Abstracts presented at the 17th International Congress on Antiphospholipid Antibodies

0005

PLATELET AND ENDOTHELIAL MICROPARTICLES DISTINGUISH HIGH-RISK (TRIPLE-POSITIVE) ANTIPHOSPHOLIPID ANTIBODY PROFILES

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Microparticles (MP) are submicron vesicles implicated in the pathogenesis of inflammation, thrombosis and malignancy. Studies on MP in patients with antiphospholipid antibodies (aPL) are sparse and inconclusive. The risk of thrombotic events increases with the number of positive tests. Patients/individuals positive for lupus anticoagulant (LAC), anticardiolipin (aCL) and anti-ß2-glycoprotein I (aß2GPI) antibodies (triple-positive), are at high risk of recurrent or first thrombotic event compared with those positive in two (double-positive) or one (single positive) test.

Aim: We aimed at finding functional alteration in the platelets and endothelial cells by measuring specific MP in individuals with triple, double and single positive aPL antibodies.

Patients and methods: Nine single positive (IgG aß2GP1 only), 9 double positive (IgG aCL and IgG aß2GP1), and 15 triple positive (LA, IgG aCL and IgG aß2GP1) individuals were studied. Platelet free plasma was prepared at room temperature by using double centrifugation, 15 minutes each, at 2,500g and stored at -80°C. APL antibodies were measured as previously described. MPs were acquired by cyflow space PARTEC flow cytometry and analysed by Partec FloMax™ software, according to ISTH SSC Working Group's suggestions. Megamix (Biocytex) was used to set up the MP gating according to the datasheet. Markers of Platelet Microparticles (PMP) were CD41a-PE and annexin-V-FITC was used to determine phosphatidylserine exposure. CD144-FITC was used as a marker of Endothelial Microparticles (EMP). Corresponding isotype controls were tested. All antibodies were from BD Pharmingen™.

Results: Median values of IgG aß2GP1 were significantly different among the single (22 CU, IQR, 20-46) double (125 CU, IQR 31-2039) and triple positive (1864 CU, IQR 916-5202) individuals (p<0.0001, Figure 1). The number of total MP was significantly higher in triple and double positive with respect to single positive group and showed a significant correlation with IgG aß2GP1 titers (Figure 3-4). Analysis of specific MP revealed that PMP number was the lowest in triple positive group and inversely correlated with IgG aß2GP1 titers (Figure 5-6). On the other hand, EMP number was higher in triple positive group and positively correlated with IgG aß2GP1 antibody titers (Figure 7-8).

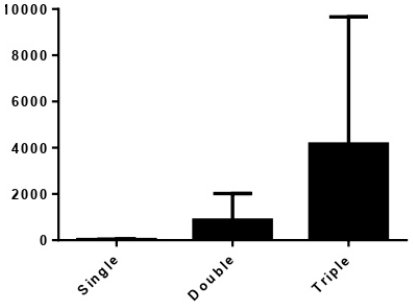

Figure 1: Median lgG aβ2GPI in single, double and triple positive groups.

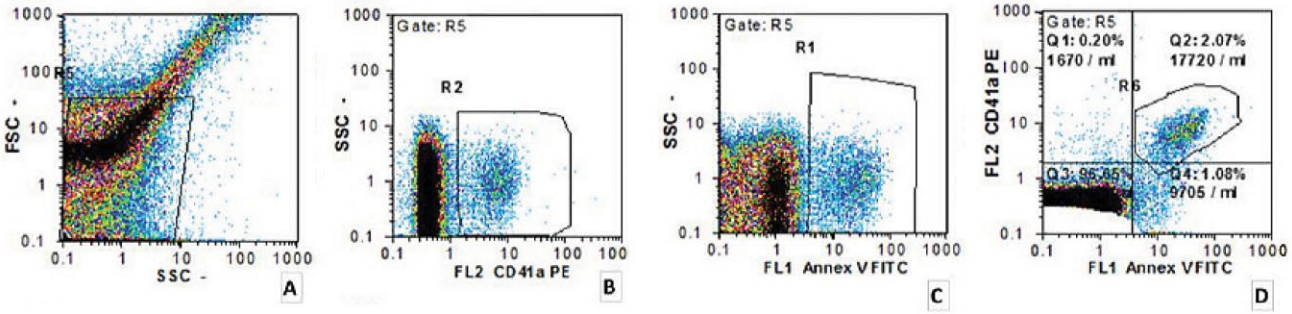

Figure 2: Flow cytometry set up and PMP concentration gating.

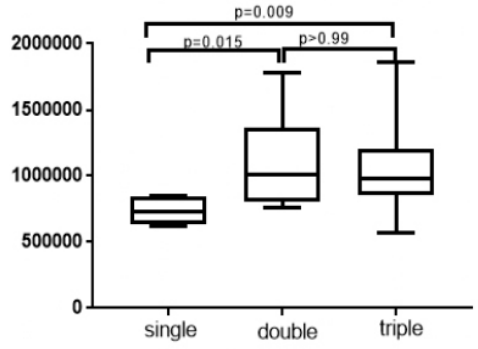

Figure 3: The number of total microparticles was compared among individuals with single, double and triple antiphospholipid antibody positivity.

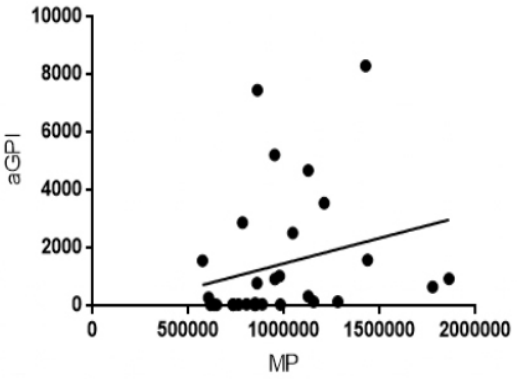

Figure 4: Positive correlation of aBetaGPI, and total microparticles.

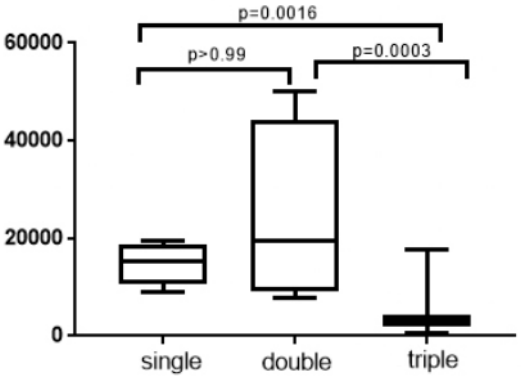

Figure 5: The number of platelet microparticles was compared among individuals with single, double and triple antiphospholipid antibody positivity.

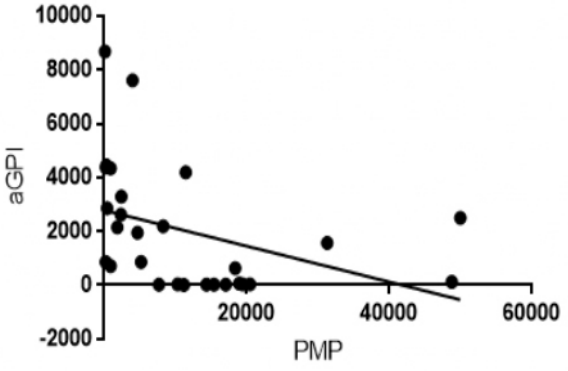

Figure 6: Inverse correlation between aβGPI, and Platelet MP.

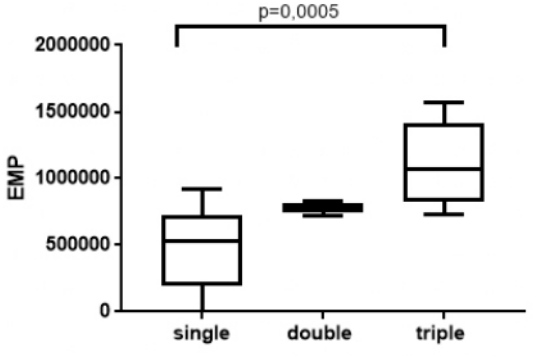

Figure 7: The number of endothelial microparticles was compared among individuals with single, double and triple antiphospholipid antibody positivity.

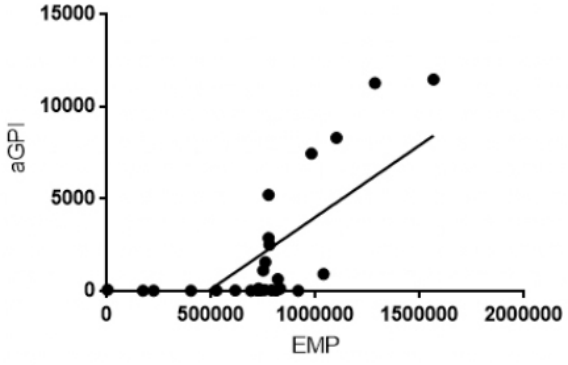

Figure 8: Positive correlation of aBetaGPI and endothelial microparticles.

Conclusions: This study shows that PMP and EMP counts are altered in aPL positive individuals and significantly in triple-positive group. Indeed, high-risk triple-positive group shows low PMP and inverse correlation with IgG aß2GP1 and high EMP with positive correlation with IgG aß2GP1 titers. PMP expose PS at the outer surface of their membrane and bind selectively to ß2GPI allowing their recognition by aß2GP1 antibodies. This mechanism is possibly involved in rapid clearance of PMP from the circulation. In addition, antibody-dependent cross-linking of ß2GP1 bound to PMP can perturb vascular endothelial cells generating EMP. The binding of ß2GPI and aß2GPI results in the activation of endothelial cells, which can further stimulate the surrounding rest cells with procoagulant and pro-inflammatory properties in a paracrine or/and autocrine manner. In conclusion, low levels of PMP and high level of EMP might in part explain the pathogenesis of thrombosis in high risk triple-positive APS patients.

Keywords: APS, platelet microparticles, endothelial microparticles, aPL profile, single-double-triple positivity.

0006

PREVALENCE OF ANTI-PHOSPHATIDYLSERINE/PROTHROMBIN ANTIBODIES AND ASSOCIATIONS WITH OTHER ANTIPHOSPHOLIPID ANTIBODIES IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME: A SYSTEMATIC REVIEW

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Antiphospholipid syndrome (APS) is an autoimmune disorder characterized by the presence of antiphospholipid antibodies (aPLs) and a wide variety of clinical symptoms, including recurrent arterial and/or venous thrombotic events and recurrent fetal loss. Accumulated evidence has highlighted the impact role of autoantibodies against phosphatidylserine/prothrombin complex (aPS/PT), in both pathological and diagnostic relevance of APS.

Aim: We aim to figure out the prevalence of aPS/PT in APS population by meta-analysis of available pooled data, and then look into two subgroups by primary and secondary APS. Furthermore, we analyzed aPS/PT among LAC positive APS population, as well as patients with double and triple positivity of aPL profile.

Patients and methods: A systematic search of PubMed, Web of Science, and the Cochrane Library from January 1990 to September 2021 was carried out according to PRISMA guidelines. Proportions and 95% confidence intervals (CIs) were calculated using random-effects model. Publication biases were evaluated via visualization of funnel plots along with Egger's and Begg's tests.

Results: Twenty-one articles about the prevalence of aPS/PT in 1853 patients with APS were deemed eligible and analyzed in our meta-analysis according to the inclusion criteria. Pooled prevalences of aPS/PT IgG alone, IgM alone, and IgG/M were 50.0%, 45.0%, and 65.0%, respectively, confirming the important role of aPS/PT in APS. No significant publication biases were detected from funnel plots or Egger's and Begg's tests. Our results suggest that aPS/PT would be the fourth laboratory marker for the diagnosis of APS.

Author	APS With LAC (n)	Anti- PS/PT IgG (n,%)	Anti- PS/PT IgM (n,%)	Anti- PS/PT IgG/M (n,%)
Bardin N	60	-	-	33 (55.0%)
Cattini MG	14	11 (78.5%)	11 (78.5%)	14 (100.0%)
Núñez-Álvarez	59	47 (79.7%)	48 (81.4%)	-
Pengo V	25	8 (32.0%)	21 (84.0%)	25 (100.0%)
Pregnolato F	77	-	-	67 (87.0%)
Valagea A	120	-	-	92 (76.7%)
Zabczyk M	63	48 (76.2%)	34 (54.0%)	-
Zhang S	165	-	-	118 (71.5%)
Zhu L	46	34 (73.9%)	35 (76.1%)	43 (93.5%)

Conclusions: The use of aPS/PT and aβ2GPI antibodies for APS evaluation is particularly appealing given the possible role of these molecules in disease pathogenesis and risk stratification. Testing for antibodies to the PS/PT complex offers comparable sensitivity with significant overlap with LAC.

Keywords: Anti-phosphatidylserine/prothrombin antibodies, antiphospholipid antibodies, systematic review.

0007

GLUCOSE FLUX AS A THERAPEUTIC TARGET IN ANTIPHOSPHOLIPID SYNDROME (APS)

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Neutrophil hyperactivity and neutrophil extracellular trap (NET) release (NETosis) appear to play roles in APS pathophysiology. Due to their significant energy requirements, it has long been thought that neutrophils rely primarily on glycolysis to fulfill their energy needs; however, accumulating evidence suggests that a variety of additional metabolic pathways guide both physiologic and pathologic neutrophil functions. In fact, our previous work characterizing the transcriptome of APS neutrophils found markedly upregulated genes to not only glycolysis, but also glycogenolysis and the pentose phosphate pathway. We now begin to characterize how neutrophil metabolism may influence APS-associated disease phenotypes.
Patients and methods: Metabolic flux of APS patient and healthy control neutrophils was assessed using a Seahorse Extracellular Flux Analyzer. Neutrophil glycogen content was assayed using a commercially available kit (Abcam). Primary human neutrophils were stimulated with phorbol myristate acetate (PMA), calcium ionophore A23187 (Ca iono), IgG purified from primary APS patients (APS IgG), or IgG purified from healthy controls (control IgG). PMA and Ca iono were chosen as mechanistic anchors given their divergent processes for triggering NETosis (NADPH oxidase-dependent and -independent, respectively). Inhibitors included 2-deoxy-D-glucose (2-DG, a competitive inhibitor of glycolysis) and 6-aminonicotinamide (6-AN, a pentose phosphate pathway inhibitor). NETosis was quantified with SYTOX Green. APS-associated venous thrombosis was modeled in C57BL/6 mice via electrolytic activation of the inferior vena cava (IVC).
Results: In the metabolic flux analysis, primary APS patients (n=27) had a higher neutrophil glycolytic capacity (a measure of the maximal glycolysis rate achievable by cells) compared with controls (mean 12.6 vs. 8.6 mpH/min; p=0.01). Glycolytic capacity correlated well with clinically relevant labs such as C-reactive protein (r=0.67, p=0.004) and neutrophil counts (r=0.56, p=0.01). Furthermore, APS neutrophils had higher glycogen stores than controls (mean 11.0 vs. 7.0 ug glycogen/10^6 cells; p=0.04). For NETosis experiments, 2-DG and 6-AN readily decreased NETosis induced by either PMA (by 41% and 60%, respectively; p<0.05) or APS IgG (by 41% and 33%, respectively; p<0.05). In contrast, Ca iono-induced NETosis was not sensitive to either inhibitor. In a mouse model of APS, transfer of APS IgG (as compared with control IgG) into mice (n=10/group) led to accrual of larger IVC thrombi at 24 hours (mean 7.5 mg vs. 4.5 mg, p=0.002). When APS IgG-treated mice were administered daily 2-DG for 1 week prior to thrombus induction, thrombus weight decreased back to baseline of 3.8 mg (p<0.001); this was accompanied by a corresponding decrease in plasma NET remnants as defined by myeloperoxidase-DNA complexes (p=0.01).
Conclusions: We demonstrate for the first time that neutrophils isolated from primary APS patients have enhanced glycolytic flux along with increased glycogen stores, which suggests metabolic specialization. In addition, APS IgG-induced NETosis mirrors that induced by PMA and relies on glycolysis and the pentose phosphate pathway. The potential clinical applicability of these studies is emphasized by the ability of 2-DG to restrain APS-associated thrombosis in mice. Numerous other studies are underway to further dissect these potentially modifiable metabolic underpinnings of APS pathophysiology.
Keywords: Metabolism, neutrophil extracellular traps.

0008

SERONEGATIVE ANTIPHOSPHOLIPID SYNDROME ASSOCIATED WITH COVID19 VACCINATION

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Seronegative APS is usually a diagnosis of exclusion and should be suspected in patients with a clinical history suggestive of APS with persistent negativity of aPL tested on at least two occasions, and when other causes of thrombosis are excluded. Apart from conventional biological markers, numerous other markers of APS have been studied such as antibodies against phosphatidyl-ethanolamine, phosphatidylserineprothrombin, igA isotypes of classic antibodies, anti-vimentin/cardiolipin, and Annexin A5, among others.
Case report: A 40-year-old female patient with a history of ischemic stroke in the right parietal lobe 2 months prior to admission, anti-SARS CoV2 vaccination with ChAdOx1 (Oxford/AstraZeneca) 4 days prior to the event, and infertility. She was admitted for left brachiocrural paresis, bradypsychia and bradylalia. Brain MRI performed showed acute ischemia right frontoparietotemporal and insular with extension to the lenticular nucleus. Echocardiogram was performed with bubble passage that evidences extracardiac shunts, and Carotid ultrasound was normal. Evaluation by hematology and rheumatology was requested for suspected thrombophilia. Prothrombin 20210, Leiden Factor V, Anti beta2glycoprotein I IgG and

IgM, Anti cardiolipin IgG and IgM, and lupus inhibitor were performed and were negative. In the context of two strokes in different territories, it was interpreted as a cardioembolic event and anticoagulation with acenocumarol was started. Hospital discharge was granted for outpatient follow-up. A month later, he evolved with edema of the right lower limb, and Homans sign. Doppler ultrasound performed showed femoral vein thrombosis up to the middle third of the popliteal vein. Laboratory was performed with normal blood count, and coagulogram with INR 1.96. PCR performed for SARS CoV2 was positive. Anticoagulation was initiated with enoxaparin 1mg/kg/day. Results were obtained from previously requested serologies: reticular cytoplasmic ANA 1:320, anti RNP positive, Anti-Ro, Anti-La, Anti-Sm, Anti DNAdc negative, and anti-phosphatidylserine IgM positive, IgG negative.
Conclusions: It is interpreted as probable seronegative APS. Hydroxychloroquine 400mg was started. Currently, it does not meet criteria for associated autoimmune disease. In patients with clinical manifestations suggestive of an antiphospholipid syndrome and negative classical antibodies, the determination of serological markers not included in the classification criteria allows the reclassification of the diagnosis in up to one third of cases. Anti-phosphatidylserine antibodies were linked in some studies to obstetric manifestations in patients with seronegative APS. COVID 19 infection has been linked to thrombotic events of probably multifactorial cause. Some authors have found the presence of antiphospholipid antibodies, but their role is still under study. On the other hand, vaccination against SARS-CoV-2 generates an immune reaction that in some patients can be expressed with thrombotic manifestations, especially with adenovirus vector vaccines. Some patients studied had antiphospholipid antibodies, but in most studies this manifestation appears to be related to the presence of antibodies to platelet factor 4.
Keywords: Seronegative antiphospholipid syndrome, COVID19 vaccination, anti-phosphatidylserine.

0009

IMPROVEMENT OF LONG COVID-ASSOCIATED BRAIN FOG AFTER COVID-19 VACCINATION IN A PATIENT WITH ANTIPHOSPHOLIPID ANTIBODIES

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Persistent impairment in sustained attention or cognitive function after coronavirus disease-2019 (COVID-19) is known as long COVID-associated brain fog which may be related to persistent viremia, relapse, reinfection or inflammatory immune reactions. Although the underlying pathogenesis of long COVID-syndrome remains unclear, several reports indicate that COVID-19 vaccines may improve symptoms associated with this syndrome including brain fog. Antiphospholipid antibodies (aPL) are frequently detected in COVID-19 patients and the presence of aPL is sometimes associated with cognitive dysfunction. Here, we report a case of a patient who experienced changes in aPL titres after COVID-19 and recovered from long COVID-associated brain fog after COVID-19 vaccination.
Methods: We designed a special questionnaire to inquire about the current health status of the patient and her persistent symptoms in the post-COVID period and measured her aPL by chemiluminescent immunoassay.
Case report: A 22-year-old woman presented to our hospital with cognitive disfunction, difficulty concentrating, chronic fatigue and widespread musculoskeletal pain. She referred that two months earlier she developed fever and was diagnosed with COVID-19 by the quantitative antigen test for SARS-CoV-2. Her fever disappeared but cognitive dysfunction and fatigue were sustained. When she came to our hospital for further examination, laboratory investigations showed positive anti-beta-2-glycoprotein 1 (beta2GP1) IgG antibody (41.6 U/mL, normal range <: 20.0 U/mL) while all other laboratory and imaging examinations were normal. There was no evidence of thrombosis. A diagnosis of chronic fatigue syndrome was made and treated it symptomatically. Three months later, anti-beta2GP1 IgG antibody was converted to negative. Seven months after COVID-19 onset, she was vaccinated with two doses of BNT162b2 messenger ribonucleic acid COVID-19 vaccine and two weeks after the second dose, her symptoms improved dramatically. Analyses of the questionnaires administered before and after vaccination, indicated that the patient's global assessment (on 100 mm visual analog scale) improved from 36 mm to 0 mm, and the Chalder fatigue scale improved from 21 to 4. Moreover, Wechsler Adult Intelligence Scale-Fourth Edition's scores improved on several items (verbal comprehension: 81 to 94, working memory: 106 to 117 and processing speed: 105 to114).
Conclusions: Vaccination against COVID-19 may ameliorate long COVID symptoms by halting the harmful immune response. Changes in aPL titres in patients with long COVID-related cognitive dysfunction may indicate that some immunological mechanisms may be involved in the brain fog.
Keywords: Anti-phospholipid antibodies, brain fog, COVID-19.

0011

PLASMIN CLEAVAGE OF BETA-2-GLYCOPROTEIN I LEADS TO NOVEL STRUCTURES AND ALTERED ANTIBODY BINDING

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Beta-2-Glycoprotein I (ß2GPI) is a serum protein of 50kDa comprised of 5 domains arranged like beads on a string. It is also the main autoantigen of Antiphospholipid syndrome (APS). Antibodies to B2GPI (aß2GPI) are diagnostic of APS and are strongly associated with clinical events including thrombosis. ß2GPI can adopt one of two structures, a circular closed structure or a linear open structure. It also has contrasting functions in complement and coagulation regulation. ß2GPI can activate plasminogen to plasmin that cleaves ß2GPI in the 5th domain removing the terminal 8 amino acids. It is unknown what this cleavage does to the structure and function of ß2GPI. This project aimed to assess the change in structures associated with plasmin cleavage and the effect on autoantibody binding.

Material and methods: Purified ß2GPI was incubated overnight with Plasmin, cleavage was confirmed through migration under reduction on a coomassie gel and purification achieved by Size Exclusion Chromatography. Purified plasmin-clipped ß2GPI was then characterized by a range of analytical and structural methods including Analytical Ultracentrifugation (AUC) and Small Angle X Ray Scattering (SAXS), supplemented by Molecular Dynamics Simulations (MD). The activity of Plasmin Cleaved ß2GPI was assessed by inhibition ELISA. Serum from APS patients was incubated in the presence or absence of either plasmin clipped or intact ß2GPI, and subsequently used in a ß2GPI ELISA to assess the fluid phase inhibition of anti- ß2GPI I antibodies.

Results: Plasmin cleavage was most successful overnight with a 1:1 ratio of plasmin to ß2GPI. Analysis by AUC showed an altered distribution of structures favoring more linear forms than circular in contrast to non-clipped which had a more even distribution between the forms. MD showed significantly increased flexibility in the plasmin clipped compared to intact ß2GPI whilst SAXS showed a novel S shaped structure mirroring the MD findings. Finally, inhibition assays showed more inhibition of antibody binding for the plasmin clipped ß2GPI compared to non-clipped (14.9%vs9.5%, p<0.05).

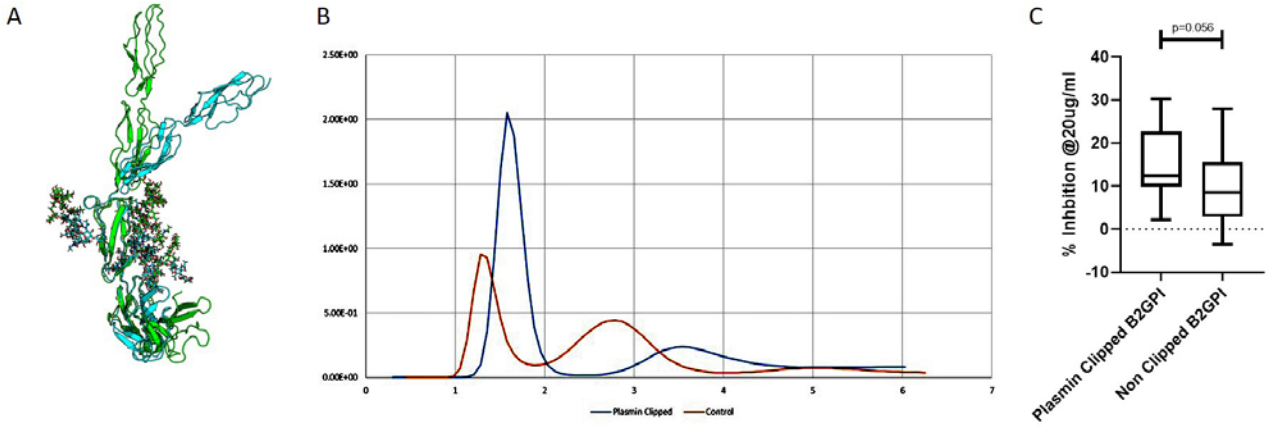

Figure 1: Plasmin cleavage of beta-2-glycoprotein I leads to novel structures and altered antibody binding.
Panel A shows two structures of B2GPI identified by Small Angle Xray Scattering, in the green is the non-cleaved healthy control B2GPI which approximates to the known linear structure (PDB:1C1Z), whilst in Blue is the plasmin clipped B2GPI structure, representing an entirely novel structure of B2GPI, these structures have been aligned by the 3rd and 4th domain and exhibits the extreme movement in the 1st and 2nd domains compared to the rest of the protein. Panel B shows the difference in Analytical Ultracentrifugation with a much larger peak for the plasmin clipped (Blue) in comparison to the orange sample (Control B2GPI) whilst the second peak has also shifted and represents a smaller proportion of the B2GPI in the Plasmin Clipped (Blue). The shift right in the AUC but retention of linear nature suggests the large peak in AUC represents the novel structure seen in panel A. Finally panel C shows the inhibition at 20ug/ml of B2GPI from either plasmin clipped or healthy control (non clipped) in the fluid phase. As can be seen greater inhibition was seen with the plasmin clipped samples (p=0.056).

Conclusions: Plasmin cleavage of the 5th domain dramatically alters the structure and function of ß2GPI, inducing a novel S shape structure with increased antibody binding.

Keywords: Autoantibodies, beta-2-Glycoprotein I, structural biology, novel structure.

0012

STRUCTURAL DIFFERENCES EXIST IN BETA-2-GLYCOPROTEIN I FROM ANTIPHOSPHOLIPID SYNDROMES PATIENTS COMPARED TO HEALTHY CONTROLS

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Beta-2-Glycoprotein I (ß2GPI) is a serum protein of approximately 50kDa and is the main autoantigen of Antiphospholipid Syndrome (APS). Antibodies to ß2GPI (aß2GPI) are diagnostic of APS and are strongly associated with clinical events including thrombosis. ß2GPI can adopt one of two structures, a circular closed structure or a linear open structure. It is proposed that these structures have different functions and thus alter disease pathogenesis. The structure of B2GPI in APS patients is poorly characterized. Here we present data comparing structure and antibody-binding properties of ß2GPI from patients with APS and healthy controls (HC).

Material and methods: ß2GPI was purified from APS and HC plasma by affinity chromatography and PEG precipitation avoiding acid steps. Samples were analyzed by ion mobility-mass spectrometry on a Waters SELECT SERIES cIMS to assess structure, and increasing voltage was applied to investigate structural dynamics. Data were processed using MassLynx v4.2 (Waters). Antibody activity was tested by inhibition ELISA, briefly: serum from APS patients was incubated in the presence or absence of either HC or APS ß2GPI and then used in a ß2GPI ELISA to assess the fluid phase inhibition of anti-ß2GPI antibodies.

Results: Similar glycoisoforms of ß2GPI were seen in HC and APS ß2GPI. A different distribution of the two known structures was seen, with APS patients displaying more linear ß2GPI compared to healthy controls at the same charge state. When voltage was applied to the linear form of ß2GPI from HC, the protein was capable of adopting a more compact form again, however this was not possible for APS ß2GPI. In an inhibition ELISA APS B2GPI from high aß2GPI positive patients (n=2) inhibited binding of anti-ß2GPI antibodies to ß2GPI significantly more than HC (19.1%vs13.5%, p=0.007).

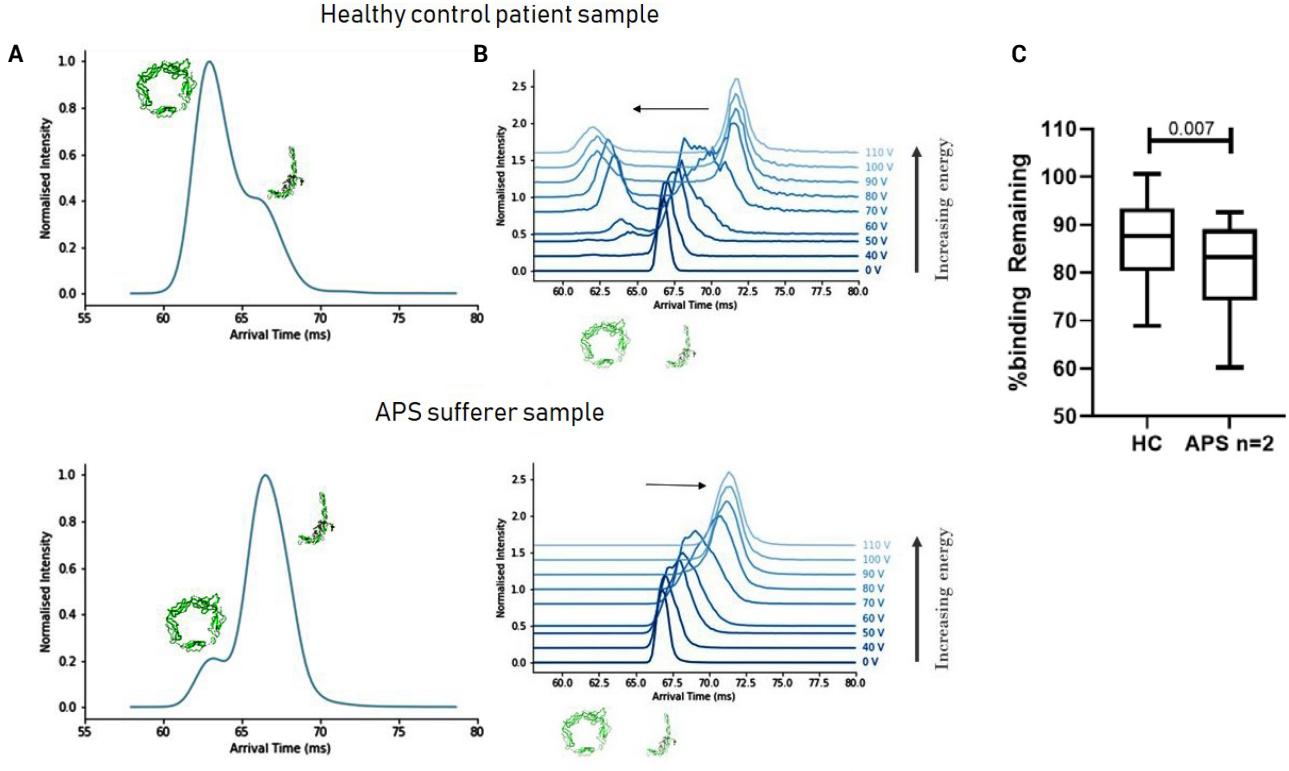

Figure 1: Structural differences exist in beta-2-glucoprotein I from APS patients compared to healthy controls.
*Panel A shows the distribution of B2GPI structures in healthy controls (top) and APS patients (bottom) at a single charge state. As can be seen the peaks are reversed with increased amounts of linear B2GPI shown in the APS samples (peak arrival ~67.5ms) and the inverse for the circular form (arrival time ~62.5ms). In panel B, when the linear form from healthy controls (Top) was then subjected to increased voltage, as can be seen the linear peak (*67.5ms) can form another peak equivalent to the circular form ("62.5ms) before progression to a superlinear form. In contrast, APS patients (Bottom) are not capable of this and progress to a superlinear form. Finally, Panel C shows blinding remaining in an anti-B2GPI ELISA using 10 APS patients serum challenged with either APS purified B2GPI (n=2) or HC B2GPI (Pooled). As can be seen APS B2GPI inhibits significantly better than healthy control equivalent.*

Conclusions: Structural differences exist in APS patients compared to controls, with more linear ß2GPI in patients and this may be explained by differences in the structural dynamics. Furthermore, these structural differences are associated with better antibody binding which may suggest that this structural difference plays a role in autoantibody production in APS.
Keywords: Beta-2-Glycoprotein I, APS, ion mobility mass spectrometry, structure.

0013

PROFILING CRITERIA AND NON-CRITERIA ANTIPHOSPHOLIPID ANTIBODIES IN ANTIPHOSPHOLIPID SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS BY LINE IMMUNO-ASSAY TECHNIQUE

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An absence of classic aPL criteria does not mean that other antibodies are not present or involved in the onset of adverse pregnancy outcomes (APO) and/or thrombotic events in patients with systemic lupus erythematosus (SLE) and/or antiphospholipid syndrome (APS). Different non-criteria (nc)-aPL have been extensively investigated, however their pathogenic role and clinical significance is not well understood. Despite a well-recognized association between the classic aPL and their role in causing obstetric/thrombotic events, there is conflicting evidence as to whether this association also exists with nc-aPL. Therefore, we examined for the presence of 2 criteria and 8 nc-aPL by a novel multiplex Line Immunodot-Assay (LIA) in patients with SLE, APS and healthy controls (HC), to assess the frequency and specificity of nc-aPL in APS, SLE and HC.
Patients and methods: Samples were obtained from subjects by informed consent at University College London Hospital, including: 20 APS, 33 SLE, 19 SLE/APS and 23 HC. Data including demographics (age, disease duration and ethnicity) plus SLE and APS phenotypes (SLE with minor organ involvement or major organ involvement, thrombotic APS (TAPS), obstetric APS (OAPS) and SLE/APS overlap patients) was collected. Serum was tested for presence of these 10 criteria and nc-aPL by LIA.
Results: Our cohort (n=95) consisted of predominantly white (>55%) females (>80%). TAPS was more frequent than OAPS (80 vs 45%) in the APS cohort and in the SLE group, major organ involvement was more common than minor organ involvement (58 vs 42%). Table 1 demonstrates the most (>47%) prevalent IgG and IgM aPL detected were aCL, aPA and anti-ß2GPI in patients with APS and SLE/APS compared with SLE (>18% prevalence) and HC (<17% prevalence). A similar pattern was observed with aPS at lower (37-45%) prevalence in APS and SLE/APS compared with SLE (15-21%) and HC (0%). A greater prevalence of IgM aAN (>53%) and aPT (>42%) were found in patients with APS and SLE/APS compared with SLE (<21% for both) and IgG aAN and aPT (<18%) in all groups. A low (<25%) prevalence of IgG and IgM aPI was found in patients with APS, SLE and SLE/APS compared with none (0%) in HC. Low (<25%) prevalence of aPI and negligible/no (<1%) prevalence of aPC, aPE and aPG were detected across IgG and IgM in all four groups.

Table 1: Characteristics of the subjects included in the study.

	APS N=20	SLE N=33	APS+SLE N=19	HC N=19
Females , N (%)	16 (80)	30 (91)	18 (95)	23 (100)
Ethnicity				
White, N(%)	19 (95)	18 (55)	11 (58)	18 (78)
Asian, N(%)	0 (0)	8 (24)	4 (21)	2 (9)
Black, N(%)	1 (5)	1 (3)	2 (10.5)	2 (9)
Other, N(%)	0 (0)	6 (18)	2 (10.5)	1 (4)
Age at serum sample (y),median (IQR)	46.5 (16.3)	45 (28.5)	51 (17)	32 (7)
Duration of disease at serum sample (y), median (IQR)	16.5 (20.3)	13 (20)	13 (15)	N/A
APS phenotype				
Thrombotic, N(%)	16 (80)	N/A	15 (79)	N/A
Obstetric, N(%)	9 (45)	N/A	11 (58)	N/A
SLE phenotype				
Mayor organ involvement, N(%)	N/A	19 (58)	11 (58)	N/A
Treatment				
Anticoagulants, N(%)	13 (87)	0 (0)	9 (60)	0 (0)
Aspirin, N(%)	4 (27)	7 (26)	0 (0)	0 (0)
Hydroxychloroquine, N(%)	2 (13)	15 (56)	8 (54)	0 (0)
Immunosuppressants, N(%)	1 (7)	16 (60)	10 (67)	0 (0)
Steroids, N(%)	2 (13)	15 (56)	8 (53)	0 (0)

Table 2: Number of study subjects with a positive result for the antibodies tested.

	APS N=20	SLE N=33	APS + SLE N=19	HC N=19
Cardiolipin (CL)				
IgG, N(%)	14 (70)	11 (33)	9 (47)	0 (0)
IgM, N(%)	11 (55)	6 (18)	13 (68)	1 (4)
Phosphatidic acid (PA)				
IgG, N(%)	13 (65)	11 (33)	10 (53)	1 (4)
IgM, N(%)	15 (75)	6 (18)	13 (68)	0 (0)
Phosphatidylcholine (PC)				
IgG, N(%)	0 (0)	0 (0)	0 (0)	0 (0)
IgM, N(%)	0 (0)	0 (0)	0 (0)	0 (0)
Phosphatidyletthanoolamine (pe)				
IgG, N(%)	0 (0)	0 (0)	0 (0)	0 (0)
IgM, N(%)	1 (5)	0 (0)	0 (0)	0 (0)
Phosphatidylglycerol (PG)				
IgG, N(%)	0 (0)	0 (0)	0 (0)	0 (0)
IgM, N(%)	1 (5)	0 (0)	0 (0)	0 (0)
Phosphatidylinositol (PI)				
IgG, N(%)	3 (15)	4 (12)	3 (16)	0 (0)
IgM, N(%)	5 (25)	1 (3)	2 (11)	0 (0)
Phosphatidyiserine (PS)				
IgG, N(%)	9 (45)	7 (21)	7 (37)	0 (0)
IgM, N(%)	9 (45)	5 (15)	8 (42)	0 (0)
Annexin A5(AN)				
IgG, N(%)	0 (0)	6 (18)	1 (5)	2 (9)
IgM, N(%)	11 (55)	7 (21)	10 (53)	2 (9)
Beta -2 Glycoprotein I (B2GPI)				
IgG, N(%)	10 (50)	10 (30)	10 (53)	4 (17)
IgM, N(%)	16 (80)	10 (30)	16 (84)	2 (9)
Prothrombin (PT)				
IgG, N(%)	0 (0)	6 (18)	1 (5)	1 (4)
IgM, N(%)	10 (50)	4 (12)	8 (42)	1 (4)

Conclusions: We found a similar prevalence of certain IgG and IgM nc-aPL with criteria aPL in patients with APS and SLE/APS compared with SLE and healthy control groups. In contrast, a greater prevalence of IgM was found for other nc-aPL in APS and SLE/APS groups and negligible/no prevalence of other nc-aPL. Further research is required to understand the significance of these findings.
Keywords: Non-criteria aPL, antiphospholipid syndrome, systemic lupus erythematosus.

0014

ASSOCIATION BETWEEN PRECONCEPTION COMPLEMENT LEVELS AND USE OF HYDROXYCHLOROQUINE WITH PREGNANCY OUTCOME IN PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME AND CARRIERS OF ANTIPHOSPHOLIPID ANTIBODIES: AN INTERNATIONAL MULTICENTER STUDY

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Complement was demonstrated to be involved in antiphospholipid antibodies (aPL)-related pregnancy loss in animal models and human disease. Hydroxychloroquine (HCQ) can control the activation of the complement system, could improve pregnancy outcome and to reduce aPL title. This study was conducted to verify the effect of HCQ in a multicenter cohort of primary antiphospholipid syndrome (PAPS) and aPL carriers pregnant women and possible correlation with preconception serum C3/C4 levels. This study was conducted to verify the effect of HCQ in a multicenter cohort of Primary APS (PAPS) and aPL carriers pregnant women and possible correlation with preconception serum C3/C4 levels.

Patients and methods: We retrospectively evaluated 164 pregnancies (22 aPL carriers - 13%) in 128 patients with confirmed positivity for aPL attending 12 referral centers from January 2010 to December 2020. All the patients were treated with combination therapy (low dose aspirin, LDA + low molecular weight heparin, LMWH), in 30 HCQ was added. 58 pregnancies (43%) had low levels of preconception C3/C4. Triple aPL positivity was observed in 54 pregnancies (40%).

Results: In the whole cohort and in the group of patients with preconception low C3/C4, the addition of HCQ on the top of combination therapy did not significantly improved the gestational outcome. In the 40 pregnancies characterized by a high-risk profile (triple aPL positivity and complement consumption) HCQ significantly improved gestational outcome.

Conclusions: The study showed that administering HCQ in addition to combination therapy can improve gestational outcome in aPL/APS high-risk patients. This observation confirms that HCQ exerts a beneficial effect on aPL pregnancies by complement inhibition as it was shown in animal models. In addition, our results provide the clinicians a useful tool to implement conventional treatment in patients at high risk of pregnancy complication or loss.

Keywords: Pregnancy antiphospholipid antibodies, complement levels hydroxychloroquine.

0015

IMMUNOSUPPRESSION IN PRIMARY ANTIPHOSPHOLIPID ANTIBODY-POSITIVE PATIENTS: DESCRIPTIVE ANALYSIS OF THE APS ACTION REGISTRY

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The APS ACTION Registry was created to study the outcomes of persistently antiphospholipid antibody (aPL)-positive patients with or without systemic autoimmune disease (SAIDx). Given that immunosuppression (IS) has been increasingly used in the management of APS patients with certain non-criteria manifestations (NCM), e.g., thrombocytopenia (TP), our primary objective was to describe the general indications for IS medications in aPL-positive patients without other SAIDx.

Patients and methods: The inclusion criteria for the registry were positive aPL based on the laboratory section of the APS Classification Criteria. Patients were followed every 9-15m. For this descriptive retrospective/prospective analysis, we included aPL-positive patients without other SAIDx or catastrophic APS, and excluded those with new SAIDx classification during follow-up. For each patient, we retrieved clinical data at baseline and follow up including diffuse alveolar hemorrhage [DAH], antiphospholipid-nephropathy [aPL-N], livedoid vasculopathy-related skin ulcers [LV], TP, hemolytic anemia [HA], and cardiac valve disease [VD]); and IS use (ever) except steroids (CS) and hydroxychloroquine (HCQ).

Results: Of 899 patients enrolled as of July 2021, 537 were included in this analysis (mean age at entry 45±13y; female 377 [70%]; and 438 [82%] met APS Classification Criteria). Of 537 patients: a) 76 (14%) were reported to use IS (ever), in 41/76 patients the indication was specifically for at least one selected NCM; and b) 141 (26%) had at least one selected NCM. In six of 6 (100%) DAH patients receiving non-CS/HCQ IS, 6/12 (50%) aPL-N, 4/13 (31%) LV, 25/34 (74%) TP, 6/7 (86%) HA, and 1/9 (11%) VD, the indication was specifically for the selected NCM (Table).

Table: Immunosuppressive medications recorded (ever) in 76 primary antipholipid antibody-positive patients (indication for selected non- criteria manifestations in 41 and others * in 35).

# of Patients	DHA	aPL-N	LV	TP	HA	VD
Reported at Baseline	5	15	25	84	11	37
Reported During Follow-up	3	3	3	4	0	6
Total (In combinations with other NCM)	8	18	28	88	11	43
(As the only (NCM)	4	4	16	70	6	25
Immunosuppression Use (Total)*	6	12	13	34	7	9
Immunosuppression Use (For NCM)	6	6	4	25	6	1
IVIG	4	1	1	18	4	1
Rituximab(RXT)	5	4	3	14	2	0
Mycophenolate Mofetil (MMF)	3	5	1	5	0	0
Azathioprine(AZT)	0	2	1	5	3	0
Plasma Exchange (PE)	1	0	0	2	0	0
Cyleophosphamide (CYC)	1	1	0	3	0	0
Belimumab (BEL)	0	1	1	1	0	0
Eculizumab (ECU)	0	0	0	2	0	0
Sirolimus (SIR)	0	0	0	2	0	0
Other***	1	0	2	1	0	0

DHA: Diffuse alveolar hemorrhage; aPL-N: aPL- nephropathy; LV: Livedoid vasculopathy; TP: persistent Thrombocytopenia <100x109/1; HA: hemolytic anemia: and VD: cardiac valve disease.
**:Immunosuppressive indications reported other than selected non-criteria manifestation (NCM) were(35/76):Lupus-like disease with musculoskeletal and/or hematologic involvement without SLE classification (n:6, methotrexate[MTX], AZT); Heparin-induced TP (n:1,IVG) Peripheral artery ischemia (n:1,IVIG,RTX): Cognitive dysfunction (n:1RXT,MMF); HWLLP (hemolysis, elevated liver enzyme, and low platelet); Syndrome (n:2,PE,IVIG); Vasculitis (n:3ATZ,CYC,MMF,MTX): Hidradenitis suppuritiva (n:1 adalimumab); Post CVA acute renal failure (n:1,PE); Interstitial lung disease (n:2IVIG,RXT,MMF,CYC); Pregnancy morbidity resistant to traditional management (n2IVIG); Peripheral artery bypass surgery (n:1 eculizumab); Primary biliary cirrhosis/autoimmune hepatitis crhon´s disease e (n;3, AZT): Myasthenia gravis (n1;AZT); Renal transplant thrombotic microangiopathy /hepato-pulmonary syndrome (n;2CYC;MMF,tacrolimus); idiopathic pachymeningitis encephalopathy (n;2, AZT,RTX,CYC); Dystonia/neuropathy (n:3,IVIG,PE,RTX,AZT,MMF,MTX); In vitrofertilization co-adjuvant treatment(n:1IVG) Anticoagulation resistant TIA (n:1,RTX); and Atopic dermatitis/alopecia (n;MMF).*
***: Some patients had more than one NCM simultaneously or at a different time points.*
****: Abatacept, MTX, Danzol and Tacrolimus.*

Conclusions: In our multi-center international cohort, 14% of aPL-positive patients without other systemic autoimmune diseases were reported to receive IS. Thrombocytopenia was the most frequent NCM, however only one-third required IS. Diffuse alveolar hemorrhage, aPL-nephropathy, and hemolytic anemia were frequently treated with IS. The benefit of IS for NCM requires further study.
Acknowledgment: Partial results of this study were previously presented as a poster at the American College of Rheumatology Convergence 2021. The APSACTION registry was created using REDCAP Provided by the clinical and translational science Center at Weill Cornell Medical College (CTSC grant UL1 TR00457).
Keywords: Antiphospholipid syndrome, immunosuppression, antiphospholipid antibodies.

0017

ANTI-CARDIOLIPIN AND ANTI-ß2-GLYCOPROTEIN-I ANTIBODY LEVELS IN PATIENTS WITH COVID-19

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High incidence of thrombosis in COVID-19 patients indicates a hypercoagulable state. Hence, exploring the involvement of antiphospholipid antibodies (aPL) in these patients is of interest. We aimed to determine anti-cardiolipin (aCL) and anti-ß2-glycoprotein-I (aß2GP1) antibody levels in hospitalized patients with COVID-19 and analyze their behavior over time.
Patients and methods: An analytical, prospective, correlational and cross-sectional study was carried out in the Biochemical Service of San Roque Hospital from Córdoba, Argentina. Group of study: 48 patients with COVID-19 of both sexes between 18-60 years. Control group: 21 healthy patients of both sexes between 18-60 years. Sera collected from patients were tested for aCL and aß2GP1 antibodies (IgM and IgG) by ELISA (Orgentec®) at the time of hospitalization, with part of the patients with COVID-19 (35/48) retested after six days. Excel® and InfoStat® were used for data analysis.
Results: Significant differences were observed between the control group and the group of study on IgM/IgG-aß2GP1 and IgG-aCL ($p<0.0001$), but not on IgM-aCL ($p=0.1335$) (Figure 1). According to the cut-off point of the commercial kit, the results were classified as positive, negative or borderline. 4%, 10%, 6% and 4% positive results were obtained for IgM-aCL, IgG-

aCL, IgM-aß2GP1 and IgG-aß2GP1, respectively (Table 1). For those patients retested after six days, significant differences were observed on IgM-aCL (increase, p=0.0156) and IgM-aß2GP1 (decrease, p=0.0150) (Table 2).

Table 1: Comparison between control and patient group.

Variable	Results	Control N	Control %	Patient N	Patient %	p-value
IgMaCL	Negative (<10MPL-U/mL) Positive (≥10MPL-U/mL)	21 0	100% 0%	46 2	96% 4%	0.3425
IgGaCL	Negative (<10MPL-U/mL) Positive (≥10MPL-U/mL)	21 0	100% 0%	43 5	90% 10%	0.1246
IgGaCL	Negative (<5 MPL-U/mL) Borderline (5-81 PL-U/mL) Positive (>8 U/mL)	21 0 0	100% 0% 0%	33 12 3	69% 25% 6%	0.0151
IgG-aB2GP1	Negative (<5 U/mL) Borderline (5-8 U7mL) Positive (>8 U/mL)	20 1 0	95% 5% 0%	41 5 2	85% 10% 4%	0.4558

Table 2: Results of aCL and aB2GP1 antibodies at day 1 and day 6.

Variable	Media	SD	Min	Max	p-value
IgM-aCL (day 1) (MPL-U/mL) IgM-aCL (day 6) (MPL-U/mL)	3.31 4.43	2.04 3.12	1 2	11 16	0.0156
IgM-aCL (day 1) (MPL-U/mL) IgM-aCL (day 6) (MPL-U/mL)	5.51 4.77	3.55 2.57	1 2	14 13	0.7252
IgG-aB2GP1 (day 1) (U/mL) IgG-aB2GP1 (day 6) (U/mL)	3.94 3.26	2.35 2.98	2 1	12 17	0.0150
IgG-aB2GP1 (day 1) (U/mL) IgG-aB2GP1 (day 6) (U/mL)	3.74 3.91	4.3 7.68	1 1	24 39	0.0556

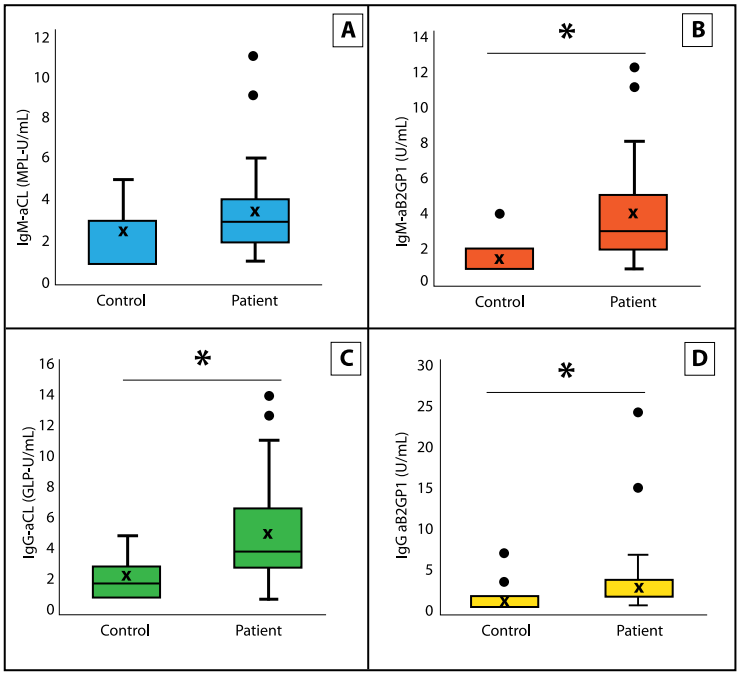

Figure: Box plot according to observed values for patient and control sera. A) IgM-aCL; B) IgM aB2GP1; C) IgG-aCL; D) IgG-aB2GP1.

Conclusions: Patients with COVID-19 show higher levels of aCL and aß2GP1 antibodies compared to healthy patients, suggesting that certain infections in genetically predisposed individuals, as well as inflammatory processes, may induce autoimmunity. Those patients with elevated values maintained them over time (day 1 and day 6), suggesting a tendency to stay that way and not a chance finding. A large-scale analysis of a COVID-19 cohort, whose antibody composition is put into context with the course of the disease and necessarily with thrombotic events, is essential. Subsequent studies with more frequent aPL testing and thus longitudinal observations in the course of the infection may provide more answers.

Keywords: antiphospholipid syndrome, anti-cardiolipin, anti-ß2-glycoprotein-I, COVID-19.

0018

ANTI-NET ANTIBODIES IN ANTIPHOSPHOLIPID ANTIBODY-POSITIVE PATIENTS: RESULTS FROM THE APS ALLIANCE FOR CLINICAL TRIALS AND INTERNATIONAL NETWORKING (APS ACTION) CLINICAL DATABASE AND REPOSITORY ("REGISTRY")

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The release of NETs by hyperactive neutrophils plays a role in the thromboinflammatory phenotype of APS. Previous work has demonstrated that some patients with APS have autoantibodies targeting NETs, which impair NET clearance and potentially activate complement. We aimed to elucidate the presence, clinical associations, and antigen specificities of anti-NET antibodies in a large, ethnically diverse cohort of aPL-positive patients.

Patients and methods: Levels of anti-NET IgG/IgM were determined in sera of 308 patients with primary APS and 81 patients who were aPL positive but without "criteria" APS manifestations or another systemic autoimmune disease diagnosis. All patients were recruited as part of the APS ACTION consortium. A positive cut-off for anti-NET level was established at the 99th percentile optical density of healthy-control samples. Multivariate logistic regression with best variable model selection was used to determine clinical associations. For a subset of patients (n=214), we profiled autoantibodies with a microarray platform that included 120 potential autoantigens.

Results: We found elevated levels of anti-NET IgG or IgM in 45% of aPL-positive patients. There was a strong relationship between anti-NET IgG and IgM ($r=0.52$, $p<0.0001$). High anti-NET levels correlated with a circulating marker of NETs, MPO-DNA complexes. Anti-NET activity also demonstrated a positive correlation with levels of traditional aPL (anti-beta-2 glycoprotein I IgG: $r=0.21$, $p<0.0001$) and anticardiolipin IgG: $r=0.19$, $p=0.0001$). When considering clinical manifestations among aPL-positive patients, positive anti-NET IgG was strongly associated with brain white matter changes after adjusting for demographic variables and criteria aPL profiles (OR=11, 95% CI 1.9 to 62), but not with other aPL-related manifestations. By immunofluorescence microscopy, we determined that high anti-NET sera more efficiently deposited complement C3d on NETs. In pursuit of the antigen specificity of anti-NET antibodies, 214 samples were analyzed by autoantibody microarray. Anti-NET IgG positivity significantly associated with the following antigens: citrullinated-histone H1 and H4, MPO-DNA complexes, nucleosomes, centromere protein A, heparan sulfate proteoglycan, laminin and collagen VI. Meanwhile, anti-NET IgM positivity associated with the following: single or double-stranded DNA, and proliferating cell nuclear antigen.

Conclusions: In summary, these data reveal high levels of anti-NET antibodies in 45% of aPL-positive patients wherein they potentially activate the complement cascade and contribute to white matter changes. While anti-NET IgM may especially target DNA in NETs, anti-NET IgG appear more likely to target protein antigens.

Keywords: Anti-NET antibodies, NETosis, non-criteria manifestations, APS ACTION.

0020

INCREASED EXPRESSION OF CD49D MARKER ON MONOCYTES IN RESPONSE TO STIMULATION BY ANTIPHOSPHOLIPID ANTIBODIES

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Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by thrombosis, obstetric complications, and the presence of antiphospholipid antibodies (aPL). Monocytes play an important role in tissue homeostasis, protective immunity, and promotion, as well as resolution of inflammation. They interact with endothelial cells via various integrins and selectins. The interaction between very late activation antigen 4 (VLA-4), an integrin dimer composed of CD49d and CD29, and its ligand, vascular cell adhesion molecule 1 (VCAM-1), is believed to be involved in inflammatory and autoimmune pathways. We aimed to determine the surface expression of CD49d in vivo on monocytes isolated from APS patients and to analyze the ability of aPL to stimulate its surface expression on monocytes in vitro.

Patients and methods: Whole blood from 19 APS patients and 13 healthy blood donors (HBDs) was stained for CD14+/CD16+ monocytes, and the CD49d marker was detected by flow cytometry. For in vitro experiments, monocytes derived from HBDs were stimulated with lipopolysaccharide (LPS) and prothrombin (PT) alone or in combination with IgG fractions isolated from the serum of a triple-positive catastrophic APS patient or HBD. Monocyte activation was determined by TNF-a ELISA in cell culture supernatants. The surface expression of CD49d on monocytes was determined by flow cytometry after 16 hours of incubation.

Results: Flow cytometric analysis of CD14+/CD16+ monocytes showed a slight increase in the percentage of CD49d+ monocytes in the group of APS patients (37.0 ± 15.8 %) compared to HBDs (30.5 ± 13.7 %), p=0.232 (Figure 1A) and a slight increase in median fluorescence intensity between the APS patients (3.46 ± 1.13 MFI) and the HBDs (2.98 ± 0.93 MFI), however, the difference was not statistically significant (Figure 1B). Monocytes stimulated with IgG from APS patient released significantly higher levels of TNF-a protein into the media compared with monocytes stimulated with IgG from HBD (18.2 µg/ml vs. 3.5 µg/ml) (Figure 1E). Stimulation with IgG from APS patient significantly increased the percentage of CD49d+ monocytes (95.1 ± 2.4 %), compared with IgG from HBD (3.79 ± 0.90 %), p<0.0001 (Figure 1C). Accordingly, the CD49d median fluorescent intensity was increased when stimulated with APS-IgG (19.8 ± 2.01 MFI) compared to HBD-IgG (1.84 ± 0.02 MFI), p=0.0004 (Figure 1D).

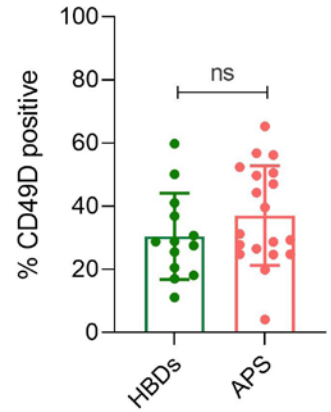

Figure A

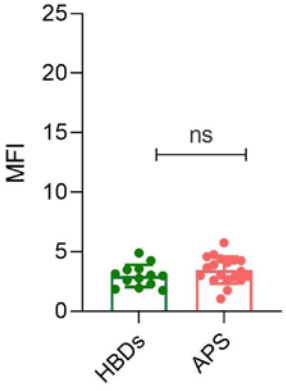

Figure B

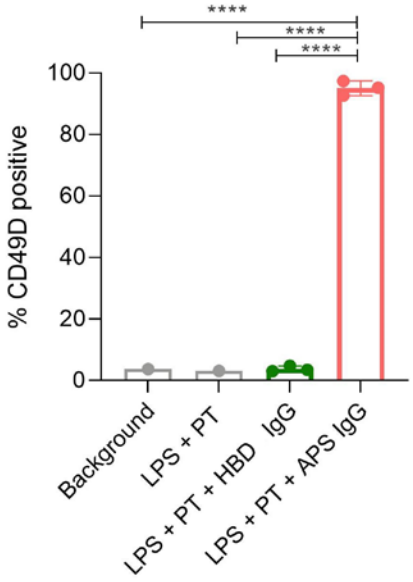

Figure C

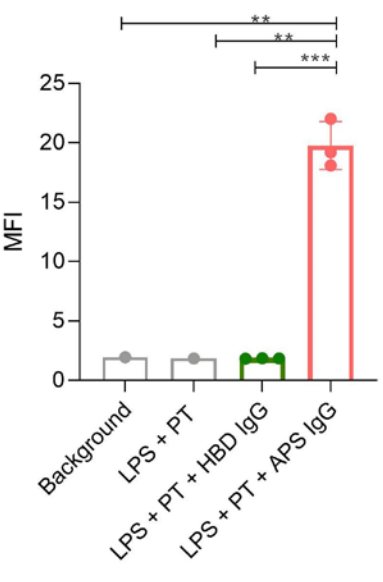

Figure D

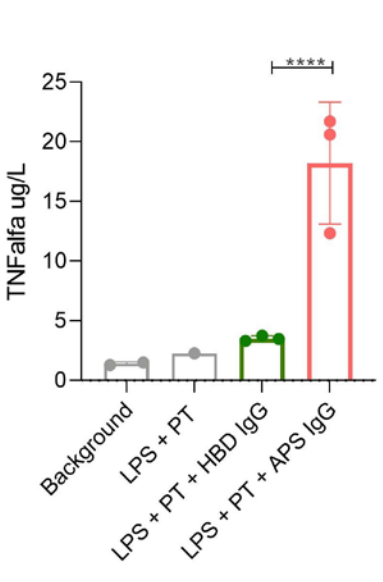

Figure E

Conclusions: Overall, our study showed that the expression of CD49d on monocytes was slightly increased in APS patients compared to HBDs. However, the patients included in the study were all in a chronic state and therefore under therapy, which may have reduced CD49d expression. On the other hand, in vitro experiments mimicking the acute phase showed that CD49d was significantly increased on the surface of monocytes after stimulation with IgG from APS patient. This suggests the possible importance of CD49d in the adhesion of monocyte to endothelial cells and their interaction during an acute event in APS patients.
Keywords: Antiphospholipid syndrome, antiphospholipid antibodies, adhesion, CD49d, monocytes.

0022

EPIDEMIOLOGY OF THE ANTIPHOSPHOLIPID SYNDROME: THE REAL-WORLD EXPERIENCE OF PIEDMONT AND AOSTA VALLEY

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Antiphospholipid Syndrome (APS) is a rare autoimmune disorder with an estimated prevalence of 40-50 cases per 100.000 persons. Patients suffering from low prevalence diseases are more to face diagnostic challenges, given the limited knowledge of most clinicians. The main aim of this study was to investigate the prevalence and incidence of APS and the time between symptoms occurrence and the diagnosis of APS patients using the Piedmont and Aosta Valley Rare Disease Registry. Secondly, to evaluate the individual impact of the diagnostic gap by gathering patients' personal experiences through a self-administered questionnaire.

Patients and methods: In order to participate in a better estimation of the epidemiology of the syndrome, we performed an analysis by using a population-based approach to investigate the clinical-epidemiological data of patients with APS in North-West Italy. We collected data from Piedmont and Aosta Valley Rare Disease Registry, as part of the National Registry of Rare Diseases (1,2). The registry includes a common dataset, including socio-demographic and disease data. In addition, personal experiences were analyzed through a self-administered questionnaire.

Results: A total of 740 APS patients included in the Piedmont and Aosta Valley Rare Disease Registry was analyzed. Median age at diagnosis was 45 years old (interquartile range 23 years), 63% of patients were diagnosed aged ≤50 years, 39% ≤40 years, and 18% ≤30 years. Taking into account that the population of the Piedmont and Aosta Valley Region is around 4.4 million (12) persons, the calculated estimated prevalence of APS in Piedmont and Aosta Valley Region is 1.68 cases per 10,000 people (Figure 1). When analyzing the data of the register in ten years (from January 2010 to January 2020), the calculated annual incidence was 1.1 cases per 100,000 people. Diagnostic delay (as defined by time between symptoms' occurrence and the diagnosis of APS) was significantly reduced over time. In particular, when comparing the diagnostic delay between patients diagnosed between 1983 to 1999 and patients diagnosed between 2000 until 2015, we found a significant statistical difference (Mann-Whithey U Test; mean rank 1216.6 vs. 1066.9, respectively; p <0.0001; Figure 1). When

analyzing the self-administered questionnaires, patients with a perception of having suffered for a diagnostic delay had a higher prevalence of symptoms suggestive of an autoimmune condition but not highly suggestive of APS (45%), followed by "extra criteria" APS manifestation (30%) and by thrombotic events (25%). The first clinical manifestation of patients who did not have the perception of having suffered a diagnostic delay was thrombotic events (45.5%), followed by autoimmune manifestation not linked to APS (45.5%), and "extra criteria" APS manifestations (9%).

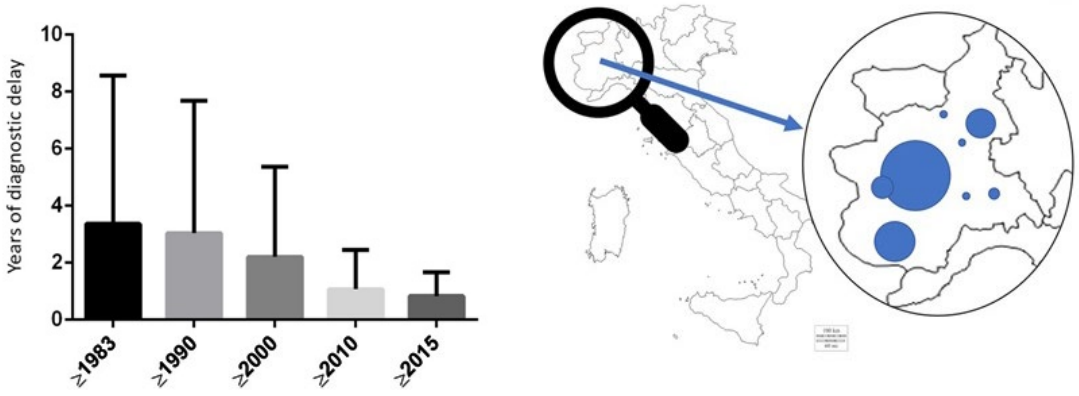

Figure:

Panel A: Box plot of diagnostic delay of antiphospholipid syndrome stratified by time period.

Panel B: Relative bubble chart of the centers that reported patients with antiphospholipid syndrome diagnosis from January 2010 to January 2020.

Conclusions: The analysis of the Rare Disease Registry of Piedmont and Aosta Valley confirmed that APS is a rare disease. While the diagnostic delay of APS has been reduced during the last years, the time between symptoms occurrence and the diagnosis of rare diseases still represents a critical issue to be addressed in order to prevent major complications.
Keywords: Epidemiology, diagnostic delay, rare diseases.

0023

ECULIZUMAB USE IN CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME (CAPS): DESCRIPTIVE ANALYSIS FROM THE "CAPS REGISTRY"

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To describe the real-world experience of eculizumab use in patients with catastrophic antiphospholipid syndrome (CAPS) according to the information provided by the "CAPS Registry".

Patients and methods: We analyzed the demographic, clinical and immunological data from all the patients included in the "CAPS Registry" treated with eculizumab and described the indications for eculizumab administration, dose, outcome, use of prophylactic vaccines and adverse effects.

Results: The "CAPS Registry" currently includes 584 patients from whom 39 (6.7%) were treated with eculizumab (it was used as a rescue therapy in 30 cases while in 6 cases it was used as first line therapy). Mean age of eculizumab treated patients was 39 years (SD=14.6), 72% were female, 77% had a primary APS and 79% had a precipitating factor before the CAPS event. Thrombocytopenia was present in 28 (72%) cases and features of microangiopathic hemolytic anemia were present in 15 (38.5%). Twenty-nine (74.4%) patients recovered from the episode of CAPS (four showed only partial remission). Symptoms worsened in 9 patients, from whom 5 finally died despite the treatment. There was only one relapse after a median follow up of 10.7 months. The most common treatment regimen was 900 mg weekly for four weeks and 1200mg fortnightly.

Conclusions: According to the real-world experience provided by the "CAPS Registry", eculizumab can be considered in some patients with CAPS refractory to previous therapies, especially if they present with features of complement-mediated thrombotic microangiopathy.

Keywords: Catastrophic antiphospholipid syndrome, CAPS.

0024

THE CLINICAL SIGNIFICANCE OF LOW COMPLEMENT LEVELS IN CAPS: A DESCRIPTIVE ANALYSIS OF 73 PATIENTS FROM THE "CAPS REGISTRY"

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To explore the prevalence and clinical significance of low complement levels in patients with catastrophic antiphospholipid syndrome (CAPS).

Patients and methods: We reviewed data from the "CAPS Registry" on C3 and/or C4 complement plasma protein levels during acute CAPS episodes. Patients were classified into those with low and normal complement levels. Data on clinical presentation, with special focus on thrombotic microangiopathy (TMA) features, diagnosis of systemic lupus erythematosus (SLE), and antiphospholipid antibody (aPL) profile were reviewed. The chi-square exact test was performed to evaluate differences between categorical data.

Results: The "CAPS Registry" includes 566 patients with a total of 578 episodes of CAPS. Three hundred ninety-nine (69%) patients were female, the mean age was 39.1 ± 16.1 years, and 342 (59.2%) had a primary APS. Data on complement plasma protein levels was available in 73 episodes from the same number of patients. Low levels of C3 and/or C4 complement plasma proteins were detected in 42 (58%) CAPS episodes. Low complement levels were more common in SLE patients (55% SLE vs. 19% No SLE; p<0.001). The frequencies of clinical TMA (72.1% vs. 80%; p=0.44) or TMA syndrome (85.7% vs. 84.4%, p=0.87), frequency of triple-aPL triple positivity (66.7% vs 33.3%; p=0.45), or the mortality (35% vs. 31.3%; p=0.74) were similar between low and normal complement groups.

Conclusions: In our study, low levels of C3 and C4 plasma proteins are detected in 58% episodes of CAPS, which were not associated with clinical presentation including TMA features, aPL triple positivity, or mortality.

Keywords: Complement, catastrophic antiphospholipid syndrome, antiphospholipid syndrome, systemic lupus erythematosus.

0026

ANTI-DOMAIN 1 ANTIPHOSPHOLIPID ANTIBODIES AS A MARKER FOR ADVERSE PREGNANCY OUTCOME IN SLE AND APS

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Lupus anticoagulant (LA) is the strongest predictor of 2nd and 3rd trimester adverse pregnancy outcome (APO) in systemic lupus erythematosus (SLE) or antiphospholipid syndrome (APS). Antibodies against β2 glycoprotein I (β2GPI) are also important in APS, particularly those against domain 1 (aD1), but current data regarding their predictive value for APOs are limited. In this pilot study, we sought to explore the value of aD1 antibodies with regard to APOs in a selected group of high-risk patients.

Patients and methods: Data were obtained from a selected subset of a prospectively-observed cohort of pregnancies with SLE, APS, or antiphospholipid antibodies (aPL) alone (PROMISSE study; NCT00198068). Selection included 32 patients with SLE but negative aPL (16 with and 16 without APO), 11 patients with SLE and positive aPL (6 with and 5 without APO), and 22 patients without SLE but positive aPL (11 with and 11 without APO). aD1 levels from early pregnancy sera were quantified using the QUANTA Flash® system; 99th percentile for positivity was determined using sera from 125 healthy, non-pregnant females. APO was defined as preeclampsia or placental insufficiency requiring delivery <34 wks GA. We compared sensitivity and specificity of positive aD1 and/or LA for APO.

Results: Significantly more cases with APO tested positive for aD1 compared to cases without APO (52% v 25%, p=0.028, Table 1). Sensitivity for APO was higher for aD1 than LA, and specificity similar to LA, as an isolated test (Table 2). The intersection of LA and aD1 performed best for specificity, and the union best for sensitivity.

Table 1: Rate of each possibility for cases with and without APO.

Mesure	All Cases N=65	Cases with APO N=33	Cases w/o APO N=32	p
aD1	25(38.5)	17(52)	8(25)	0.028
LA	22(33.8)	13(39)	9(28)	0.337
LA U aD1	33(50.8)	19(58)	14(44)	0.265
LA ∩ aD1	14(21.5)	11(33)	3(9)	0.019

Values presented a frequency (column percent).
LA-lupus anticoagulant; aD1- anti – Domain 1 antibody at the 99th percentile threshold (18.5).
APO- adverse pregnancy outcomes.
U *denotes union; possibility of both LA and aD1.*
∩ *denotes intersection: possibility of both LA and aD1.*

Table 2: Sensitivity and specificity of each positivity or APO.

Measure	Sensitivity	Specificity
aD1	0.52(0.35-0.68)	0.75(0.58-0.87)
LA	0.39(0.25-0.56)	0.72(0.55-0.84)
LA U aD1	**0.58(0.41-0.73)**	0.56(0.39-0.72)
LA ∩ aD1	0.33(0.20-0.50)	**0.91(0.76-0.97)**

95% confidence interval presented Parenthetically.
Best in each category is bolded.
LA-lupus anticoagulant aD1– Domain 1 antibody at the 99th percentile threshold (18.5).
APO- adverse pregnancy outcomes.
U *denotes union; possibility of both LA and aD1.*
∩ *denotes intersection: possibility of both LA and aD1.*

Conclusions: In subjects with SLE, APS, or aPL, sensitivity of aD1 positivity for APO was superior to that of LA. Combined measures of LA and/or aD1 improves sensitivity and specificity. These preliminary data suggest that elevated aD1 results are associated with APOs and that aD1 results contribute additional information beyond that of LA. Additional study is in progress to determine predictive value of aD1 positivity in a high-risk population.
Keywords: Antiphospholipid antibodies, systemic lupus erythematosus, obstetric antiphospholipid syndrome, pregnancy.

0027

INTRACRANIAL VESSEL WALL MRI IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME: A CASE SERIES STUDY

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Cerebrovascular disease is one of the major features of antiphospholipid syndrome (APS) as well as systemic lupus erythematosus (SLE). The differentiation between cerebral vasculitis and atherosclerosis is challenging and important to provide appropriate treatment for patients with primary APS (pAPS) and/or SLE with APS (SLE-APS). Magnetic resonance (MR) vessel wall imaging (VWI) can detect concentric vessel wall enhancement reflecting vasculitis and has been used to diagnose cerebral vasculitis. We report five cases of APS patients with cerebral vascular stenosis who were evaluated by intracranial MR-VWI.
Patients and methods: This case series study comprised patients with APS and subjective neurological symptoms including migraine, vertigo, dysarthria, numbness, or depression who had intracranial vessel stenosis detected by MR imaging (MRI)/MR angiography (MRA), and then underwent intracranial VWI at our department from July 2018 to July 2021. MR-VWI consisted of 1.5-T MRI, which obtained T1-weighted 3-dimensional fast-spin echo. Patients' clinical/laboratory manifestations and MRI/MRA findings were collected and analyzed.
Results: MR-VWI was performed in five APS patients, one pAPS and four SLE-APS, with intracranial vessel stenosis detected by MRI/MRA. All were women. Case 1: a 47-year-old manifested vertigo. MR-VWI showed a concentric enhancement at cortical branch of the middle cerebral artery. Laboratory data revealed low CRP levels and high anti-DNA antibody titers. Case 2: an 18-year-old manifested depression. MR-VWI showed concentric enhancements at arteries distributed in the parietal and temporal lobes. Laboratory data showed low CRP levels, hypocomplementemia, and high anti-DNA antibody titers. Case 3: a 39-year-old manifested dysarthria caused by cerebral infarction of the left thalamus detected by MRI. The

enhancements of MR-VWI at vertebral arteries was non-concentric. She had a history of hypertension and dyslipidemia, and Laboratory data showed low CRP levels. Case 4: a 33-year-old manifested migraine. Laboratory data showed low levels of CRP levels and hypocomplementemia. Case 5: a 61-year-old manifested numbness in the lower limbs. She had a history of hypertension. Laboratory data showed low CRP levels, hypocomplementemia, and elevated anti-DNA antibody titers. Case 4 and Case 5 showed no findings in MR-VWI. Cases 1 and 2 were treated with immunosuppressive therapy for vasculitis, improving their symptoms. Case 3 was treated with anticoagulant drugs for thrombosis. In case 4, a diagnosis of migraine was considered. In case 5, transverse myelitis was suspected and treated with immunosuppressive therapy, and the symptoms resolved. Case 4 was diagnosed with pAPS, and the other four cases were diagnosed with SLE-APS.
Conclusions: In our series, three of the five APS patients had contrast enhancement in the intracranial vessel wall, two of which had concentric enhancement and one of which had non-concentric enhancement. Intracranial MR-VWI might detect cerebral vasculitis and therefore could be a useful tool for the diagnosis of neuropsychiatric manifestations in patients with APS.
Keywords: SLE, APS, cerebral vasculitis, arteriosclerosis, MR-VWI.

0028

ASSOCIATION BETWEEN ANTINUCLEAR ANTIBODIES AND PREGNANCY OUTCOME IN PATIENTS WITH RECURRENT PREGNANCY LOSS

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Although an association between antiphospholipid antibodies (aPLs) and recurrent pregnancy loss (RPL) has been established, the possibility that antinuclear antibodies (ANA) may be involved in patients with RPL who have no aPLs remains controversial. We therefore conducted the present study to evaluate whether ANA affects subsequent live births in patients with RPL.
Patients and methods: All were seen in our hospital from 2006 to December 2019. The following pre-pregnancy tests ruled out uterine malformations, and antiphospholipid syndrome (APS), an abnormal chromosome in either partner. Lupus anticoagulant by APTT and RVVT and ß2glycoproteinI dependent anticardiolipin antibody were measured to diagnose for APS. Since some unexplained patients wished for medication, such patients were also excluded from the analysis. Thus, the present cohort study included 798 patients with a history of two or more pregnancy losses and the subsequent pregnancy. ANAs were measured by indirect immunofluorescence on Hep-2 cell slides. The protocol was reviewed and approved by the institution's Research Ethics Committee.
Results: The rate of ANA-positive patients was 39.0 % (390/1000) when the 1:40 dilution result was positive. With a 1:160 dilution, it was 3.50 % (35/1000). With the use of the 1:40 dilution, analyzing only live births and euploid miscarriage, live birth rates were 92.4 % (220/238) for the ANA-positive group and 92.0 % (346/376) for the ANA-negative group. With the use of the 1:160 dilution, live birth rates were 92.4 % (220/238) for the ANA-positive group and 92.0 % (346/376) for the ANA-negative group. Subgroup analyses were performed for each pattern on immunofluorescence staining, but there was no significant difference in the live birth rate between the two groups. ANA-positive patients were found to have APS with an odds ratio of 4.1.
Conclusions: We examined whether ANA predict the subsequent pregnancy prognosis for 798 patients with RPL, however, we found no predictive value of ANA. ANA is a biomarker for autoimmune diseases screening such as SLE, but it does not seem to be a biomarker for prognosis of pregnancy in patients with RPL. It is more important to accurately diagnose and treat APS, which is often associated with ANA-positive patients, in order to improve their pregnancy outcome.
Keywords: Recurrent pregnancy loss, antinuclear antibodies, antiphospholipid antibodies.

0031

ASSESSING THE CARDIOVASCULAR RISK IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: QRISK AND GAPSS SCORES HEAD TO HEAD

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Cardiovascular diseases (CVDs) represent one of the most life-threatening conditions that can affect SLE patients. Assessing the potential CVD risk of these patients is still a challenge and an important aspect in the clinical practice. Recently the QRISK3 score has attempted to encompass for SLE augmented thrombotic risk by adding items (such as corticosteroid use) that are missing in traditional CVD risk scores. The aim of this study was to apply and compare the QRISK3 and the

adjusted Global Antiphospholipid Syndrome Score (aGAPSS), a validated score to assess CVD and overall thrombotic risk in aPL positive patients, in a cohort of SLE patients with and without a concomitant diagnosis of APS.

Patients and methods: 25-85 years old patients attending San Giovanni Bosco Hospital (Turin) during a period of 6 months (Sep 2019 – Feb 2020) with a confirmed diagnosis of SLE (according to 2019 ACR/EULAR classification criteria) and/or a diagnosis of SAPS (according to Sidney criteria) were included in the study. QRISK3 has been calculated using the official online calculator (https://qrisk.org/). aGAPSS has been calculated using the validated point values based on aPL profile and independent risk factors: aCL=5, aβ2GPI=4, LA=4, aPS/PT=3, hyperlipidemia=3, hypertension=1.

Results: The analysis included a cohort of 142 SLE patients: 34 SAPS (23.9%) and 108 SLE patients without APS (76.1%), with a mean age of 48±12.9 (SAPS=51.6±12.8/SLE without APS=46.9±12.8). Table 1 summarizes patient's characteristics. When focusing on cerebrovascular/coronary events, we found a statistical significance with respect to aGAPSS (pt with event =10.1±6.2 vs. pt without event=5.8±6.1; p=0.007), but not QRISK3. Also, a significant association was observed between the occurrence of these events and high risk aGAPSS: p=0.03 for aGAPSS≥8, p=0.01 for aGAPSS ≥9, p=0.008 for aGAPSS ≥10. Moreover, the aGAPSS but not the QRISK3 resulted to strongly correlate with the occurrence of any thrombotic event, both at the uni- and multivariate analysis (univariate: pt with event =8.17±7.1 vs. pt without event= 5.41±5.6; p=0.012 / multivariate: p=0.009). The same was observed for gender: male gender resulted to correlate with the occurrence of any thrombotic event at both uni- and multivariate analysis (p=0.017 and p=0.03, respectively). Finally, when focusing on aPL profile, regardless the diagnosis, we found a statistical significance only with respect to aGAPSS (aPL+ =9.6±6.3 vs. aPL- = 4.1±5.1; p<0.001).

PATIENTS	CHARACTERISTICS
Age (m ±sd)	Tot=48 ±12.83
	SAPS=51.61 ±12.82
	SLE w/o APS=46.87 ±12.83
Females, n(%)	Tot=120/142(84.5%)
	SAPS=22/34(64.7%)
	SLE w/o APS=98/198(90.74%)
THROMBOTIC	EVENTS
Thrombotic event, n(%)	Tot=48/142(33.8%)
	SAPS=33/48(68.75%)
	SLE w/oAPS=15/48(31.25%)
Arterial Thrombosis, n(%)	Tot =22/142(15.49%)
	SAPS=19/22(86.36%)
	SLE w/o APS =3/22(13.64%)
Venous thrombosis, n(%)	Tot=32/142 (22.53%)
	SAPS=18/32(56.25%)
	SLEw/o APS=14/32(43.75%)
Stroke, n (%)	Tot=13/142(9.15%)
	SAPS=13/13(100%)
	SLEw/o APS=0/13(0%)
	Tot =6 /142(4.22%)
TIA, n(%)	SAPS=6/6(100%)
	SLE w/o APS=0/6(0%)

Conclusions: By encompassing factors that can contribute to CVD development in complex/autoimmune diseases, QRISK3 has been shown to be more accurate than traditional risk score in predicting SLE patients CVD risk. Nonetheless, the results of this analysis showed how the aGAPSS still seems to be the most valuable tool for this purpose when facing SLE patients. Moreover, the significance observed when focusing on patients' aPL profile, suggests that adding this item to the QRISK3 could be a useful strategy to improve it.

Keywords: Cardiovascular risk, aGAPSS, QRISK3.

0032

EVALUATION OF NON-CRITERIA MANIFESTATIONS OF ANTIPHOSPHOLIPID SYNDROME IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ACCORDING TO ANTI-PHOSPHOLIPID ANTIBODY PROFILE

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To compare the presence of non-criteria non-thrombotic manifestations of APS in patients with SLE and APS, SLE with positive aPL, SLE with negative antibodies and different outcomes such as mortality, hospitalizations and damage score.
Patients and methods: Observational, analytical and cross-sectional multicenter study. Data were obtained from the review of the RELESSAR database. We included patients ≥ 18 years with diagnosis of SLE according to modified ACR 1984 criteria. The diagnosis of APS was made according to the Sidney Criteria 2006. The sample was classified into three groups based on the presence of established APS (Group 1), aPL carrier (Group 2) and aPL negative (Group 3). Non-criteria manifestations were described and compared in the three groups. Continuous variables were compared by Student's or Mann Whitney's T test, and categorical variables by Chi^2 test or Fisher's exact test. In cases where a significant difference was found between the groups, multiple post hoc comparisons were made.
Results: One thousand two hundred and two patients were included, 1,110 (92.3%) were women. One hundred and sixty patients (13.3%) had APS (group 1), 241 (20.04%) were aPL carrier (group 2) and 801 (66.6%) were negative for aPL (group 3). Patients with APS were older than patients in group 2 [42.6 (SD 13.5) vs 38 (SD 14.2), p 0.001] and 3 [42.6 (SD 13 .5) vs 39.5 (SD 14.1) p 0.004]. The disease duration was longer in patients with APS compared to patients with SLE and negative aPL (138 months (SD 113) vs 101 (SD 113) (p <0.001). Table 1 shows non-thrombotic manifestations in the three groups. A higher percentage of patients with hemolytic anemia was observed in the APS group (p=0.001) and in the aPL carrier group (p=0.018) compared to negative aPL group. Patients with APS showed a higher proportion of thrombocytopenia when compared to patients with negative aPL (p=0.039). Acute cranial/peripheral neuropathy was more frequently observed in APS group compared to aPL-negative group (p=0.006). APS group was significantly associated with hospitalizations due SLE flares, morbidity and damage index. A higher proportion of patients in the APS group had thrombotic events compared to aPL carrier and aPL negative groups (p<0.05).
Keywords: APS, SLE.

Table 1: Non-criteria non-thrombotic manifestations.

	APS (group 1)	aPL + (group 2)	aPL - (group 3)	p
Hemolytic anemia	31 (19.9%)	37(15.4%)	75(9.47%)	<0.001
Thrombocytopenia	41 (26.6%)	56 (23.4%)	138 (17.6%)	0.011
Depression	23 (14.8%)	17 (7.05%)	92 (11.6%)	0.041
Acute Neuropathy	10 (6.62%)	9.(373%)	14(1.77%)	0.002

Conclusions: In this nation-wide SLE cohort, neurological and hematological manifestations were frequently observed in patients with secondary APS. Moreover, these patients had higher rate of hospitalization, damage score and comorbidities.

0033

ANTI-ß2-GLYCOPROTEIN I ANTIBODIES CAUSE ACTIVATED PROTEIN C RESISTANCE BY INTERFERING WITH FACTOR V CLEAVAGE AT ARGININE 506

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The acquired thrombotic risk factor known as lupus anticoagulant (LA) is detected as a phospholipid-dependent prolongation of the clotting time and can be caused by autoantibodies against ß2-glycoprotein I (ß2GPI). LA is associated with activated protein C (APC) resistance, which might contribute to thrombotic risk in patients with LA. How anti-ß2GPI antibodies cause APC resistance is currently unclear. We have previously shown that anti-ß2GPI antibodies cause LA by attenuating factor (F)V activation by factor (F)Xa through a direct interaction with FV. As FV is central to the anticoagulant properties of APC, we hypothesized that the interaction between ß2GPI-antibody complexes and FV also causes APC resistance. Here, we want to investigate how anti-ß2GPI antibodies induce APC resistance.
Material and methods: The effects of model monoclonal anti-ß2GPI antibodies on APC resistance were studied in plasma and with purified coagulation factors.
Results: Anti-ß2GPI antibodies with LA-activity caused APC resistance using LA-sensitive clotting assays targeting both common and intrinsic coagulation pathways. APC resistance was only observed at limiting phospholipid concentrations, underlining the association between APC resistance and LA. Anti-ß2GPI antibodies only interfered with APC-mediated cleavage of FV, not when FVa was activated: When FV is activated the inhibitory effects of anti-ß2GPI antibodies on APC activity in plasma are lost. Also, anti-ß2GPI antibodies had no effect on APC-mediated FVa inactivation in a purified system indicating that these antibodies should have an effect on the inactivation of FVIIIa. Analysis of FV cleavage patterns after incubation with APC indicated that anti-ß2GPI antibodies attenuated APC-mediated cleavage of FV at two different positions: R506 and R306. APC-mediated cleavage at R506 is required for FV cofactor activity during inactivation of FVIIIa by APC. Assays with purified coagulation factors confirmed that anti-ß2GPI antibodies interfered with the cofactor function of FV during inactivation of FVIIIa.
Conclusions: Anti-ß2GPI antibodies with LA activity contribute to a procoagulant state by causing APC resistance via interference with the cofactor function of FV during inactivation of FVIIIa.
Keywords: Activated protein C resistance, anti-beta-2 glycoprotein I antibody, lupus anticoagulant.

0034

OBSTRUCTIVE SLEEP APNEA (OSA) IS ASSOCIATED WITH HIGHER DAMAGE MEASURED BY DAMAGE INDEX FOR ANTIPHOSPHOLIPID SYNDROME (DIAPS) AND INCREASED LEVELS OF VON WILLEBRAND FACTOR (VWF) IN PATIENTS WITH THROMBOTIC PRIMARY ANTIPHOSPHOLIPID SYNDROME (PAPS)

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Obstructive sleep apnea (OSA) has been associated with an increased risk of thrombotic-related events, such as myocardial infarction and cerebrovascular diseases in the general population. Thus, understanding the impact of OSA in patients with thrombotic primary antiphospholipid syndrome (tPAPS) is important to determine potential non-traditional factors that may contribute to thrombotic recurrence in those patients. We aimed to evaluate: 1) the frequency of OSA in tPAPS; 2) the differences in APS characteristics, damage accrual measured by Damage Index for Antiphospholipid Syndrome (DIAPS) and levels of biomarkers associated with thrombosis (von Willebrand factor - vWF) between tPAPS patients with and without OSA; 3) and the performance of screening tools for OSA in this scenario.
Patients and methods: We consecutively enrolled 60 patients with tPAPS (Sydney criteria). Damage accrual was measured by DIAPS. vWF antigen levels were determined using ELISA (Abcam™). OSA was evaluated using a portable sleep monitor (Embletta Gold, Natus Medical Inc., Ontario, Canada). OSA was defined by an apnea-hypopnea index (AHI) >=15. Patients with and without OSA were compared regarding APS clinical and laboratory characteristics, damage accrual and vWF levels, using standard statistical procedures. For the diagnostic yield analysis, we applied four different screening tools for assessing OSA (Epworth Sleepiness Scale [ESS], Berlin questionnaire, NoSAS score [Neck circumference, Obesity, Snoring, Age, Sex], and STOP-Bang [Snoring, Tiredness, Observed apnea, Pressure (high blood), BMI, Age, Neck circumference, Gender]) and compared their performance using ROC curves.

Results: Out of 60 patients who underwent sleep monitoring, 52 were included for analysis (8 patients were excluded due to low quality of sleep data). The majority of patients were females (82.7%) and whites (76.9%). The mean age and body-mass index were 48±14 years and 31.1±6.5 Kg/m², respectively. OSA was diagnosed in 13 patients (25.0%). Patients with OSA were older (56.9±10.7 vs. 44.6±13.8, p=0.006) and had higher neck and waist circumferences, waist-to-hip ratio and systolic blood pressure levels. Patients with OSA had a trend for previous arterial events (61.5% vs. 33.3%, p=0.073). We also found higher levels of vWF (38.9 [26.45-56.3] vs. 32.6 [20.4-38.3] mUI/mL, p=0.038) and higher DIAPS (5 [2.5-9.5] vs. 2 [1-5], p=0.020) in patients with OSA (vs. without OSA). Among screening tools, NoSAS had the highest area under ROC curve (0.806, 95% CI: 0.672-0.939, p=0.001), followed by STOP-Bang (0.772, 95% CI: 0.607-0.938, p=0.004).
Conclusions: The frequency of OSA was strikingly high in our cohort. tPAPS patients with OSA had numerically higher rates of previous arterial events and also significantly higher levels of vWF and higher damage accrual than those without OSA. NoSAS appears to be the best screening tool for OSA in patients with PAPS.
Keywords: Obstructive sleep apnea, von Willebrand factor, damage.

0035

CLINICAL DELPHI ON APL NEGATIVIZATION: REPORT FROM THE ITALIAN SOCIETY OF RHEUMATOLOGY WORKING GROUP ON ANTIPHOSPHOLIPID SYNDROME

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The rate of antiphospholipid antibodies (aPL) negativization in antiphospholipid syndrome (APS) patients is uncertain, but it is estimated to be as high as 8%. aPL disappearance seems to be more frequent in patients positive for one single test aPL and appears to be related with the immunosuppressant/immunomodulatory treatment undertaken by the patient. Currently, a consensus definition of aPL negativization is lacking, as well as international recommendations on how to approach treatment in patients with a persistent aPL negative seroconversion. The aim of our work was to evaluate the clinical approach and level of consensus among experts from the APS Study Group of the Italian Society for Rheumatology (SIR-APS) in different clinical scenario addressing aPL negativization and its definition, investigating the level of existing consensus.
Patients and methods: We applied a survey methodology, already described elsewhere, with the purpose to detangle difficult-to-manage clinical scenarios not fully covered by existing evidences. Most of the questions were intentionally dichotomous, to obtain a straight answer. Nonetheless, a free-text option allowed to elaborate on the selected response, or to provide arguments for an alternative response
Results: A structured survey was circulated among 30 experts. Up to 90% of the interviewed experts agreed on defining aPL negativization as the presence of two negative determinations, one year apart (90%).Almost full consensus exist among experts in some clinical settings, including: a) the role of aPL negativization in the management of a thrombotic event determined by concomitant presence of cardiovascular risk factors, both modifiable and not modifiable (90%); b) approach to young patients with triple aPL positivity who experienced pulmonary arterial thrombotic event and tested negative for aPL detection after five year of vitamin K antagonist (VKA) treatment (90%); c)the use of "extra criteria" aPL antibodies testing before pondering VKA suspension (93%).
Conclusions: Consensus is extremely useful to support the management of patients with APS in areas where controlled data are missing. A substantial agreement exists among expert in defining aPL negativization as the presence of two negative determinations, one year apart. On the contrary, VKA suspension should be embraced with extreme caution when it comes to APS patients, particularly if they experienced arterial thrombotic events and/or tested positive for triple aPL. Nevertheless, VKA cessation might be considered when risk factors are carefully monitored/treated and the presence for "extra criteria" aPL is ruled out.
Keywords: Antiphospholipid antibodies, aPL antibodies negativization, risk of thrombotic recurrence.

0036

IDENTIFICATION OF DIFFERENT POPULATIONS OF PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES USING THROMBIN GENERATION ASSAY AND LUPUS ANTICOAGULANT

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Among antiphospholipid antibodies (aPL) positive patients, the so-called "tetra-positive" (persistently positive for LA, aCL, aß2GPI and aPS/PT) are now recognized as those at higher risk. Also, when considering single-positivity, LA has been considered the strongest risk factor for the development of thrombosis. Nonetheless, risk stratification in these patients remains a clinical challenge. We aimed to evaluate the role of Thrombin Generation Assay (TGA) in distinguishing various populations of aPL positive patients (regardless LA status) and its association with ß2GPI-dependent and aPS/PT antibodies.

Patients and methods: 108 patients were tested with TGA and divided as follows: 21 patients with aPS/PT IgG/IgM (medium/high titres) (Group 1), 29 with aß2GPI IgG/IgM (medium/high titres) (Group 2), 31 with aPS/PT and aß2GPI IgG/IgM (medium/high titres) (Group 3) and 27with aPS/PT and/or aß2GPI IgM (low titers) (Group 4). 31 healthy donors (HDs) and 24 controls treated with VKA but without other autoimmune conditions were also included.

Results: The most deranged TGA and LA profiles were observed in patients with both aPS/PT and aß2GPI at medium/high titers when compared to those with an isolated positivity for aPS/PT or aß2GPI (at medium/high titers) and patients with aPS/PT and/or aß2GPI IgM at low titres (Figure 1A). Similarly, patients with aPS/PT and/or aß2GPI at medium/high titres presented with the higher rate of clinical manifestations. In particular, when comparing Group 1and 4 we found a statistical difference in the number of thrombotic events (21 vs. 15; p<0.05), venous events (9 vs. 3; p<0.05), recurrence of thrombosis (19% vs. 0%; p<0.05) and number of recurrent thromboses (3 vs. 0; p<0.05). Group 2 and 4 showed differences in the occurrence (50% vs. 20%; p<0.05) and number of venous events (13 vs. 3; p<0.05) and occurrence of TIA (3 vs. 0; p<0.05) and DVT (8 vs. 2; p<0.05). When comparing Group 3 and 4 we found differences in the number of thrombotic events (36 vs. 15; p<0.05), the occurrence and number of venous events (46% vs. 20%; p<0.05), occurrence of TIA and DVT (4-11 vs. 0-2; p<0.05), occurrence and number of recurrent thromboses (29%-5 vs. 0; p<0.05) and occurrence of arterial thromboses (21% vs. 0%; p<0.05).When comparing the TGA curves of APS patients, asymptomatic aPL+ subjects, HDs and controls treated with VKA, we observed that aPL+ patients (particularly those with a confirmed diagnosis of APS) showed a characteristic profile (Figure 1B). Moreover, both in aPL+ subjects and in the control groups we observed a correlation between TGA and LA parameters.

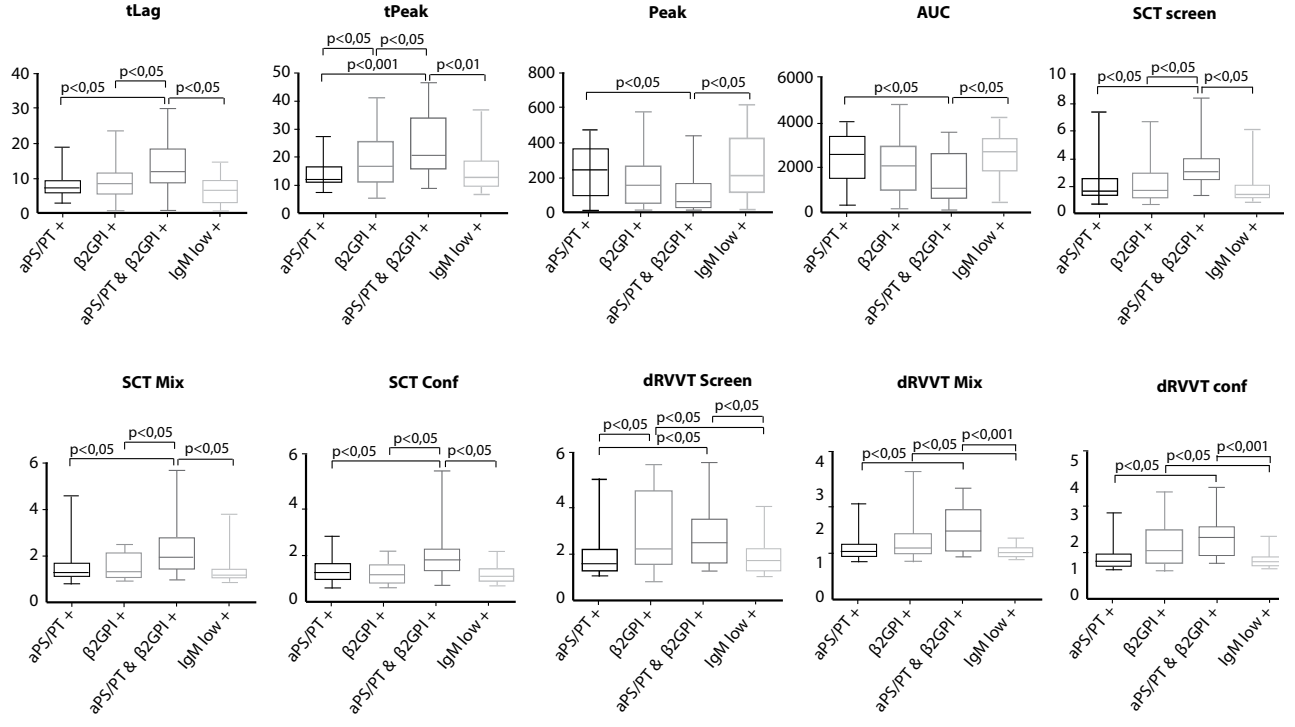

Figure 1A

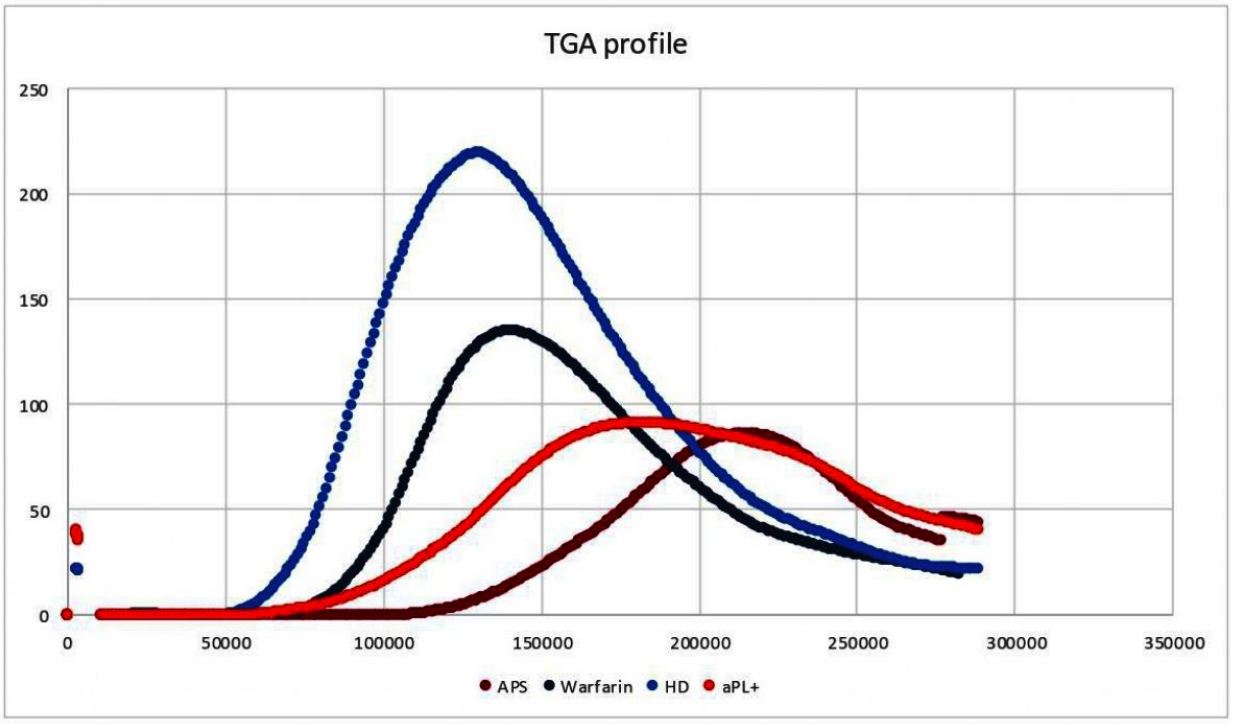

Figure 1B

Conclusions: TGA seems a valuable approach to stratify aPL+ patients according to their risk profile. The differences among groups and different populations of autoantibodies specificities obtained from this test can be considered a translational validation of the increased thrombotic risk of patients with triple or tetra aPL-positivity.
Keywords: Thrombin generation assay, lupus anticoagulant, risk stratification.

0037

WHOLE EXOME SEQUENCING IN ANTIPHOSPHOLIPID SYNDROME GENETIC FACTORS: A PILOT EXPERIENCE

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Antiphospholipid syndrome (APS) aetiology is still unknown but, similarly to other autoimmune conditions, the high heterogeneity of its manifestations and clinical course is presumably due to the occurrence of different mechanisms and alterations at diverse levels and pathways. The first genetic studies in APS focused mainly on the HLA region, but recent data highlighted the role of other genes in APS susceptibility, primarily those involved in the immune response and in the haemostatic process. Given this, we aimed to deepen the investigation of APS genetic background starting from a case of familial APS, analyzing two triple-positive siblings with thrombotic APS.
Patients and methods: Genomic DNA was extracted from peripheral blood of the two siblings. Samples underwent Whole Exome Sequencing (WES) on a 100X coverage and Burrows-Wheeler Alignment tool (BWA) was used to align the reads to the human reference genome (GRCh37/hg19 assembly). 99.50% of the targeted bases had at least 10X coverage for all the three donors, moreover the mean sequencing depth on target regions was 170X for patient 1, 205X for patient 2. The resulting single nucleotide polymorphisms (SNPs) have been analyzed through a step-by-step process based on their frequency population (using Genome Aggregation Database), their predicted effects on the protein (using VarSome) and a literature research about the genes carrying them. Also genes previously associated with a pro-thrombotic tendency and with APS have been analyzed in the two patients.
Results: The WES highlighted the presence of more than 120000 SNPs for each patient. The step-by-step process led to reduce the list of SNPs of interest to 27 missense mutations. The complete literature research referred to the genes carrying these mutations allowed to further reduce their number, focusing on 7 genes exerting a role potentially involved in APS pathogenesis and development. In particular, these genes (PLA2G6, HSPG2, BCL3, ZFAT, ATP2B2, CRTC3 and ADCY3) take part in the immune response and the vascular homeostasis. The list of the DNA missense variants of interest found in our

cases of familial APS is resumed in Table 1. No mutations on genes previously associated with APS (B2GPI, PF4V1, SELP, TLR2, TLR4, GP Ia, GP1BA, F2R, F2RL1, TFPI, F3, VEGFA, FLT1, and TNF) or known to be associated with a pro-thrombotic state (F5, F2, MTHFR, F13A1, PROC, PROS1, FGB and SERPINE1) have been found in the WES analysis.

GENE	FULL NAME	SNP	CHR	COORDINATE	TRANSCRIPT	VARIANT EFECT
CROCC	Ciliary rootlet coiled-coli/Rootlein	rs1444279934(A/T)	1	17270657	NM_014675.3	Missense variant (p.Gln624Leu)
HSPG2	**Herpan sulfate proteoglycan2**	**rs766963773(C/T)**	**1**	**22207015**	**NM_005529.5**	**Missense variant (p.Arg679His)**
KIF14	Kinesin family member 14	rs373895990(C/T)1	1	200573037	NM_014875.2	Missense variant (p.Arg598Gln)
ADCY3	**Adenylate cyclasse3**	**rs754839662(C/T)**	**2**	**2505928**	**NM_004036.3**	**Missense varian (Val759Met)**
GRM7	Glutamate metabotropic receptor7	rs1480175679(A/C)	3	7494339	NM_181874.2	Missense variant (p.Lys407Thr)
SRGAP3	SLIT-ROBO Rho GTPase activating protein 3	rs7641347118(C/T)	3	9146464	NM_014850.3	Missense variant (p.Arg108Gln)
ATP2B2	**ATPase plasma membrane Ca+2 transporting 2**	**rs751257556(G/A)**	3	**10382352**	**NM_001001331.2**	**Missense variant (p.Ala985val)**
OXNADI	OxidoreductaseNDA binding domain containing1	rs1456594626(T/G) rs1159857217(T/A) rs1390159575(C/G)	3	16343175 16344176 16343177	NM_138381.3	Missense variant (p.Phe159Glu)
PDZD2	PDZ domain containing2	rs1345334581(C/G)	5	32098731	NM_178140.2	Missense variant (p.Pro2737 Ala)
FAT2	FAT Atypical cadherin 2	rs761199516(C/A)	5	150945648	NM_001447.2	Missense variant (p.Ala949Ser)
OR2FI	Olfactory receptor family 2 subfamily F member 1	rs777034277(T/C)	7	143657370	NM_0123669.2	Missense variant (p.Phe103Leu)
ZFAT	**Zinc finger and A-T-Hook domain containing**	**rs748138009(G/A)**	**8**	**135596174**	**NM_020863.3**	**Missense variant (p.Arg930Cys)**
IFNA17	**Interferon alpha 17**	**c.338A>T**	**9**	**21227835**	**NM_201268.2**	Missense variant (p.TyR113Phe)
ZNF462	Zinc finger protein 462	C.226A>T	9	109686419	NM_021224.4	Missense variant (p.Asn 76Tyr)
MRPL48	Microchondrial ribosomal protein L48	rs745995390(G/T)	11	73555903	NM_016055.5	Missense variant (p.Aps85Tyr)
LTBP2	Latent transforming growth factor beta binding protein 2	rs1310944162(G/A)	14	74995323	NM_000428.2	Missense variant (p.Ala744Val)
CRTC3	**CREB regulatedtranscription coactivator 3**	**c.163C>T**	**15**	**91083301**	**NM_022769.4**	**Missense variant (p.Leu55Phe)**
USP32	Ubiquitin specific peptidase 32	c.1169T>C	17	58313569	NM_032582.3	Missense variant (p.Leu390Pro)
IMPA2	Inositol monophoshatase 2	rs1423846345(T/C)	18	12009980	NM_014214.2	Missense variant (p.Vall10Ala)
MUC16	Mucin 16	rs200972932(C/T)	19	9067504	NM_024690.2	Missense variant (p.Glu6648Lys)
CC2DIA	Colied.-coil an C2 domain containing 1A	c.794G>T	19	14028928	NM_017721.4	Missense variant (p.Arg265Leu)
MAP3K10	Mitogen-activated protein kinase kinase kinase 10	c.358G>A	19	40698296	NM_002446.3	Missense variant (p.Glu120Lys)
BCL3	**BCL3 transcription coactivator**	**rs747655476(C/A)**	**19**	**4526063**	**NM_005178.4**	**Missense variant (p.Thr381Asn)**
MCM8	Minichromosome maintenance 8 homologus recombination repair factor	rs768426546(G/A)	20	5955350	NM_001281521.1	Missense variant (p.Arg451 His)
PLA2G6	**Phospholipase a2 group VI**	**rs780423461(C/G)**	**22**	**38528920**	**NM_003560.2**	**Missense variant (p.Cys332Ser)**

Conclusions: To a certain extent, this results can be seen as a proof of concept of the high complexity of APS. Efforts to interpret the genetic risk factors involved in the heterogeneous clinical features of the syndrome and its development, for instance the integration of WES and network-based approaches, might be helpful to identify and stratify patients at risk of developing APS.

Keywords: Whole exome sequencing, antiphospholipid antibodies, aPL genetics.

0039

ANALYSIS ON AUTOANTIBODIES MODIFICATIONS AFTER ANTI-SARS-COV2-VACCINATION IN A COHORT OF PATIENTS WITH TRIPLE POSITIVITY FOR ANTIPHOSPHOLIPID ANTIBODIES

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Vaccines anti-severe acute respiratory syndrome coronavirus type 2 (SARS-CoV2) showed a good efficacy in prevention of severe coronavirus disease-19 [1]. Their potential in induction of autoantibodies (abs) has not been well established [1]. One recent study demonstrated an increase of abs' titre after anti-SARS-CoV2 vaccination only in patients with already pre-existing positivity [2]. In contrast, patients without abs before did not respond with sustained autoantibody production upon vaccination [2]. This study aims to evaluate the potential induction of abs after SARS-CoV2 vaccination in a cohort of patients with triple positivity for antiphospholipid antibodies (aPL).

Patients and methods: Eighteen subjects were enrolled (M/F= 17/1; median age=52 years; 5 PAPS, 5 SLE-associated APS, 8 aPL carriers). Serum samples were collected before the first (T0) and at least one month after the second administration (T1) of the anti SARS-CoV-2 vaccination: 16 patients were vaccinated with BNT162b2, 1 with mRNA-1273 and 1 with Gam-COVID-Vac. A wide panel of abs were evaluated through routinely methods.

Results: None developed additional autoimmune signs/symptoms upon vaccination. Patients majority did not display new autoantibody positivity (Table 1). Changes were observed in 3 patients: 1) one aPL carrier ANA negative at T0 became ANA positive with homogenous pattern at T1 (negative anti-dsDNA and anti-ENA); this patient was actually ANA positive in her clinical history; 2) one aPL carrier patient affected by SLE, who was IgM and IgG aCL and IgG aBeta2GPI positive at T0, turned positive for IgM and IgA aBeta2GPI; 3) one aPL carrier patient affected by Behçet Disease, who was positive for IgM aCL and for IgM aBeta2GPI at T0, turned positive for IgA aCL and IgA aBeta2GPI. All emerging aPL were low titre.

Table 1: Autoantibodies titre pre (To) and post (T1) anti-SARS-Cov-2 vaccination.

Autoantibodies	Pre-vaccine Level(T0)	Post-vaccine level(T1)	P-value*	Patients positive T0	Patients positive at T1	p-value**
Anti-dsDNA (n.v <27 IU/ml)	28.7 (21.8-64.5)	25.8 (15.9-68.5)	0.163	7/18 (38.9%)	6/18 (33.3%)	0.729
aCL IgG (n.v <20 CU)	88.1 (27.1-210.9)	68.2 (18.8-181.3)	0.118	15/18 (83.3%)	13/18 (72.2%	0.691
aCL IgG (n.v <12 IU/ml)	11.9 (11.2-77.2)	11.2 (11.2-24.5)	04.32	9/18 (50%)	7/18 (38.9%)	0.502
aCL igM (n.v <20CU)	20.8 (5.935.9)	8.9 (3.3-21.6)	**0.006**	9/18 (50%)	5/18 (27%)	0.171
aCL IgM (n.v <12 IU/ml)	30.4 (18.1-170.8)	23.8 (11.2-82.3)	**0.029**	14/18 (77.8%)	12/18 (66.7%)	0.457
aCL IgA (n.v <12 IU/ml)	11.7 (11.2-30.9)	11.2 (11.2-17.6)	0.029	8/18 (44.4%)	6/18 (33.3%)	0.494
aß2GPI IgG (n.v <20 CU)	230.4 (110.1-971.91)	242.3 (33.765.9)	0.083	16/18 (88.9%)	14/18 (77.8%)	0.658
aß2GPI IgG (n.v <20 CU)	9.3 (9.3-128.1)	19.4 (9.3-126.9)	0.844	8/18 (44.4%)	9/18 (50%)	0.738
aß2GPI IgM (n.v <20 CU)	16.9 (3.6-51.3)	6.8 (1.5-23.1)	**0.041**	**7/18 (38.9%)**	5/18 (27.8%)	0.480
aß2GPI IgM (n.v <20 IU/ml)	19.8 (11.1-78.8)	9.9 (9.3-52.4)	0.109	8/18 (44.4%)	7/18 (38.9%)	0.735
aß2GPI IgA (n.v <20 IU/ml)	20.8 (9.3-39.9)	9.3 (9.3-37.8)	0.080	10/18 (55.6%)	7/18 (38.9%)	0.317

*Antiphospholipid antibodies were determined with chemiluminescence (CU) and Home-made ELISA (IU/ml) methods of detection. Pre and post-vaccine values are expressed as median (IQR). In blood, statistically significant comparison. *Willcoxon singed-rank test for paired variables was applied. **Chi-square test or Fisher exact test were applied.*

dsDNA=double-stranded DNA; aCL: anti-cardiolipin; aß2GPI: anti-beta2-glycoproteinl; n.v.; normal value.

Conclusions: Anti-SARS-CoV2 vaccination didn't induce clinical signs of autoimmunity in our cohort. Autoantibodies serology remained mostly stable. Few patients experienced the emergence of low titre aPL, possibly as an expected inter-assay variation rather than an evolving "serological flare". References: [1] Ishay Y et al. Int Immunopharmacol. 2021; [2] Thurm C et al. medRxiv 2021.
Keywords: Anti-SARS-Cov-2 vaccination, autoimmunity, antiphospholipid antibodies.

0040

PEDIATRIC ANTIPHOSPHOLIPID SYNDROME: CLINICAL FEATURES AND THERAPEUTIC INTERVENTIONS AT A SINGLE CENTER

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Pediatric antiphospholipid syndrome (APS) is a thromboinflammatory disease characterized by the presence of circulating antiphospholipid antibodies (aPL) and either thrombotic events or pregnancy morbidity. The objective of this study was to review a large institution's experience to better understand the characteristics of children with APS.
Patients and methods: We conducted a retrospective review of pediatric APS at a tertiary referral center. The electronic medical record system was queried from 2000 through 2019, and 21 cases were included based on meeting the revised Sapporo Classification criteria by age 18 or younger. Included cases were assessed for clinical and laboratory features, therapeutic management, and outcome data.
Results: Twenty-one patients were included with a median age at diagnosis of 16 years and median follow-up of 5.8 years. Secondary APS was slightly more common than primary APS (11 vs. 10 cases) and was primarily diagnosed in the context of systemic lupus erythematosus. Over at least 12 weeks, 64% of the cohort was positive for anti-β2GPI antibodies, 81% for anticardiolipin antibodies, and 52% for lupus anticoagulant; there were no statistically significant differences between the primary and secondary APS groups with regards to which aPL were positive. About half of all patients in the cohort (10, 48%) were triple positive for all three aPL tests. All patients were treated with some form of antiplatelet or anticoagulant therapy. Significantly more patients with secondary APS (64%) as compared with primary APS (20%) were treated with aspirin (p=0.04). Most patients were treated with either warfarin or low-molecular-weight heparin at some point in their course; a small number of patients were treated with a direct oral anticoagulant or with fondaparinux. Almost half of patients (43%) had recurrent thrombosis, typically when patients were subtherapeutic or non-adherent with anticoagulation. Two-thirds of patients (67%) also had at least one "non-criteria" manifestations of APS including thrombocytopenia (52%), autoimmune hemolytic anemia (43%), and livedo reticularis/racemosa (24%). To quantify damage accrued over time, Damage Index in Patients with Thrombotic APS (DIAPS) scores were calculated based on the clinical status at the patient's most recent contact with their physician. Damage measured via the DIAPS demonstrated similar median scores in primary and secondary APS (1.5 and 1.2, respectively). Three patients had a score of 3 or higher.
Conclusions: This case series of pediatric APS adds important context regarding potential phenotypes displayed by children with APS. Frequent recurrent events while subtherapeutic underscore the need for consistent therapeutic anticoagulation. High prevalence of non-criteria clinical manifestations highlights the need to consider these characteristics when developing pediatric-specific classification criteria and when considering this relatively rare diagnosis in pediatric practice. Within our cohort of 21 patients, 3 accumulated severe damage based on their DIAPS score, which emphasizes the potential long-term burden of pediatric APS.
Keywords: Pediatrics, recurrent thrombosis, non-criteria features, damage index.

0042

INTERACTION OF ANTIPHOSPHOLIPID ANTIBODIES AND AUTOANTIGENS IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

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Antiphospholipid syndrome (APS) is an autoimmune disease characterized by thrombotic events and pregnancy complications with persistently positive antiphospholipid antibodies (aPL) which recognize the phospholipid-binding proteins. Recently, studies have shown that the complexes of misfolded proteins with major histocompatibility complex class II (MHC II) molecules are major targets of autoantibodies in autoimmune diseases. Our previous study identified overexpressed PT/MHC II complexes on HEK293T cell-surface by a mouse monoclonal phosphatidylserine-dependent anti-prothrombin antibody (aPS/PT). Further, phorbol myristate acetate (PMA) treated human monocyte cell line (THP-1) synthesized PT. Hence, we

hypothesized that the PT/MHC II complexes on cell-surface of monocytes might be one of the potential antigenic targets for aPS/PT. The aim of this study is to evaluate the existence of prothrombin-expressed monocytes (PT-mono) in patients with APS (Experiment I) and to understand the role of PT-mono in the thrombophilia of APS (Experiment II).
Patients and methods: Experiment I: 1) Peripheral blood mononuclear cells (PBMCs) were isolated from 18 patients with APS and Flow cytometry was performed to identify PT-mono. 2) Proximity ligation assay (PLA) was applied to confirm the association between PT and HLA.
Results: Experiment I: 1) Cell-surface PT was detected on monocyte in two out of 18 APS patients and aPS/PT binding to the monocyte was confirmed. 2)The immunofluorescence staining, and PLA identified PT/HLA complex expressed on monocyte surface in patients with APS.
Conclusions: We have identified the novel expression of PT-mono in APS patients, and thrombogenicity of aPS/PT, represented by TF induction in vitro, was confirmed in this experience. The PT/MHC II complexes on cell-surface of monocytes might be considered as one of the antigenic targets for pathogenic aPS/PT.
Keywords: Antiphospholipid syndrome, phosphatidylserine-dependent anti-prothrombin antibody (aPS/PT), monocyte, major histocompatibility complex class II.

0043

MICROGLIAL ACTIVATION MEDIATED BY ANTI-β2GPI ANTIBODY LEADS TO COGNITIVE IMPAIRMENT AND ANXIETY-LIKE BEHAVIOR IN MICE MODEL

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Neuropsychiatric involvements include the most serious organ dysfunctions in systemic lupus erythematosus. Antiphospholipid antibody (aPL) is a significant risk factor for developing neuropsychiatric lupus. Cognitive impairment is present in 19–40% of aPL-positive patients and 42–80% of primary APS patients. However, the pathogenic role of aPL in central nervous system have not been clarified. We aimed to investigate the effect of aPL on neuropsychiatric manifestations and central neuronal cells in a mouse model.
Material and methods: We previously generated mouse monoclonal aPL against β2 glycoprotein I (β2GPI), named WBCAL-1, via hybridoma derived from NZW×BXSB F1 mice. We implanted 6- to 8-week-aged C57BL/6 mice with osmotic pumps to continuously infuse 200 μg of either WBCAL-1 or an IgG control antibody directly into the 3rd ventricle for 2 weeks. Behavior phenotyping and histopathological examination of the brain were performed after antibody infusion. We employed a novel object recognition test (NORT) to assess cognitive function, and the elevated plus maze test (EPM) to evaluate anxiety-like behavior. We identified the localization of β2GPI and IgG antibody deposition by immunohistochemistry. We also analyzed microglial activation and neuronal cell phenotypes using Iba-1, CD68 and NeuN.
Results: WBCAL-1 infused mice had a significantly lower discrimination index in NORT and shorter time in open arm in EPM than IgG infused control mice, indicating that WBCAL-1 contributed to cognitive dysfunction and anxiety. We detected β2GPI in the CA2 region of the hippocampus in wild type mice, and IgG deposition occurred in the same region of WBCAL-1 injected mice. Mice with WBCAL-1 injection demonstrated more CD68+Iba-1+ activated microglial cells in the hippocampus and lower NeuN expression of CA3 neurons than mice with an IgG control antibody injection.
Conclusions: Mice with the intracerebroventricular infusion of aPL showed an altered microglial activation status as well as neuronal phenotypes in the hippocampus, which might lead to cognitive impairment and anxiety-like behavior.
Keywords: Antiphospholipid syndrome, anti-β2GPI antibody, mouse model, cognitive impairment, anxiety.

0044

POSITIVE AUTOANTIBODIES IN A WOMAN WITH SARS-COV-2 INFECTION

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To provide evidence of the possible role of SARS-CoV-2 as an environmental trigger of autoimmunity.
Case Report: A 32-year-old woman with no history of autoimmune disease was admitted to the Rawson Hospital with a one-week diagnosis of COVID-19, with dermal, geographic, erythematous, pruritic and papuloid lesions in the upper and lower limbs, abdomen, neck and scalp, and thrombocytopenia. On physical exam, she presented polyarthritis in her knees, ankles and wrists. The patient reported arthralgia and synovitis in previous months with morning stiffness lasting 30 minutes. Her mother has rheumatoid arthritis. Diagnostic suspicion: thrombotic thrombocytopenic purpura (TTP) secondary to

COVID-19 vs autoimmune disease. Specialized laboratory carried out in the San Roque Hospital laboratory included: anti-nuclear antibodies (ANA), extractable nuclear antigens (ENA), anti-cardiolipin IgG/IgM, anti-B2-glycoprotein-I IgG/IgM and antimitochondrial antibodies (AMA) (Figure).

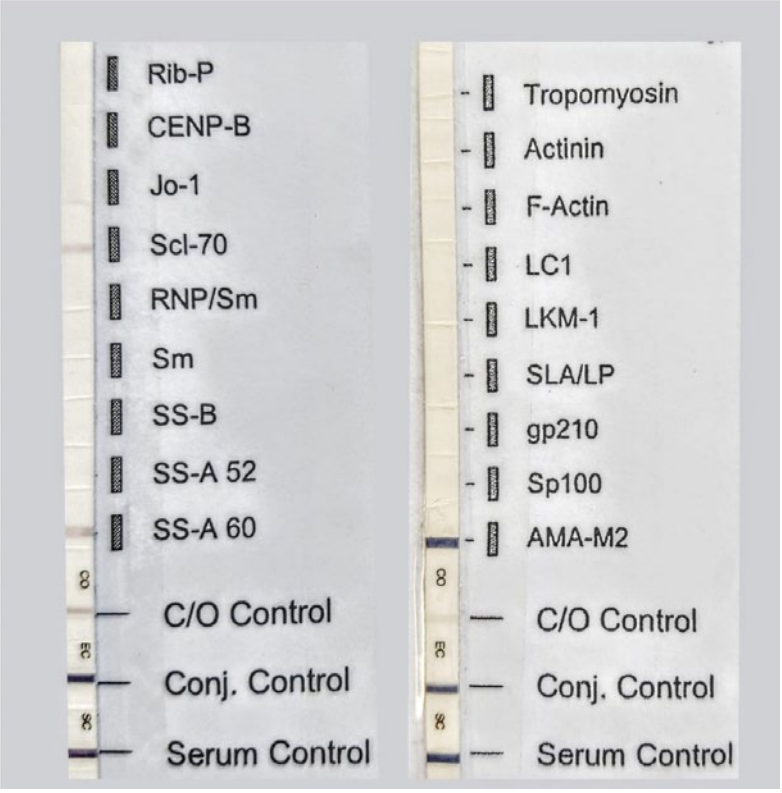

Figure: Linear immunoassay (LIA), left ENA panel, SS-A-60(+), Scl-70 (+); right: liver autoimmunity panel AMA-M2 (+).

Conclusions: The concept that infections promote autoimmunity in genetically susceptible individuals is reinforced. According to the evidence, SARS-CoV-2 mediates an autoimmune response through molecular mimicry and bystander activation; together with the exacerbated inflammatory response, it would favor multi-organ disease and autoimmunity. 10 days after the beginning of the infection, the patient manifests symptoms compatible with rheumatic disease, which supports the viral role as a precipitant in autoimmunity, and the family history confirms the importance of the genetic component in the autoimmune response. In this case, a wide generation of autoantibodies with various specificities associated with pathologies such as APS, scleroderma and PBC was found. Evidence of SARS-CoV-2 mediated autoimmunity could be considered a serious complication that is associated with a worse prognosis. Therefore, early diagnosis and knowledge of the mechanisms involved is essential to control and prevent the incidence or exacerbation of autoimmune manifestations.

Keywords: Autoantibodies, SARS-CoV-2, anti-phospholipid syndrome.

0045

ABUNDANCE OF B CELL RECEPTORS HARBORING ELONGATED POLYTYROSINE AND POLYSERINE RICH MOTIFS WITHIN THEIR HEAVY CHAIN CDR3 DISTINGUISHES CATASTROPHIC AND ANTIPHOSPHOLIPID SYNDROME

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Antiphospholipid syndrome (APS) is defined by arterial and/or venous thrombosis and/or pregnancy morbidity along with persistent circulating antiphospholipid antibodies (aPL). Central to APS pathogenesis are B cells that generate autoreactive antibodies, including anticardiolipin antibodies (aCL), and anti-ß2-glycoprotein-I antibodies (anti-B2GPI). Several studies have implicated specific germline and/or antigen-driven somatic hypermutations within the complementarity determining

regions (CDRs) of pathogenic antibodies in APS, as well as other thrombotic disorders. Nevertheless, the B cell repertoire in thrombotic APS remains poorly characterized. Recently, autoreactive and platelet activating pathogenic antibodies harboring elongated tyrosine rich CDR3 motifs were reported in patients with heparin-induced thrombocytopenia (HIT). Whether such antibodies are present in APS and their potential role, if so, has not been determined.

Material and methods: We leveraged single cell immunoprofiling to characterize the presence of antibodies harboring elongated tyrosine rich CDR3 motifs in the circulating B cell repertoire obtained from peripheral blood mononuclear cells (PBMC) from patients with thrombotic and catastrophic APS as well as healthy individuals. We also correlated the abundance of these antibodies with criteria aPL and inflammatory cytokines in plasma. The modified Ham (mHam) test was used to assess functional complement activation in plasma in plasma from all of the subjects studied (Chaturvedi et al. Blood 2020).

Results: B cell clones containing elongated polytyrosine rich CDR3 motifs were most abundant in patients with a diagnosis of catastrophic APS (n=3), and were markedly elevated in patients with APS (n=4) compared to healthy counterparts (n=3) (Table 1). Elongated polytyrosine rich CDR3 motifs from CAPS patients contained penta-tyrosine (Y5), hexa-tyrosine (Y6), hepta-tyrosine (Y7), and octa-tyrosine (Y8) motifs (Table 2) and contained more tyrosine residues than the penta-tyrosines previously reported in HIT. In addition, all of the polytyrosine containing motifs CDR3 motifs were present on the heavy chain and ware followed by MDVW motif of IGHJ6. The presence of B cell clones containing elongated polytyrosine rich CDR3 motifs exhibited significant positive correlations with complement activation measured by mHAM test (r=0.728, p=0.0032), criteria aPLs including anticardiolipin antibodies (aCL) and anti-ß2-glycoprotein-I antibodies (anti-B2GPI), as well as plasma inflammatory cytokines; TNFa (r=0.901, p=1.5x10 -5), IL-23 (r=0.780, p=0.0016), IL-17C cytokines (r=0.729, p=0.0033), sICAM1 (r=0.740, p=0.0025), sVCAM1 (r=0.764, p=0.0015), (Figure 1). The presence of elongated polytyrosine rich CDR3 motifs was also associated with the increase abundance of polyserine rich CDR3 motifs that were present predominantly in patients with CAPS.

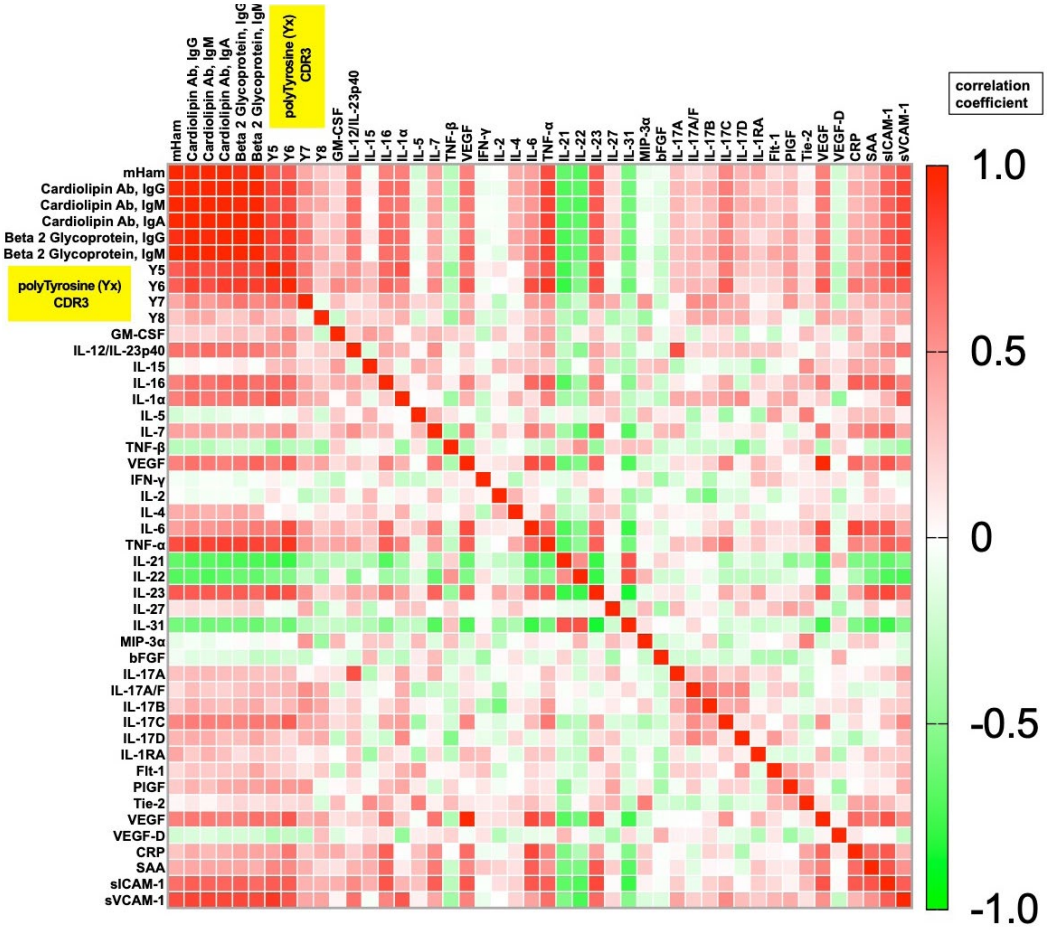

Figure 1: Correlation matrix. Spearman's correlations of criteria antibodies, elongated PolyTyrosine rich clones (y5, Y6, Y7, Y8) and inflammatory markers in plasma of study subjects. Key to the right of the correlation matrix represents the correlation coefficient [p= 1 negative correlation (green) to p=1 positive correlation (red)].

Cohort Clinical Presentation, and CAPS diagnosis				APS Laboratory Criteria						PolyTyrosine-Rich CDR3 clones Tyrosine Y(X)				PolySerine Rich CDR3 clones Tyrosine S(X)		
Patient	Presentation		CAPS	Cardiolipin IgG	Cardiolipin IgM	Cardiolipin IgA	B2GPI IgG	B2GPI IgM	LAC	Y5	Y6	Y7	Y8	S_4	S_5	S_6
N 1	Healthy	Healthy	No	N/D	N/D	N/D	N/D	N/D	N/D	15	2	0	0	4	0	0
N 2	Healthy		No	N/D	N/D	N/D	N/D	N/D	N/D	7	3	0	0	8	0	0
N 76	Healthy		No	N/D	N/D	N/D	N/D	N/D	N/D	10	0	0	0	2	0	0
APS 1	APS (Arterial Thrombosis), ITP, MI, CAPS	CAPS	Definite	150	38	43	150	52	Positive	94	35	6	0	34	5	1
APS13	APS, Thrombophlebitis, DVT		Probable	103	<9	<9	150	<9	Positive	52	16	2	0	14	0	0
APS 21	APS (DVT, RVT, PE, SVCT), HIT, PAD, Calciphylaxis, DAH, CKD		Probable	51	<9	<9	134	<9	Positive	15	5	0	0	3	0	0
APS 2	APS(PE), ITP	Thrombosis	No	110	35	<9	109	30	Positive	24	5	0	1	8	0	0
APS 52	PE, lupus anticoagulant disorder		No	<9	<9	<9	9	<9	Positive	14	5	0	0	4	0	0
APS 70	APS		No	40	12	<9	54	<9	Indeterminate	24	3	0	0	7	1	0
APS 71	APS, DVT, lacunar infarct		No	90	14	<9	107	<9	Indeterminate	10	2	0	0	3	0	0

Table 1: Clinical characteristics, laboratory criteria, and prevalence of elongated PolyTyrosine Rich and PolySerine and Domains within their Heavy Chain CDR3 Y (x).

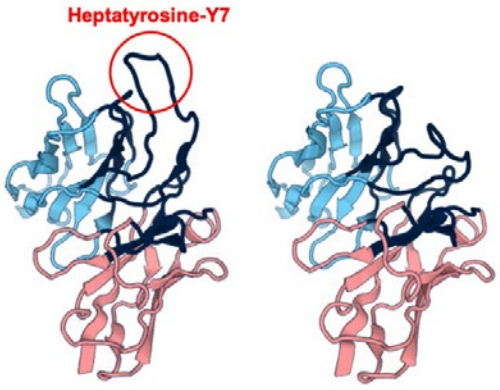

Figure 2: Variable fragment (Fv) Modeling PolyTyrosine-Rich Domains (Heptatyrosine-Y7) (left) vs PolyTyrosine devoid CD3.

HCDR3 (Amino acids)	igh v genes	Modification	igh j genes	Isotype
CARDVAGMTYYYYYYYMDVW	IGHV3-21	insertion	IGHJ6	IGHM
CARDYRPYYYDSSGYYYYYYYGMDVW	IGHV3-21	insertion-deletion	IGHJ6	IGHM
CARDQAAREYYYYYYYMDVW	IGHV3-48	insertion	IGHJ6	IGHD
CARDGSSPYYYYYYYMDVW	IGHV4-61	insertion	IGHJ6	IGHM
CARDSNGDYQYYYYYYYMDVW	IGHV3-33	insertion	IGHJ6	IGHM
CARTRYDFWSGYYYYYYYGMDVW	IGHV3-33	insertion-mismatch-deletion	IGHJ6	IGHM
CVKEARITGTTGYYYYYYYMDVW	IGHV3-64D	insertion	IGHJ6	IGHM
CAREGGGGAGSRGYYYYYYYMDVW	IGHV1-69D	insertion	IGHJ6	IGHM
CARGQNQPGPSSLYYYYYYYMDVW	IGHV3-33	insertion	IGHJ6	IGHM
CARDIADRYYYDSSGYYYYYYYGMDVW	IGHV1-46	insertion-deletion-mismatch	IGHJ6	IGHM

Table 2: Genotypic characterization of elongated PolyTyrosine-Rich Domains (Heptatyrosine-Y7) within complementarity-determining regions (HCDR3) from catastrophic APS patients.

Conclusions: These preliminary studies provide the first characterization of the prevalence of B cell clones containing elongated polytyrosine rich CDR3 motifs, previously reported in HIT, within the B cell repertoire of APS patients. Notably, the abundance of these B cell clones is markedly elevated in patients with CAPS and is associated with elevated levels of inflammatory cytokines TNFa, IL-23, IL-17C, sICAM1, and sVCAM1. Validation studies in larger cohorts from APS patients and other thrombotic disorders are ongoing.

Keywords: Catastrophic anti-phospholipid syndrome.

0046

HIGH PLASMA C5B-9 AND C5A LEVELS DURING QUIESCENT PHASES ARE ASSOCIATED TO SEVERE ANTIPHOSPHOLIPID SYNDROME SUBSETS

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High plasma C5a and C5b-9 levels are considered a clear sign of complement activation. We aimed to evaluate the clinical significance of these two complement activation products during quiescent phases of thrombotic antiphospholipid syndrome (APS) by comparing their plasma levels in the different clinical subsets and relating them to the clinical characteristics and antiphospholipid antibody profile of the patients.
Patients and methods: Primary APS patients with arterial, venous or small vessel thrombosis constituted our study population. The three APS patient subsets studied were: i) thrombotic patients responsive to anti-vitamin K therapy, generally affected with a single thrombotic event (TAPS); ii) patients with rethrombose despite seemingly adequate treatment with a vitamin K antagonist; i.e. patients refractory to standard anticoagulant therapy (RAPS); iii) patients with catastrophic APS (CAPS). One plasma sample from each eligible APS patient was collected from January 2009 to January 2021 during a quiescent disease phase at least one year after APS diagnosis. The control population was constituted by healthy subjects matched for sex and age with the quiescent APS patients. All the samples were stored at -80° C until they could be analyzed. Plasma C5a and C5b-9 levels were assessed using commercial ELISA assays.
Results: The study population was constituted by 62 quiescent APS patients: 40 were affected by TAPS, 13 by RAPS and 9 by CAPS. A plasma sample was taken from all quiescent APS patients at different times after APS diagnosis (median=7 years, IQR=11). The control population was constituted by 30 healthy blood donors. Data analysis uncovered that both the C5a and C5b-9 values in the healthy controls were significantly lower than those in the quiescent APS patients (p=<0.0001 and p<0.0001, respectively). Moreover, the TAPS patients had significantly lower C5a and C5b-9 levels with respect to the RAPS (p=0.0249 and p=0.0002, respectively) and CAPS patients (p=0.0332 and p=0.0002, respectively). In addition, the levels of C5a significantly prevailed in small vessels thrombosis with respect to the venous one (p=0.0166) and those of C5b-9 in small vessels thrombosis with respect to both the venous and arterial one (p=0.0037 and 0.0088, respectively). In accordance with data from the literature, triple antiphospholipid antibody positivity defined as IgG and/or IgM anticardiolipin antibodies plus IgG and/or IgM anti-beta2 Glycoprotein I antibodies plus lupus anticoagulant, was considered a laboratory risk factor for thrombosis. The C5b-9 levels were significantly higher in the triple antiphospholipid positive with respect to the single or double positive patients (p=0.0248). The ROC curve showed that the best cut-offs for C5a and C5b-9 levels had a higher sensitivity, specificity and likelihood ratio in the CAPS and RAPS groups than they did in the TAPS subset.
Conclusions: In the future, if these data are confirmed by further larger scale studies, they could attribute an important role to the complement system in the pathogenesis of thrombosis in APS and contribute to stratify the risk in APS patients by identifying those who may develop further thrombotic events as well as benefit from complement inhibitors in the event of an acute episode unresponsive to conventional treatment.
Keywords: antiphospholipid syndrome, thrombosis, complement, activation.

0047

ENDOTHELIAL CELL-DERIVED EXTRACELLULAR VESICLES, ANTIPHOSPHOLIPID ANTIBODIES AND ß2 GLYCOPROTEIN I. COULD NEW INTERACTIONS CHANGE THE CURRENT APPROACH TO THE LUPUS ANTICOAGULANT PARADOX?

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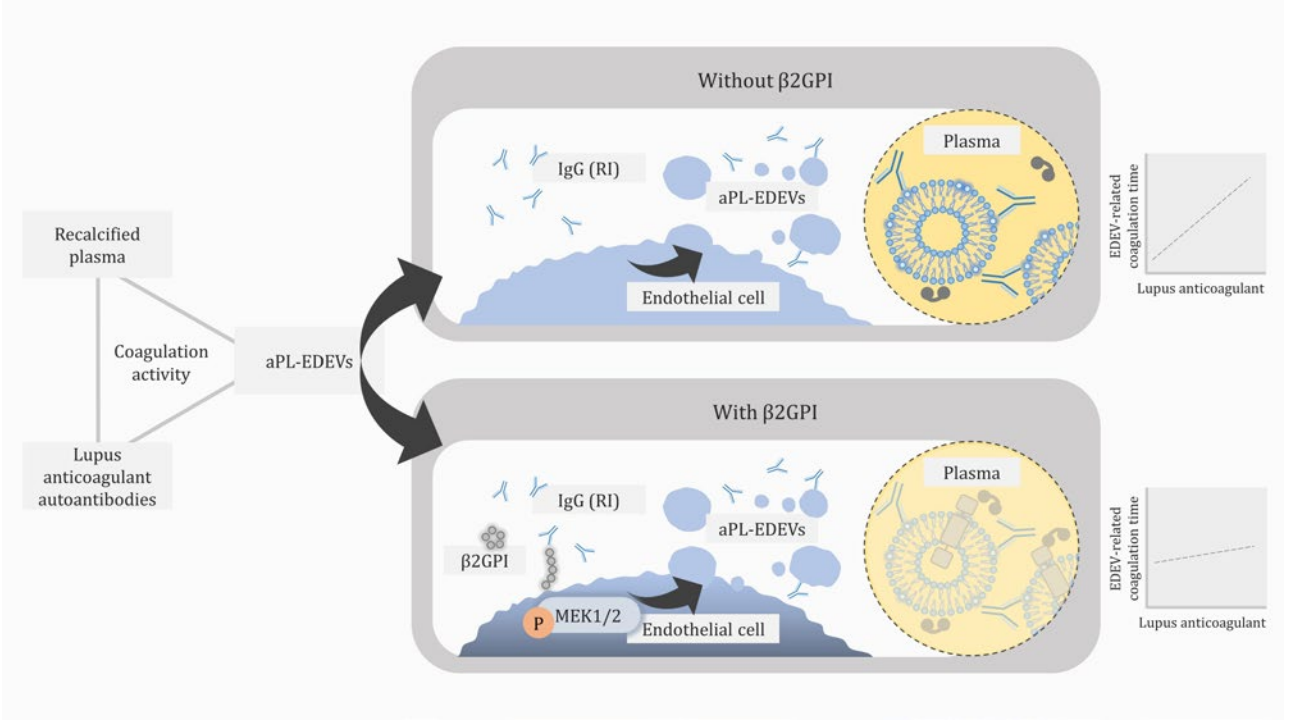
Antiphospholipid antibodies (aPL) lead to a hypercoagulable state in vivo. Paradoxically, some of these autoantibodies behave as inhibitors of the coagulation cascade in vitro, a phenomenon known as lupus anticoagulant (LA). Likewise, patients with LA and other aPL have an increased quantity of plasma medium/large extracellular vesicles, which are membrane fragments with putative procoagulant properties. This work explores how the clotting process is modified in vitro by the complex interaction between plasma, endothelial-cell derived medium/large extracellular vesicles released upon stimulation with aPL (aPL-EDEVs) and the same autoantibodies that condition the release of aPL-EDEVs.
Patients and methods: We employed a primary model of endothelium stimulated with immunoglobulin G from patients with different clinical presentations of APS; patients with non-aPL-related clinical manifestations (either vascular thrombosis or

pregnancy-related morbidity); and healthy seronegative women with proven gestational success. aPL-EDEVs resulting from this model were analyzed by flow cytometry, and their coagulation properties were compared using a recalcified plasma-based assay.
Results: Our results show that, in principle, the coagulation activity of aPL-EDEVs is mainly conditioned by the LA-like activity of autoantibodies. Nevertheless, in the presence of ß2-glycoprotein-I during endothelial cell stimulation (as would occur in vivo), the coagulation activity of aPL-EDEVs is proportionally restored in a mitogen-activated protein kinase kinases 1 and 2 (MEK1/2) pathway-dependent manner.



Conclusions: aPL can exhaust the coagulation properties of aPL-EDEVs. However, ß2-glycoprotein-I, the primary cofactor of aPL, is sufficient to eclipse, but not overwhelm, this anticoagulant effect. This balance poses an alternative explanation for why the LA phenomenon has not been shown to be significant in vivo with some exceptions, but also why aPL-EDEVs have not been shown to represent a direct procoagulant mechanism in antiphospholipid syndrome. As a new hypothesis, we propose that LA-like antibodies preferentially form immune complexes with extracellular vesicles, and these complexes could lead to thrombosis by indirect means.
Keywords: Thrombosis, cell-derived extracellular vesicles, lupus coagulation inhibitor.

0048

ANTIPHOSPHOLIPID ANTIBODIES PROFILE IN SAMPLES OF PATIENTS WITH OBSTETRIC COMPLICATIONS ATTENDED AT A GENERAL HOSPITAL.

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Antiphospholipid Antibodies (aPL): Lupus Anticoagulant (LA), Anticardiolipin Antibodies IgG and IgM (ACA G and M) and ß2glycoprotein I Antibodies IgG and IgM (B2GPI G and M) are associated with obstetric complications and pregnancy morbidity.
Aim: To determine the profile of aPL in patients with obstetric complications attended at our laboratory.
Patients and methods: Material and Methods: Data obtained retrospectively since January 2019 to December 2021 from laboratory database. Patients (p): 100 (15-49 years); Samples (s): 104. The obstetric complications studied were: Group 1: Two abortions < 10 weeks: 5s; Group 2: Three abortions < 10 weeks: 14 s; Group 3: One abortion > 10 weeks: 22 s; Group 4: Pre-eclampsia: 15 s; Group 5: Fetal Death: 38 s; Group 6: Placental Abruption: 2 s; Group 7: Intrauterine growth restriction: 1 s and Group 8: Syndrome HELLP (Hemolysis, elevated liver enzymes and low platelet count): 7 s. LA was detected according to the guidelines of the ISTH. ACA (>40 GPL/MPL) and B2GPI (>20U) were measured by a standardized ELISA.
Results: Results: In Group 1, 6 and 7 all the aPL were negative, in Group 2 LA was positive in 14%, ACA G in 7%, ACAM in 14%, B2GPI G in 0% and B2GPI M in 14% of the samples. In Group 3 LA was positive in 5%, ACAG in 0%, ACAM in 23%, B2GPIG

in 0%, B2GPIM in 9% of the samples. In Group 4: LA was positive in 27%, ACAG 7%, ACAM 13%, B2GPIG 7% and B2GPIM in 7% of the samples. In Group 5: LA was positive in 8%, ACAG 8%, ACAM 16%, B2GPIG 3% and B2GPIM 5% of the samples. In Group 8: LA was positive in 17%, ACAG 14%, ACAM 0%, B2GPIG and B2GPIM 0% of the samples.
Conclusions: Conclusions: The total percentage of positivity was 7,96% (41/515 s). In the population studied LA was more prevalent in Pre-eclampsia (4/15), ACAG in HELLP (1/7), ACAM in one abortion >10 weeks (5/22), B2GPIG in Pre-eclampsia (1/15) and B2GPIM in three abortions <10 weeks (2/14). The antibodies with the highest number of positives was ACAM (15/104). More studies are needed to establish the association between aPL and pregnancy morbidity.
Keywords: Antiphospholipid antibodies, obstetric complications, pregnancy morbidity.

0049

CUTANEOUS MANIFESTATIONS IN ANTIPHOSPHOLIPID SYNDROME. CASE REPORT

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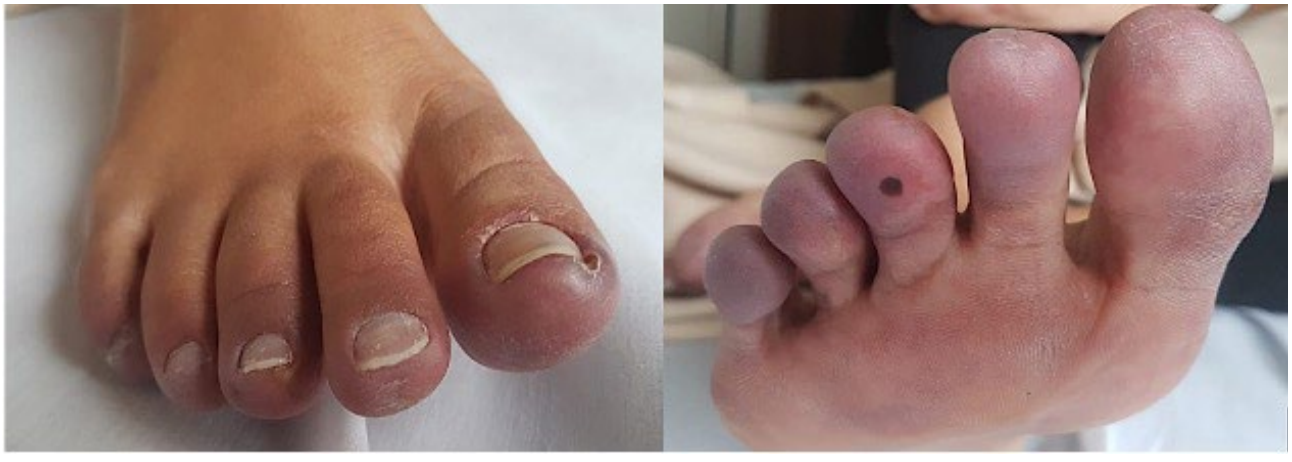
The clinical manifestations of APS are varied, being very common skin manifestations, which are observed in 49% of patients with APS and can be the first symptom in 30.5-41% of cases. The pattern of cutaneous presentation is variable and can sometimes make diagnosis difficult. Many skin manifestations have been described in patients with APS, including livedo reticularis, ulcers, and skin necrosis.
Case report: We present a 24-year-old female patient, originally from Brazil, with no relevant history. She was admitted due to a symptomatology of approximately 8 months of evolution characterized by acrocyanosis in all the extremities, associated in the last 3 months with petechiae in the lower limbs. On physical examination: diastolic murmur in aortic focus 3/6, acrocyanosis, livedo reticularis, hematomas and petechiae in the lower limbs, small periungual ulcer in the 1st right toe (Image 1), normal and symmetrical peripheral pulses, the rest without pathological findings. Within the complementary studies on admission, it was observed thrombocytopenia of 90000 per mm³, slightly increased nitrogen levels that normalize after hydration, negative cryoglobulins and non-reactive viral serologies. Peripheral blood smear: mild anisocytosis, no evidence of schistocytes. Lupus inhibitor, anti-cardiolipin IgG and IgM, and anti-B2 glycoprotein IgG and IgM all positive, ANA 1/80 speckled pattern, normal C3 and low C4. Normal capillaroscopy. Upper and lower limb arterial Doppler with preserved flow. Transesophageal echocardiogram: trivalve aortic valve with thickened leaflets in all its extension, cottony images in the extremities of the aortic valve that does not allow coaptation, severe moderate aortic regurgitation. Given the suspicion of APS with extra criteria clinical manifestations (livedo, thrombocytopenia, and valvular disease) associated with triple positivity of antibodies, a skin biopsy of foot lesions was performed, which reported: dermis and hypodermis with small vessel thrombosis. Although she has positive ANA and hypocomplementemia, now it does not meet the criteria for classification of SLE, but it is important to take this into account during follow-up.
Results: Among the possible clinical manifestations of APS, deep vein thrombosis is the most frequent presentation. However, there are other manifestations called “extra criteria”, equally frequent, such as thrombocytopenia, neurological manifestations (chorea), nephropathy associated with antiphospholipid antibodies, heart valve involvement and livedo reticularis, which must be considered. Many skin manifestations have been described in patients with APS, including livedo reticularis, ulcers, and skin necrosis. Most can be explained by vascular occlusion, frequently demonstrable by histopathological examination. Many nonspecific skin lesions (pseudovasculitis) are also seen, including red, purple macules, small red or cyanotic lesions on the hands and feet, localized necrosis, bruising, and painful skin nodules; these can easily be mistaken clinically as "vasculitis" if a biopsy is not taken.



Conclusions: It is important to characterize the cutaneous manifestations of APS, mainly livedo reticularis, since they make up a subgroup with a higher risk of arterial thrombosis, cerebrovascular events, and pregnancy morbidity and, therefore, may require closer monitoring.
Keywords: APS, livedo reticularis.

0050

DIFFERENCES IN LUPUS ANTICOAGULANT FINAL DIAGNOSIS IN VITAMIN K ANTAGONIST PATIENTS ANTICOAGULATED

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The detection of lupus anticoagulant (LA) in patients who are on vitamin k antagonist (VKA) treatment is still an unresolved issue. Dilution of patient's plasma into pooled normal plasma (NPP) prior LA testing is recommended by some guideline but the dilution reduces sensitivity and can generate false negative results. The last ISTH guideline suggests that the dilution of patient's plasma into NPP is not reliable solution in patients on VKA. The aim of this study is to compare LA final diagnosis between diluted with NPP (1:1) or undiluted VKA patient plasma to perform LA tests.
Patients and methods: Population: 70 patients with anti-phospholipids syndrome before beginning anticoagulation with VKA. All patients were studied for the second time to confirm diagnosis, three months after starting VKA treatment. At moment of this study all patients have an international normalized ratio (INR) < 3. Preanalytic variables according by ISTH last guideline. Method: dilute and confirm Russell´s viper venom time (dRVVT and cRVVT) and silica clotting time (SCT) were used. All clotting assay were performed in STA Compact Max analyzer.
Results: Taking into account both assay in undiluted plasma 22/70 patients are LA negative. 42 of the 70 samples were positive by Russell in undiluted plasma but only 10 / 70 were positive by Russell assay in diluted plasma. The Kappa value for the measure of agreement between dilute and undiluted Russell assay was 0.20 (95 % CI=0.004-0.404) .37/70 were negative by SCT assay in undiluted plasma and 31 / 70 were negative in dilute plasma. 26/70 were positive for diluted and undiluted sample by SCT. Only 5/70 were positive by SCT in the mixing and negative in undiluted plasma. The kappa was 0.655 (0.477-0.833)
Conclusions: Although dilution of the patient's plasma in PNP is widely used, according with these results, it is not a good option because it could give false negative or positive diagnosis, depending of the assay and the INR level. The discrepancy using the mixture or not is greatest in Russell`s assay.
Keywords: Lupus anticoagulant, diagnosis, vitamin K antagonist.

0051

HIGH LEVELS OF SOLUBLE TRIGGERING RECEPTOR EXPRESSED ON MYELOID CELLS-1 PREDICT MANIFESTATIONS OF ANTIPHOSPHOLIPID SYNDROME

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Triggering receptor expressed on myeloid cells-1 (TREM-1) is an amplifier of TLR4 pathway which is involved in antiphospholipid syndrome (APS). Recently, it has been shown a plasmatic sTREM-1 level significantly higher in thrombotic primary APS patients compared controls. This study aimed to investigate the predictive value of plasmatic sTREM-1 level on the occurrence of thrombotic event or death in patients with APS, antiphospholipid antibodies (aPL) and/or systemic lupus erythematosus (SLE).
Patients and methods: Serum sTREM-1 levels were measured in 114 patients with APS, isolated aPL and/or SLE who were followed up. Clinical and laboratory characteristics were recorded. Risk factors for the occurrence of an event, defined by thrombosis, death and obstetrical morbidity (for women only) were analyzed by multivariate Cox model.
Results: sTREM-1 levels tended to be higher in primary APS patients than patients with isolated aPL. Patients with nephropathy, diabetes, hypertension, dyslipidemia had a significant higher level of sTREM-1 than other patients. Nineteen (17%) patients had thrombotic events, 5 patients died and 3 women had obstetrical morbidity during follow-up. An elevated sTREM-1 level was an independent risk factor for the occurrence of thrombotic event or death in patients and for obstetrical morbidity in women.

Conclusions: High sTREM-1 levels are predictive of the occurrence of thrombotic events or death (and obstetric events in women) in a cohort of aPL patients and/or SLE. The sTREM-1 level could represent a new biomarker of thrombotic risk or death in APS.
Keywords: Antiphospholipid syndrome, TREM-1, thrombotic risk.

0053

HEALTH INFORMATION-SEEKING BEHAVIOUR AMONG FRENCH-SPEAKING PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

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Antiphospholipid syndrome is a complex disease inducing various troubles in everyday life. Poor information levels have been correlated to lower health-related quality of life. Our objective was to assess health information-seeking behavior among French-speaking patients with antiphospholipid syndrome: main sources of information, perceived quality of information given, main subjects of concern.
Patients and methods: Thus a 3-section survey was conducted in June 2021: sources of information, perception of received information, free text responses about APS. Participants were patients followed within the Regional Competence Center for Rare Vascular and Systemic Autoimmune Diseases, Nancy Academic Hospital, France, with diagnosis of APS (Sapporo-Sydney criteria). A systematic review of French-language online forums and social media contents was conducted at the same time. All posts in French containing keywords about APS, available online between January 1st 2001 and July 31st 2021, were analyzed. Text analytics methods were performed on both free text data from the questionnaire and the internet review. Text segments were analyzed through Descending Hierarchical Analysis to identify clusters of concepts related to APS for the patients.
Results: Among the 75 respondents in our center, 88% reported the specialist physician as their main information source, followed by the general practitioner (36%). Web sources were rarely reported to be used (under 25%). Patients reported being well informed about their disease, and 79% were looking for further information about it. Information provided by a specialist physician was judged useful for 75% of respondents, easily understandable for 71% of them and reliable for 82% of them. Information provided by their general practitioner was judged useful for 48% of respondents, easily understandable for 61% of them and reliable for 71% of them. Information provided by medical websites was judged useful for 67% of respondents, easily understandable for 71% of them and reliable for 75% of them. For the web analysis we extracted 590 posts from 16 different websites, representing 68459 words. Textual analysis showed three main clusters of important subjects for patients: the first group was pregnancy, fertility issues and lupus; the second group APS related diseases, thrombosis, mechanisms, lab tests results, anticoagulant treatments, and research/actuality about APS; the third group included everyday life, travel, VKA, burden (physical, emotional, administrative), hopes and support.
Conclusions: Specialist physicians and general practitioners were main sources of information for many French patients in our center, despite increasing internet use for health information-seeking purpose. Information level was rather good. APS patients seemed to be careful with information and willing to learn about their diseases. We identified main 3 major clusters with major subjects of concern.
Keywords: Information, social media, quality of life.

0054

CLINICAL OUTCOMES AND FACTORS ASSOCIATED WITH RELAPSE AND MORTALITY AMONG PATIENTS WITH NEW ONSET DIFFUSE ALVEOLAR HEMORRHAGE AND ANTIPHOSPHOLIPID SYNDROME: A MULTI-CENTER STUDY

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To describe the clinical outcomes of incident diffuse alveolar hemorrhage (DAH) in patients with antiphospholipid syndrome (APS) from a multi-center institution in the USA.
Patients and methods: We conducted a multi-center, retrospective, cohort study of patients with APS-associated DAH from Mayo Clinic sites in Minnesota, Arizona, Wisconsin, and Florida. We identified enterprise-wide patients with APS and DAH. We included those with persistent (+) antiphospholipid antibodies (aPL) according to Sydney criteria and DAH defined as radiographic findings and a progressively bloody bronchoalveolar lavage (BAL) fluid and/or >20% hemosiderin-laden

macrophages in BAL, or biopsy with evidence of DAH and capillaritis. Only incident DAH cases were included, the date of first DAH episode was considered the index date. We excluded patients with DAH explained by another condition. We abstracted demographics, systemic lupus erythematosus (SLE) diagnosis, APS manifestations, and aPL; symptoms, laboratory, radiologic, BAL findings, and treatments at DAH; and clinical outcomes (relapse and mortality). Patients were followed until death or lost to follow-up. Descriptive statistics were used to summarize data, Kaplan-Meier methods were used to estimate relapse and mortality rates over time, and Cox models were used to evaluate factors associated with relapse and mortality.

Results: The study population included 61 patients with APS and incident DAH. Mean age was 44.2 years and 48% were female. 87% were non-Hispanic White, and 30% had SLE. Median APS duration was 53.6 mos, and the median follow-up was 32.3 mos. 85% had a history of vascular thromboembolism, 36% of stroke, 28% of myocardial infarction, and 17% of pregnancy morbidity; their most common "non-criteria" manifestations were thrombocytopenia (51%), and valve thickening/dysfunction (43%). Lupus anticoagulant (LA) was (+) in 85%, 73% had (+) anticardiolipin (aCL) IgG, 12% had (+) aCL IgM, 59% had (+) beta-2 glycoprotein I (B2GPI) IgG, 7% had (+) B2GPI IgM. 47% were triple (+) (LA + aCL IgG or IgM + B2GPI IgG or IgM). At DAH, 90% of patients had dyspnea, 79% had cough, and only 59% had hemoptysis; 18% had platelets count <50K/μL, and 55% had an INR <2. The majority (87% and 90%) had ground glass or consolidations on CT and radiographs, respectively. 90% had a (+) bronchoscopy. 74% of patients were anticoagulated prior to DAH, 48% received pulses of steroids, 13% CYC, 23% MMF, 20% RTX and 20% PLEX. 20 patients relapsed and the relapse rate was 36.9% by 1 year, 13 patients (65%) relapsed within 6 mos (Figure 1A). Factors associated with relapse within 6 mos included triple(+) (HR 6.23) and platelet count <50K/μL (HR 4.71). The estimated mortality at 1 and 5 years was 19.2% and 38.2% (Figure 1B). Factors associated with mortality were platelet count <50K/μL (HR 5.88) and age (HR 1.44, per 10 years). No medications were associated with decreased relapse or mortality. SLE was not associated either.

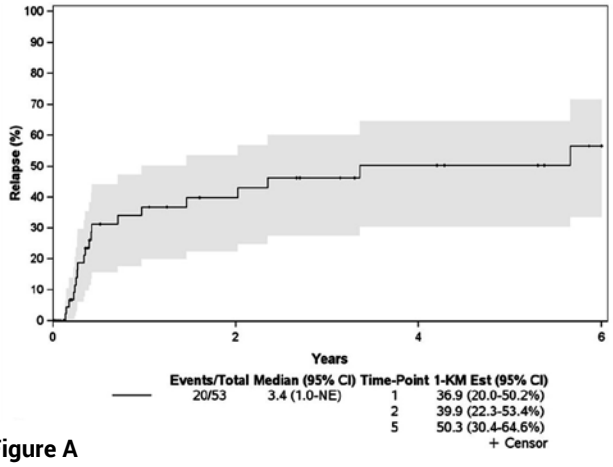

Figure A

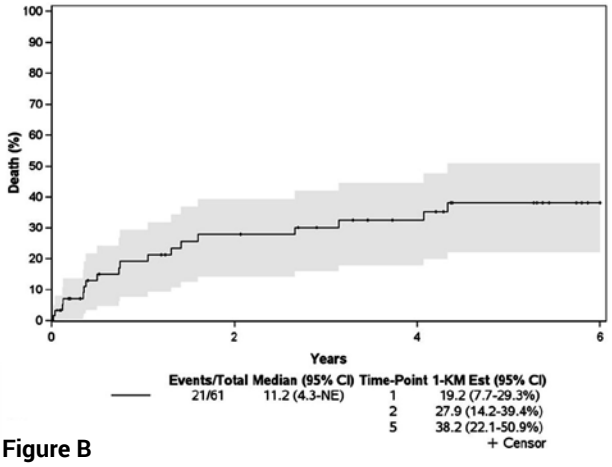

Figure B

Conclusions: Patients with incident DAH and APS had a high mortality and most patients relapsed within 6 mos. Triple positivity and thrombocytopenia were risk factors for relapses. Thrombocytopenia was associated with mortality.

Keywords: Antiphospholipid syndrome, diffuse alveolar hemorrhage, clinical outcomes.

0055

TRIPLE APL POSITIVITY IS ASSOCIATED TO RECURRENT THROMBOTIC EVENTS IN VENOUS AND ARTERIAL DISTRICTS: ANALYSIS OF A MULTICENTRIC EUROPEAN APS COHORT

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Recurrent thrombotic events are not uncommon in the field of Antiphospholipid Syndrome (APS). Generally, a first arterial thrombosis is followed by an arterial event and an initial venous thrombosis is followed by a venous event, but switches among vascular sides were described. However, factors determining the predilection for the venous or arterial circulation are not known. The aim of this study is to analyze the clinical and serological features of APS patients affected by recurrent thrombosis in both venous and arterial vessels.

Patients and methods: A retrospective analysis enrolling consecutive patients with diagnosis of primary thrombotic APS (Miyakis et al. 2006) was performed. Patients with APS associated to other connective tissue diseases were excluded as well as women who presented with obstetric events as first antiphospholipid antibodies (aPL)-related manifestation. All the subjects were followed during 1985-2019 period in four European Centers (Paris, Lille, Rouen, in France and Brescia in Italy).
Results: The cohort included 415 patients (69% females; median age at onset: 34.0 [25.0-29.0] years). The initial event was venous in 62% of the cases, mainly deep vein thromboses (61%) and pulmonary embolism (26%); in 38% it was arterial, among which strokes (73%) and myocardial infarctions (10%) prevailed. During follow-up, despite the standard therapy (anticoagulant in 69%, antiaggregant in 56%, combination in 36%), at least one recurrent event occurred in 176/415 (42%) subjects. The comparison between patients who suffered from recurrent events and patients who did not is reported in Table 1. In addition, among recurrences, vascular side switches occurred in 54/176 (31%) cases. Comparing patients who experienced thrombotic events in both venous and arterial circulation with those who did not, the former presented more frequently triple aPL positivity (65% vs 39%; p:0.005), while no differences in demographics, initial presentation and concomitant risk factors were observed. At the last evaluation, "switching patients" were more frequently treated with anticoagulant and antiaggregant in combination (20% vs 11%; p:0.083) and with immunomodulants/immunosuppressants (37% vs 20%; p:0.014).

Table 1: Comparison between patients who suffered from recurrences and those who did not.

	PATIENTS WITH RECURRENCIES 176(42)	**PATIENTS WITH NO RECURRENCIES 239(58)**	**P<0.05**
Males	65 (37)	64 (27)	0.027
Age at onset, years	35 (26-50)	34[25-48]	0.621
Initial arterial event	52 (30)	105 (44)	0.003
Initial venous event	124 (70)	134 (56)	0.003
Complete aPL profile available	143/176	200/239	-
Single aPL positivity	46 (32)	68 (34)	0.722
Double aPL positivity	32 (22)	53 (26)	0.383
Triple aPL positivity	65 (45)	79 (40)	0.271
±1 CV risk factor	129 (73)	148 (62)	0.015
Arterial hypertension	65 (37)	62 (26)	0.016
Obesity	27(15)	22 (9)	0.906
Diabetes	17(10)	12 (5)	0.754
Smoke	58 (33)	82 (34)	0.073
Dyslipidemia	56 (32)	67 (28)	0.404
Hyperhomocysteinemia	13 (8)	24 (10)	0.348
Tested for congenital thrombophilia	134/177	161/239	-
Factor V mutation	6 (4)	9 (6)	0.665
Factor II mutation	5 (4)	5 (3)	1.000
ATIII deficiency	3 (2)	1 (0.6)	0.333
Protein C deficiency	2 (1.5)	4 (2.5)	0.692
Protein S deficiency	9 (7)	3 (1.8)	0.036
21 acquired thrombophilic risk factor	68 (39)	93 (39)	0.955
Trauma / surgery / immobilization	29 (16)	24 (10)	0.853
Hormonal therapy	29 (16)	58 (24)	0.054
Pregnancy / post-partum	11 (6)	20 (8)	0.417

Results are presented as median [1st-3rd quaartile] or number (%). Continuous variables were compared with Mann-Whitney test; Categorical variables were compared with Chi-Scruared or Fisher exact test. In bold, statistically significant comparisons. Abbreviations: aPL= antiphospholipid antibodies, AT = anti-thrombin, CV= cardiovascular.

Conclusions: In this large APS patients' cohort, thrombotic events occurred both in venous and arterial districts in 54/415 (13%) subjects, especially in triple aPL positive patients. Triple aPL positivity defines the serological profile at highest risk of thrombosis and it seems associated to an increased possibility of switch in the involved vascular side.
Keywords: Antiphospholipid syndrome, recurrent thrombotic events, triple aPL positivity.

0056

ACCRUAL DAMAGE IN ANTIPHOSPHOLIPID SYNDROME IS ASSOCIATED WITH THROMBOSIS AND TRIPLE ANTIPHOSPHOLIPID ANTIBODIES POSITIVITY. A RETROSPECTIVE SINGLE CENTER STUDY

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To assess the frequency of accrual damage in antiphospholipid syndrome (APS) and to evaluate the association with different laboratory and clinical APS subsets.
Patients and methods: Medical records of 273 patients, 229 (83.9%) female and 44 (16.1%) males with a mean (±SD) age at diagnosis of 38 (±13.3) years, followed prospectively from 1990 to 2021 were reviewed.
Results: Ninety-five (34.8%) presented pregnancy morbidity alone, 141 (51.6%) thrombosis alone and 37 (13.6%) both thrombosis and pregnancy morbidity. A single, double or triple antiphospholipid antibodies (aPL) positivity was registered, respectively in, 83 (30.4%), 81 (29.7%) and 109 (39.9%) of the patients. Following a mean (±SD) follow up of 209.6 (±94.5) months, a total of 40 (14.7%) organ damage accrual was recorded. This included neurological damage in 9 (22.5%) patients, hemiparesis in 8 and cognitive dysfunction/dementia in one case, cardiac valvopathy in 5 (12.5%) patients of which 3/5 (60%) require valve replacement with mechanical valve in two cases and bioprosthetic in one. Chronic heart failure was found in 4 (10%) patients, chronic renal failure in 10 (25%), amputation due to peripheral arterial thrombosis in 6 (15%), visual loss in 2 (5%), post thrombotic syndrome in 2 (5%), adrenal insufficiency in one (2.5%) and both chronic renal failure and post thrombotic syndrome in one (2.5%) patient. Both thrombotic and thrombotic and pregnancy morbidity subsets were significantly associated with a higher rate of damage accrual compared with pregnancy morbidity alone, respectively p<0.0001 (OD 0.03; 95% CI: 0.004-0.2) and p=0.0006 (OD 0.04; 95% CI 0.005-0.3). Regarding laboratory subsets, triple aPL positivity was significantly associated with a higher rate of damage accrual compared to single and double aPL, respectively, p=0.0017 (OD 0.2; 95% CI: 0.09-0.6) and p=0.004 (OD 0.2; 95% CI: 0.1-0.6).
Conclusions: Overall, our data show a higher frequency of damage accrual in APS patients. Both thrombosis and thrombosis and pregnancy morbidity APS clinical subsets as well as triple aPL laboratory APS feature were significantly associated with a higher rate of damage accrual. These findings should be in mind when counselling APS patients and might help guide clinicians in therapeutic decision.
Keywords: Damage accrual, antiphospholipid syndrome, antiphospholipid antibodies.

0059

ANTIPHOSPHOLIPID SYNDROME (APS) AS FIRST MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A CASE REPORT

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APS is characterized by clinical (thrombosis/pregnancy loss) and laboratory criteria (antiphospholipid antibodies-aPS). These antibodies, mainly lupus anticoagulant (LAC), are frequently associated with thrombotic events. We report the case of a patient, who developed several thrombotic events under anticoagulation with apixaban, without known diagnosis of SLE.
Case report: 49-year-old patient with a history of superficial vein thrombosis (SVT) of the right upper limb (RUL) 2017 and fugax amaurosis in left eye 2018. Entered the Emergency Department due to pain, and swelling in right lower limb (RLL). Extensive deep vein thrombosis (DVT) from femoral vein to solea veins and unprovoked pulmonary embolism (PE) were diagnosed, and anticoagulation with apixaban. After 30 days, he presented impairment of symptoms. A new venous ultrasound was performed, which confirmed progression of thrombosis to external iliac vein. Laboratory tests showed accelerated erythrocyte sedimentation rate and mild anemia. An angiotomography showed lymph node enlargement in right ileofemoral region and hospitalization was decided. A stent was placed in the femoral vein, with partial improvement. The patient evolved with bilateral SVT RUL.
Results: Apixaban was discontinued and enoxaparin was started. No neoplastic process was observed in PET TC scan. Thrombophilia studies and antibodies testing were positive for (LAC), anticardiolipin: IgG:154 U/mL y antib2-glycoprotein: IgG:95 U/mL antibodies, antinuclear antibodies:1/1280 (homogeneous pattern), strong positive anti-DNA antibodies, complement C3 and C4 in low values, anti Ro SS-A antinuclear antibody. The diagnosis of APS secondary to SLE was based on clinical and laboratory criteria. Treatment was switched to warfarin and hydroxychloroquine was added. Nephrotic syndrome was diagnosed later. Laboratory showed Hematocrit:27%, Hemoglobin:8.5g/dl, Leucocytes:3100/mm^3,

Serum protein:5.3g/dl, Albumin:2.5g/dl, Triglycerides:247, Reticulocytes:1.8%, Direct Antiglobulin Test:(+), 24-Hour Urine: Microalbuminuria:> 2gr, Proteinuria:8gr. A renal biopsy reported a proliferative lupus nephropathy and immunosuppressive therapy (IS) was started. He developed reactivation of multimetameric herpes zoster. The patient improved clinical and laboratory parameters and IS was switched to mycophenolate and tacrolimus.
Conclusions: Patient with DVT progression under DOAC that arrived to the diagnosis of SAF y developed SLE with lupus nephropathy Given the increasingly widespread use of DOACs in acute DVT and PE, another pathology should be suspected (cancer, autoimmune) in patients with poor response to treatment. Early diagnosis is key in order to optimize treatment.
Keywords: Antiphospholipid syndrome, systemic lupus erythematosus.

0060

COVID-19 AS AN INCREMENTAL TRIGGER OF AUTOIMMUNITY

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For many years it has been known that a large variety of viruses are capable of leading to immunomodulation. Viruses may affect the immune system through multiple molecular mechanisms and might contribute to the development of autoantibodies (auto-Abs) and autoimmune diseases, such as Sjögren's syndrome, multiple sclerosis, and rheumatoid arthritis. Some of the most well-known viruses with immunomodulatory ability are the Coxsackie B virus (CVB), rotavirus, influenza A viruses (IAV), herpes viruses, and given many recent studies, the SARS-CoV-2, which was found as well to bear such a powerful influence. There is an association between COVID-19 and the development of over 15 separate types of autoantibodies and above 10 distinct autoimmune diseases. Numerous studies have examined the prevalence of auto-Abs in COVID-19 patients since their existence in an individual might be the first easily measurable indication of a sub-clinical autoimmune reaction, reflecting a hyper-activation of polyclonal B cells.
Immune-mediated blood disorders may be the most common group of newly diagnosed autoimmune manifestations in COVID-19 patients. Due to the high risk of thrombosis in COVID-19 patients and their significant impact on survival, multiple auto-Abs associated with thrombosis were studied, including anti-phospholipid antibodies (aPL). According to aPL data in COVID-19 patients from different cohorts, the positive rate of aPL and its subtypes is broad, ranging from 24.2% to 57.1%. Yet the pathological significance of aPL in SARS-CoV-2 infected patients remains unclear; it is essential to remember that COVID-19 significantly increases the inflammatory state and may cause endothelial cells damage, both increasing the risk of thrombus formation independent to aPL. It is essential to determine the pathological significance of aPL in SARS-CoV-2 infected patients to evaluate the need to use therapeutic options in such patients in the acute and chronic phases of the disease.
Conclusions: Therapeutic options for COVID-19 patients with aPL might not be identical to the classical treatment of anti-phospholipid syndrome and catastrophic anti-phospholipid syndrome. Further research is needed to evaluate the most beneficial combinations of the wide variety of available therapies. Notably, thrombotic complications and coagulopathy triggered by SARS-CoV-2 have distinct clinical and laboratory features from other coagulation disorders, including the anti-phospholipid syndrome; thus, suffusion evaluation is crucial to perform suffusion evidence-based medicine.
Keywords: COVID-19, SARS-CoV-2, anti-phospholipid antibodies, antiphospholipid syndrome, autoantibodies, autoimmunity.

0062

A DECONSTRUCTIVE ANALYSIS OF THE OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (APS)

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Defined more than 20 years ago, the APS criteria were last updated in 2004. Most obstetric complications are not due to APS. APS is present in our societies and women frequently believe that APS is the cause of their obstetric complication. The clinical application of many observations has yet to be determined since the evidence we have is still insufficient and the management often uncertain. Deconstruction, form of philosophical and literary analysis, derived mainly from work begun in the 1960s by the French philosopher Jacques Derrida. To "deconstruct" an opposition is to explore the tensions and contradictions between the hierarchical ordering assumed (and sometimes explicitly asserted) in the text and other aspects of the text's meaning. The point of the deconstructive analysis is to restructure, or "displace" the opposition, not simply to reverse it. Deconstruction works in to lay bare and to expose what has been hidden from view. Deconstruction's influence widened to include a variety of other disciplines, such as medical practice.

Material and methods: This work is only referred to the called non-thrombotic obstetric APS and do not is applicable to other clear well established autoimmune diseases (LES, Rheumatoid Arthritis etc.). Material: The International Classification Criteria propose to define the APS (Miyakis et als. 2006, JTH p295); the use in the "real-world" and daily medical practice of the antiphospholipid antibodies (aPLa). Argentine experience (Grand B et al.2017, rpth p1140, 1449) and information from media and social media. Method: In 1st column we describe the traditional "scientific perspective of the classical APS"; in the 2nd column the social widespread and real-world use of aPLa and the 3rd we propose what is needed to be deconstructed before new/future classifications of APS.
Results: Table: Deconstructing the APS.

TRADITIONAL	REAL WORLD PRACTICE	NEED TO DECONSTRUCT
International consensus statement on an updated classification criteria for definite APS was designed mainly for clinical studies. The obstetric APS is considered different from thrombotic APS	Impact on individual care, use for diagnosis and treatment. Wrong diagnostic of APS, overdiagnosis. Women feel ill when aPla are detected and demands to screen before getting pregnant or "in vitro" fertilizations failures (IVFF)	This daily practice and define clearly in future meetings how information will be published. Discuss previous impact in daily care of pregnancy complications and future direction in this area.
Scientific medicine for research purposes. APS is defined as a "rare", systemic autoimmune disease	A disease is "socially constructed". Political force. Media and social media patient`s forum. Not a rare disease for women at reproductive age.	Medicalization of deviance. Led to sickness in the healthy. Patients ought to be aware of what APS is and what APS is not.
Muyakis et al. (2006) Criteria: Recurrent early abortion: the most sensitive, low specificity Preeclampsia and placental insufficiency: insensitive or non-specific Fetal death: the most specific	aPLa screening in pregnancy morbidity for diagnosis women`s collectives that demand a law to study thrombophilia. They ask: why we have to wait 2 or 3 abortions?	The real cause of early recurrent abortion is other (embryo aneuploidy, abnormal karyotypes, that dramatically increase with maternal age) Need to discuss with a multidisciplinary team, with the participation of high risk pregnancy obstetricians and reproduction specialists
14th TASK Force Obstetric APS. Except for fetal death there are limitations in the quality of data supporting the association of antiphospholipid antibodies (aPLa) with obstetric complications	First line treatment heparin + low doses of aspirin use as the gold standard for the 3 criteria with lack of good established evidence in preeclampsia and intrauterine growth restriction	Should early recurrent abortion be a criterion? Should early preeclampsia be a criteria or only a risk factor? It seems that only fetal death is specific for APS
Source of treatment information: small trials, retrospective and prospective observational studies	Overdiagnosis, overtreatment Hydroxychloroquine added when results from trials are yet ongoing. Lack of accepted evidence	Firs "do not harm". Means that in an explicit way International Societies need to refer to this real world situation (deconstruction) for a future classification criterion update.

Conclusions: APS has become a familiar concept and the truth for daily practice in women with pregnancies complications. We propose an effort to open a new way of looking the APS at health care. We need to give a correct answer to women at reproductive age and not create false expectative when detecting aPLa. The APS International Classification Criteria contrasts with daily practice. Patients ought to be aware of what APS is and what APS is not. After deconstruction of the APS a new reconstruction of this syndrome can open a clearer way for the diagnosis and treatment.
Keywords: Deconstruction, obstetric antiphospholipid syndrome.

0063

ANTIPHOSPHOLIPID SYNDROME (APS): MATERNAL AND PERINATAL OUTCOME AFTER TREATMENT WITH LOW MOLECULAR WEIGHT HEPARIN (LMWH) AND LOW DOSE ASPIRIN (LDA). RETROSPECTIVE ANALYSIS.

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Antiphospholipid Syndrome (APS) is an autoimmune condition characterized clinically by thromboembolic events and/or adverse pregnancy outcomes in the presence of persistent circulating antiphospholipid antibodies (aPLa). The antibodies currently included in the classification criteria are lupus anticoagulant (LA), anticardiolipin antibodies (aCL) and anti-beta 2-glycoprotein I antibodies (anti-beta2GPI). Treatment with LDA plus heparin at prophylactic dosage is recommended as first line therapy.
Patients and methods: 33 pregnancies (one twin pregnancy) in 27 patients that fulfilled the revised classification criteria of APS (Sydney 2006) were included. Period: 2010-2020. Classification 1) Thrombotic: 1 (stroke); 2) Pregnancy morbidity: 21 a) Fetal death (FD): 9; b) Severe preeclampsia (sPE) or placental insufficiency (PI):9; Recurrent pregnancy loss (RPL):3;

thrombotic + obstetric: 5. According to laboratory categories 14/27 pt were in category I (6 double and 8 triple positivity); 13 were in category IIa only LAC (+). Treatment: Initial prophylactic doses of enoxaparin 40 mg + LDA and intermediate or therapeutic doses in that patients with thrombotic APS.
Results: There were 30 newborns (2 were twins), 2 FD (24 and 33 weeks), 2 early abortions. There were 4 neonatal deaths in women with previous sPE or PI (1/4 y 3/4 respectively). One woman with triple positivity and previous thrombotic and obstetric APS developed a peripartum deep vein thrombosis. Patients with previous sPE and PI showed the poorest response to first line therapy.
Conclusions: Our results suggest that current first line therapy for APS in pregnancy prevent obstetric complications in women with history of RPL or FD, but not in those with previous sPE and/or PI. The poorest obstetric outcome was also observed in women with triple positivity. The division into two groups of obstetric APS (RPL/FD and PI/sPE) and the triple positivity might facilitate the choice of early additional therapy in these women. The most appropriate prophylactic treatment strategy for fetal growth restriction prevention in APS is still debated.
Keywords: Obstetric antiphospholipid syndrome, pregnancy, low molecular weight heparin.

0067

CHRONIC PULMONARY THROMBOEMBOLISM (PTE) AS A FORM OF PRESENTATION OF PRIMARY ANTIPHOSPHOLIPID SYNDROME (APS) AND POSSIBLE COMPLICATIONS ASSOCIATED WITH SURGICAL RESOLUTION

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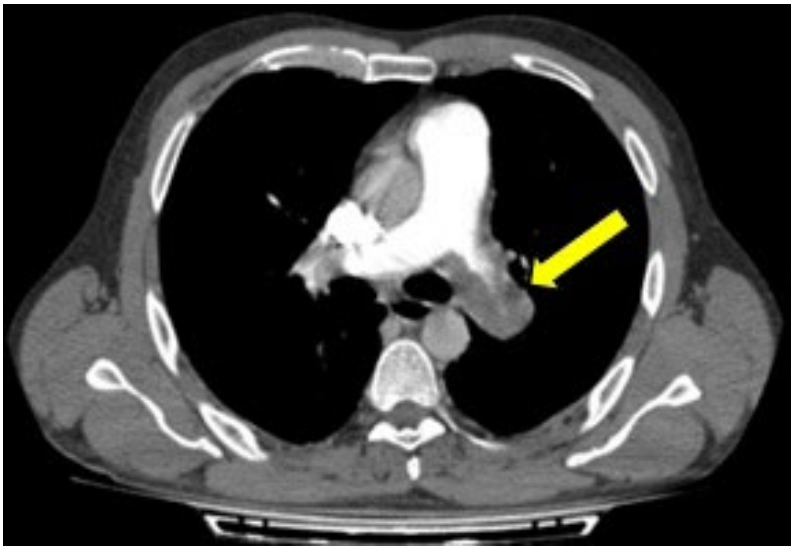
PTE is an arterial thrombotic event that can occur in APS, and may lead to the development of chronic thromboembolic pulmonary hypertension (CTEPH), a potentially fatal complication. Pulmonary endarterectomy (PEA) represents the gold standard treatment to reverse CTEPH, with a huge prognostic impact. This surgery requires a maneuver called deep hypothermic circulatory arrest (DHCA). Associations have been reported between this procedure and subsequent neurological complications.
Case report: A 48-year-old male patient, previously healthy, with a 7 month-history of dry cough, pleuritic pain and progressive dyspnea, weight loss of 8 kg and mild hemoptysis in recent days. Chronic PTE (image) was diagnosed, with echocardiogram-estimated pulmonary artery systolic pressure of 103 mmHg, associated with thrombocytopenia (68,000/mm^3) and prolonged coagulation times. Blood exams showed: false positive VDRL, decreased C4, positive IL, aCL IgM > 150 and IgG 147 and anti-β2 glycoprotein 1 IgM 121.8 and IgG > 150, ANA 1/320, anti-DNA 1/20, anti-La + (78U). Treatment with anticoagulation, hydroxychloroquine and sildenafil was started. Subsequently, PEA with extracorporeal circulation was performed. It was well tolerated, obtaining a right heart catheterization-measured pulmonary artery mean residual pressure of 15 mmHg. Seven months after surgery, the patient experienced seizures and attentional mild cognitive impairment associated with depression. MRI of the brain showed bilateral periventricular and subcortical foci of gliosis. Simple brain CT and EEG were normal, with INR 2.5. Aspirin, statins and carbamazepine were added, with which the seizures were controlled. Nevertheless, cognitive impairment and depression persists to this date.



Conclusions: Here we report a rare case of thrombotic APS, with PTE and CTEPH at onset that required PEA under DHCA. This procedure has a high mortality rate and further complications. Although good recovery was observed, the patient subsequently presented severe neurological compromise despite being on anticoagulant and immunomodulatory treatment, with proper management of cardiovascular risk factors. This raised the discussion whether the neurological symptoms were due APS damage, or were major surgery associated sequela.

Keywords: Antiphospholipid syndrome (APS), chronic pulmonary thromboembolism (PTE) primary, neurological complications.

0070

A DISTINCT POPULATION OF MONOCYTES IN APS/SLE PATIENTS: THE ROLE OF COMPLEMENT

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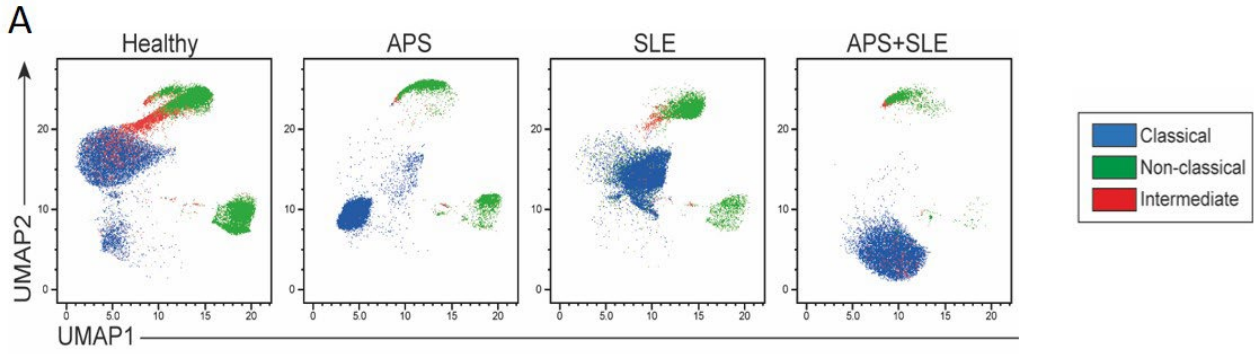
Antiphospholipid syndrome (APS) is an autoimmune disorder characterized by both the presence of distinct clinical outcomes (thrombosis and/or pregnancy morbidity) and autoantibodies, including anti-Beta-2-Glycoprotein I antibodies. APS may occur in isolation (primary APS) or in combination with other autoimmune disorders, most commonly Systemic Lupus Erythematosus (SLE). The pathogenesis of APS is multifactorial, with strong evidence supporting a central role for complement and coagulation cascades and the aberrant function of pro-inflammatory monocytes that upregulate coagulation pathway components such as tissue factor (TF). Our study utilizes mass cytometry (CyTOF) to quantify complement and coagulation marker expression in PBMCs of APS/SLE patients relative to healthy individuals, and with a focus on monocyte subsets.

Patients and methods: Peripheral blood was collected from APS (n=2), SLE (n=4) or APS/SLE (n=4) patients attending the UCLH Rheumatology outpatient clinic, and from healthy controls (n=4). PBMCs were separated by SepMate density-based centrifugation and stored in liquid nitrogen until analysis. Cells were thawed on ice and rested for 90 minutes before staining. PBMCs were stained for CyTOF using the Fluidigm commercial M1/M2 monocyte-focused kit with the addition of custom conjugated antibodies to measure complement and coagulation proteins (PAR1, Tissue Factor (TF), C3, C5-C9 and C3aR). Cells were stained as per manufacturer's instructions and acquired on a Helios mass cytometer. Analysis was carried out using Flow Jo software and GraphPad Prism.

Results: APS/SLE patients had higher global frequencies of C3+ and C5-C9+ leukocytes than SLE, APS or healthy donors. C3aR and TF expression was comparable between groups while the frequencies of PAR1+ leukocytes were elevated in patients with SLE. Monocytes represented a substantial proportion of C3, C3aR and C5-C9-expressing cells in all groups, with the primary elevation of C3+ and C5-C9+ frequencies in APS/SLE patients observed in this subset. The expanded population of C3hi monocytes in APS/SLE patients was determined to be a CD36hiCD33hi classical monocyte subset expressing the markers CD206 and CD163. Healthy individuals possessed similar frequencies of this phenotypic subset but lacked C3 expression.



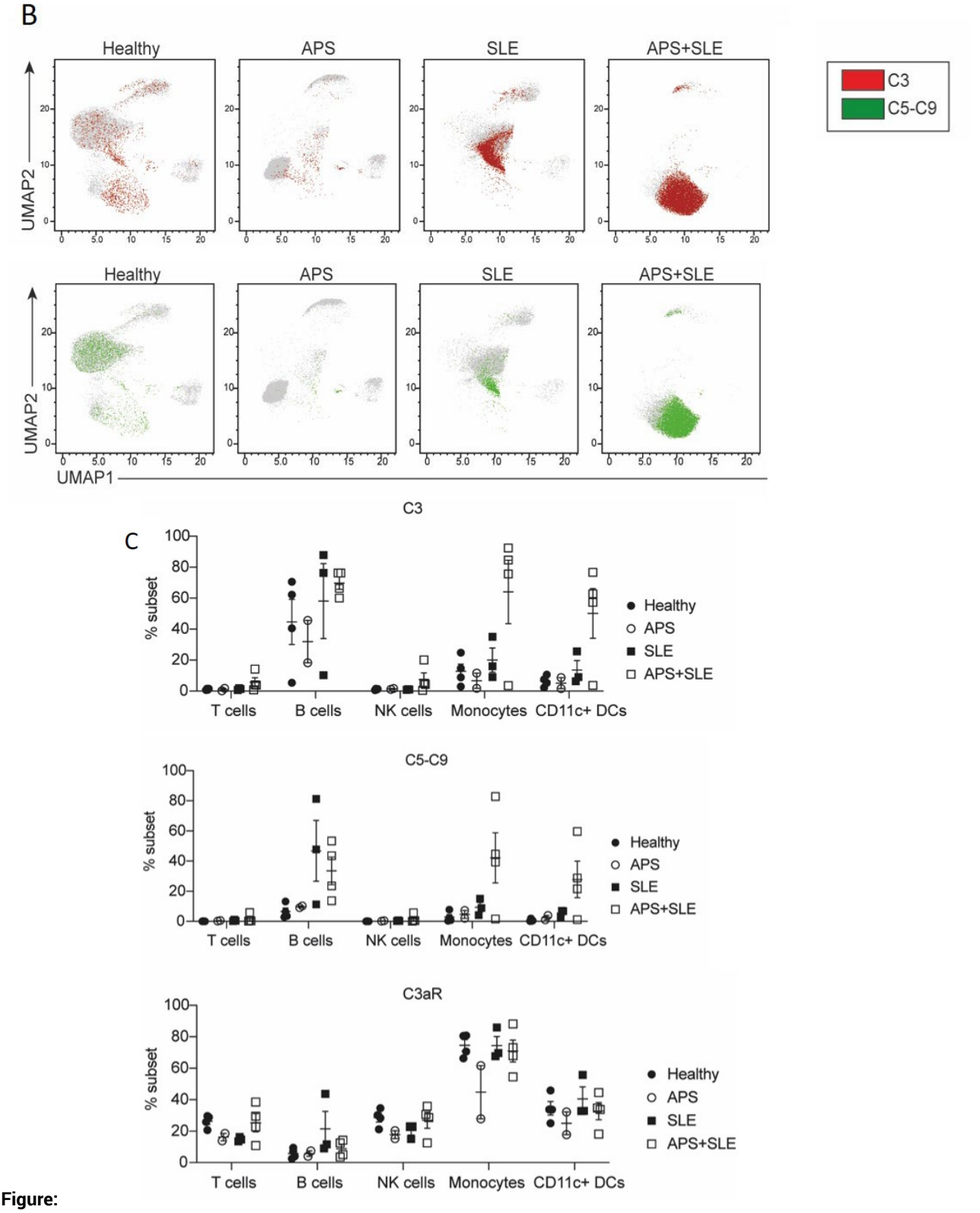


Figure:

A) Two-dimensional UMAP projection of CyTOF data of total monocytes from the PBMCs of APS, SLE, APS/SLE patients and healthy controls. This indicates the groupings of classical, non classical and intermediate monocytes, as can be seen APS-SLE classical monocytes cluster differently to Healthy, APS alone and SLE alone. Further analysis (B) shows a large proportion of cells expressing C3 (red) and C5-C9 (green) are classical monocytes with increased expression in the APS/SLE patients. Panel C shows this increased expression of C3 and C5-C9 is in multiple cell types but most strikingly monocytes. These data reveal substantial heterogeneity between patient groups and highlight a distinct cluster of monocytes in APS/SLE patients that are present at lower densities and with lower C3/C5-C9 expression in healthy individuals and are absent in patients with APS or SLE-only.

Conclusions: Our data suggests a cellular dysregulation resulting in aberrant activation of a subset of classical monocytes in APS/SLE patients which contain high intracellular levels of C3 and C5-9. Further study is required to phenotypically and functionally characterize this subset of cells to understand the potential impact on disease pathogenesis.
Keywords: Monocytes, CyTOF, APS, SLE, complement.

0071

DAMAGE INDEX FOR ANTIPHOSPHOLIPID SYNDROME (DIAPS) MISSES SOME ACUTE THROMBOTIC NEUROLOGIC EVENT-RELATED DAMAGE

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Neurologic involvement in thrombotic antiphospholipid syndrome (APS) is common and leads to morbidity. The damage index for APS (DIAPS) misses some neurologic event-related damage. We aim to characterize the cumulative prevalence of damage related to acute thrombotic neurologic events not included in DIAPS.
Patients and methods: Single-centre retrospective analysis of thrombotic APS patients (2006 Sydney criteria). Damage was assessed using DIAPS. Only acute thrombotic neurologic events were considered. All damage events not captured by DIAPS were recorded as follows: a) stroke with sensory deficits (paraesthesia/anaesthesia); b) cerebellar stroke with ataxia; c) cerebral sinus venous thrombosis (CSVT). We excluded ophthalmologic damage as it is a component of DIAPS.
Results: A total of 197 patients followed for 43 (median 10) years were identified. The median age at diagnosis was 40 (interquartile range, 51-28) years; 71.1% were female; 66% had primary APS. We identified 149 events in 113 (113/197, 57.4%) patients (Table 1), the most common being stroke affecting the cerebral cortex (52.3%), followed by transient ischaemic attacks (TIA) (32.2%), CSVT (10.1%) and cerebellar stroke (5.4%). Damage arose in 68 (45.6%) cases. Only 39 (57.4%) of these were already scored by DIAPS, of which 89.7% (n=35) were related to cortical stroke with motor deficits. Thirty-five patients (35/197, 17.8% of all patients) experienced 29 damage events (42.6% of damage) not recorded in DIAPS: 13 patients (11.5% of affected patients) experienced 14 sensory deficits (20.6% of damage); cerebellar stroke affected 4.1% of patients (n=8) and led to damage in 75.0% (6/8) of cases; CSVT, which affected 6.6% of patients (n=13), led to damage in 61.5% (8/13) cases.

Table 1: Distribution of acute thrombotic neurologic events and its damage.

N,(%)	**Affected Patients** 113(57.4[b])	**Total Events** 149 (100.0)		**Damage** 68 (45.6)	
			Total Events 68 (100.0)	In DIAPS 39 (57.4)	Not in DIAPS 29 (42.6)
Cortical Stroke Motor deficit Sensory deficit Aphasia Other[a]	62 (54.9;31.5[b]) 34 (30.1;17.3[b]) 13 (11.5;6.6[b]) 3 (2.7;15[b]) 2 (1.8;1.0[b])	78 (52.3)	54 (79.4) 35 (51.5) 14 (20.6) 3 (4.4) 2 (2.9)	39 (100.0) 35 (89.7) 0 3 (7.7) 1 (2.6)	15 (51.7) 0 14 (48.3) 0 1 (3.4)
Transient ischaemic attack	30 (26.5;15.2[b])	48 (32.2)	0	-	-
Central sinus venous thrombosis	13 (11.5;6.6[b])	15 (10.1)	8 (11.8)	0	8 (27.6)
Cerebellar Stroke	8 (7.1;4.1[b])	8 (5.4)	6 (11.8)	0	6 (10.7)

[A] Stroke – related parkinsonism (n=1) and stoke with dyspraxia (n=1); [b]% of all patients (n=197).

Conclusions: Most acute thrombotic neurologic event-related damage came from motor deficit secondary to cortical strokes, which are well represented in the current DIAPS. However, DIAPS failed to score more than 40% of damage events in nearly 18% of all patients.
Keywords: Antiphospholipid syndrome, damage index, neurologic events.

0073

HETEROGENEITY OF THE TYPE I INTERFERON SIGNATURE AMONG ANTIPHOSPHOLIPID ANTIBODIES POSITIVE SUBJECTS

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Type I Interferons (IFN) are central players in the pathogenesis of several autoimmune conditions. To date, a limited number of evidences is available on the specific role of IFN activation in antiphospholipid antibodies (aPL) positive patients, including aPL carriers, primary antiphospholipid syndrome (PAPS) and those APS subjects who presented with an associated autoimmune disease (secondary APS, SAPS), such as systemic lupus erythematosus (SLE). The aim of this study was to evaluate the differential expression of IFN stimulated genes (ISG) among different subsets of aPL positive subjects.

Patients and methods: For the purpose of the study, a total of 112 patients attending the San Giovanni Bosco Hospital (Turin, Italy) were enrolled, including 31 PAPS, 25 SAPS, 27 SLE patients without aPL, 29 aPL carriers (mean age 48.3±13.3 years, 76% female). Nineteen subjects were also recruited as healthy controls (HCs). Gene expression was evaluated by RT-PCR in whole blood for the following genes: IFI6, IFI44, IFI44L, MX1, IFI27, OAS1 and RSAD2. Normalized gene expression levels (Z-scores) were averaged into a global IFN signature (IFN score). Differences were measured by Kruskal-Wallis tests and associations among genes were studied by cluster and correspondence analyses. Correlations among genes were plotted by network analyses.

Results: An overall activation of ISG was noted across APS subsets, but certain differences were noted among genes. Whereas some ISG were already upregulated in the aPL positive group compared to HC (IFI44, IFI44L, MX1, IFI27, OAS1 and RSAD2, all p<0.050), other ISG were only in increased SLE (IFI6), MX1 differed between SLE and SAPS, and IFI27 and OAS1 showed differences between PAPS and SAPS. The composite IFN score revealed quantitative differences in the IFN pathway activation across APS subsets, being elevated in aPL carriers/PAPS groups compared to HCs (both p<0.050) and increasing in SAPS (p<0.010) and SLE (p<0.001) groups. Network analyses (Figure 1A) revealed qualitative differences in the gene-gene correlation networks: (i) weaker structures were found in HCs and aPL carriers, compared to stronger and higher-degree networks in SAPS and SLE groups; and (ii) the influence of each node was different across groups. Unsupervised cluster analysis identified 3 clusters (I to III) based on ISG patterns (Figure 1B). Clusters usage differed among APS subsets, thus correlating clinical status (Figure 1C). Distinct groups of ISG positively correlate to aPS/PT IgG titre in aPL carriers and PAPS groups (all rho>0.500), whereas no associations were retrieved in SAPS or SLE. No associations with previous thrombotic events were observed in any subset, although IFN composite score and several ISG correlate with the number of thrombotic recurrences under anticoagulation (all rho>0.400). No associations with GAPSS were observed.

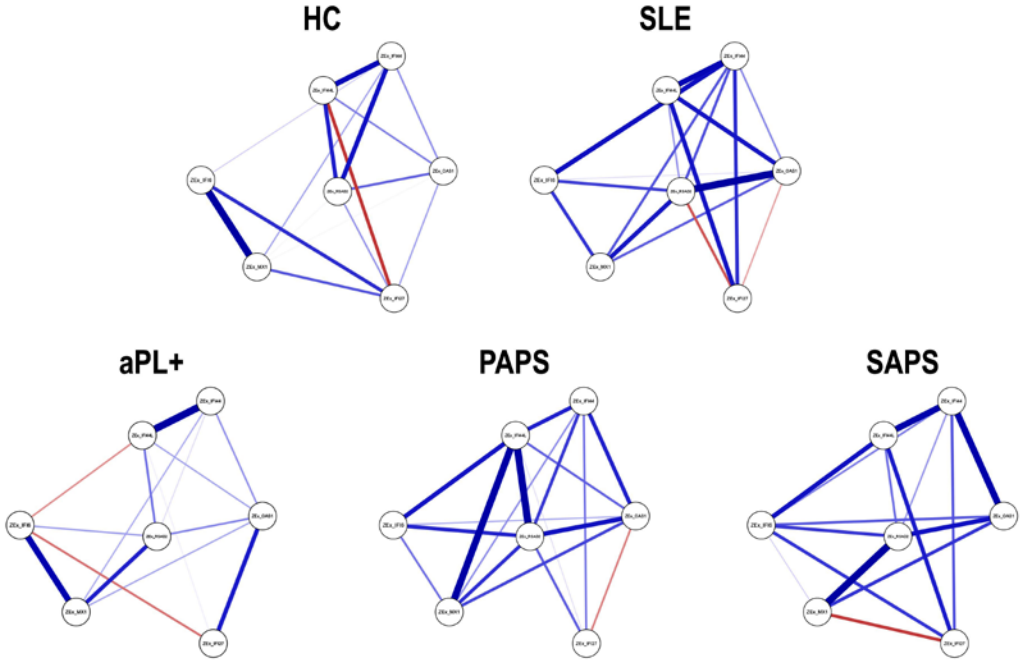

Figure 1A

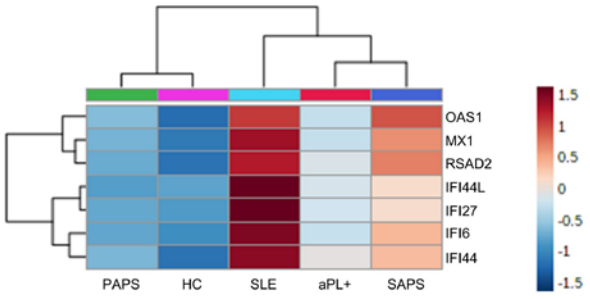

Figure 1B

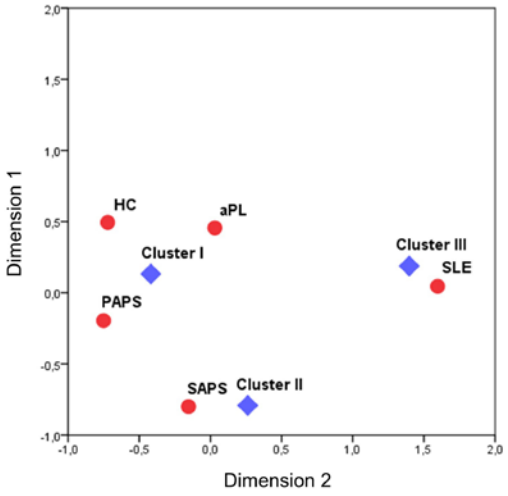

Figure 1C

Conclusions: An overall IFN pathway activation has been observed in aPL positive patients and across all APS subsets. Qualitative and quantitative differences across the APS spectrum can be identified, leading to the identification of distinct IFN signatures with different clinical value.
Keywords: Interferon signature, phenotyping, antiphospholipid antibodies.

0074

ANTIPHOSPHOLIPID COEXISTENCE WITH ANTI-ADAMTS13 ANTIBODIES: REPORT OF TWO PATIENTS FOCUSING ON CLINICAL MANIFESTATIONS AND AUTOANTIBODIES INTERRELATIONS OVERTIME

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Primary antiphospholipid syndrome (APS)/antiphospholipid antibodies (aPL) associated with acquired thrombotic thrombocytopenia purpura (TTP) has only been described in ten cases in literature.
Patients and methods: A 46-year-old woman with asymptomatic lupus anticoagulant (LA) since 2018 presented a placental rupture and urgent cesarean in 2019. A week later, under prophylactic enoxaparin, she initiated spontaneous ecchymosis with abdominal pain and thrombocytopenia (10000/mm^3), hemolytic anemia, hepatitis and hypertension. Patient had 9% schistocytes and undetectable ADAMTS13 activity. A positive anti-ADAMTS13 inhibitor (21 U/ml) diagnosed patient of TTP. Plasmapheresis, corticoids and caplacizumab achieved complete response in one month. Until now, LA persisted positive, and no thrombotic episode occurred. On follow-up, ADAMTS13 antibodies have been intermittently positive with concomitant protease deficiency but without clinical recurrences of TTP, so immunosuppression was not applied. Patient two is a 43-year-old man that in 2010 presented a respiratory viral infection followed by abdominal pain, thrombocytopenia (5000/mm^3), hemolytic anemia, hepatitis and renal insufficiency. Antiphospholipid antibodies were negative. Schistocytes (6%) and decreased ADAMTS13 activity led to TTP diagnosis. Sixteen sessions of plasmapheresis were completed achieving TTP remission. In 2015, TTP recurrence occurred after a streptococcal pharyngitis. Normalization of platelet count succeed after 11 sessions of plasmapheresis. In 2017 a second recurrence of TTP occurred requiring plasmapheresis and rituximab. During hospital stay he presented a venous thrombosis associated to intravenous catheter and laboratory showed positivity for anticardiolipin IgG (46 CU) and anti-B2glycoprotein I IgG (103 CU). Several months later, LA was firstly identified as positive and in subsequent follow-up years triple positivity for aPL persisted while no other recurrence of ADAMTS13 inhibitor antibodies happened.

Antiphospholipid coexistence with anti-ADAMA13 antibodies: tow patients´ description focusing on clinical manifestations and autoantibodies interrelations overtime. PATIENT 1					
	LA detection 2018	**TTP diagnosis June 2019**	**Follow-up Oct 2019**	**Follow-up Oct 2020**	**Follow-up Oct 2021**
Clinical Manifestations	No	Ecchymoses in puerperium Platelets 10000/mm^3 Hemolytic anemia Elevated liver enzymes 9% schistocytes	No	No	No
Treatment	No	Plasmapheresis, corticoids caplacizumab	No	No	No
ADAMST13 activity	NP	0%	14%	4%	0%
ADAMST13 antibodies	NP	Pos+ (21U/ml)	Neg	Pos+(42U/ml)	Pos+(33U/ml)
La **DRVVTr** **SCTr**	Pos+ Neg 1.70	Np	Pos+ Neg 1.70	Pos+ Neg 1.43	Pos+ Neg 1.68
aCL IgG	Neg	Np	Neg	Neg	Neg
aCL IgM	Neg	Np	Neg	Neg	Neg
AntiB2GPI IgG (CU)	Neg	Np	Neg	Pos+(24)	Neg
AntiB2GPI IgM	Neg	Np	Neg	Neg	Neg

Results: We observed that the development/detection of antiphospholipid and anti-ADAMTS13 autoantibodies is not usually concomitant. Along with that, and despite the associated presence of LA, TTP clinical presentation of our first patient was as expected without further complications. On the other hand, TTP immunosuppressant regimens in our patients did not prevent the appearance/persistence of aPL antibodies along time.
Conclusions: The association of aPL/APS and TTP is extremely rare and, although sharing a thrombotic-based mechanism, clinical forms are not much more severe. Both entities would maintain their independence in clinical and serological evolution and therapeutic responses.
Keywords: Antiphospholipid syndrome, thrombotic thrombocytopenic purpura, anti-ADAMTS13.

0075

HYPOPROTHROMBINEMIA-LUPUS ANTICOAGULANT SYNDROME (HLAS). CLINICAL SUSPICION AND DIAGNOSIS IN AN ADULT PATIENT.

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Hypoprothrombinemia-Lupus anticoagulant syndrome (HLAS) is a rare, acquired disorder caused by anti-prothrombin antibodies, reported in almost a hundred cases in literature.
Case report: A 47-year-old man was referred to our hospital in 2021 for concomitant prolongation of activated partial thromboplastin time (aPTT) and prothrombin time (PT) observed in the study of a 2-month hematuria after a lithiasic renal colic. In 1993 patient underwent a corneal transplantation secondary to ocular traumatism, the several surgeries without hemorrhagic complications. In 2018 he suffered a nephritic colic that needed shock wave lithotripsy without complications; prolongation of coagulation times was identified (aPTT ratio 3.5, 120 sec and PT ratio 1.64, 47%), normal thrombin time, with positive lupus anticoagulant (LA) (Diluted Rusell Viper Venom time ratio 2.3), anti-cardiolipin (aCL IgG 160 GLP) and anti-Beta2GlycoproteinI (IgG 180 U/ml). In 2019 immune study revealed positive ANA 1/320, negative antiDNA and low C3 and C4 complement. Patient did not have pass thrombotic events or APS criteria. Based on PT prolongation we assessed coagulation factors and antiprothrombin antibody. Results confirmed normal FVII and X levels and decreased factor II (16%) with positive antiprothrombin antibodies (DRG DiagnosticsR ELISA test). Other factors with decreased levels (V 42%,

VIII 4.6%, IX 0%, XI 21%) were attributed to in vitro interference with LA phenomenon. A 1:1 dilution of patient´s and normal plasma nearly corrected PT but not aPTT. We diagnosed the patient of HLAS associated with LA.
Results: We present a case of HLAS in a triple positive aPL adult male that presented with minor bleeding, an uncommon profile of a disease that commonly affects pediatric age (<16 years), predominates in women, and is associated with infections or lupus. However, hematuria or minor mucosal bleeding, low complement levels, artificial reduction of other coagulation factors and typical normalization of PT and not aPTT mixing test (due to non-neutralizing nature of antiprothrombin antibody) are common features of HLAS reflected in our patient.
Conclusions: In patients with LA and associated PT and aPTT prolongation, with or without bleeding complications, a hypoprothrombinemia-Lupus anticoagulant syndrome should be suspected. Diagnosis is confirmed with decreased factor II levels (<40%) and presence of antiprothrombin antibodies.
Keywords: Antiphospholipid, hypoprothrombinemia-lupus anticoagulant syndrome, HLAS, anti-prothrombin antibodies.

0077

IS THERE ANY ASSOCIATION BETWEEN ANTIPHOSPHOLIPID ANTIBODIES AND CELIAC DISEASE?

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We studied the prevalence of celiac disease (CD) in patients with positivity for at least one antiphospholipid antibody.
Patients and methods: We analyzed 50 patients whose APS profiles were positivity, presuming that they suffer from APS according to international consensus at the time of sampling, 39 female (F) and 11 male (M); age: 27 -77 years, median 35.5. Along 50 individuals as control group (GC), 31 F and 19 M age 26-59 years, median 39.8; constituted by healthy individuals without a history of thrombosis and / or obstetric complications, without pre-existing autoimmune disease, or intolerance to gluten. We perform: aCL IgG and IgM (Quanta Flash Inova): negative <20, indeterminate 20 -40, positive> 40 (aCL IgG CU / ml, aCL IgM CU / ml); and aβ2GPI IgG and IGM (Quanta Flash Inova): negative <15, indeterminate 15 - 20, positive> 20 CU. The serological profile tested to evaluate celiac disease (Quanta Lite INOVA) consists of anti-Tranglutaminase IgA antibodies (h-tTG IgA U / ml), anti-Tranglutaminase IgG (h-tTG IgG U / ml), anti-deaminated peptides of Gliadin IgA (Gliadin II IgA U / ml) and deaminated peptides of Gliadin IgG (Gliadin II IgG U / ml): Negative <20 U / ml; Weak positive 20-30 U / ml and Positive moderate to Strong Positive> 30 U / ml. By indirect immunofluorescence (INOVA imprints with monkey esophagus sections), anti-Endomysium IgA and IgG antibodies. Reference value: Negative. Lupus anticoagulant (AL) was analyzed according guides ISTH 2009.
Results: See Tables.

	Control Group	Control Group	Control Group	APS Group	APS Group	APS Group
	Positive	Indeterminate	Negative	Positive	Indeterminate	Negative
aCL IgG	0	3	47	15	0	35
Acl IgM	14	4	32	27	0	23
a ß2GPI IgG	6	12	32	13	0	37
a ß2GPI IgG	10	2	38	19	0	31
LA	1	-	49	17	-	33
Triple positivity	0	-	-	18	-	32

	Control Group	Control Group	APSI Group	APS Group
	Positive	Negative	Positive	Negative
h-Ttg IgA	1	49	0	50
h-Ttg IgG	1	49	0	50
Gliadin II IgA	1	49	0	50
Gliadin II IgG	1	49	0	50
Endomysium IgA	1	49	0	50
Endomysium IgG	1	49	0	50

Conclusions: We did not find an association between APS antibodies and celiac disease; perhaps some of them had high antibodies titers or triple positive.
Keywords: Antiphospholipid antibodies, celiac disease, triple positivity.

0079

HYPOPROTHROMBINEMIA-LUPUS ANTICOAGULANT SYNDROME (HLAS) CASE: LACK OF RESPONSE TO RITUXIMAB AND CORRELATION WITH PERIPHERAL B-CELL SUBSET ANALYSIS

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The eradication of anti-prothrombin antibodies in hypoprothrombinemia-Lupus anticoagulant syndrome (HLAS) is based in corticoids alone or combined with immunosuppressants. Only six patients treated with rituximab had been reported.
Case report: A 47-year-old man was referred for hematuria and prolonged activated partial thromboplastin time (aPTT) and prothrombin time (PT). Similar coagulation alterations were present since 2018 when a study confirmed the presence of lupus anticoagulant (LA) and anticardiolipin/anti-B2glycoproteinI. Patient had no thromboembolic history. In present study we found decreased factor II activity (16%) with presence of anti-prothrombin antibodies and diagnosed a HLAS associated with LA. We started immunosuppressants due to persistent inhibitor. First attempt with high-dose corticoids and immunoglobulins resulted in partial increase of FII (32%) but same PT prolongation (22 secs, 42%), TTPA (4.4 ratio, 129 sec) and LA positivity. We infused cyclophosphamide (800 mg/monthly x 2 months) and no response was achieved (FII 18%, positive anti-prothrombin antibody) at two months. Rituximab (1000mg, 2 infusions separated 15 days) was applied with no changes in FII deficiency (19%) and positivity of LA and anti-prothrombin antibodies. To deepen in the reasons of failure with antiCD20 rituximab, we analyzed B-cell population. Three months after infusion, total plasma CD19+ B cells persisted depleted (0.09%). Proportion of B-cell subsets were immature transitional CD24highCD38high 0% (N 2-11), naïve IgD+CD27neg 17% (N 48-72), preswitch memory IgD+CD27+ 32% (N 12-100), switch memory IgD-CD27+ 50% (N 10-22), CD19+CD21low 48% (N 2-6) and plasmablast IgD-CD27++ 34% (N 4-17). Along last year of follow-up, no recurrence of bleeding has occurred.
Results: In our patient, rituximab did not eradicate anti-prothrombin antibodies. Previous reports of HLAS treated with rituximab regimens brought heterogeneous results; two patients achieved complete responses, two partial remissions with FII activity at 30-40% without hemorrhagic symptoms, and last two cases did not respond. We have reported the first analysis of subpopulations of peripheral B lymphocytes in HLAS. We evidenced changes compatible with rituximab-depletion period (scarce number of CD19+ cells along with a highest proportion of IgD−CD27+ memory B cells and plasmablasts) however that fact did not correlate/predict a serologic remission of anti-prothrombin and LA. Auto reactive antibody secreting cells (short-lived proliferating plasmablasts, long-lived plasmatic cells) resistant to antiCD20 inhibition could possibly explain that fact.
Conclusions: Rituximab shows irregular outcomes in the eradication of anti-prothrombin antibodies and does not seem a reasonable first-line approach in HLAS.
Keywords: Antiphospholipid syndrome, hypoprothrombinemia-lupus anticoagulant syndrome (HLAS), anti-prothrombin antibodies.

0080

PRIMARY ADRENAL INSUFFICIENCY ASSOCIATED WITH ANTI-PHOSPHOLIPID SYNDROME

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APS is a form of acquired thrombophilia induced by autoantibodies, characterized by the presence of thrombotic phenomena and/or obstetric events. The Adrenal insufficiency (ISR) is a rare entity, characterized by partial or complete loss of adrenal steroid secretion. Autoimmune adrenalitis is responsible for 70-90% of these cases. Bilateral adrenal secondary hemorrhage and/or thrombosis to APS represents less than 1% of the cases.
Case report: A 38-year-old female patient with a history of deep vein thrombosis, pulmonary thromboembolism, and spontaneous abortion 20 days ago, anticoagulated with acenocoumarol. In subtherapeutic range of anticoagulation in the last 3 months. Medical consultation due to asthenia, anorexia, abdominal pain, nausea, and vomiting. On examination, normal vital signs, cutaneous hyperpigmentation. Abdomen distended and painful in diffuse form. Blood chemistry tests: Hb 15 gr%, GB 8230, platelets 284000, CPK 62 UI/l, g 0.90 g/l, ESR 64 mm/h, Na 134 meq/l, K 4.53 meq/l, creatinine 0.92 mg%, RIN 1.60. Abdominal CT: increased size of both adrenals, greater density at the level of the medulla. With contrast enhances

only the cortical. Impressive bilateral adrenal hemorrhage. Abdominal MRI: both adrenal glands markedly enlarged, the right measuring 38 x 21 mm and the left one 41 x 34 mm. Inside, hyperintense content is observed on T2 and hypointense on T1 with a liquid appearance. In the periphery, hyperintensity is shown in the T1 sequence with fat suppression compatible with a hematic component. Plasma cortisol was measured at 1.2 µg/dL, ACTH at 88.4 pg/ml. TSH 5.74 µUL/ml, FT4 1.07 ng/dl. FAN negative, anti-DNA negative, normal complement, B2 glycoprotein IgG 2 U/ml, IgM 6.2 U/ml. Anti cardiolopins Ig G 6.8 GPL, IgM 5 MPL. Lupus anticoagulant Strongly positive (persistent after 12 weeks). Negative anti adrenal ac. Negative thrombophilia profile. A diagnosis of ISR secondary to bilateral adrenal hemorrhage due to APS is made. Replacement began with oral hydrotisone 15 mg, fludrotisone 0.1 mg/day, enoxapraine 80 mg every 12 hours, associated with ASA. With clear improvement of her symptoms.
Conclusions: Among the most common causes of primary ISR are autoimmune adrenalitis and tuberculosis. APS is a rare etiology, and its pathogenesis would be involved in both supraadrenal vein thrombosis and subsequent hemorrhagic infarction of the glands, as well as possible spontaneous hemorrhage in patients previously anticoagulated. The clinical presentation is similar in the different aetiologies, with symptoms of hypoadrenalism that can be life-threatening if not detected early. Cases associated with APS may concomitantly involve thrombosis in another part and adrenal hemorrhage is usually bilateral. ISR is rarely the debut form and usually appears in patients with previous thrombotic events. CT and MRI show structural changes that can help the diagnosis, as well as possible differential diagnoses. Hormone replacement therapy and anticoagulation are the mainstay of the treatment.
Keywords: Suprarrenal insufficiency, bilateral adrenal hemorrhage, antiphospholipid syndrome.

0084

TRIPLE POSITIVE ANTIPHOSPHOLIPID SYNDROME: CLINICAL MANIFESTATIONS

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The concept of triple positive antiphospholipid syndrome (APS) emerged as a tool to identify those patients with a higher thrombotic risk despite adequate treatment. In addition, triple positive carriers have been associated with a high frequency of development of clinical manifestations: obstetric and/or thrombotic. However, in clinical practice it is difficult to identify high-risk patients.
Case reports: Case 1. Female, 37 years. October 2020 cesarean section due to selective intrauterine growth restriction and preeclampsia at 31 weeks pregnant. Nine days after, extensive ischemic stroke due to obstruction of the right middle cerebral artery, with a left faciobrachial crural motor focus. r-TPA was performed. She started on enoxaparin prophylaxis and aspirin due to risk of hemorrhagic transformation. Five days later a proximal deep venous thrombosis was diagnosed. Actual treatment: vitamin K antagonist plus aspirin. Laboratory for APS: October 2020 aCL IgM 14 IgG 23, LA positive, aβGP1 IgM15 IgG16. February 2021 aCL IgM 90 IgG 38, LA positive, aβGP1 IgM51 IgG24. No new thrombotic events to date. Case 2. Female, 46 years. Acute myocardial infarction at 26 years old without major cardiovascular risk factors and normal coronary angiography. In 2012 persistent triple positive APS. She remained anticoagulated for 2 years and then discontinued on her own. She continued on aspirin. 10 years later diagnosis of systemic lupus erythematosus (SLE) treatment with hydroxychloroquine. In 2021 ACL IgM 30 IgG 188, LA positive, aβGP1 IgM15 IgG 222.No new thrombotic events to date. Case 3. Female, 36 years. Medical history of Hashimoto thyroiditis and episcleritis. Later, autoimmune hemolytic anemia (meprednisone and then rituximab). Celiac disease (positive antibodies and HLA DQB). Arthralgias with elevated anti citrulline peptide. Laboratory for APS: November 2020 aCL IgM 11 IgG 36, LA positive, aβGP1 IgM 37 IgG17. April 2021 aCL IgM 37 IgG 11, LA positive, aβGP1 IgM40 IgG10. Oral contraceptives are discontinued and ASA is started.
Results: Triple-positive APS patients are associated with high thrombotic risk, both obstetric and thrombotic, like case 1. However, not all cases have the same behavior. Case 2, presents a high-risk laboratory profile, SLE and arterial thrombosis. She remained only with ASA and prophylaxis in risk situations and did not repeat complications. Case 3, represents a challenge due to underlying immunological disease and high-risk profile. These patients are prone to developing complications and treatment is unclear (from no treatment to aspirin to anticoagulation). She has not developed any complications to date.
Conclusions: APS is a disease with high clinical diversity. There are identified risk factors for thrombotic recurrence and worse evolution: triple positivity antibodies, arterial thrombosis, concomitant immunological disease. We present these patients to show that we still need new tools that allow us to identify high risk patients and optimize treatment.
Keywords: thrombosis, triple positive APS, clinical diversity.

0085

PEPTIDE MICROARRAY BASED ON R39-R43 OF DOMAIN I OF ß2-GLYCOPROTEIN I DETERMINED ANTIGENIC SPECIFICITY OF ANTIPHOSPHOLIPID ANTIBODIES

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Antiphospholipid antibody syndrome is an autoimmune disease characterized by the presence of antiphospholipid antibodies and clinical manifestations such as recurrent thromboembolic or pregnancy complications. Although cryptic epitope R39-R43 belonging to beta-2-glycoprotein 1 (ß2GP1) has been identified as the main antigenic determinant for antiphospholipid antibodies (aPL), we have recently demonstrated that the epitope is a motif determined by the polarity, rather than by the sequence or charge of amino acids. In the present study, we wanted to identify the exact association of residues needed to obtain the highest aPL affinity.
Material and methods: Based on the epitope R39-R43 and our identified motif, we generated a printed peptide microarray of 676 different peptides. These peptides have been then screened for their ability to interact with the plasmas from 11 well characterized APS patients and confirmed by surface plasma resonance assay.
Results: We identified a peptide which selectively bound IgG derived from APS patients with 100 times more affinity than ß2GP1, Domain I or epitope R39-R43. Based on this peptide, we are able to inhibit the activity of IgG derived from APS patients in vitro. We have also generated a monoclonal IgG antibody against this peptide. Using both, peptide, and monoclonal antibody, we have been able to develop a fully standardized indirect colorimetric immunoassay with a sensitivity improved of twice that of the current most sensitive chemiluminescence immunoassay (CLIA) reaching 84% (n=371).
Conclusions: The identification of the optimized peptide offers a new standardized and accurate tool for diagnostics of APS. Furthermore, having increased affinity for aPL, this peptide could represent a useful tool to prevent recurrent pregnancy loss or represent a prevention strategy for APS as an alternative to the use of anticoagulants.
Keywords: aPL, epitope, diagnostic standardized, ELISA.

0086

DECIPHERING THE INTRICACIES OF DIAGNOSIS OF ANTI-PHOSPHOLIPID SYNDROME DURING INFANCY

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In this study, we aim to: 1) present the immunological work-up of a complex clinical case suggestive of infantile APS and 2) illustrate how the normal immunoglobulin physiology during pregnancy and neonatal period impacts on diagnosis.
Case report: A 5-month old baby, born to consanguineous parents, initially presented with a seizure. MRI brain showed evidence of stroke in the fronto-parietal area, which had appearances suggestive of a thrombo-embolic stroke. Past history: preterm delivery; fetal anemia due to Rh alloimmunization; mechanical ventilation for respiratory distress as a neonate. In the family history, the mother had a history of recurrent pregnancy morbidity.
Results: IgG cardiolipin antibodies were positive at 71 GPL (NR < 10), IgG beta-2-glycoprotein-I antibodies 80 U/ml (NR<7), confirmed on subsequent repeat testing. IgM antibodies and lupus anticoagulant were negative. Thrombophilia screen and genetic testing were not contributory. The mother was negative for all aPL, including lupus anticoagulant.

Collected time 15.31 AST **Collected date** 12/07/21		
TEST		**UNITS**
Anti cardiolipin Ab IgG	71.00 *1	GPL
Anti cardiolipin Ab IgG Int	Positive 1 *1	
Anti cardiolipin Ab IgM	1.40 *1	MLP
Anti cardiolipin Ab IgM Int	Negative 2*1	
Anti B2 Glycoprotein IgG	80.00 01*1	U/mL
Anti B2 Glycoprotein IgG Int	Positive 01 3 *1	
Anti B2 Glycoprotein IgM	<2.90 01*1	U/mL
Anti B2 Glycoprotein IgM Int	Negative 01 3 *1	

Lab view	24/09/21 9:32 AST	17/07/21 08:41 AST
Lupus anticoagulant		
Lupus anticoagulant APTT		See LA comment ratio Auth (verified)
Lupus anticoagulant comment		Lupus anticoagulant comment Auth (verified)
Immunology		
Cardiolipin IgG		1.0 GPL units Auth (verified)
Cardiolipin IgG Interp		Negative* Auth (verified)
Cardiolipin IgM		1.1 MPL unit Auth (verified)
Cardiolipin IgM Interp		Negative* Auth (verified)
Cardiolipin IgG/IgM		Image attached Auth (verified)
Anti-Beta2 Glycoprotein antibodies		Image attached Auth (verified)
Anti-Beta2 Glycoprotein IgG		1.0 unit/mL Auth (verified)
Anti-Beta2 Glycoprotein IgG Interp		Negative* Auth (verified)
Anti-Beta2 Glycoprotein IgM		2.4 unit/mL Auth (verified)
Anti-Beta2 Glycoprotein IgM Interp		Negative* Auth (verified)

Conclusions: The initial impression was that the IgG aPL detected in this young baby were derived from the mother therefore would be transient, not diagnostic of APS, and not needing treatment. However simultaneous negative testing of mother, and knowledge of normal immune mechanisms during pregnancy and neonatal period, confirmed that these were IgG aPL produced by the baby. (Most IgG is transferred in the 3rd trimester - but this baby was premature. Half-life of IgG is 3 weeks, therefore after 6 months, most IgG is from the baby). The baby's clinical course was complicated by a further stroke, confirmed on MRI. The baby did indeed fulfill both clinical and laboratory criteria for APS.
Keywords: Anti-phospholipid, thrombosis pregnancy stroke.

0091

IMMUNOGENICITY, SAFETY AND ANTIPHOSPHOLIPID ANTIBODIES AFTER SARS-COV-2 INACTIVATED VACCINE IN PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Coronavirus disease 19 (COVID-19) has an increased risk of coagulopathy with high frequency of antiphospholipid antibodies (aPL). The recent reports of thrombosis associated with the adenovirus-based vaccines raises concern that SARS-CoV-2 immunization in primary antiphospholipid syndrome (PAPS) patients may trigger a dysregulated immune response with possible clotting complications. Therefore, the objectives of this study were to assess immunogenicity, aPL production and safety of Sinovac-Coronavac, an inactivated vaccine against COVID-19 in PAPS patients. To assess immunogenicity, safety and aPL production after Sinovac-Coronavac vaccine in PAPS patients.
Patients and methods: This prospective controlled phase 4 study of SARS-CoV-2-naive PAPS patients and a control group (CG) consisted of a two-dose Sinovac-CoronaVac (D0/D28) and blood collection before vaccination (D0), at D28 and 6 weeks after second dose (D69) for immunogenicity/aPL levels. Outcomes were seroconversion (SC) rates of anti-SARS-CoV-2 S1/S2 IgG and/or neutralizing antibodies (NAb) at D28/D69. Safety and aPL production: anticardiolipin (aCL) and anti-beta2-glycoprotein-I (aßGPI) were also assessed.
Results: Forty-four PAPS patients and 132 CG had comparable age (p=0.982) and sex (p>0.999). At D69, both groups had high and comparable SC (83.9% vs. 93.5%, p=0.092) as well as NAb positivity (77.4% vs. 78.7%, p=0.440), and NAb-activity [64.3% (49.0-77.0) vs. 60.9% (45.6-81.3), p=0.689]. Of note, for D28, the antibody response was very low and also similar in both groups SC (25.8% vs. 30.6% p=0.609). Antiphospholipid levels remained stable throughout the study at D0 vs D28 vs D69 (IgG aCL p=0.058; IgM aCL, p=0.091; IgG aßGPI, p=0.513 and IgM aßGPI, p=0.468). Thrombotic event up to 6 months or other moderate/severe side effects were not observed.
Conclusions: We provide novel evidence that Sinovac-CoronaVac vaccine has a high immunogenicity and excellent safety profile in PAPS. We further demonstrated that this vaccine did not trigger thrombosis or induced changes in aPL-related antibodies production. Our findings support the recommendation of SARS-CoV-2 vaccination for PAPS patients.
Keywords: Antiphospholipid syndrome, COVID-19, SARS-CoV-2 vaccine.

0093

TWIN PREGNANCY IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

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Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease that affects predominantly women during their reproductive years. A better understanding of the disease, the advances of the treatment and creation of specialized multidisciplinary groups has led to dramatic improvement in disease management and pregnancy outcome over the last 20 years. However, Maternal and fetal complications are still present. Risk factors for fetal and obstetric complications are disease activity at the conception and during pregnancy, lupus nephritis (LN), arterial hypertension, positive antiphospholipid antibodies (APL), antiphospholipid syndrome (APS) and anti-Ro/SSA antibodies. Moreover, twin pregnancy (TP) has consistently been associated with severe maternal and perinatal morbidity and its occurrence with SLE and APS is rare. We describe a twin pregnancy and its complications in SLE and APS patient.

Case report: A 27 years old woman with 28 weeks dichorionic diamniotic twin unplanned pregnancy was referred to our tertiary maternity hospital. She had a medical history of SLE (Cutaneous, Hematological and renal involvement), immune thrombocytopenia and non-terminal chronic renal disease secondary to lupus nephritis diagnosed 8 years ago. She had anti-Ro positive and triple positivity of antiphospholipid antibodies (LA, aCL Ig G and B2GPI Ig G). The immunosuppressive therapy was azathioprine 100 mg /d, prednisone 20mg/d, Hydroxycloroquine 400mg/d, and she also was treated with low dose aspirin, prophylactic dose of enoxaparin, folic acid and 16UI of levemir insulin for steroids induced diabetes. Her blood test showed HB level of 10.3 g/d, WBC of 10.2200 and platelets of 93.000/mm^3. Renal function was impaired (serum creatinine 2.57mg/dl, Uric acid 8.7 mg/dl) with proteinuria in a 24-hour urine test (0.10 grs), Fetal echocardiography was performed without congenital heart block and valve disease. On the third day of hospitalization the patient presented premature rupture of membranes, with spontaneous onset of labor. Cesarean section was performed due to breech presentation of the first fetus. The first male newborn weight was 870 grs with an Apgar score of 4/7 and the second female newborn weight was 1030 grs with Apgar score 4/7 with 27 gestational age. Ten days after cesarean section a subaponeurotic hematoma was diagnosed requiring surgical intervention. She had impairment of her renal function and it returned to her previous level in the late puerperium.

Conclusions: Pregnancy in SLE and APS women should be planned and a multidisciplinary evaluation is crucial, with adequate treatment and management of comorbidities. Preterm birth is the most frequent complication associated with a twin pregnancy.

Keywords: Twin pregnancy, systemic lupus erythematosus, antiphospholipid syndrome.

0094

METABOLIC SYNDROME IN PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Metabolic Syndrome (MS) is highly prevalent in rheumatic diseases and it is recognized as a new independent cardiovascular risk factor. Objective: to study the frequency of MS in patients with Primary Antiphospholipid Syndrome (APS).

Patients and methods: We studied patients with APS according to Sydney Criteria at Rheumatology Unit in Córdoba Hospital and Center of Research of Immunopathology and Rare Diseases of University of Torino in Italy from May 2013 to July 2021 and a control group matched age and gender. Clinical and demographic characteristics were analyzed. Sera samples were tested for lipid profile (cholesterol (CT), HDL, LDL, triglyceride (TG)), glucose, insulin level (IN), TSH, free T4, uric acid, and autoantibodies. MS was defined by 3 different criteria: World Health Organization (WHO), Adult Treatment Panel III (ATPIII) and International Diabetes Federation (IDF). Chi^2 test, Fisher's test, Student's test or Wilcoxon test were performed. $p<0.05$ was considered statistically significant.

Results: 120 APS patients were included, 104 females, with mean age of 36.2 years old and 120 as a control group, 100 females with mean age of 36 years old. 47.5% (n=57) of APS patients had thrombotic manifestations (arterial (AT)/ venous thrombosis (VT)) without pregnancy morbidity, 60.6% had pregnancy morbidity and 9,6% had both thrombosis and pregnancy morbidity. 69% of patients had aCL Ig G, 40% aCL Ig M, 58% LA, 43% AntißGP1 and 51% had double positivity and 14% triple positivity. Weight, abdominal circumference and body mass index (BMI) were 70.20 kg, 89.3 cm, and 26.46 in APS patients

and 69 kg, 84.2, 24.8 in the control group. (p=0.54, p=0.006, p=0.01). Glucose level CT, HDL, LDL, TG and IN were 99.3, 176, 60.9, 112, 107, 12.9 in APS patients and 96.7, 183, 65, 114, 95 and 10 in the control group (p=0.21, p=0.07, p=0.002, p=0.68, p=0.09, p=0.01). MS data according to OMS, ATPIII, and IDF definition in APS patients and control group are shown in Table. Regarding APS patients, APS who met one of the MS criteria were more frequently thrombotic APS (APS-MS+ 68.8% vs APS-MS- 39.8%; p=0.004) and AT (APS-MS+ 40.6% vs APS-MS- 19.3%; p=0.01) but less frequently pregnancy morbidity (APS-MS+ 40.8% vs APS-MS- 67.1%; p=0.01) and recurrent abortions (APS-MS+ 20.0% vs APS-MS- 45.6%; p=0.02).

Ms Criteria	APS (n=120)	Controls (n=120)	p
ATP III	15 (12.7) /118*)	8 (6.7)	0.1145
OMS	10 (8.3)	7 (5.8)	0.4504
IDF	32 (26.7)	8 (6.7)	0.00003
MS total#	36 (30.0)	8(6.7)	0.000003

Conclusions: Frequency of MS is high in APS patients and it is associated with thrombotic APS, particularly arterial thrombosis. MS is a known risk factor for cardiovascular disease, morbidity and mortality in systemic autoimmune diseases. A tight control of this condition in the early stages of disease should be recommended.
Keywords: Metabolic syndrome, antiphospholipid syndrome.

0095

CORONARY ARTERY DISSECTION ASSOCIATED WITH ANTIPHOSPHOLIPID SYNDROME PRESENTING AS ACUTE CORONARY SYNDROME

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Antiphospholipid syndrome (APS) is a multisystem autoimmune disease associated with recurrent arterial and venous thrombosis and pregnancy loss. Cardiac manifestations include valve abnormalities, coronary artery disease, myocardial dysfunction, pulmonary hypertension and intracardiac thrombi. Coronary artery dissection (CAD) is an unusual cause of acute coronary syndrome, rapidly gaining recognition over the last decade. It occurs predominantly in young women and in autoimmune diseases and coronary angiogram often lacks typical atherosclerotic features. We present a rare case of male patient who had CAD of left anterior descending coronary artery which presenting acute coronary syndrome with intracardiac thrombi with a known diagnosis of APS.
Case report A 36 years old man was referred for cardiac and rheumatology evaluation to our hospital. He had a medical history of primary APS diagnosed 8 years ago. He had 3 episodes of deep vein thrombosis and pulmonary emboli (PE) with triple positivity of antiphospholipid antibodies (LA, aCL Ig G and B2GPI Ig G) without treatment. He also had a history of overweight, smoking and cocaine consumption in the past. Four months before, he developed acute dyspnea and he was diagnosed of PE and he received thrombolytic therapy and he was discharged with oral anticoagulation. Two months later, he developed severe chest pain while he was at rest. ECG showed negative T wave from V1 to V3, and his cardiac enzymes were within normal limits. He received nitrates, statins, low molecular heparin and aspirin. He was discharge with oral anticoagulation with warfarin plus aspirin with INR of 3. Transthoracic echocardiography showed left ventricular dilatation with regional wall motion abnormalities and intracardiac thrombi of 33x22x39mm that it also was seen in cardiac MRI. (Image 1). Coronary angiogram showed left anterior descending CAD. Warfarin and aspirin treatment was prescribed.

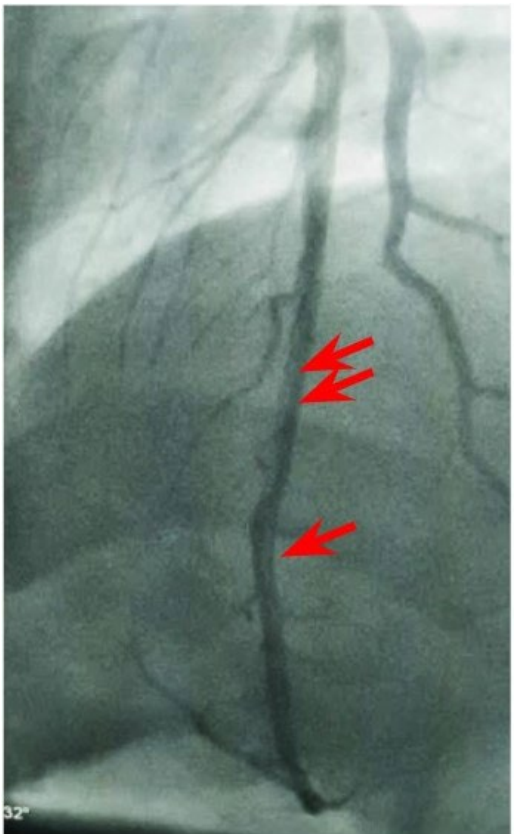

Image 1: Coronary angiogram showing left anterior descending CAD.

Conclusions: APS can lead to CAD and it should be considered in the setting of acute coronary syndrome in APS. Although the management of such patients is not well established, it should be based on the intensive antithrombotic therapy.
Keywords: Coronary artery dissection, antiphospholipid syndrome.

0096

INTRACARDIAC THROMBI IN ANTIPHOSPHOLIPID SYNDROME

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Antiphospholipid syndrome (APS) is a multisystem autoimmune disease associated with recurrent arterial and venous thrombosis and pregnancy loss. Cardiac manifestations include valve abnormalities, coronary artery disease, myocardial dysfunction, pulmonary hypertension and intracardiac thrombi. A potentially life-threating but treatable manifestation of APS is intracardiac thrombus (IT). Thrombus formation can cause embolic pulmonary and systemic events and it remains uncertain about the mechanism of its formation. IT can occur in all cardiac chambers and needs to be differentiated from intracardiac myxoma. Echocardiography and cardiac MRI are the best tools for IT diagnosis. We present 2 cases of IT in APS.
Case reports: Case 1: A 39 year old woman who had a medical history of systemic lupus erythematosus diagnosed 3 years previously, she developed severe headache with right hemiparesis that fully recovered in 4 hours. Brain MRI showed left frontal diffusion restriction focus and carotid ultrasound without atherosclerotic lesions. Doppler Transthoracic echocardiography showed a mobile mass 22x 10 mm attached to the left atrial wall. (Image 1) Cardiac MRI showed 2 intracardiac thrombi attached by pedicle to posterior free wall of atrium (Image 2). A laboratory investigation revealed; Lupus anticoagulant (LA) positive, Anticardiolipin Ig G (ACL Ig G), Ig M (ACL Ig M) (-), Anti BGPI Ig G e IG M (-). She started on enoxaparin (therapeutic dose) and warfarin with a target 2.5-3. She stayed for 5 days in the hospital with improvement of her symptoms and repeated echocardiography showed fully resolution of IT 6 months later. Case 2: A 36 year old man was referred for cardiac and rheumatology evaluation to our hospital. He had a medical history of primary APS diagnosed 8 years ago. He had 3 episodes of DVT and pulmonary emboli (PE) with triple positivity of antiphospholipid antibodies (LA, ACL Ig G and Anti-B2GPI Ig G) without treatment. He also had a history of overweight, smoking and cocaine consumption in the past.

Four months before, he developed acute dyspnea and he was diagnosed of PE and he received thrombolytic therapy and he was discharged with oral anticoagulation. Two months later, he developed severe chest pain while he was at rest. ECG showed negative T wave from V1 to V3, and his cardiac enzymes were within normal limits. He received nitrates, statins, Low weight molecular heparin, and aspirin. He was discharge with oral anticoagulation with warfarin plus aspirin with INR of 3. Transthoracic echocardiography showed left ventricular dilatation with regional wall motion abnormalities and intracardiac thrombi of 33x22x39mm that it also was seen in cardiac MRI. Warfarin and aspirin treatment was prescribed.

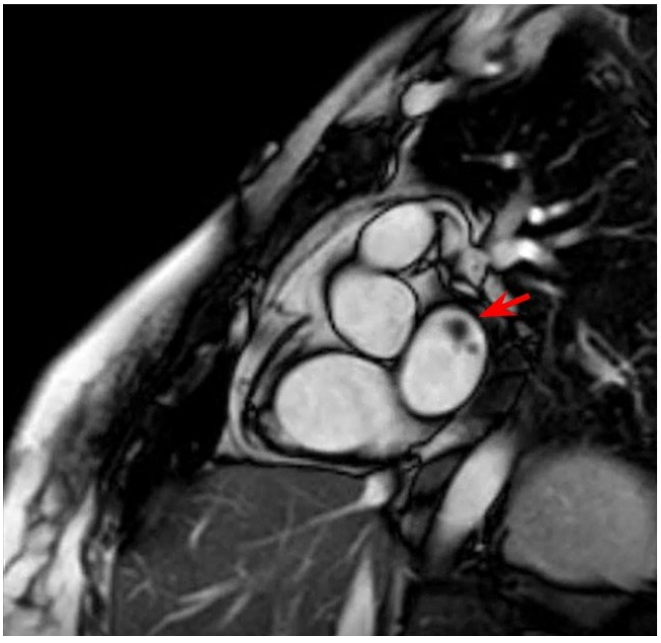

Image: Cardiac MRI IT attached by pedicle to posterior free wall of atrium.

Conclusions: It has rarely been reported in APS patients. This cardiac manifestation should be considered because early diagnosis and proper management with anticoagulant therapy are essential to prevent mortality.
Keywords: Intracardiac thrombi, antiphospholipid syndrome.

0097

FREQUENCY OF ANTIPHOSPHOLIPID ANTIBODIES DETECTED IN PREGNANT WOMEN WITH SARS-COV-2 INFECTION AND IMPACT ON PREGNANCY OUTCOME: A SINGLE-CENTER PROSPECTIVE STUDY ON 151 PREGNANCIES.

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At the beginning of the SARS-CoV-2 pandemic in Italy at the end of February 2020, there was a lack of information about the impact of the infection on pregnancy and its capability to induce de novo autoantibodies. It became clear soon that thrombosis was a manifestation of COVID-19, therefore the possible contribution of de novo antiphospholipid antibodies (aPL) raised research interest. We aimed at screening for aPL those pregnant patients that resulted positive for SARS-CoV-2 by nasopharyngeal swab upon admission to the Obstetric Department between March 2020 and July 2021.
Patients and methods: The study included 151 women who were hospitalized either for a symptomatic SARS-CoV-2 infection or for other reasons (obstetric complication, labour and delivery) and found incidentally positive at the entry swab. All these women underwent the search for aPL by means of Lupus Anticoagulant (LAC), IgG/IgM anti-cardiolipin (aCL), IgG/IgM anti-beta2glycoprotein I (aB2GPI). Data about biomarkers of inflammation, obstetric complications, neonatal complications and patients' comorbidities were collected.
Results: Sixteen patients (10.6%) were positive for aPL, all of them at low titre. The Table shows aPL profile and pregnancy outcomes upon symptomatic SARS-CoV-2 infection or not. Pneumonia was diagnosed in 21 women (5 with positive aPL)

and 5 required ICU admission (2 with positive aPL). Obstetric complications occurred in 11/16 (69%) aPL positive and in 38/135 (28%) patients. Only one case of maternal thrombosis occurred in an aPL negative woman. aPL positivity was checked after at least 12 weeks in 6/16 women (37.5%): 3 had turned negative; 1 tested positive for IgG and IgM aB2GPI as in the first detection; 1 remained positive for IgG aCL but turned negative for aB2GPI; 1 turned negative for LAC but displayed a new positivity for IgG aCL at high titre.

		Patients with SARS CoV-2symptomatic infection		Patients with SARS-CoV-2 asymptomatic infection	
	Total of Patients:151	40 (26.49%)		111 (73.51%)	
aPL positivity	**Total aPL positive: 16/151(10%.6%)**	6•		10	
	LAC test positive	4/6	66.6%	4/10	40%
	aCL IgG and or igM positive	1/6	16.7%	4/10	40%
	aß2GPI IgG and / or IgM positive	1/6	16.7%	4/10	40%
	Single aPL	5/6	83.3%	7/10	70%
	Double aPL	1/6	16.7%	3/10	30%
	Triple aPL	0/6	0%	0/10	0%
	Age Median IQR	34.58 Y 8.37 (27.87-36.25		31,35 y 8.00 (27.76-35.76)	
	Gestational week at admission (Median)	24.5 w		36 w	
	Obstetric complications	3º/6	50%	8ºº/10	80%
	Maternal thrombosis	0/6	0%	0/10	0%
	Neonatal complications	2/6	33.3%	1/10	10%
	Comorbidities	4/6	66.6%	2/10	20%
	Total aPL negative: 135/151 (89.4%)	34••		101	
	Age Median IQR	38,81 y 8,21 (27,84-36,05)		30,47 y 8,24 (27,87-36,12)	
	Gestational week at admission Median	30W		39W	
	Obstetric complication	7*/34	20.6%	31**/101	30.7%
	Maternal thrombosis	1/34	2.9%	0/101	0%
	Neonatal complications	2/34	5.9%	14/101	13.9%
	Comorbidities	11/34	32.4%	21/101	20.8%

• 5/6 patients (83.4%) presented pneumonia, 1/6 (16.6%) presented dyspnea, 2 pregnant women with pneumonia needed ICU admission (33.4%).
•• 15/34 patients (44.1%) presented pneumonia, 3/34 (8.8%) needed ICU admission.
ºAmong these, 1 patient presented preeclampsia (16.6%) and 1 had threatened preterm labour (16.6%).
ººAmong these 1 patient presented HELLP syndrome (10%) (this woman had double profile), there have been 2 cases of preeclampsia (20%) and an early miscarriage at 13.6 w (10%).
** Among these there have been 2 cases of preeclampsia (5.9%) and a CID (2.9%).*
*** Among these there have been 5 cases of preeclampsia (5%) and 2 isolated hypertensions (1,9%) and one threatened preterm labour (1%).*

Conclusions: The frequency of positive aPL in pregnant women with SARS-CoV-2 infection was low in our cohort and they mostly presented as single positive, low titre, transient antibodies. The rate of obstetric complications was higher in aPL positive women as compared to negative ones but other risk factors may have been contributed, including a full-blown picture of COVID-19. Moreover, not all the complications could be attributable to aPL, while typical aPL-related events such as preeclampsia were observed in both aPL positive and negative women.

Keywords: Antiphospholipid antibodies, COVID-19, autoimmunity.

0101

REFRACTORY EVANS SYNDROME AS A SEVERE MANIFESTATION OF ANTIPHOSPHOLIPID SYNDROME AND/OR SYSTEMIC LUPUS ERYTHEMATOSUS

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Evans Syndrome (ES) is defined as autoimmune hemolytic anemia (AHIA) coexisting immune thrombocytopenia (TBP) or autoimmune neutrophenia. The incidence of AHIA in APS is 6.6 % and TBP is 22-42%. Also ES has been frequently associated with systemic lupus erythematosus (SLE) in young people, it is difficult to control and the presence of TBP increases mortality.
Case report: 64-year-old male, from Córdoba, APS during stroke in 2011, anticardiolipin (ACL) antibodies (AB): Ig G > 140gpl, Ig M > 31 mpl, beta 2-glycoprotein 1 (B2-GP1): IgM: 24IU/mL, IgG: 159 IU/mL and TBP. Hospitalization in 2017: TBP (71000), persistent elevated ACL and B2-GP1, lupus anticoagulant (LA) +, ANA + 1/160, speckled and nucleolar pattern, hypocomplementaemia, negative AntiDNA and ENAS, ESR 40, CRP 2.2, lymphopenia; Brain MRI with putaminal hemorrhage and hyperintensive lesion in flair and T2 in bilateral fronto-temporal sulci. AntiSarsCoV2 last vaccination on 08/04/2021. He presented with seizures, head trauma and dyspnea, pallor, bibasal velcro cracklesand drowsiness, Hb: 4.8, plaq: 9000, GB: 10200, direct Coombs ++++, APP 28%, KPTT 150", LDH 1044, BI 2.23, creatinine 1.41, urea 54, CT: compatible with bilateral pneumonia (CAP), he was admitted and initially received dexamethasone 8 mg/8 hs and multiple transfusions. Then, he was treated with Methylprednisolone (MPDN) 500 mg IV/3 days, romiplostim, and MPDN 60 mg/d; bone marrow puncture resulted in normal medullogram. Doppler echocardiogram: Moderate increase in LA, EF 70%, normal PASP. Ultrasound with normal splenoportal axis; C3 41, C4 4, ANA (-), ACL andB2-GP1in high titers. We added hydroxychloroquine 400 mg/d, and Rituximab (RTX) 500mg/week IV x 4. He was discharged with GB 3900, Hb level of 11 and platelet count of 49000. In the 2nd admission he had fever, GB 1900 (Li 58), Hb level 12.7, platelet count 39000. Lungs CT showed bilateral infiltrates. After ruling out infectious disease, he received filgrastrim + MPDN 500 mg IV x 3. In external control he showed Hb 12.8, GB 8760, plaq 32000. 3rd admission: fever and leukopenia (GB 500), Hb 13.1, plaq 11000, ESR 16, BT 1.68, BI 1.29, LDH 261. It was detected IgG and IgM for CMV, so foscarnet was indicated for 7 days+ MPDN EV 500mg x 3 + Gamma globulins (Gamma) 400mg/kg/day x 5 days. He was discharged with GB 10580 (NS 88, Li 9), Hb 11 and plaq 34000. The last admission, he had fever for 4 days, rhinorrhea, dyspnea, severe pancytopenia and bilateral CAP with multiple organ failure; he was treated with several transfusions, empirical ATB and MPDN 500mg IV x 3 + Gamma 400mg/kg/day x 5 days, without response and death.
Conclusions: We present this case report with the aim of showing the fatal outcome of hematologic compromise of SLE plus APS and the refractory treatment.
Keywords: Evans syndrome, systemic lupus erythematosus, antiphospholipid syndrome.

0102

KIDNEY TRANSPLANT IN LUPUS NEPHROPATHY AND THEIR RELATIONSHIP WITH ANTIPHOSPHOLIPID ANTIBODIES. EXPERIENCE OF A SINGLE CENTER

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Introduction Kidney transplant (KT) represents a therapeutic option in patients with lupus nephritis (LN) in end-stage renal disease (ESRS). The presence of antiphospholipid antibodies (APL) has been associated with an increased risk of thrombosis, graft loss and death. To evaluate the characteristics and evolution of the KT recipient, according to their AFL profile.
Patients and methods: Analytical, retrospective study in Lupus patients with KT (ACR 82-97).
Results: In 27/41 (66%) Lupus patients with KT the AFL profile was known: 15 AFL-positive patients (group I) and 12 AFL-negative patients (group II) were compared. Table 1 shows the characteristics of this patients. Dialysis and renal transplantation occurred at younger age in patients with negative AFL (p= 0.05 and p=0.02), respectively. Thrombotic events were presented only in patients of group I and the localizations were arteriovenous fistula, superior vena cava, dialysis catheter and central nervous system. Graft loss occurred in 25.9% of cases: 4 due to chronic graft nephropathy, 1 BK virus infection, 1 renal artery thrombosis (with positive AFL), and 1 focal segmental glomerulosclerosis. When both groups were compared, no statistically significant differences were found in causes of graft loss and graft survival (p=0.96). Six patients (22.2%) died: 3 infected, 2 cardiovascular diseases, 1 cancer. No differences in mortality between the groups were found, although it was associated with the presence of anti-B2 GPI IgG antibodies (p=0.043).

Table 1: General characteristics.

	Total (n=27)	Group 1 AFL+(N=15)	Group 1 AFL- (N=12)	P-value
Female n (%)	23(85.2%)	13(86.7%)	10(83.3%)	1
Ayes at dialysis (years) Median [Q1, Q3]	31.9[23.3, 38.0]	37.3[31.6, 40.4]	23.5[20.9, 30.7]	0.05
Aye at renal transplant(years) Median [Q1, Q3]	41.1[39.9 ,47.3]	43.7[41.6, 49.2]	32.7 [28.2, 38.1]	0.02
Peritoneal dialysis n(%)	1(3 .70%)	1(6.67%)	0(0%)	1
Hemodialysis n (%)	26 (96.3%)	14(93.3%)	12(100%)	1
Time from dialysis to transplant (months) Median [Q1, Q3]	99.2[66.9, 135]	101[74.6, 136]	89.3[54.5, 128]	0.29
Graft survival time (months) Median [Q1, Q3]	73.1[51.4, 109]	75.7[57.3, 111]	72.7[51.5, 98.8]	0.96
Thrombosis n(%)	4(14.8%)	4(26.7%)	0(0%)	0.11
Graftloss n(%)	7(25.9%)	4(26.7%)	3(25%)	1
Morality n(%)	6(22.2%)	4(26.7%)	2(16.7%)	0.66

Conclusions: AFL profile was studied in a 66% of KT lupus patients. Only the patients with positive AFL suffered thrombotic events (26%). Although no significant difference was found between groups related to graft loss, one patient with positive AFL presented a renal artery thrombosis. The presence of anti-B2 GPI IgG Ab was associated with mortality.
Keywords: Kidney transplant (KT), antiphospholipid antibodies (APL), thrombosis.

0103

SERONEGATIVE ANTIPHOSPHOLIPID SYNDROME OR SEVERE LUPUS FLARE: A DIAGNOSTIC CHALLENGE. CASE REPORT

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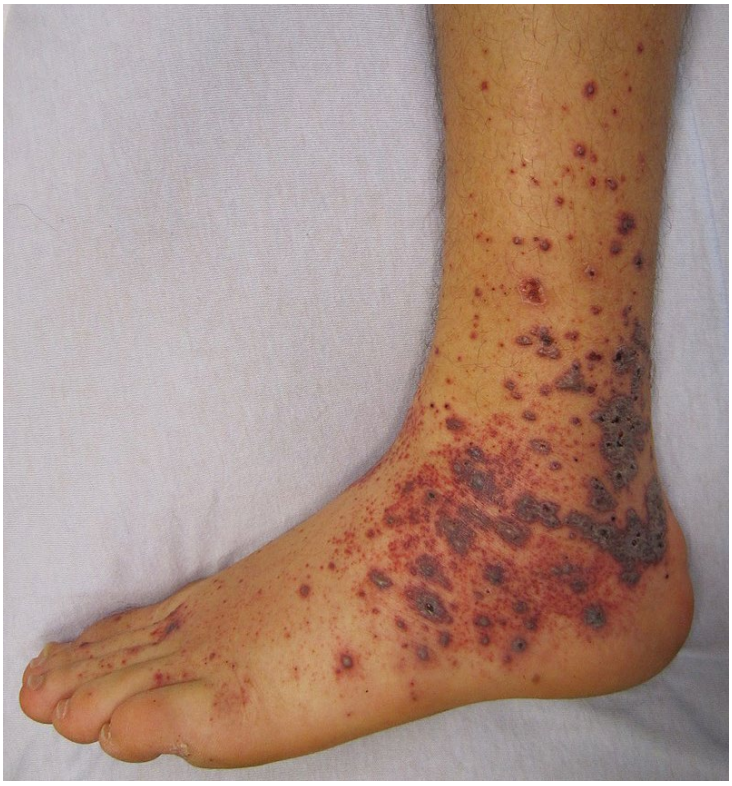
Case report: A 52 year-old women, Systemic Lupus Erythematosus (SLE) diagnosed 20 years ago, presented with photosensitivity, malar rash, hair loss, vasculitic skin lesions and polyarthritis. ANA 1/5120 nuclear pattern and anti ds-DNA positive. She received treatment with prednisone and hydroxychloroquine with adequate therapeutic response. - In 2012: Ischemic stroke not attributable to arterial hypertension or vasculitis. Magnetic resonance imaging (MRI): extensive right temporoparietal infarction with multiple ischemic images in the right supratentorial white matter. Secondary Antiphospholipid Syndrome (APS) was also ruled out due to negative antiphospholipid antibodies (aPL) (2 previous negative tests in 2003 and 2007). Treatment with aspirin and rosuvastatin were started. -In 2015: severe flare with skin and joint involvement, necrotic skin lesions in lower limbs and polyneuropathy (SLEDAI 2K: 17). Laboratory test showed hypocomplementemia, thrombocytopenia and thrombophilia tests (aPL, protein C and S deficiency, antithrombin III deficiency, factor V Leiden mutation, prothrombin 20210) were negative. Furthermore, demyelinating polyneuropathy in electromyography and vasculitis associated with multiple intraluminal thrombi in skin biopsy were found. She received treatment with methylprednisolone pulses 1 g/day for 3 days, cyclophosphamide i.v. 1 g monthly for 6 months and oral anticoagulation with improvement of clinical features. Due to cutaneous thrombosis, a history of stroke and multiple ischemic lesions on MRI, a diagnosis of seronegative APS was established. There were no new ischemic events to present.



Conclusions: We present a patient with a long history of thrombotic events, with seronegative aPL and some clinical and laboratory manifestations also attributable to SLE activity. The diagnosis of seronegative APS should be formulated only after the exclusion of other inherited and acquired thrombophilic conditions. Its recognition is important to adopt the most appropriate anti-thrombotic strategy to reduce the rate of recurrences. Several different antibodies to a number of antigens are involved in seronegative APS. The most studied antibodies are those against phosphatidylethanolamine, phosphatidic acid, phosphatidylserine, phosphatidylinositol, vimentin/cardiolipin complex, and annexin A5. The routine testing of these non-criteria antibodies has not yet been standardized for clinical practice.
Keywords: Seronegative antiphospholipid syndrome, systemic lupus erythematosus.

0104

RETINAL VEIN OCCLUSION IN A YOUNG PATIENT WITH CO-EXISTING ANTIPHOSPHOLIPID SYNDROME AND FACTOR V LEIDEN MUTATION: A CASE REPORT

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Retinal vein occlusion (RVO) is associated with arterial cardiovascular risk factors and no routine testing for heritable thrombophilia is recommended. However, some data suggests that up to 10% of patients with RVO fulfill Antiphospholipid Syndrome (APS) criteria and are associated with a high-risk "antiphospholipid profile." The utility of antiplatelet or anticoagulant therapy for RVO is unknown. Some reports suggest monotherapy with low-dose aspirin for those APS patients with no previous thrombotic event and anticoagulation is recommended for those with prior vascular or thrombotic events, based on a low level of evidence. To the best of our knowledge, no reports of concomitant APS and hereditary thrombophilia in an RVO patient have been published so far; and therefore, there is no clear evidence on how to treat these cases.
Case report: We describe a case of a 37-year old female patient with no previous history of thrombosis, obstetric events or cardiovascular risk factor who had an acute visual field defect and decreased visual acuity of the right eye. She was diagnosed with RVO by her ophthalmologist. She started treatment with intravitreal Bevacizumab and she was referred to our Hematology Department. We indicated treatment with aspirin. Thrombophilia studies were requested.
Results: Consistent results were found for two thrombophilias: Heterozygous Factor V Leiden mutation and positive serology for APS (13.6 U Anti-ß2-glycoprotein I antibodies, 27 GPL IgG and 12 MPL IgM anticardiolipin antibodies, negative Lupus Anticoagulant). Diagnosis of primary APS was confirmed on a second test 12 weeks after the initial laboratory tests.

Given the high thrombotic risk of the coexisting thrombophilias, the patient started treatment with acenocoumarol. In the following weeks, the patient achieved a partial improvement of the visual alteration.
Conclusions: The presentation of RVO in young patients with no classical risk factors requires a hematologic evaluation to determine a possible thrombophilic state that can explain the pathogenesis of the thrombosis. This is an unusual case of an RVO secondary to co-existing thrombophilia in a patient with no traditional risk factors. Further studies are needed to better define the optimal therapy of RVO in the setting of APS and other thrombophilias.
Keywords: Retinal vein occlusion, antiphospholipid syndrome, factor V Leiden.

0105

CLINICAL OUTCOMES IN ARGENTINIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

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To describe the clinical characteristics of a cohort of patients with SLE and aPL and/or secondary APS and to determine associated variables.
Patients and methods: SLE patients (ACR 1997 and/or SLICC 2012) with a minimum follow-up of 6 months, assisted between January 2008 and December 2018 in 10 rheumatology centers in Argentina were included. Patients with positive aPL (who did not meet criteria for APS) and patients with a diagnosis of secondary APS were selected. We evaluated demographic, clinical, laboratory variables, causes of death and mortality. Statistical analysis: descriptive statistics, Chi^2 test and Fisher's exact test. Regression analysis.
Results: 382 patients were included; 90% women and 82% mestizos. Mean time of disease duration was 4.1 ± 6.7 years, mean age at last visit or death was 37.2 ± 12.7 years and 92% of the patients received treatment with Hydroxychloroquine for a mean time of 53 ± 59 months. -Sixty patients (16%) had at least one positive aPL test and did not meet classification criteria for APS, 10% (6) had triple positivity. Eight patients had a history of miscarriage, 3 preterm deliveries and 1 arterial thrombosis. When evaluating clinical manifestations of SLE, a significant association was found between aPL and renal involvement (p=0.03), osteoarticular involvement (p=0.02) and hypocomplementemia (p=0.04). Four patients died: 2 from septic shock, 1 from pneumonia, and 1 from unknown cause. -Forty-three (11%) patients had diagnosis of APS; 26 thrombotic (20 arterial thrombosis, 4 venous and 2 mixed), 12 obstetric and 5 with obstetric and thrombotic manifestations, and 9.3% (4) had triple positivity for aPL Patients with APS presented a higher frequency of central nervous system involvement (p=0.01) and greater accrual damage measured by SLICC/SDI (p=0.02). Eight patients died; 2 due to catastrophic APS, 2 to septic shock, 1 to acute myocardial infarction, 1 to hemorrhagic stroke, 1 to respiratory distress, and 1 from unknown cause. Renal involvement (RR 3.3), cardiac involvement (RR 2.7), central nervous system involvement (RR 2.1), arterial thrombosis (RR 2.3), hyperlipidemia (RR 2.4), number of infections (RR 1.2) and last SLEDAI (RR 1.1) were independently associated with mortality in this group of patients with SLE. The presence of aPL and APS were not associated with mortality.
Conclusions: In this SLE cohort from Argentina, 11% met criteria for APS and 16% had at least one positive AFL determination. APS was associated with CNS involvement and accrual damage. - Antiphospholipid antibodies and APS were not associated with mortality, although 2 patients died of catastrophic APS.
Keywords: Lupus, antiphospholipid antibodies, antiphospholipid syndrome.

0106

DIGITAL ISCHEMIA IN ANTIPHOSPHOLIPID SYNDROME: ABOUT A CASE

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Antiphospholipid syndrome (APS) is a systemic autoimmune disorder with vascular and obstetric manifestations associated with thrombotic and inflammatory mechanisms, it can occur in association with other autoimmune diseases, mainly systemic lupus erythematosus (SLE). Acute or subacute ischemic compromise of one or more fingers is a clinical scenario that we occasionally face and in most cases, it presents with preserved peripheral pulses, so vascular pathology is usually initially ruled out.
Case report: 39-year-old woman from Salta capital, diagnosed in 2005 with SLE and APS, who debuted with thrombocytopenia, malar rash, photosensitivity, alopecia, headache, Raynaud's, positivity for antinuclear antibodies (homogeneous pattern) low C4, anticardiolipin IgG antibody and positive IgM in different determinations (29.9 U/ml-85.3 U/ml/41.4 U/ml-39.2 U/ml/74.5 U/ml-25.8 U/ml) positive lupus anticoagulant and KPTT prolongation. As background, she had two spontaneous abortions, hypothyroidism, in 2015 Evans syndrome with a good response to pulses of methylprednisolone + cyclophosphamide 1000 mg, and episodes of seizures with brain MRI without alterations. In January 2018, in outpatient follow-up with meprednisone 10 mg/day, hydroxychloroquine 400 mg/day, enalapril 20 mg/day, amlodipine 10 mg/day, folic acid 5 mg/day, lamotrigine 200 mg/day, levothyroxine 75 mg/day, aspirin 100 mg/day, with poor adherence. She was admitted for pain in both feet of 3 months of evolution with intensification 10 days before admission, on physical examination she presented ischemia/necrosis of the 2nd and 3rd toes of the left foot and of the 4th and 5th toes of the right foot. Methylprednisolone 500 mg pulses were administered for 3 days, cyclophosphamide 1000 mg, analgesia and anticoagulation. She evolved with a hypertensive crisis and sepsis with a focus on the skin and soft tissues (cellulitis on the left foot), for which she was admitted to the critical care unit where antibiotic treatment was started. On the second day of hospitalization, she was referred to the trauma service and amputation of the 2nd left toe was performed. Evolution: she completed 10 days of antibiotic treatment and requested voluntary discharge. She then administered two pulses of cyclophosphamide and due to lack of response, she continued with rituximab, later abandoning treatment.
Conclusions: Anticoagulation remains the cornerstone of thrombotic APS treatment. Immunosuppressive drugs may be a therapeutic option in patients with refractory APS symptoms who experience recurrent ET despite standard therapy. A better understanding of the pathophysiological mechanisms of APS will help identify new therapeutic targets and a balance between anticoagulation and immunomodulatory drugs for the different manifestations.
Keywords: Antiphospholipid syndrome.

0107

ANTIPHOSPHOLIPID SYNDROME SECONDARY TO LUPUS AND ITS RELATIONSHIP WITH RENAL FAILURE. DATA FROM THE LUPUS REGISTRY OF THE ARGENTINIAN SOCIETY OF RHEUMATOLOGY (RELESSAR-TRANS)

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The aims of this study are: A: To analyze within the RELESSAR registry those patients with antiphospholipid antibodies (aPLs) and/or Antiphospholipid Syndrome (APS) and their characteristics. B: To evaluate the association with Lupus Nephropathy (LN) and with renal failure defined as dialysis or renal transplant.
Methods: Retrospective, observational and analytical study.
Results: 1422 SLE patients were registered, 38.5% presented aPLs and 11.25% APS. A: APS or aPLs positive patients were older (42.6 vs 38.8 yo, p <0.001), had longer SLE evolution (112 vs 71.2 m, p<0.001), more prevalence of myocardial infarction (5.1% vs 0.7%, p<0.001), pulmonary embolism (6.4% vs 0.4%, p <0.001), stroke (19.4% vs 1.7%, p<0.001), peripheral arterial disease (4.5% vs 0.9%, p=0.003), vasculitis (14.6% vs 7.01%, p= 0.003), organic brain syndrome (10.3% vs 3.9%,

<0.001), headache (18.1% vs 11.8%, p=0.016), neuropathy (1.9% vs 0.3%, p=0.002), cancer (5.8% vs 2.4%, p=0.033) and gastroduodenal ulcers (10.1% vs 4.4%, p = 0.006). They had more hospitalization (2.29±1.6 vs 1.70±1.3, p<0.001), greater Charlson (2.43 vs 1.93, p<0.001) and damage indices 1.5 vs 0.9, p<0.001), more history of Rituximab treatment (10.1% vs 3.4%, p <0.001) and use of aspirin (42.0% vs 13.7%, p < 0.001) and oral anticoagulants at last evaluation (39.3% vs 2.6%, p < 0.001). B: 611 patients (43%) had LN. Patients with LN and APS or aPLs (28%) had more rebiopsies (7.1% vs 3.4%, p=0.053). 33/611 (5%) progressed to renal failure, they showed similar frequency of aPLs (28% vs 38.8%) and APS (12.1% vs 11.2%), had more arterial hypertension (54.5% vs 21.8%, p<0.001), hospitalizations (97% vs 53.7%, p <0.001), serious infections (48.5% vs 13.8%, p <0.001), Charlson index (3.00 vs 1.00), SLICC (4.00 vs 1.00, p <0.001) and mortality (21.9% vs 1.9%, p <0.001). In the multi regression model: stroke (12.5% vs 3.44%, p=0.027), use of cyclophosphamide (77% vs 28.2%, p <0.001) and recurrent NL (63.0 % vs 15.3%, p <0.001) remained associated to renal failure.

	SAF (N=160)	No SAF (N=1262)	P-value	Total (N=1422)
Lupus Nephritis, n(%)(*4)	63(39.4)	548(43.4)	0.598	611(43.0)
Class II	8(18.6)	70(15.8)		78(16.7)
Class III	10(23.3)	71(16.0)		81(16.7)
Class IV	20(46.5)	233(52.6)		253(52.1)
Class V	1(2.3)	32(7.2)		33(6.79)
Class IV and V	2(4.6)	13(2.9)		15(3.0)
Creatinine Median [Q1,Q3] (*920)	1.2[0.8, 1.6]	1.0[07, 1.9]	0.883	1.0[07,1.9]
Proteinuria, Median [Q1,Q3](*920)	3.5[1.5,15]	4.00[1.7,52]		3.9[1.7,5.1]
Arterial Hypertension n(%)(*67)	20(13.4)	155(12.9)	0.947	175(12.9)
Hematuria n(%)(*137)	5(3.4)	55(4.8)	0.430	60(4.6)
Renal relapse n(%)(*345)	15(121.1)	157(13.5)	0.262	172(16.0)
Re-biopsy , n(%)(*743)	5(7.1)	21(3.4)	0.053	26(3.8)
Hitolic change, n(%)(*1088)	5(17.2)	41(13.4)	0.571	46(13.7)
Microangiopathy (n%)(*48)	1(0.6)	6(0.4)	0.561	7(0.5)
Dialysis, n(%)(*124)				
Past	1(0.680%)	23(2.00%)	0.643	24(1.85%)
Present	2(1.36%)	18(1.56%)		20(1.54%)
Renal transplant, n(%) (*137)	1(0.676%)	2(0.176%)	0.307	3(0.233%)

Conclusions: Patients with SLE and APS had more severe disease. Renal failure was associated with surrogates of poor evolution; highlighting the relationship with stroke, recurrent NL and treatment with cyclophosphamide, but not with the presence of aPLs or APS.

Keywords: SLE, APS, lupus nephritis.

0108

THE ASSOCIATION OF ANTIPHOSPHOLIPID ANTIBODIES WITH PREVIOUS SARS-COV-2 INFECTION AMONG ELECTIVE KNEE REPLACEMENT PATIENTS

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Acute SARS-CoV-2 infection is associated with antiphospholipid antibodies (aPL), though it is unclear if aPL contribute to COVID19 hypercoagulability, or if aPL persist. We evaluated patients undergoing elective total knee replacement (TKR) for osteoarthritis, and compared aPL-positivity in those with and without previous SARS-CoV-2.

Patients and methods: We recruited patients between 10/2020 and 10/2021. Subjects were screened for previous SARS-CoV-2 infection with a serum nucleocapsid IgG, and positive cases matched on age (+/- 5y), gender, and body mass index (BMI kg/m^2 < 35 vs. > 35) to SARS-CoV-2 IgG negative controls. aPL (lupus anticoagulant [LA], anticardiolipin antibodies [aCL] IgG/M/A, and anti-ß2-glycoprotein-I [aß2GPI] IgG/M/A] were performed pre-operatively on all subjects, and 6 weeks later in the SARS-CoV-2 IgG positive cases.

Results: 73 SARS-CoV-2 cases were matched to 73 controls. Average age 63.2 years (SD 8.0), 53.4% women, BMI 31.9 kg/m^2 (SD 6.0), 78.8% Caucasian. 46/73 cases (63%) reported symptoms of COVID19; time between COVID19 and surgery was 243.3 days, (range: 17–597). A higher proportion of SARS-CoV-2 cases reporting > 5 symptoms had at least one aPL positivity at baseline (6/15 [40%] vs 17/58 [29%]) and at 6 weeks (3/6 [50%] vs 16/52 [31%]). 21% of SARS-CoV-2 cases and controls were positive for at least one aPL; the most common aPL type/isotype was aCL IgM (11% in SARS-CoV-2 positive cases and 15% in SARS CoV-2 negative controls). Other aPL types/isotypes ranged between 1-3%. Of 73 SARS-CoV-2 positive cases, 58 (80%) had 6-week follow-up; of 12 aPL-positive SARS-CoV-2 cases re-assessed at 6 weeks, 6/12 (50%) had disappearance of aPL (Table).

# of patients (%)	SARS-CoV-2 positive (baseline) N=73	SARS-CoV-2 positive (6 weeks) N=58*	SARS-CoV-2 negative (baseline) N=73
LA Bordeline (+)**	1 (1%)	-	1 (1%)
LA (+)***	1 (1%)	-	0
aCL IgG (+)			
• 20-39U	1(1%)	1/1	0
•> 40U	2 (3%)	0/1	0
• Mean (range) (+ve only)	44U (34-57)	47U	-
aCL IgM (+)			
• 20-39U	5 (7%)	4/4	11 (15%)
•> 40U	3 (4%)	0/2	-
• Mean (range) (+ve only)	49 U (21-50)	30 U (24-39)	25 U (20-36)
aCL IgA (+)			
• 20-39U	1 (1%)	0/1	1 (1%)
•> 40U	0	-	0
• Mean (range) (+ve only)	26 U	-	24U
aβGPI IgG (+)			
• 20-39U	1 (1%)	1/1	0
•> 40U	1 (1%)	0/0	0
• Mean (range) (+ve only)	50U (24-76)	21U	-
aβGPI IgM (+)			
• 20-39U	2 (3%)	1/1	1 (1%)
•> 40U	2 (3%)	1/1	1 (1%)
• Mean (range) (+ve only)	67U (24-150=	35U (21-48)	50U (37-62)
aβGPI IgA (+)			
• 20-39U	1 (1%)	-	2 (3%)
•> 40U	0	-	0
• Mean (range) (+ve only)	37U	-	30U (22-38)
At least one aPL (+)	15 (215)	6 (10%)	13 (21%)

Conclusions: Regardless of previous SARS-CoV-2 infection, approximately one-fifth of patients undergoing elective TKR had positive aPL, mostly low level (20-39U) aCL IgM. Half of SARS-CoV-2 nucleocapsid IgG positive patients who were initially aPL-positive were aPL-negative at 6-week follow-up. Our ongoing study will assess whether aPL persist at 6 months, if number of COVID19 symptoms are associated with aPL persistence, and if aPL are associated with any clinically relevant outcomes in TKR patients after SARS-CoV-2.

Keywords: Anti-phospholipid, novel Corona virus, Knee arthroplasty.

0109

LUPUS ANTICOAGULANT-HYPOPROTHROMBINEMIA SYNDROME ASSOCIATED WITH SLE.

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Lupus anticoagulant-hypoprothrombinemia syndrome (LAHPS) is a rare and acquired disorder characterized by Factor II deficiency due to anti-prothrombin antibodies and the presence of lupus anticoagulant (LA). It is more frequent in pediatric age than in adults, mostly in women. It is mainly associated with autoimmune diseases and infections.

Case report: 19-year-old male with no prior comorbidities. Began with macroscopic hematuria, without other symptoms, he consulted with prolonged PT and aPTT, Factor II deficiency and positive lupus anticoagulant, and normal renal function. He was treated with meprednisona 40 mg in a descending dose until suspension, not repeating bleeding. After a month he was admitted to hypertension, with purpura in the lower limbs, 2/6 edema Godet +. Splenomegaly 177mm, tricytopenia, renal failure, proteinuria, hypocomplementemia, prolonged PT and aPTT. Microscopic hematuria. Renal ultrasound with increased echogenicity and normal size. Renal Doppler and splenoportal axis without particularities. In the context of nephritic syndrome, with clinical criteria of SLE ACR / EULAR 2019: 13 (Leukopenia: 3, low C3 and C4: 4, AL +: 2, proteinuria 1.5 gr / 24 hrs: 4), he received methylprednisolone´s pulses and hydroxychloroquine. A skin biopsy reported purpuric superficial perivascular dermatitis with signs of leukocytoclastic vasculitis. Renal biopsy: diffuse lupus nephropathy class IV, IA 6/24, CI 0/12. He started receiving cyclophosphamide´s pulses (1 gr). He evolved without presenting bleeding, with improvement in blood count, coagulogram and renal function parameters.

Laboratory variables	1st admission	2nd admission	
	Pre treatment	Pre treatment	Post Corticoid
Hb GB/ lymphocytes Platelets	13,5g/dL 5800mm^3/40% 188.000mm^3	11,2g/dL 2900mm^3/33% 126.000mm^3	10g/dL 4600mm^3/13% 195.000mm^3
Urea/ creatinine	43/0,9 mg/dL	69/1,87mg/dL	50/1.4mg/dL
aPPT AL/ACL/B2GP	91seg Positive /Neg/Neg	74seg Positive /Neg/Neg	38seg
TP/RIN	25% /1,98	40%1,93	68%/1,3
Factor II (vn 70 -120%)	13%	19%	
DNA	Negative	Positive 1/320	
SM	Negative	Positive weak	
ANA	1/1280 mottled	1/640 homogeneous	
Proteinuria 24hs.	Negative	1,55 gr	
Complement	ND	C3: 14 C4: 2	

Conclusions: We present a case of a patient with SLE and a rare association of lupus anticoagulant and anti-prothrombin antibodies. In a patient with bleeding, associated with hypoprothrombinemia and LA, LAHPS should be suspected. Screening for autoimmune diseases, especially SLE, is highly suggested. Early initiation with high doses of corticosteroids can reverse the hemorrhagic manifestations.

Keywords: Lupus- anticoagulant-hypoprothrombinemia.

0110

ARGENTINE REGISTRY OF ANTIPHOSPHOLIPID ANTIBODIES OF THE ARGENTINE SOCIETY OF RHEUMATOLOGY (GESAF-SAR): BASELINE AND PROSPECTIVE DATA OF THE FIRST 329 PATIENTS

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To describe sociodemographic, clinical and laboratory characteristics of baseline and follow-up visits of patients with aPL from the Argentine Registry of aPL, coordinated by APS Study Group of Argentine Society of Rheumatology.

Patients and methods: A multicenter, prospective study of aPL carriers was performed. Inclusion criteria were positive aCL with levels 20-40 GPL or MPL in at least two separate determinations 12 weeks apart, or >=40 GPL or MPL in at least one determination and/or positivity for new aPL. Twenty-five Argentine centers participated. Demographic, clinical manifestations, treatments, activity and mortality were analyzed at baseline, at 12 (T1) and 24 months (T2). A descriptive cross-sectional analysis of data collected from May 2019 to February 2022 was performed.

Results: 329 patients were analyzed, 279 (84.8%) were female with mean age at inclusion of 32.9 years (SD 11.4) Ninety (27.4%) patients classified as Obstetric APS, 115 (35.0%) as Thrombotic APS and 29 (8.8%) as Thrombotic and Obstetric APS, 32 (9.7%) patients had aPL with "non-criteria" manifestations and 38 (11.6%) positive aPL without clinical manifestations. 120 (38.8%) patients had primary APS and 84 (27.2%) associated with autoimmune disease (AID). 67 patients (21.8%) developed arterial thrombosis, 89 (29.3%) venous thrombosis, 11 (3.61%) small vessel disease and 5 (1.52%) CAPS. One hundred seventy-nine women had at least one pregnancy; 249 (45.1%) of 552 pregnancies had live births, 49 (8.88%) preterm delivery (< 34 weeks), 191 (34.6%) pregnancy loss (< 10 weeks) and 105 (19.02%) (> 10 weeks) at baseline. The aPL profile was 207 (62.9%) for LA, 182 (55.3%) for aCL IgG, 160 (48.6%) for aCL IgM, 139 (42.2%) for aB2GLPI IgG and 96 (29.2%) for aB2GLPI IgM. 106 (32.2%) patients continued their follow-up at T1, 15 (4.6%) were lost to follow-up and 6 (1.8%) patients died within 12 months. There were 68 follow-up visits at T2, one patient died during this period. At T1, 1 venous thrombotic event was recorded and 9 (10.3%) patients had 1 pregnancy, of which 100% were live births. At T2, 2 venous thrombotic

events were recorded, 6 (10.7%) women had 1 pregnancy with 4 live births and 1 abortion (<10 weeks). Regarding SARS-Cov2 infection, 13 (12.3%) were recorded at T1, and 13 (19.1%) at T2. 82 patients (47.1%) were vaccinated for Covid-19, 27 (25.5%) at T1, 55 (80.9%) at T2. Mild adverse effects were described, without association with thrombotic events.

Table: Baseline sociodemographic characteristics.

	Total: (N=329)
Age at inclusion Mean (SD)	4.17 (13.0)
Age at meeting criteria Mean (SD)	36.6 (11.7)
Age at first clinical manifestation Mean (SD)	32.9 (11.4)
Female Sex, n(%)	279 (84.8)
Ethnic distribution n(%)	
Amerindian	8 (2.4)
Caucasian	135 (41.0)
Mestizo	150 (45.6)
Arterial Hypertension, n(%)	72 (23.3)
Diabetes, n(%)	13 (4.2)
Dyslipidemia, n(%)	44 (14.2)
Obesity (BMI>30) n(%)	60 (20.4)
Smoking, n(%) (active smoker and ex-smoker)	61 (1.7)
Associated autoimmune desease[1] n(%)	147 (51.8)
Systemic Lupus Erythematosus n(%)	123 (75.0)
Socioeconomic level n(%)	
Low	23 (7.0)
Medium-high	48 (14.6)
Medium	129 (39.2)
Medium-low	74 (22.5)
Education Mean (SD)	14 (22.5)
Classification at cohort entry n (%)	
Obstetric APS	90 (27.4)
Thrombotic APS	115 (35.0)
Thrombotic and Obstetric APS	29 (8.8)
aLP with non-criteria manifestations	32 (9.7)
Asymptomatic aPL	38 (11.6)

Conclusions: We updated baseline and follow-up data of GESAF-SAR registry patient. The majority of patients had thrombotic and obstetric APS with small group of asymptomatic aPL. Clinical and immunologic characterization as well as the follow of patients is very relevant for clinical practice.

Keywords: Argentine Registry, APS Study Group.

0111

FREQUENCY OF DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A PROGRAM OF CONTINUOUS EVALUATION OF PATIENTS WITH ARTHRALGIAS AND DETECTION OF ANTIPHOSPHOLIPID ANTIBODIES

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Arthralgias are a frequent reason for consultation in medical practice in the Rheumatology office. Probable etiologies include entities with a good prognosis, such as osteoarthritis (OA), to inflammatory diseases with high morbidity and mortality, such as rheumatoid arthritis (RA) and systemic autoimmune diseases (SAIDs). The latter include pathologies in which diagnosis is usually difficult and in which speed is essential to minimize complications. Among them, systemic lupus erythematosus (SLE) is the one most frequently associated with the presence of antiphospholipid antibodies. Due to the probable prognostic implications, it is of interest to investigate its presence and evaluate the existence of differential clinical characteristics between these patients and the rest of the patients with SLE in the cohort. Objectives: To describe the frequency of SLE in a cohort of patients who consulted for arthralgia. Detect the presence of antiphospholipid antibodies in patients with a recent diagnosis of SLE.
Patients and methods: Prospective cohort study, where patients over 18 years of age who were admitted for polyarthralgia to a comprehensive evaluation program were included. At the first (baseline) visit, the following were performed: laboratory studies (including acute phase reactants, RF (rheumatoid factor), ACPA, and ANA), X-rays of the hands and feet, ultrasound of the hands with power Doppler technique, and a rheumatological interview where Sociodemographic data (age, sex), clinical data (time of evolution of arthralgia, comorbidities) and clinimetry (global VAS of the patient, joint count, HAQ) were collected. Each evaluator was unaware of the data from the other studies performed (laboratory, imaging, and clinical). In the subsequent visits (only patients who completed at least 2 visits were included) the results were evaluated and the definitive diagnosis of EAS, ANI or RA was established or not. In turn, patients with a final diagnosis of SLE underwent a measurement of IgM and IgG anticardiolipin antibodies (Ab), IgM and IgG anti-B2 Microglobulin Ab, and lupus anticoagulant.
Results: A total of 1052 patients were included, where 74.4% were female and the mean age was 53.6 years, SD: 14.5. The overall median delay to diagnosis was 38 months and 60% of the total had comorbidities.
Conclusions: The frequency of SAEs in our arthralgia cohort was 9.7% (101), where SLE represents 45% of them, among these 10% (CI: 0.6-17) had antiphospholipid antibodies at the time of diagnosis. The history of ischemic stroke was the most important differential clinical characteristic with the rest of the patients with SLE in the cohort.
Keywords: Systemic lupus erythematosus, antiphospholipid antibodies.

0112

ACUTE MYOCARDIAL INFARCTION AS THE FIRST CLINICAL MANIFESTATION OF ANTIPHOSPHOLIPID SYNDROME IN A 5 YEAR OLD CHILD. A CASE REPORT

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Antiphospholipid Syndrome (APS) is a systemic autoimmune disease characterized by both venous and arterial thrombotic events and obstetric complications that affect various organs and systems in patients with positive antiphospholipid antibodies (aPL). In pediatrics, it can present as deep vein thrombosis, pulmonary thromboembolism, renal thrombotic microangiopathy, livedo reticularis and chorea, among others. Coronary ischemic events in patients with APS have not been frequently reported in children. We present a pediatric patient with AMI as the first manifestation of APS.
Case report: A 5-year-old female patient in follow up by hematologists due to hemolytic anemia (Coombs+) and coagulogram alterations (KPTT/quick) since she was 4 years old, asymptomatic from the clinical point of view. She required hospitalization because of general malaise, with worsening of the anemia and persistence of the alteration in the coagulogram. On physical examination, she presented tiredness, skin pallor without any other associated clinical manifestation. In the immunological exams, severe hypocomplementemia was found, along with FAN +1/1280 (homogeneous), RF negative, Anti DNA +1/20, Ro+, aCL IgM/G+, B2GP IgM >300, B2GP IgG 27, Lupus anticoagulant +++, VDRL 8dils. Direct Coombs: +++. Other laboratory parameters without relevant findings. An initial cardiological evaluation revealed minimal pericardial effusion, with normal coronary arteries. Not meeting the criteria for Juvenile Systemic Lupus Erythematosus at the onset of APS, initial treatment consisted of red cell transfusion and methylprednisolone pulses, followed by meprednisone at 2mg/kg/day PO. During of her hospitalization she presented an episode of precordial pain that radiated to both upper limbs, which responded to a double dose of NSAIDs and morphine. Re-evaluated by cardiology, the ECG showed ST elevation in the inferior face D2-D3 and aVF with a Q of 8mm and PR 0.18mm, ST depression in the right cavities (V3, V4R, V1, V2) and lateral face. Echocardiogram: dyskinesia LVS with altered posterior face contractility ddvi 4 dsvi 3.2, left coronary artery 0.34 maximum

in its origin and length, CD 0.23. Cardiac enzymes: troponin: 17750 ng/ml, elevated CPK- Mb. Assuming acute myocardial infarction (AMI), she was transferred to intensive care unit for cardiac monitoring and treated with enoxaparin 2U/kg/day every 12h SC, gamma globulin 1gr/kg and steroids PO as treatment of the APS and support of the ischemic event. In the following controls, as a cardiological sequela, dilated cardiomyopathy of 4 mm, moderate MR 18 mmHg was detected. To date, in treatment with enalapril and spironolactone, she was switched to ASA and acenocoumarol, with steroids in tapering.
Conclusions: Acute Myocardial Infarction is a rare presentation of APS in pediatric patients. The report of this clinical case highlights the importance of systemic involvement and monitoring of noble organs in this syndrome.
Keywords: Acute myocardial infarction, pediatrics, antiphospholipid syndrome.

0113

POSITIVE LUPUS ANTICOAGULANT TEST IN A PATIENT WITH ADULT-ONSET STILL'S DISEASE WITH ADENOVIRUS INFECTION: A CASE REPORT

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Case report: A 39 years old, female was admitted due to 72 hours of fever of up to 39º degrees associated with peripheral edema in the hands and feet and pruritic erythematous-papular rash. Laboratory evidenced leukocytosis of 13,500 white blood cells per mm^3 with predominance of neutrophils (80%), erythrocyte sedimentation rate was 50 mm/hr and increased C reactive protein with no evidence of anemia or thrombocytopenia. Imaging, bacteriological and mycological studies and test for Sars Cov2 were negative. Viral and toxoplasmosis serologies were negative with the exception of adenovirus test which showed mild positive values for immunoglobulin M and high values for immunoglobulin G. Antinuclear antibodies, Rheumatoid Factor and ANCAs were negative. The patient presented elevated ferritin; however, the assessment of glycosylated ferritin was not performed. With suspected Adult-onset Still's disease (AOSD), treatment with prednisone 40 mg was indicated with resolution of the fever. Oral methotrexate 15 mg and folic acid 5 mg weekly at discharge were indicated. Fifteen days later, the patient attended a medical check-up, in which there was evidence of improvement in skin lesions and arthralgia, and the patient did not report new fever records. A new laboratory was performed in which antinuclear antibodies, rheumatoid factor and ANCA antibodies remained negative. A lupus inhibitor study was requested, which was positive, with negative anti cardiolipins and anti-beta 2 glycoproteins. Gradual reduction of prednisone is started. Interconsultation with Hematology is requested for a positive lupus inhibitor. Hematology requested new laboratories 12 weeks later which reiterated negative anticardiolipins and beta 2 glycoproteins and lupus inhibitor remained positive. Expectant management was decided. In the following control two months later, the patient persisted in clinical and laboratory remission and for this reason it was decided to suspend oral corticosteroids.
Results: Most studies of AOSD are limited to isolated reports or small cohorts of patients. Virus infection is a primary factor that has been implicated in the initiation of autoimmune diseases. Elevated serum ferritin is frequent in AOSD patients, being present in up to 70% of them, and these elevations correlate well with disease activity. Four clinical conditions may be associated with high ferritin levels the macrophage activation syndrome (MAS), AOSD, catastrophic antiphospholipid syndrome (CAPS), and septic shock. These disorders are characterized by life-threatening hyperinflammation with high levels of ferritin and cytokine storm, clinically presented as multiorgan failure. Jaeger et al in 1993 described the presence of positive lupus anticoagulant test in 4 children one week after the clinical onset of adenovirus infection. All coagulation abnormalities returned to normal within 4 to 12 weeks. There was no clinical evidence of thrombosis. No reports of prevalence of antiphospholipid antibodies and lupus anticoagulant test were found in patients with Still's disease.
Conclusions: Although there are only few reports of positive tests for antiphospholipid syndrome in patients who suffered from adenovirus infection we cannot forget that most adenovirus infections go unnoticed due to the low number of symptoms and for this reason it is very complex to analyze the true impact on the pathophysiology of autoimmune diseases. However, the role of ferritin as an acute phase reactant and its increase in Still's disease as well as in CAPS allows us to ask whether the positivity of the lupus anticoagulant test in this patient is more than a mere coincidence.
Keywords: Still's disease, lupus, adenovirus.

0114

INCIDENCE OF RECURRENT THROMBOTIC EVENTS IN A LARGE SINGLE-CENTER PRIMARY ANTIPHOSPHOLIPID SYNDROME COHORT: RESULTS FROM APS-RIO AFTER 600 PATIENTS-YEAR OF FOLLOW-UP

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The aim of this study is to estimate the incidence rate of new thrombotic events in a large single center prospective cohort of PAPS patients after approximately 5.5 years of its creation, and to understand risk factors associated with the occurrence of a first incident thrombotic event.

Patients and methods: All patients fulfilled the updated criteria for PAPS. For the calculation of the incident thrombosis rate, patients could contribute with more than one event since all of them were continuously at risk of thrombotic events. For the analysis of risk factors associated with the occurrence of a first incident thrombotic event, patients were followed until the occurrence of a first thrombotic event (incident cases) or until their last outpatient visit (non-incident cases). For statistical analysis, we used Kaplan-Meier curves, log-rank test, and Cox proportional hazards (including variables with p<0.10 in the univariate analysis), as appropriate.

Results: We included 135 PAPS patients. Most of them were females (85.2%) and the mean age at baseline was 43.2±12.6. Arterial hypertension and diabetes were present in 40.0% and 10.4%, respectively. Total follow-up was 601.8 patients-year. During our study, 23 thrombotic events (10 ischemic strokes, 12 venous thromboses, and 1 thrombotic microangiopathy) were diagnosed in 20 patients, which led to an incidence rate of 3.82 cases per 100 patients-year. INR values at the time of thrombosis was known in 19 events; in 12 of them (63.2%), INR was within the proposed target. When we analyzed the occurrence of a first thrombotic event, the cumulative incidence was 14.8% at the end of 66 months. The mean time for the occurrence of a first thrombotic event was 33.1±19.4 months. In the multivariate analysis, diabetes independently correlated with the occurrence of a first thrombotic event (HR 3.3, CI95% 1.1-5.6, p=0.021) (Table1/Figure 1).

Table 1: Univariate and multivariate analysis of potential risk factors associated with incident thrombosis in PAPS patients.

Variables	Univariate			Multivariate			
	HR	95% CI	P value	B (slope)	HR	95%CI	P value
Age (baseline)	1.02	0.98-1.05	0.412				
Gender	0.57	0.19-1.72	0.320				
Race	0.71	0.28-1.79	0.459				
Livedo	2.31	0.94-5.65	0.067	0.834	2.30	0.94-5.64	0.068
Thrombocytopenia	0.75	0.10-5.62	0.781				
Hypertension	1.72	0.71-4.15	0.229				
Diabetes	3.32	1.20-9.16	0.020	1.196	3.31	1.12-5.64	0.021
Hyperlipidemia	1.91	0.79-4.58	0.150				
Obesity (BMI≥30)	0.73	0.29-1.83	0.501				
Triple positivity	0.33	0.08-1.41	0.133				
aGAPSS	0.95	0.85-1.07	0.389				

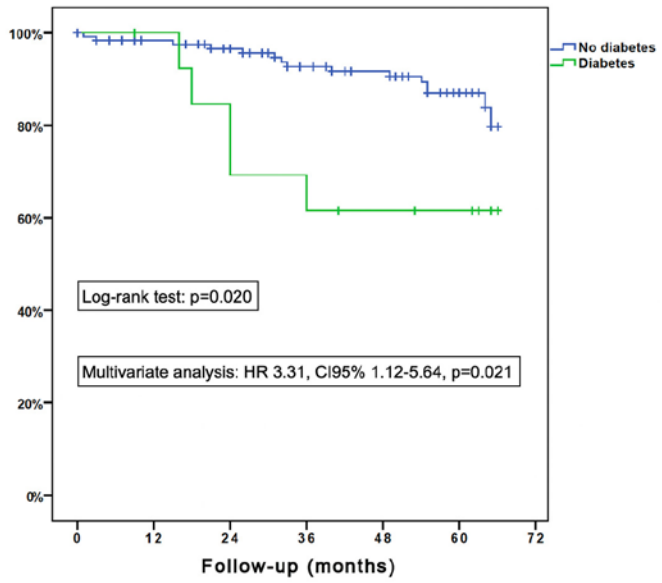

Figure: Survival analysis comparing PAPS patients with without diabetes.

Number at risk of event

Follow up (mo)	12	24	36	48	60	66
Diabetes	13	12	9	7	6	1
No diabetes	113	194	92	84	64	4

Conclusions: Incident thrombotic events were common in our cohort, most of them with INR within target. Diabetes was associated with a 3-fold risk of a new first thrombotic event in primary APS patients.
Keywords: Antiphospholipid syndrome, cohort, thrombosis.

0116

"EXTRA-CRITERION" MANIFESTATIONS DUE TO NEPHROPATHY DUE TO APS: CASE REPORT

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Antiphospholipid syndrome (APS) is an acquired autoimmune thrombophilia characterized by recurrent vascular thrombosis and/or pregnancy morbidity, in the presence of persistent antiphospholipid (aPL) titers. Clinical phenotypes outside the Sapporo classification criteria have been evaluated, including 5 clinical profiles: asymptomatic positivity for aPL; obstetric APS; thrombotic APS; microvascular APS; catastrophic APS (CAPS); and nonthrombotic APS: thrombocytopenia, heart valve disease. A case of nephropathy associated with APS is presented
Case report: A 42-year-old man, with high blood pressure, chronic kidney disease and myocardial infarction, was admitted to the emergency room due to a 3-day history of dysarthria, motor aphasia, dysgraphia associated with right hemiparesis and syncopal episodes; normotensive physical examination, no arrhythmias, no skin lesions, neurological examination with mental examination with motor aphasia, agraphia, alexia, strength and reflexes 4 limbs normal, brain MRI with acute ischemic event (Image), extension studies with thrombocytopenia, positive aPL , and proteinuria (Table); A renal biopsy was taken with findings of membranoproliferative nephropathy and thrombotic microangiopathy. With the studies obtained, cerebrovascular accident (CVA) of the left middle cerebral artery (LMCA) was considered as a thrombotic manifestation of APS with a first triple positive set and "extra-criterion" manifestations due to severe thrombocytopenia and nephrotic syndrome secondary to APS nephropathy. Anticoagulation is started, but a decrease in platelets to 1,500 is documented, steroid pulses are indicated, without response. Subsequently, he presented a new acute event with right hemiparesis, with MRI with stroke in new territories of the IMCA with hemorrhagic transformation, immunoglobulin was indicated due to refractoriness to steroids with recovery of platelet count, and initiation of cyclophosphamide due to renal involvement, presenting adequate medical evolution.

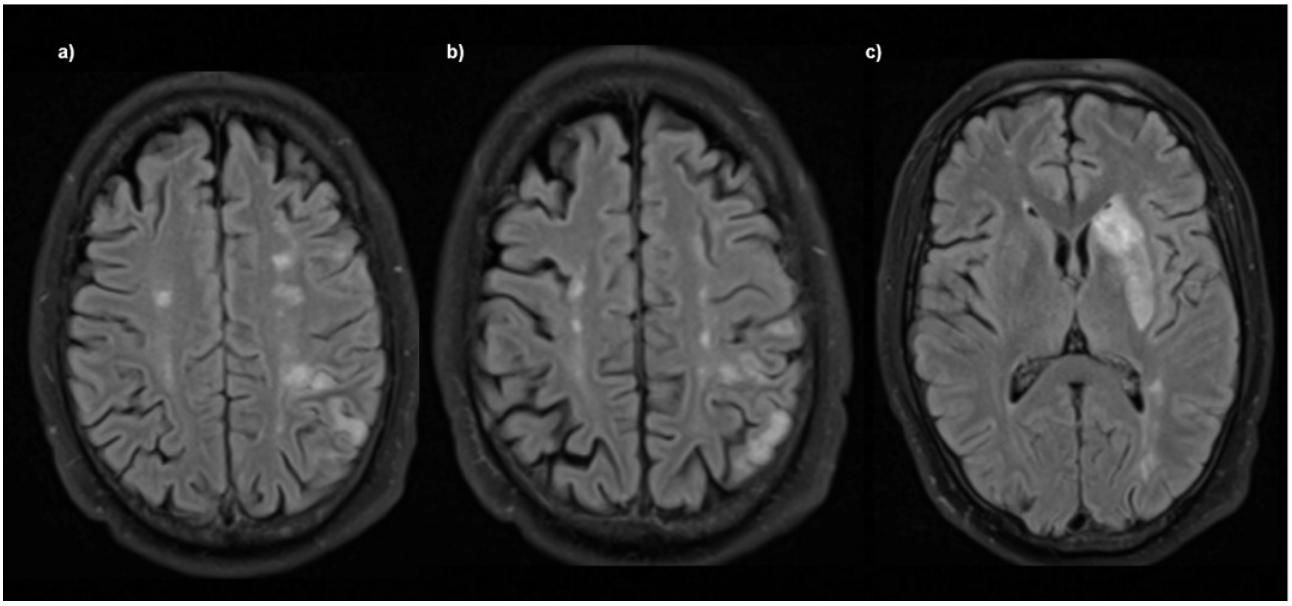

Image: Magnetic resonance imaging.

Laboratory Test	Value	Reference Value
Hemoglobin (g/dL)	15	12-16
Platelet count	37.000	150.000-450.000
Peripheral blood smear	No abnormal cells	-
BUN (mg/dL)	33	12-20
Creatinine(mg/dL)	1.8	0.7-1.0
Clinical urine test	Protein 150 mg/dl , red blood cells 5-10	
partial thromboplastin time (ptt) seg	94	30
24-hours urine proteins (gr)	4.9	0-0.15
ANA	AC-0	-
AntiDNA (Ul/mL)	0	0-200
Anti Ro (Ul/mL)	1.26	0-20
Anti La (Ul/mL)	1.25	0-20
AntiSM (Ul/mL)	1.76	0-20
AntiRNP (Ul/mL)	2.24	0-20
Dilute Russell Viper Venom Time (Ratio)	2.02	0-1.2
B2 Glycoprotein IgG (Ul)	25	>20
B2 Glycoprotein IgM (Ul)	5	>20
Anticardiolipin IgG (GPL)	45	>40
Anticardiolipin IgM (GPL)	18	>40
C3(mg/dL)	122	85-113
C4(mg/dL)	37	15-67

Conclusions: The extra-criterion microthrombotic manifestations of APS include kidney involvement due to aPL nephropathy, it has a low prevalence, it is characterized as a vascular nephropathy with occlusive lesions of small vessels, related to refractory arterial hypertension, CKD, hematuria, proteinuria associated with positivity of lupus anticoagulant, hypocomplementemia, with indication of immunomodulation.

Keywords: Antiphospholipid syndrome, nephropathy, thrombotic microangiopathy.

0119

INCIDENCE AND PREVALENCE OF ANTIPHOSPHOLIPID SYNDROME IN A HEALTH MANAGEMENT ORGANIZATION (HMO) IN ARGENTINA

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Epidemiological data on Antiphospholipid Syndrome (APS) is scarce. Our objective was to assess incidence and prevalence rates of APS using data from a tertiary university hospital-based health management organization (HMO).
Patients and methods: APS cases were identified by different methods: patients (a) with diagnosis of APS, recurrent abortions and/or fetal death in HMO electronic medical records, (b) with a Lupus anticoagulant (LA), IgG/IgM anticardiolipin and/or IgG/IgM ß2glicoprotein positive test in laboratory database, (c) included in the Institutional Registry of Thromboembolic Disease. Medical records of all cases retrieved by these methods were reviewed, definite APS was diagnosed if updated international consensus (Sydney) classification (ICS) criteria were fulfilled. Global, age-specific, and sex-specific incidence and prevalence rates were calculated for members of the Hospital Italiano Medical Care Program (HIMCP). For the incidence study members with continuous affiliation = 1 year from January 2000 to January 2015 were followed until he/she voluntarily left the HIMCP, APS was diagnosed, death, or study finalization. Prevalence was calculated on January 1st 2015.

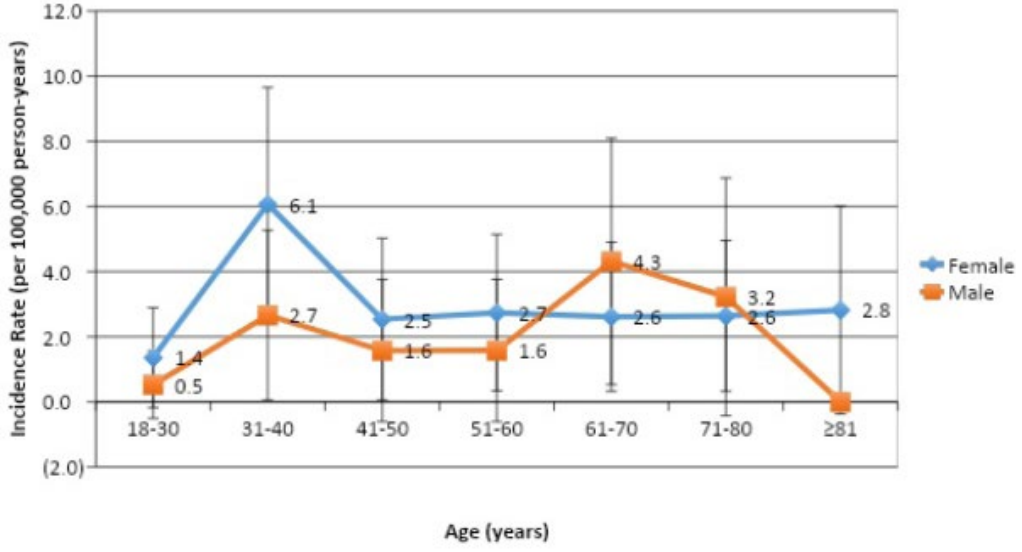

Figure: APS incidence rates per gender 100,000 persons-years.

Results: A total of 349,775 persons contributed a total of 2,073,438 person-years (py). 53 incident cases of APS were identified during the study period. Incidence rates are reported as cases per 100,000 py: APS overall incidence rate was 2.6 (95% CI 1.9-3.2). In our population, age-specific incidence and prevalence rates in female patients peaked in the third decades of life (associated with obstetric morbidity) and in male in the sixth decades. On January 1st 2015, 55 APS prevalent cases were identified from a denominator population of 135,750 HIMCP members. Prevalence rate was 40.5 per 100,000 persons (95% CI 29.8-51.2).
Conclusions: Incidence and prevalence rates were similar to previous reports. Incidence and prevalence rates in women were higher in the young population, associated with obstetric morbidity.
Keywords: Antiphospholipid syndrome.

0120

IMPACT OF ANTIPHOSPHOLIPID ANTIBODY PROFILE ON DAMAGE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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The aim of this study is to evaluate the impact of the Antiphospholipid Antibodies (aPL) profile on damage in patients with systemic lupus erythematosus (SLE).

Patients and methods: A retrospective analysis of patients with SLE according to the 2012 Systemic Lupus International Collaborating Clinics (SLICC) Criteria, who were included in the Argentine Registry of aPL of the Argentine Society of Rheumatology (SAR) and the Lupus Registry of the SAR, was performed. Sociodemographic, clinical, serological variables, SLE activity using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), and damage measured by the SLICC Damage Index (SDI) were evaluated. The conclusions were obtained with a significance level of 5%.

Results: 1,690 patients were included, of whom 1,541 (91.12%) were women, with a median age of 37.0 [27.6, 47.2] years. 458 (27%) met the Sydney Classification Criteria for Antiphospholipid Syndrome (APS) (203 thrombotic, 217 obstetric, and 38 thrombotic and obstetric). Regarding the aPL profile, 69 (4.08%) had triple positivity, 140 (8.28%) double positivity, 198 (11.72%) one aPL positivity, and 1283 (75.92%) negative aPL. The median of the SDI = 1 [0, 1.00]. 917 (54.26%) patients presented damage, being in 78.95% (n=724) of the cases moderate (SDI =1-2), and in 21.04% (n=193) severe (SDI >2). Median SLEDAI was 2.00 [0, 4.00] and adjusted Global Antiphospholipid Syndrome Score (aGAPSS) 1.00 [0, 4.00]. Patients with negative aPLs had a median SDI of 0 [0, 1.00] while those with positive aPL had a median SDI of 1.00 [0, 2.00] (p< 0.001). No statistically significant differences were found between the aPL profile and SLEDAI The variables associated with the SDI were studied after adjusting a logistic regression model. Probability of presenting harm (SDI >0) was 6% higher for each year of SLE duration [OR= 1.06 CI95 (1.04-1.09)]; 2.6 times higher for those with hypertension vs without hypertension [OR= 2.63, CI95 (1.80-3.88)]; 50% higher for those receiving maximum prednisone dose >10mg/day vs ≤10mg/day [OR= 1. 51, CI95 (1.04-2.20); 2.9 times higher for thrombotic APS vs Obstetric APS [OR=2.898, CI95(1.67-5.22)], 68% higher for Single positive [OR= 1. 67, CI95 (1.03-2.82)] or Double positive [OR= 1.68, CI95 (0.93-3.11) vs Negative patients; and 93% higher for those with Triple positive vs Negative [OR= 1.94, CI95(1.00-3.88)].

	SDI 0 (N=773)	SDI1-2 (N=724)	SDI>2 (N=193)
Age media [Q1,Q3]	38 [25.6,43.8]	39.2 [29.1,49.4]	44.4 [33.4,55.3]
Female Sex, n (%)	722 [93.4]	644 (89.0)	175 (90.7)
SLEDAI Median [Q1,Q3]	1.00 [0,4.00]	2.00 [,.4.00]	200 [0,6.00]
Duration of SLE Median [Q1,Q3]	5.00 [2.00,10.0]	8.00 [3.00,14.0]	120 [6.00,20.0]
aGAPSS Median [Q1,Q3]	0 [0,3.00]	1.00 [0,5.00]	3.00 [0,500]
Arterial Hypertension, n(%)	109 [14.5]	195 [27.6]	77 [41.6]
Dyslipidemia, n(%)	100 (15.1)	136 (20.9)	53 (30.6)
Diabetes n(%)	12 (1.55)	32 (4.42)	13 (6.74)
Smoking, n(%)	131 (18.2)	161 (23.9)	48 (25.9)
Aspirin, n(%)	80 (11.9)	156 (25.3)	34 (21.1)
Oral Anticoagulants, n(%)	24 (3.39)	76 (11.6)	26 (14.6)
Corticosteroids, n(%)	400 (55.3)	403 (60.1)	139 (76.0)
Prednisone dose >10mg/day, n(%)	496 (76.7)	494 (82.2)	142 (82.1)
Hydroxychloroquine, n(%)	665 (92.6)	589 (87.6)	138 (76.7)
Anticardiolipin IgM positive, n(%)	92 (14.5)	140 (21.9)	45 (26.0)
Anticardiolipin IgG positive, n(%)	101 (15.9)	153 (23.9)	53 (30.6)
Anti B 2 Glycoprotein 1 IgM Positive n(%)	38 (7.74)	51(10.2)	13 (10.1)
Anti B 2 Glycoprotein 1 IgG Positive n(%)	26 (55.3)	58 (11.7)	15 (11.7)
Lupus anticoagulant positive , n(%)	86 (14.6)	138 (23.0)	35 (22.2)
Thrombotic APS, n(%)	40 (5.17)	120 (16.6)	43 (22.3)
Obstetric APS, n(%)	85 (11.0)	98 (13.5)	34 (17.6)
Thrombotic y Obstetric APS, n(%)	5 (0.647)	23 (3.18)	10 (5.18)
aPLs Negatives , n(%)	631 (81.6)	520 (71.8)	132 (68.4)
aPLs Single Positive, n(%)	74 (9.57)	91 (12.6)	33 (17.1)
aPLs Double Positive, n(%)	50 (6.47)	77 (10.6)	13 (6.74)
aPLs Triple Positive, n(%)	18 (2.33)	36 (4.97)	15 (7.77)

Conclusions: The risk of presenting damage is higher in patients with SLE with aPL. Tight control of cardiovascular risk factors, use of low doses of steroids, and the evaluation of aPLs profile is essential in this group of patients.
Keywords: Antiphospholipid antibodies, damage, systemic lupus erythematosus.

0121

LOSS OF OPPORTUNITIES IN THE DIAGNOSIS AND TREATMENT OF PRIMARY OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (POAPS). FROM THEORY TO REALITY

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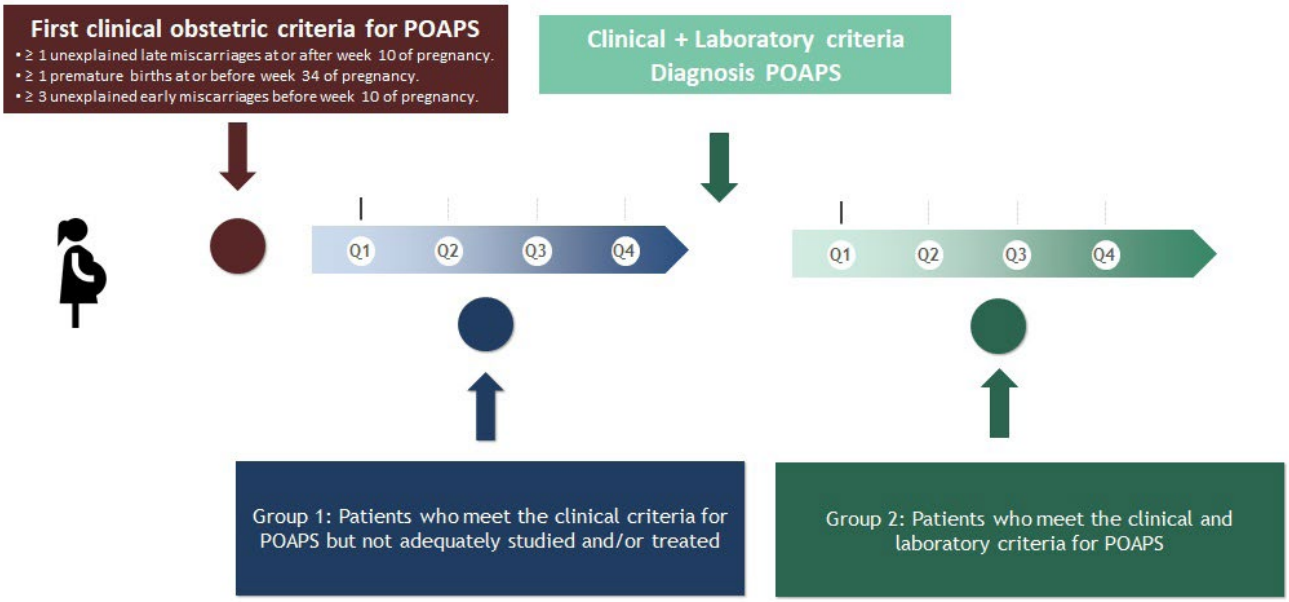
The aim of this study is to evaluate the impact of treatment in patients with POAPS
Patients and methods: We retrospectively studied 99 patients [median age: 32 years; (28-37)] diagnosed with POAPS, strictly according to the international criteria. We evaluated the obstetric history that occurred after meeting the clinical criteria for POAPS. Pregnancies were separated into 2 groups (Figure): Group 1: Pregnancies of patients who meets the clinical criteria for POAPS, but before the diagnosis. These pregnancies were defined as extra-pregnancies. Group 2: Pregnancies of patients after the diagnosis of POAPS (meets the clinical and laboratory criteria), treated with heparin + aspirin. Obstetric and clinical variables from all patients, were recorded. We compared pregnancy outcomes between group 1 and Group 2.



Results: 28,3% (28/99) patients were diagnosed with POAPS without presenting any pregnancy until diagnosis. 71,7% (71/99) patients had at least one extra-pregnancy before the diagnosis of POAPS. We compared 134 pregnancies in Group 1 with 99 pregnancies in Group 2 (Table). Treatment with heparin and aspirin in group 2 was associated with better pregnancy outcomes ODDS 6.7185 (3.596 - 12.5523), p: <.0001.

	Group 1	Group 2	p
Pregnancy Loss	58,2% (78/134)	17,2%(17/99)	<0.00001
Miscarriage	34,3%(46/134)	10,1% (10/99)	0.0001
Fetal Loss	23,8% (32/134)	7,1%(7/99)	0.001
Live births	41,8% (56/134)	82,8%(82/99)	<0.00001

Conclusions: The underdiagnosis of POAPS leads to the occurrence of preventable obstetric events, a loss of time resulting in a loss of lives. Heparin and aspirin treatment was associated with better obstetric outcomes.
Keywords: POAPS, heparin, aspirin.

0123

ARE NON-CRITERIA ANTIPHOSPHOLIPID ANTIBODIES SILENCED WITNESSES OF THE ANTIPHOSPHOLIPID SYNDROME?

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Antiphospholipid syndrome (APS) is a systemic autoimmune condition characterized by the presence of antiphospholipid antibodies (aPL) associated with vascular thrombosis or pregnancy complications. Clinical symptoms are accompanied by laboratory tests to detect a variety of aPL. We analyze the profile of aPL among APS subsets by including non-criteria aPL to unravel whether aPL play a different role in vascular and pregnancy complications.

Patients and methods: APS patients assisted at HUVH with obstetric (OAPS, n=31), thrombotic (TAPS, n=26), non-criteria clinic OAPS (OMAPS, n=26), non-criteria laboratory OAPS (NC-OAPS, n=16), or non-criteria laboratory TAPS (NC-TAPS, n=12) were screened for the presence of aPL with the line immunodotblot assay from Generic Assays GmbH. Immunodoblot slides tested for IgG or IgM aPL against cardiolipin (aCL), phosphatidic acid (aPA), phosphatidylinositol (aPI), phosphatidylcholine (aPC), phosphatidylethanolamine (aPE), phosphatidylglycerol (aPG), phosphatidylserine (aPS), ß2-glycoprotein-1 (aß2-GPI), annexin V (aAnV), and prothrombin (aPT) were scanned and quantified with Gel-Doc XR and Quantity-One software (Bio-Rad). A group of age & gender-matched healthy donors (n=79) was used to stablish the cutoff for every aPL. Analysis was done in R software (v4.1.2).

Results: Principal component (PC) analysis of aPL reactivity clearly discriminates IgG from IgM aPL reactivities (Fig. 1). aPS IgG associates with aPA and aCL IgG and contribute to define dimension 1 (Fig. 1,2). aPS IgM highly associates with aCL and aPA IgM and are the main contributors to dimension 2 (Fig. 1,2). aPE IgG also highly associates with aPG IgG (Fig. 2). aAnV and aPC reactivities are the minor contributors to this bidimensional reduction. aPL reactivities of OAPS patients are similar to the OMAPS and NC-OAPS. Interestingly, OAPS patients cluster differently from TAPS patients. We found that, aPA, aPS, aß2-GPI and aPT IgM reactivities are higher in OAPS patients and aCL, aPI and aAnV IgG reactivities are higher in TAPS patients. Finally, with a cutoff of 95% percentile, TAPS patients significantly test more positive for aCL and aAnV IgG than OAPS patients, who test more positive for aPA, aPS and aß2-GPI IgM.

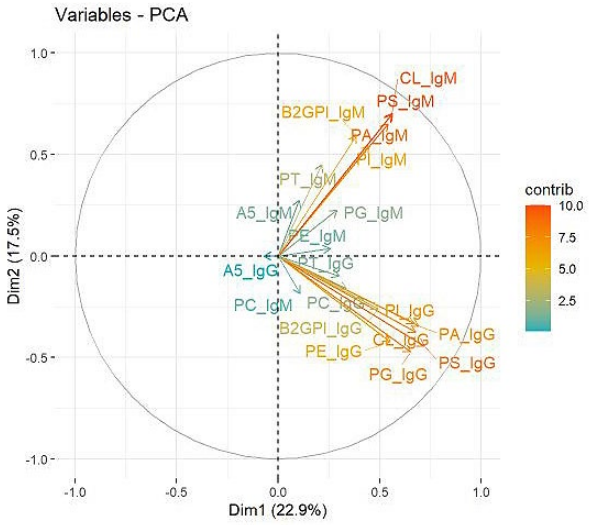

Figure 1: PC analisys.

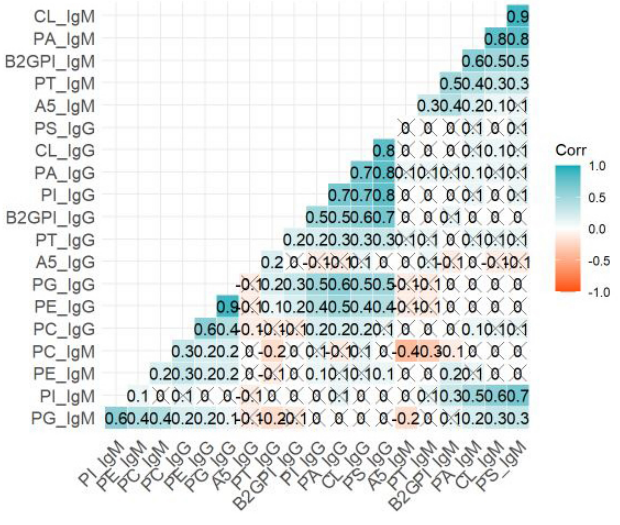

Figure 2: Correlations.

Conclusions: A subset of aPL reactivities associate between them (aPS, aPA and aCL; or aPE and aPG). Different aPL reactivity exists between OAPS and TAPS patients, suggesting that both subsets of APS patients develop a different set of aPL. Funding: This study was supported by Ona Futura Fundacio and Gravida, Barcelona.
Keywords: antiphospholipid antibodies, TAPS, OAPS, non-criteria aPL.

0124

MATERNAL AND FETAL OUTCOMES IN WOMEN WITH OBSTETRIC ANTIPHOSPHOLIPID SYNDROME: REGISTRY OF ANTIPHOSPHOLIPID ANTIBODIES OF THE ANTIPHOSPHOLIPID SYNDROME (APS) STUDY GROUP

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The aim of this study is to evaluate maternal and fetal outcomes in women with Obstetric APS and their relationship with general, laboratory and treatment variables.

Patients and methods: Descriptive, retrospective, cross-sectional, multicenter study in women admitted at baseline visit into the Registry of APS study group was conducted. Data from the ARTHROS Web platform until February 28 of 2022 was reviewed. All women who classified in the obstetric APS group were included and then divided according to whether or not they presented at least one maternal complication that included the presence of hypertensive disorders, placental injury and/or puerperium and fetal complications (gestational losses, defects in fetal growth) were considered in each pregnancy. Women with thrombotic and obstetric, non-thrombotic and obstetric manifestations and those with asymptomatic antiphospholipid antibodies were excluded. For all statistical tests with a two-tailed probability, $p<0.05$ was considered statistically significant. R software was used for all data analysis.

Results: Of the 329 patients included in the registry, 85% (278) were women, 61 presented APS. Forty-three were classified as having obstetric APS upon entering the cohort, with a total of 61 pregnancies in this group, mean age of 31.7 ± 5.25 years. Of the 43 patients included, 52.4% (11) were mestizos, 19% (4) obese and 28.6% (6) sedentary. Twenty-one (48.8%) presented at least one maternal or fetal complication, 76.2% (16) in the first pregnancy and 19% (4) in the second (Table 1). No association was found between the presence of Systemic Lupus Erythematosus (SLE) and adverse outcomes (p=0.464). When comparing pregnancies with and without maternal and fetal complications, a higher frequency of pregnancies planned was observed 89.7% (35) vs 63.6% (14) in the group without complications (p=0.02). Laboratory: 42.9% (9) were double positive for APS antibodies and 28.6% (6) simple and triple positive, respectively, no differences were observed between patients without complications. No association was found comparing combination of treatments received between patients with and without maternal and fetal complications (p=0.313).

Table 1. Complications of pregnancies.

Outcomes	n=61
Live births	
Yes	48
No, abortion < 10 wks	9 (14.8%)
No, death ≥10 < 27 wks	3 (4.9%)
No , late death ≥27 wks	1 (1.6%)
Placental insufficiency	7 (11.5%)
Preeclampsia	6 (9.8%)
Eclampsia	0 (0%)
HELLP	0(0%)
Placental hematoma	1 (1.6%)
Abruption	2 (3.3%)
Postpartum	2 (3.3%)

Conclusions: Pregnancy planned with the doctor could be a strategy to reduce the various maternal and fetal complications in obstetric APS.

Keywords: Obstetric APS, maternal complications, fetal complications.

0125

ANTIPHOSPHOLIPID ANTIBODIES IN ACUTE AND POST-ACUTE PHASE OF HOSPITALIZED COVID-19 PATIENTS

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Clinically significant coagulopathy and multiple infarcts were described in patients with COVID-19 along with the presence of antiphospholipid antibodies (aPL). The effect of autoantibodies on disease progression, and whether autoantibody reactivities prelude systemic autoimmune diseases or Long-COVID (LC) are not yet well-defined and will be part of this investigation.
Patients and methods: In total, 88 COVID-19 hospitalized patients in March-April 2020 in two tertiary hospitals (HUVH and AXA) were tested for aPL of the IgG and IgM isotypes using a line immunoassay developed by GA Generic Assays GmbH. aPL against cardiolipin, phosphatidic acid, phosphatidylinositol, phosphatidylethanolamine, phosphatidylglycerol, phosphatidylserine, ß2-glycoprotein-1, annexin V, and prothrombin were detected. A cohort of 20 healthy blood donors was used to setup the cut-off for the determination of aPL positivity.
Results: Serum samples from 88 COVID-19 patients collected during the first wave of pandemic in HUVH and AXA were tested for SARS-CoV-2 PCR positivity and IgG/IgM anti-SARS-Cov-2 antibody presence. IgM or IgG aPLs, including non-criteria aPLs, were detected in 30 patients (34.09 %), whose 10 (33,3%) showed more than 1 positivity. aPL positivity was equally distributed for gender (Odds Ratio [OR]=0.72, 95% CI [0.26.-1.90], p-value=0.505) and age (p-value=0.233). Some of these patients persistently showed aPL positivity all along the time that they were in-hospital. aPL positivity in men but not in women correlated with longer hospitalization stays (14.5 [11.0-17.7] vs 20.5 [18.3-40.3] days, p-value<0.005) as well as with higher levels of ferritin on admission (639.5 [331-963.5] vs 1021 [630-2209] ng/ml, p-value<0.05). But, no aPL positivity was associated with COVID-related thrombotic events [OR=0.76, 95% CI (0.07-5.01), p-value=1] nor severe COVID-19 [OR=1.09, 95% CI (0.26-4.09), p-value=1]. In a multivariate analysis based on clinical data acquired on admission, patients are grouped by their levels of ferritin, IL-6 and by their monocyte and PMN numbers and inversely correlated with the glomerular filtration rate. In a principal component analysis, although coagulation variables were contributing to the dimension´s variance, no association of aPL positivity was observed with any of these variables. Finally, the follow-up of these patients at 18 months of discharge rendered 10 patients died and 7 developed LC. Both, death and LC associated with COVID-19 severity once corrected by age (p-value<0.0001); but neither associated with aPL positivity (p=0.286).
Conclusions: aPL positivity was detected in 34.1% of acute Covid-19 hospitalized patients and correlated with higher ferritin levels and longer hospitalization stays for men, but neither associated with disease severity nor LC. Funding: This study was supported by Ona Futura Fundacio and Gravida, Barcelona.
Keywords: Antiphospholipid antibodies, COVID-19 severity, Long-COVID.

0126

THE EFFECT OF AVERAGE ADJUSTED GLOBAL ANTI-PHOSPHOLIPID SYNDROME SCORE (AGAPSS) ON RECURRENCE OF CLINICAL MANIFESTATIONS IN APS PATIENTS. A RETROSPECTIVE LONGITUDINAL STUDY

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Several factors have been associated with increased risk of clinical manifestations in patients with antiphospholipid syndrome (APS), such as the antiphospholipid antibody (aPL) profile (i.e. triple positivity), rate of aPL persistence over time, and association with other autoimmune diseases. The Global APS Score (GAPSS) and its "adjusted" version (aGAPSS), consider the aPL profile along with cardiovascular risk factors (arterial hypertension and dyslipidemia). They have been suggested as a tool for predicting thrombotic and obstetric manifestations in primary and associated APS. Various authors associated the baseline GAPSS/aGAPSS with the recurrence of clinical manifestations in patients with APS. However, aPL can fluctuate over time and cardiovascular risk factors can be modified by lifestyle and treatment. Moreover, patients with thrombotic APS treated with anti-vitamin K (AVK) agents can suffer from fluctuations in the anticoagulation intensity, measured by international normalized ratio (INR), because of several factors, contributing to thrombosis recurrence. To overcome these issues, we performed a retrospective longitudinal study to assess the effect of the average aGAPSS over time on recurrence of clinical manifestations despite appropriate treatment in APS patients, taking into account the percentage of time spent within the therapeutic range (TTR) in patients under AVK.
Patients and methods: 200 APS patients (138 with primary APS and 62 associated to other autoimmune diseases) were

included. The aGAPSS was calculated for each patient at baseline and on a yearly basis for either up to 6 years (minimum 3 years) or right before the clinical event in patients who experienced thrombosis or pregnancy morbidity. The average score per patient was computed and considered the reference aGAPSS. In patients who had a new thrombosis under anticoagulant treatment, TTR was calculated based on the INR values of the 6 months before the thrombotic episode. In patients without thrombosis TTR was calculated on the base of the INR values of the last 6 months of follow-up.
Results: 70 patients presented recurrence despite treatment: 58 (29%) thrombotic, 9 (5%) obstetric and 3 (1.5%) both. Higher average aGAPSS values were found in patients who experienced clinical recurrence in comparison to patients who did not [8.81 (C.I. 7.53-10.08) vs 6.38 (C.I. 5.64-7.12), p = 0.001]. Patients with thrombotic recurrence presented higher aGAPSS in comparison to patients with obstetric recurrence [9.48 (C.I. 8.14-10.82) vs 4.25 (C.I. 0.85-7.65), p = 0.006]. Moreover, patients with arterial-arterial thrombosis and patients with venous-arterial/arterial-venous thrombosis showed higher aGAPSS than those with venous-venous thrombosis recurrence [10.41 (C.I. 8.45-12.37) and 10.94 (C.I. 8.49-13.39) vs 6.63 (I.C. 4.39-8.87), p = 0.01 and p=0.01 respectively]. TTR was not statistically different between patients who had thrombosis recurrence and patients who had not.
Conclusions: Our data support the role of periodic (annual) monitoring of the aGAPSS score in predicting clinical manifestations recurrence, especially arterial thrombosis, in patients with APS.
Keywords: Antiphospholipid syndrome, aGAPSS, systemic lupus erythematosus, recurrence, thrombosis.

0127

CLINICAL PHENOTYPES IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS (CSLE) AND ANTIPHOSPHOLIPID ANTIBODIES

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The reported frequencies of antiphospholipid antibodies (aPL) in pediatric SLE patients have ranged from 20 to 85% (aCL pts) and from 10 to 60% (in LA pts). This wide variability in the frequency of aPL reported in cSLE may be due to differing sensitivities of assays and heterogeneity in SLE population. Antiphospholipid antibodies in cSLE are related to increased risk of arterial and venous thrombotic; different neurological manifestations and autoimmune cytopenias. Objective: To analyze the prevalence, clinical phenotype and evolution of the disease in a cohort of cSLE and aPL (+).
Patients and methods: Observational retrospective study of patients with cSLE (ACR'97), <18 ys at diagnoses (1990-2018) aPL positive patient was defined as the presence of aCL (IgM/IgG >40 UPL/ml) and/or B2GP1 (IgM/IgG >Pc 99) and/or LA in at least 2 determinations separated by 12 weeks. Demographic, clinical, activity (SLEDAI '92) and damage (SLICC '96), laboratory and therapeutical variables were analyzed. Thrombotic (arterial/venous and fetal loss) and non-thrombotic manifestations associated with APS (as livedo reticularis, neurological disease, heart valve disease, and autoimmune cytopenias) were analyzed. Statistical Analysis: Chi² —T test. ANOVA. SPSS 15.0
Results: 79 out of 188 cSLE (42%) had aPL (+) antibodies, 86% (68 pts) were female, X age at diagnoses: 12.7 ys (IQR: 10.4-14.6) and X follow-up time: 4.9 ys (IQR: 3.3-6.7). aPL profile: aCL 75% (59 pts), B2GP1 45% (36 pts) and LA+ 45% (36 pts). aPL (+) titers were moderate/high in 69 pts (87%). Double positivity of aPL was found in 35% (28 pts) and triple in 16% (13 pts). The clinical phenotypes were – the thrombotic one: arterial thrombosis 10 pts (53%) (CNS and peripheral vascular); venous thrombosis 6 pts (32%) and fetal loss 3 pts (16%). Recurrent thrombosis in 6 pts (32%). Non-thrombotic Phenotype, 50 pts (63%): 26 neurological manifestations (headaches and cognitive dysfunction), 19 with cardiac involvement (non-infectious endocarditis more frequently), 19 hemolytic anemia, 18 thrombocytopenia and livedo reticularis. The entire cohort received hydroxychloroquine and corticosteroids; and 87% (60 pts) immunosuppressive drugs. Patients under thrombosis received aspirin and anticoagulant therapy and only one third of patients with non-thrombotic disease received aspirin prophylaxis. When the cSLE cohort was compared regarding the presence or not of aPL, we found that those with aPL (+) were younger at diagnosis (12.7 vs. 13.7 ys p.038), have a higher SLEDAI (14.8±6.2 vs. 12.9±6.4 p.042); developed more non-thrombotic neurological (33% vs. 18% p.008) and cardiac manifestations (28% vs 14% p.02) and livedo reticularis (23% vs 5% p.0001). Disease course was severe in this group: multi-organ compromise (48% vs 28% p.002) with more admissions to PICU (33% vs 13% p.04). On the last visit, they accumulated a higher dose X of steroids (23.2 ± 17.8 vs. 15.4 ±12.4 g. p.001) and organ damage (49% vs 30% p.02). There were no differences in mortality rate in both phenotype patients.
Conclusions: The presence of aPL (+) in moderate/high titers in our cSLE cohort was associated with younger age at diagnosis, development of thrombotic events (secondary APS) and a more severe disease with higher morbidity.
Keywords: Antiphospholipid antibodies, childhood-onset systemic lupus erythematosus, antiphospholipid syndrome.

0128

INVESTIGATION FOR ANTIPHOSPHOLIPID ANTIBODIES IN PATIENTS PRESENTING WITH PULMONARY EMBOLISM DURING COVID-19 DISEASE

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Positive antiphospholipid antibodies-APA, have been referred in patients presenting with Deep Vein thrombosis-DVT in COVID-19 patients. Aim: To investigate the presence of APA in patients presenting with Pulmonary Embolism during COVID-19 disease.
Patients and methods: We investigate 10 patients with pulmonary embolism during COVID-19 disease, median age 49 years, 6 men, 4 women for the presence of APA and analytically anticardiolipin antibodies IgM, IgM, anti-b2- GPIa IgG, IgM and lupus anticoagulant (DRVVT test)
Results: In 5 out of 10 patients positive APA were found, and analytically 3 patients had anticardiolipin antibodies IgM in moderate titles, three had positive lupus anticoagulant (by DRVVT method) and 2 had anti-b2 GPIa IgM antibodies in moderate to high titles. Two patients had double positivity for Anticardiolipin IgM and lupus anticoagulant and one patient had positive anti-B2 GPIa IgM and lupus anticoagulant. All 5 patients had no previous history of DVT or known systematic autoimmune disease. 3-6 months after Pulmonary Embolism the antibodies remained positive in 4 out of 5 patients.
Conclusions: High incidence of APA in patients with Pulmonary Embolism during Covid-19 disease is shown in our case-series. 3-6 months after the DVT episode APA remain positive in 4 out of 5 patients, and there are still in follow-up. If there is a causative link between those antibodies and the thrombosis is still unclear and should be proven by larger randomized and also follow-up studies
Keywords: Antiphospholipid antibodies, COVID-19, pulmonary embolism.

0130

COMPARISON OF GESTATIONAL OUTCOMES OF PATIENTS WITH PRIMARY APS AND ARTERIAL THROMBOSIS TO PATIENTS WITH ARTERIAL THROMBOSIS AND NEGATIVE APL

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The aim of this study is to compare gestational outcomes of pregnant patients with history arterial thrombosis and primary APS to patients with arterial thrombosis and negative aPL.
Patients and methods: Cohort study with retrospective data collection of patients with history of arterial thrombosis, that occurred before or during pregnancy, that were followed in Prenatal Care for Autoimmunity and Thrombophilia (PrAT) at Hospital Universitário Pedro Ernesto – Rio de Janeiro, Brazil. All patients were tested for antiphospholipid antibodies at least once, while patients with positive aPL were retested after 12 weeks. Patients with lupus and arterial thrombosis were excluded from the analysis.
Results: 31 pregnancies in 50 patients were evaluated. Of these, 13 tested positive for aPL and 18 were negative. Three patients of APS group also had venous thrombosis, while nine patients of negative aPL had history of both arterial and venous thrombosis. All patients in Group 1 used anticoagulant during pregnancy, while 66% of group 2 used this medication. The most frequent antibody in patients with APS was lupus anticoagulant (46.1%) and two patients were triple positive. Patients with APS had a lower mean age (28.4 + 7.2 x 31.8 + 5.4 p = 0.05) and both groups were similar considering primiparity (23% x 22.2%, p = 0.47). Among adverse obstetric outcomes (described in Table 1 and 2), Group 1 (APS) had a higher frequency of preeclampsia (46.1% x 16.7% p=0.04) and lower birthweight (2.216 + 1094 x 3010 + 692, p = 0.04) than group 2. Patients with APS had more frequently premature delivery, lower gestational age at delivery and lower Apgar score at 5 minutes, although the differences did not reach statistical significance in this study. There were two miscarriages and one stillbirth in APS group.

Table 1

Variables	PAPS (n=13)	PAPS (n=13)	aPL negative (n=18)	aPL negative (n=18)	RR	CI 95%	P value
	n	%	n	%	-		
Miscarriage	2	15.4	0	-	-		0.08
Oligohydramnios	3	23	0	-	-		0.03
Intrauterine growth restriction	3	23	2	11.1	2.33	0.29 -22.55	0.21
Premature rupture of membranes	3	23	2	11.1	2.33	0.29 – 22.55	0.21
Preeclampsia	6	46.1	3	16.7	4.07	0.78 – 25.3	0.04
Premature delivery	5	45.5	3	16.7	3.94	0.69 – 26.01	0.06
Stillbirth and neonatal death	1	9	0	-	-		0.18

Table 2

Variable	PAPS (n=11)	PAPS (n=11)	aPL negative (n=18)	aPL negative (n=18)	p value
	n	%	n	%	
Delivery	-	-	-	-	-
vaginal	7	63.6	6	33.3	0.06
C-section	4	36.4	12	66.7	0.06
Gestational age (weeks) mean + - SD	34.8+-4.9	-	37.6 +-2.1	-	0.09
Newborn weight mean + - SD	2216 +- 1094.7	-	3010+-692.8	-	0.04
Small for gestational age	3	27.3	1	5.6	0.07
5 min Apgar score	6.9+-3.8	-	9+-0.8	-	0.09
Admission to Nicu	3	27.3	4	22.2	0.38

Conclusions: Patients with arterial thrombosis and APS have increased risk of adverse obstetric events compared to patients with arterial thrombosis that test negative for aPL.
Keywords: Arterial thrombosis, antiphospholipid syndrome, adverse birth outcome.

0131

CHARACTERISTICS OF PATIENTS WITH BUDD-CHIARI SYNDROME IN A SINGLE CENTER COHORT OF ANTIPHOSPHOLIPID SYNDROME

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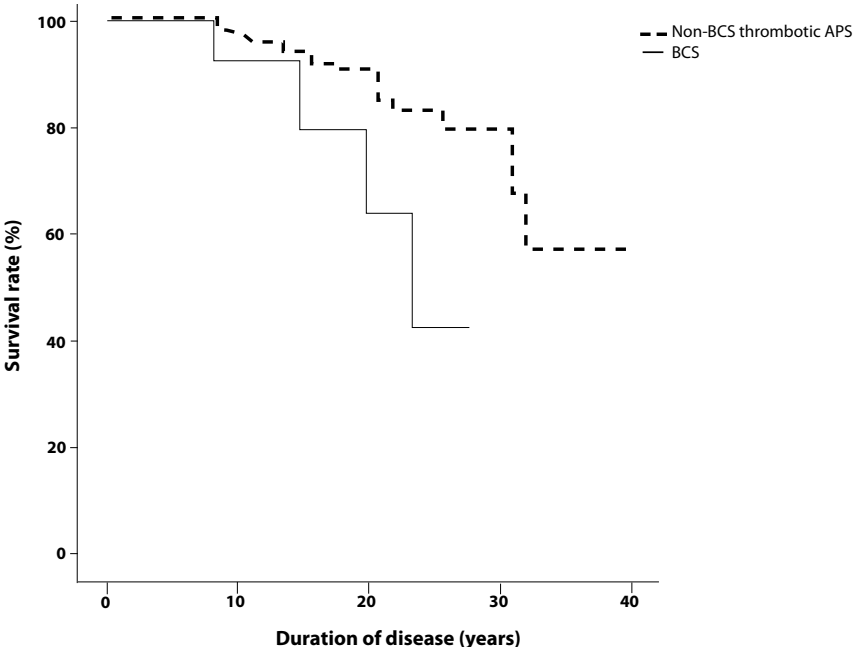
Herein we aimed to identify the clinical characteristics and prognosis of APS patients with Budd-Chiari syndrome (BSC) in a single center cohort of patients with APS.
Patients and methods: Of 237 patients with APS (± SLE) followed up between 1982 and 2021, 15 with BCS and 176 with non-BCS vascular thrombosis were included in the analysis. Data regarding demographics, clinical and laboratory characteristics, and mortality were retrieved from the updated existing database.
Results: Characteristics of the patients with BCS (n=15) and non-BCS thrombotic APS (n=176) are shown in Table 1. Mean age at diagnosis of BCS was 30±11.3. Nine (60%) of the patients with BCS had history of thrombosis and 5 (33.3%) had previous pregnancy morbidity. The most common presenting symptom was abdominal pain (73%) followed by ascites (40%), liver enzyme abnormalities (20%), autoimmune cytopenia (20%) and abdominal wall venous collaterals (13%). The most affected vascular segments were hepatic veins (86.6%) and vena cava inferior (80%) (66.6% had both). Ascites (46.2%) and esophageal varices (46.2%) were most common complications of portal hypertension. Radiologically, abdominal venous collaterals (66.6%) were most common findings followed by splenomegaly (60%) and hepatomegaly (53.3%). Six patients had liver cirrhosis (40%). Hereditary thrombophilia was studied in 13 patients and 3 had heterozygous mutations of Factor V Leiden. At the time of BCS diagnosis, 7 patients were on anticoagulation (4 on VKA, 3 on LMWH prophylaxis). Of patients on VKA, 2 had INR between 2 and 2.5, and 2 < 2. Two patients had SLE flare at the time of BCS diagnosis. BCS group had higher damage (DIAPS>= 3) and aGAPSS compared to non-BCS thrombotic APS group. Four patients died due to sepsis and 1 due to bleeding after kidney biopsy. Patients with BCS had significantly lower survival rate compared to those with non-BCS thrombotic APS (73.3% vs 90.9%, P=0.03) (Figure 1).

Table: Demographic, clinical and laboratory characteristics of the patients with BCS and non-BCS thrombotic APS.

	BCS (N=15)	Non-BCS Thrombotic APS (n=176)	p
Female , n(%)	9 (60)	142 (80.7)	0.066
Age, years (mean±SD)	41.6 (10.3)	47.9 (12.1)	**0.038**
Age at diagnosis years (mean±SD)	26.5 (10.9)	32.9 (11.6)	**0.044**
Disease duration years (mean±SD)	15 (7.1)	14.9 (8.1)	0.975
SLE, n (%)	8 (53.3)	91 (51.7)	0.560
Recurrent thrombosis, n (%)	11 (73.3)	66 (37.5)	**0.008**
Pregnancy morbidity n (%)	6 (40)	65 (36.9)	0.509
Livedo reticularis, n (%)	1 (6.7)	34 (19.3)	0.198
Thrombocytopenia, n (%)	7 (46.7)	56(31.8)	0.186
Heart valve disease, n (%)	5 (33.3)	72 (40.9)	0.388
aLP Profile **La** **aCL IgG/IgM** **aβ2GPI IgG/IgM** **Triple positive**	 9 (60) 13 (86.7) 11 (73.3) 7 (46.7)	 119 (93) 116 (65.9) 74 (42) 38 (21.6)	 0.367 0.081 **0.019** **0.036**
aGAPSS (mean±SD)	11.1 (3.2)	9.6 (3.8)	0.111



Number at risk					
BCS	15	13	5	0	0
Non-BCS thrombotic APS	176	123	48	10	0

Figure: Kaplan-Meier estimates of survival in BSC and non-BSC thrombotic APS groups.

Conclusions: BCS may be the first event or occur later in APS. It is associated with high damage and decreased survival. APS patients with high risk aPL profile, new onset abdominal pain and abnormal liver enzymes should be evaluated for BCS. Effective anticoagulation and control of SLE flares may help to prevent BCS.

Keywords: Antiphospholipid syndrome, Budd-Chiari syndrome, venous thrombosis.

0132

PATIENTS WITH DVT AND PRIMARY APS HAVE WORSE OBSTETRIC OUTCOMES THAN PREGNANT WOMEN WITH DVT AND NEGATIVE APL

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The aim of the study is to compare gestational outcomes of pregnant patients with history or current of deep venous thrombosis (DVT) and primary APS to patients with DVT and negative aPL.
Patients and methods: Cohort study with retrospective data collection of patients with history of DVT, that occurred before or during pregnancy, that were followed in Prenatal Care for Autoimmunity and Thrombophilia (PrAT) at Hospital Universitário Pedro Ernesto – Rio de Janeiro, Brazil. All patients were tested for antiphospholipid antibodies at least once, while patients with positive aPL were retested after 12 weeks. Patients with lupus were excluded from the analysis.
Results: 174 pregnancies in 164 patients with history of DVT were evaluated. Of these, 37 fulfilled APS criteria and 127 were aPL negative. All patients in group 1 (primary APS) used anticoagulant during pregnancy, while 97.6% of group 2 used this medication. Patients with APS had a higher mean age (32.5 x 30.4, p 0.05) and more history of miscarriage (43.2% x 18.9%, p = 0.002), with no difference in relation to primiparity (24.3% x 29.1%, p = 0.29). In this group, the most frequent antibody was lupus anticoagulant (67.6%), with five triple positive patients. In both groups, the most frequent site of DVT was in the lower limbs (75.6% and 89.7%, respectively). Among adverse obstetric outcomes, Group 1 (APS) had worse obstetric outcomes (described in Tables 1 and 2), such as higher frequency of oligohydramnios (8.1% vs. 1.6%, p = 0.04), intrauterine growth restriction (16.2% vs. 4.7). %, p = 0.01), prematurity (18.9% x 7.9%, p = 0.03) and lower birth weight (2,831g + 627 x 3,215g + 541, p = 0.001). The only case of intrauterine fetal death occurred in APS group.

Table 1

Variable	PAPS (n=37)	PAPS (n=37)	aPL negative (n=127)	aPL negative (n=127)	RR	CI 95%	p value
	n	%	n	%	-	-	-
Oligohydramnios	3	8.1	2	1.6	5.43	0.78 -47.28	0.04
Intrauterine growth restriction	6	16.2	6	4.7	3.86	1.10-13.5	0.01
Premature rupture of membranes	2	5.4	12	9.4	0.54	0.08-2.30	0.23
Preeclampsia	5	13.5	8	6.3	2.31	0.64-7.65	0.09
Premature delivery	7	18.9	10	7.9	2.71	0.90-7.81	0.03
Stillbirth and neonatal death	1	2.7	0	-	-	-	-

Table 2

Variable	PAPS (n=37)	PAPS (n=37)	aPL negative (n=127)	aPL negative (n=127)	p value
	n	%	n	%	-
Delivery					
Vaginal	12	32.4	54	42.8	0.13
C-section	25	67.6	72	57.2	0.13
Gestational age (weeks) mean+-SD	37.4+-2.4	-	37.9+-1.7	-	0.15
Newborn weight mean +- SD	2831.9+-627	-	3215+-541.2	-	0.001
Small for gestational age	5	13.5	15	11.9	0.38
5 min Apgar score	8.7+-1.8	-	9+-0.81	-	0.5
Admission to NICU	5	13.5	9	7	0.12

Conclusions: The presence of aPL in patients with history of DVT is associated with worse pregnancy outcomes. Our study suggests that investigation for APS is important for the adequate follow-up of pregnant women with a history of DVT.
Keywords: Venous thrombosis, antiphospholipid syndrome, adverse birth outcome.

0133

ISCHEMIC AND HEMORRHAGIC SYMPTOMS IN A PATIENT WITH ACQUIRED HEMOPHILIA AND ANTIPHOSPHOLIPIDS ANTIBODIES

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We herein present infrequent association between acquired hemophilia and antiphospholipid antibodies in a patient with symptoms of ischemic and bleeding.
Case report: A 38-year-old female patient, physician, she had arterial hypertension treated with nevibolol 2.5 mg daily and bronchial hyper reactivity. Four months before the first consultation, she was seen by a neurologist cause repeated episodes of aphasia. A brain MRI performed was normal. She received diagnosed a transient ischemic attack and aspirin was prescribed. One months later, she had spontaneous hematomas in the extremities, the mouth .and had an episode of digestive bleeding due to an esophageal hematoma. The patient went to the hematologist, who requests laboratory studies. The results of the tests were platelets 322.000 mm^3, white cell count 8.900 mm^3 differential count normal, hematocrit 30 (%) Hb 9.6 (mg/dl) MCV 75 (fl), Prothrombin time 90% aPTT 64 (fail to corrected with normal plasma) ESR 25, Factor VIII 1.5%, Factor II, V, VII-X, IX, X, vW ag all normal, RF 9.3 (UI/ ml) ANA (Hep-2) 1/ 320 homogeneous. She was diagnosed factor VIII acquired hemophilia. Prednisone 1 mg/kg daily azathioprine 1 mg/kg/ d was prescribed and she was referred for consultation with a rheumatologist.
Results: At the first consultation, the patient presented bruises and photosensitivity no referred other articular or extra-articular rheumatic manifestations. She had no history of gynecological, obstetric, toxic or allergies, she had gallbladder surgery. She had and aunt with rheumatoid arthritis. On physical examination, she weighed 98 kg, and had a height 172 cm, vital signs were normal, she had bruises on the extremities, the rest without particularities Laboratory showed iron deficiency anemia with normal liver and kidney function tests, including 24-hour proteinuria. The electrophoretic proteinogram, LDH C3 and C4 normal. The studies of auto antibodies DNA, Ro, La, Sm, RNP, all negative, test direct coombs negative, too. Chest x-ray and electrocardiogram performed were normal. The results of lupus anticoagulant were positive and anticardiolipins ab IgG 27gpl (moderate titles). Hepatitis B, C and HIV serology were negative. Two months after receiving azathioprine and corticosteroids, he presented a factor VIII value of 28% with symptoms of bruising in the mouth. Rituximab 1.000 mg was prescribed, two doses at 14 days' interval. Two months later of the first infusion the patient had no symptoms, the factor VIII were 100% and antiphospholipids antibodies negative. The azathioprine was discontinued. The prednisone was tapering. She received hydroxiclhoroquine 400 mg, calcium 500 mg plus Vitamin D 800 U daily, Trimethoprim sulfamethoxazole 3 times a week.
Conclusions: The patient was diagnosis of acquired thrombophilia A and ischemia, associated with antiphospholipid antibodies and autoimmunity.
Keywords: Acquired hemophilia, antiphospholipid antibodies.

0134

THE EUROPEAN REGISTRY ON OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (EUROAPS): A SURVEY OF 1048 CONSECUTIVE CASES

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The aim of this study is to analyze the clinical features, laboratory data and fetal-maternal outcomes, and follow them up on a cohort of 1048 women with obstetric antiphospholipid syndrome (OAPS).
Patients and methods: The European Registry of OAPS became a registry within the framework of the European Forum on Antiphospholipid Antibody projects and was placed on a website in June 2010. Thirty hospitals throughout Europe have collaborated to carry out this registry. Cases with obstetric complaints related to antiphospholipid antibodies (aPL) who tested positive for aPL at least twice were included prospectively and retrospectively. Ten-year survey results are reported.
Results: 1048 women were included. All cases fulfilled the Sydney classification criteria. According to the lab categories, 318 (30.3%) were in category I, 374 (35.6%) in IIa, 229 (21.8%) in IIb and 127 (12.1%) in IIc. Miscarriages were the most prevalent clinical manifestation in 409 cases (39%). Moreover, the presence of early preeclampsia (PE) and early foetal growth restriction (FGR) appeared in 194 (18.5%) and 170 (16.2%), respectively. In this series, 469 (44.92%) women received the recommended OAPS treatment. Patients with recommended treatment had a really good live-birth rate (84.4%) while patients with no treatment showed a poor birth rate (52.4%). Histopathological results of 177 placentas were obtained, showing mixed thrombotic and inflammatory etiology among the findings: 118/177 (66.6%) with thrombus and infarcts, 126/177 (71.1%) with inflammation.
Conclusions: In this series, recurrent miscarriage is the most frequent poor outcome. To avoid false-negative diagnoses, all laboratory category subsets were needed. OAPS cases have very good fetal-maternal outcomes when treated.
Keywords: Antiphospholipid antibody, antiphospholipid syndrome, obstetric antiphospholipid syndrome, pregnancy autoimmune disorders, registry.

0136

MULTIMODAL OPHTHALMOLOGIC EVALUATION CAN DETECT RETINAL INJURIES IN ASYMPTOMATIC PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME

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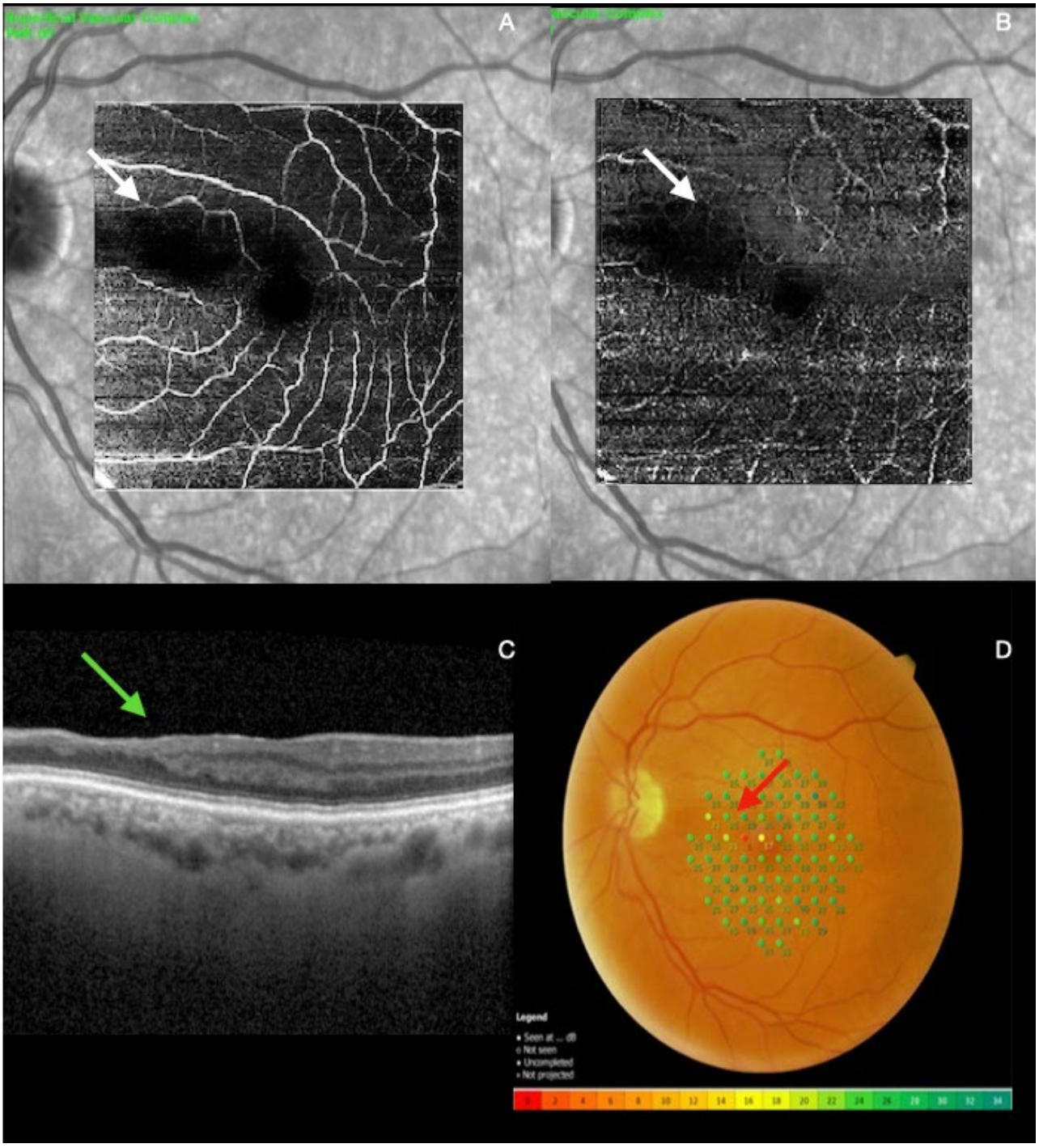
The aim of this study is to perform a multimodal ophthalmologic evaluation, including the use of Optical Coherence Angiotomography (OCTA), in patients with thrombotic Primary antiphospholipid syndrome (PAPS) without ocular complaints and compare with healthy individuals.
Patients and methods: We analyzed PAPS patients followed at our tertiary Rheumatology outpatient clinic. All patients fulfilled Sydney APS classification criteria (2006). We evaluated only ocular asymptomatic patients with no previous of any ocular disease. Antiphospholipid antibodies and clinical APS manifestations were compared between patients. A complete multimodal ophthalmological examination was performed including optical coherence tomography, OCTA and microperimetry.
Results: We included 104 eyes of 52 subjects (26 patients with thrombotic PAPS without ocular complaints and 26 healthy individuals). Among PAPS patients, 21 were female (80.8%) and 21 (80.8%) were Caucasians. Mean age of PAPS patients was 46.5 ± 11.8 years and control group was 46.3 ± 11.3 years. Venous and arterial thrombosis were present in 65.4% and 34.6% of them, respectively. Obstetrical criteria were present in 34.6%. Lupus anticoagulant was present in all PAPS patients. PAPS patients presented with 19.2% of ophthalmologic findings against none of the healthy individuals (p=0.05). The most common retinal change was paracentral acute middle maculopathy (PAMM) (3 patients, 5 eyes) - which is characterized by the infarction of the inner nuclear layer due to ischemic events located in the intermediate and deep capillary plexus of the retina, followed by drusen-like deposit - extracellular deposits of lipids, proteins and cellular debris, which accumulate below the retinal pigment epithelium (RPE) and appear as small, yellow deposits on fundus eye exams (1 patient, 2 eyes) and pachychoroid pigment epitheliopathy (1 patient, 1 eye), characterized by focal RPE abnormalities overlying abnormal and permanent increase in choroidal thickness (pachychoroid disease), without the presence of subretinal fluid. Hypertension and hyperlipidemia were present in 100% of the PAPS patients with PAMM, while only six patients (26.1%) with PAPS without PAMM presented these two risk factors together (p=0.03).



Conclusions: PAMM was observed in 11.5% of PAPS patients with no previous ocular complaints. Hypertension concomitant with hyperlipidemia were the most common associated risk factors for PAMM in patients with PAPS. Prospective studies are important to study the prevalence of PAMM in this population.
Keywords: Optical coherence tomography angiography, venous thrombosis, arterial thrombosis, retina, paracentral acute middle maculopathy, blood vessels, primary antiphospholipid syndrome.

0137

COMPARISON OF PLACENTAL VASCULAR OBSTETRIC CRITERIA (OAPS) AND NON CRITERIA (NC-OAPS) ANTIPHOSPHOLIPID SYNDROME

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Placental vascular derived complications usually translate in high-risk pregnancies with fetal death or prematurity consequences. Antiphospholipid antibodies (APL) are the only thrombophilic disorders to be evaluated according to different guidelines. Sydney Antiphospholipid criteria were intended for clinical trials. In daily practice we usually face women who do not fulfill these criteria but still are high risk cases and may be underrepresented. Objective: to compare clinical OAPS versus NC-OAPS in women with APL-related placental vasculopathy.

Patients and methods: Methods: Retrospective multicenter observational study. We analyzed and compared those complications that occur in late second and third trimester. Inclusion criteria: women 18-50 years old with a history of OAPS: stillbirth (SB), early and severe preeclampsia (EPE)< 34 weeks or prematurity due to placental insufficiency (PI) and NC-OAPS: late onset PE after 34 week (LPE), late intrauterine growth restriction (LIGR), preterm birth: >34<37 weeks (PT), abruptio placentae (AP). Laboratory inclusion criteria: LA and/or aCL IgG, IgM and/or antiB2GPI IgG/ IgM positivity, tested at least twice, 12 weeks apart. It was used either Sapporo or the 99th percentile. Data were analyzed with chi square.

Results: 87 women, median age 33 years (22–50). OAPS:57 (65%): 36%EPE, 45% SB, 7% EPE + SB, 5% PI; NC-OAPS: 30 (34,45 %):36% LPE,30% LIGR, 6% PT, 26% AP. We didn´t find significant difference between clinical OAPS and NC-OAPS and placental infarcts/villous thrombosis (P=0,9), arterial/ venous thrombosis (vascular clinical criteria) P=0,55; triple positive laboratory test (P=0,87), transient antiphospholipid (P=0,87), positive lupus anticoagulant (P=0,59). 45 OAPS women had 57 pregnancies after the index event. All pregnancies were treated with heparin and ASA with 82,7 % live births and 2617 g median birth weight. 20 NC-OAPS women had 23 pregnancies. 21/23 pregnancies were treated with heparin and ASA with 78,2 % Live births and 2863 g median birth weight. No significant difference in live births (P=0,82) and median birth weight (P=0,77) between OAPS and NC-OAPS respectively. Interestingly 8 OAPS women had a recurrent event in next pregnancy 4 as OAPS but 4 were NC-OAPS (1 AP, 2 LIGR, 1 PT).

Conclusions: Conclusion: According to our results, we did not find any difference in laboratory parameters and/ or treatment response between clinical OAPS and NC-OAPS in our patients. There may be many biases derived from the multicenter and retrospective design. Considering the high risk that means underrepresented cases, we recommend that NC-OAPS should be evaluated in a prospective and bigger trial.

Keywords: Obstetric antiphospholipid syndrome, non-criteria obstetric antiphospholipid syndrome pregnancy.

0138

COMPARATIVE STUDY OF OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (OAPS) AND NON-CRITERIA OBSTETRIC APS (NC-OAPS): REPORT OF 1744 CASES FROM THE EUROAPS REGISTRY

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The aim of this study is to compare clinical features, laboratory data and fetal-maternal outcomes between 1048 women with obstetric APS (OAPS) and 696 with antiphospholipid(apL)-related obstetric complications not fulfilling Sydney criteria (non-criteria OAPS, NC-OAPS).

Patients and methods: This was a retrospective and prospective multicenter study from the European Registry on Obstetric Antiphospholipid Syndrome.
Results: A total of 1760 women were included. Altogether, 1048 cases (OAPS group) fulfilled the Sydney classification criteria and 696 (NC-OAPS group) did not. Sixteen NC-OAPS cases were excluded for presenting thrombosis during follow-up. All cases were classified as category I (triple positivity or double positivity for aPL) or category II (simple positivity). Overall, aPL laboratory categories showed this distribution: 28.91% in OAPS vs 17.09% in NC-OAPS for category I, and 71.09% in OAPS vs 78.16% in NC-OAPS for category II, and 4.88% of NC-OAPS presented positivity only for atypical aPL antibodies. Clinical differences were observed between groups without major differences in treatment rates, livebirths and thrombotic complications. In the NC-OAPS group, 195/696 (28.01%) did not fulfil Sydney criteria (subgroup A), 190/696 (27.29%) had a low titre and/or non-persistent aPL positivity but did meet the clinical criteria (subgroup B) and 311/696 (44.68%) had a high aPL titre but did not fulfil Sydney clinical criteria (subgroup C).
Conclusions: Significant clinical and laboratory differences were found between groups. All laboratory categories were well represented. Fetal-maternal outcomes were similar in both groups when treated.
Keywords: Antiphospholipid, antiphospholipid antibodies, antiphospholipid syndrome, non-criteria antiphospholipid syndrome, obstetric antiphospholipid syndrome, outcomes, treatment.

0139

DOES PREGNANCY INCREASE ACCRUAL DAMAGE IN LUPUS?

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The aim of this study is to evaluate accrual damage in women with or without pregnancy, and its relationship with renal failure and dialysis and the autoantibodies profile.
Patients and methods: A multicenter, cross-sectional, study from the RELESSAR registry was performed. SLE patients of 41 centers of Argentina, who fulfilled ACR 1997 criteria, during 2017 and 2018 were included. Sociodemographic data, autoantibody profile, the number of pregnancies and maternal and fetal complications were analyzed. Accrual damage was evaluated by SLICC-SDI index and it was present when scoring was more or equal than 1. Preeclampsia, eclampsia, fetal death, preterm delivery, and miscarriage were evaluated.
Results: 1390 patients were included. 892 (64.2%) had one pregnancy or more (PW), 471 (33.9%) were never pregnant (NP), and 1,9% missing data. 89,5% had no complication in PW group and 427 (53.5%) of them had accrual damage. 94 (10.5%) PW had complications, and 59 (62.8%) had accrual damage. Demographic and Clinical data are shown in Table. There was no relationship between the number of pregnancies and accrual damage (0.075). Comparing PW vs NP regarding to SDI, the women who had at least one pregnancy had higher SDI (p=0.012), and the SDI was higher when we compared complicated pregnancies vs normal (p 0.001). Accrual damage was no related to pregnancy in lupus nephritis patients.

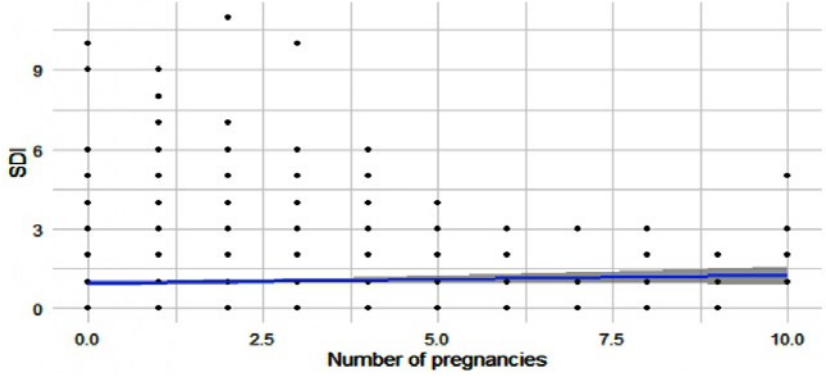

Table: Features of woman with or no pregnancy.

Features	Pregnancy, (n892)	Non pregnancy (n471)	p value	Total (N=1363)
Age at diagnosis (mean±SD)	31.9 [24.3,40.5]	22.9 [17.6,28.6]	<0.001	28.4 [21.0,37.8]
Disease duration mean (SD) months	112 (100)	90.5 (86.3)	<0.001	104 (96.1)
Socioeconomic level, n(%)				
high	4 (0.4)	7 (1.49)	0.010	11 (0.8)
Middle high	84 (9.4)	45 (9.5)		129 (9.4)
Media	341 (38.2)	212 (45.0)		553 (40.6)
Lower Media	382 (42.8)	179 (38.0)		561 (41.2)
Education (years) mean (SD)	11.8 (3.9)	13.3 (3.5)	<0.001	12.4 (3.9)
APS, n(%)*(777)	111 (13.4)	35 (7.6)	0.002	146 (11.4)
Smoking, n(%) *(777)				
Never	562 (66.4)	342 (77.7)	<0.001	904 (70.3)
Smoker and past Smoker	284 (18.6)	98 (22.2)		382 (29.6)
Diabetes, n(%)*(37)	37 (4.2)	4 (0.8)	<0.001	41 (3.0)
Hypertension, n(%)*(32)	37(4.2)	4 (0.8)	<0.001	296 (22.2)
Seizures, n(%)*(26)	31 (3.5)	28 (5.9)	0.055	59 (4.4)
Lupus nephritis n(%)*(12)	515 (57.7)	263 (55.8)	0.59	778 (57.1)
Renal Failure, n (%)*(99)	17 (2.0)	11(2.5)	0.701	28 (2.2)
Depression, n(%)*(18)	109 (12.4)	33 (7.0)	0.002	142 (10.6)
SDI, Median [Q1,Q3]	1.0[0,1.0]	0[0,1.0]	0.011	1.0[0,1.0]
Serology, n (%)				
Anti DNA*(24)	315 (36.0)	131 (28.3)	0.008	446 (33.3)
AntisSm*(186)	236 (30.3)	156 (39.1)	0.003	392 (33.3)
Low Complement *(46)	184 (21.3)	126 (27.7)	0.003	310 (23.5)
Kidney damage, n(%)*(144)	58 (7.2)	25 (5.9)	0.479	84 (6.7)
Corticoids, the highest does , n(%)				
Less than 10 mg of prednison2	301 (63.9)	180 (65.9)	0.946	487 (64.6)
10-30mg/d	122 (25.9)	66 (24.2)		190 (25.2)
>30-60mg/d	40 (8.4)	23 (8.4)		65 (8.6)
>60mg/d	8 (1.7)	4 (1.4)		12 (1.5)
Missing	421 (47.2)	198 (42.0)		636 (45.8)
Antimalarial, n (%)*(99)	723 (87.6)	404 (91.0)	0.090	1146 (88.8)

Conclusions: Accrual damage is not related with pregnancy history in SLE and lupus nephritis patients of RELESAR registry. However, complicated pregnancies can impact in more accrual damage.

Keywords: Accrual damage, antiphospholipid syndrome, systemic lupus erythematosus.

0140

MULTIMODAL OPHTHALMOLOGIC EVALUATION CAN DETECT RETINAL INJURIES IN ASYMPTOMATIC PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME SECONDARY TO SYSTEMIC LUPUS ERYTHEMATOSUS

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The aim of this study is to perform a multimodal ophthalmological evaluation, including the use of Optical Coherence Angiography (OCTA), in patients with APS secondary to SLE (APS/SLE) without complaints or history of eye problems and to compare the findings with SLE patients and healthy individuals.
Patients and methods: We analyzed APS/SLE patients followed at our tertiary Rheumatology outpatient clinic. All patients fulfilled Sydney APS classification criteria (2006) and the diagnosis of SLE was based on the revised criteria of the American College of Rheumatology. SLE activity was classified according to the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K) criteria. Laboratory tests were performed at the moment of the ophthalmological examination. The study consisted on the comparison of 3 groups of ocular asymptomatic subjects: A - patients with APS secondary to SLE (APS/SLE) and no systemic disease activity (defined by SLEDAI-2K = 4); B - patients with SLE without APS and no systemic disease activity; C - healthy individuals without comorbidities. The groups were matched for sex and age. A complete multimodal ophthalmological examination was performed including optical coherence tomography, OCTA and microperimetry.
Results: One hundred and fifty eyes of 75 subjects (25 individuals each group) were included. There was a female predominance (88%) and mean age of the patients was 42.3 ± 8.6 years. Antinuclear antibodies were detected in all patients. Among antiphospholipid antibodies (aPL), lupus anticoagulant was detected in 24 of 25 patients of APS/SLE (96%) and 2 of 25 SLE patients (8%) ($p<0.001$). All patients were without disease activity. Ophthalmologic findings were observed in 9 (36%) APS/SLE patients, 11 (44%) SLE patients and none (0%) of healthy individuals ($p<0.001$). Drusen-like deposits (DLDs) were the most common retinal finding in both lupus groups with 16% (4 patients, 8 eyes) in the APS/SLE group and 24% (6 patients, 11 eyes) in the SLE group. Half of patients affected by DLDs had no previous history of lupus nephritis. DLDs consist of extracellular deposits of lipids, proteins and cellular debris, which accumulate below the retinal pigment epithelium. In APS/SLE patients, the most relevant changes observed were paracentral acute middle maculopathy (PAMM) - which is characterized by the infarction of the inner nuclear layer due to ischemic events located in the intermediate and deep capillary plexus of the retina (2 patients, 3 eyes) and homonymous quadrantanopsia (1 patient). Triple positivity to aPL in the APS/SLE group was present in two patients (100%) with PAMM versus four patients (16%) without PAMM ($p=0.05$). Mean values of adjusted Global AntiphosPholipid Syndrome Score (aGAPSS) in our patients with PAMM and APS/SLE patients was 14 ± 0 and without PAMM was 9.69 ± 3.44 ($p = 0.09$).
Conclusions: DLDs was the most common retinal finding in both SLE groups, even without associated nephritis. PAMM was observed in 8% of APS/SLE patients with no previous ocular complaints. Triple positivity to aPL and high aGAPSS were the most common associated risk factors for PAMM in the APS/SLE group.
Keywords: Antiphospholipid syndrome, Systemic lupus erythematosus, Optical Coherence Tomography Angiography, Venous thrombosis, Arterial thrombosis, Retina.

0141

EXTENSIVE SKIN NECROSIS IN PREGNANT WOMAN: AN UP-TO-DATE VIEW OF ANTIPHOSPHOLIPID SYNDROME

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Case report: 23-year-old female. Medical History: 2-year diagnostic of Graves-Basedow disease, treated with methylmercaptoimidazole, during 21-week pregnancy. Current illness: Presents painful skin lesions of acute appearance, on the face, arms and thighs of a burning nature, with progressive appearance of new lesions and increase in size of pre-existing ones. Afebrile, without other accompanying sign-symptoms. Physical exam: fair general condition, lucid, HR: 120 bpm, RR: 16 rpm, BP. 100/60 mmHg. Thyroid gland enlarged, mobile, without thyroid murmur. Normal uterine tone, fetal heart rate: 144 bpm. Skin and skin appendages: Symmetrical polymorphous erythematous-violaceous lesions, with well-defined borders, raised, ranging from 5 to 20 cm in diameter, some harden on palpation, without crepitus, secretion or signs of phlogosis, distributed on the face, lateral region of both arms, inner and outer region of the thighs, not present on scalp, torso, legs, palms and soles. Mucosal: two painless oral ulcers, with sharp edges, clean base. Entry Laboratory: Hct: 33,3%, Hb: 11,3 g/dl, MCV: 85 fl, MCHC: 34 g/dl. Leukocytes: 3650/ml, segmented neutrophils: 2560/ml, Lymphocytes: 800/ml, Platelets: 189000/ml. ESR: 45 mm/h. Hepatogram and complete urine: normal, PT: 79, KPTT: 49,1. TSH: <0,005 uU/ml,

T4L: 1,68 ng/dl, TSHrAb: 15,10 UI/l (Up to 1,75). Immunological Panel: anti-histone antibodies: NEGATIVE, Ac ANCA-c y ANCA-p: NEGATIVE, cryoglobulins: NEGATIVE, ANF: 1/1280 homogeneous pattern, Ac anti DNA: POSITIVE 1/40, Ac anti La/SSB: 29,9 U/ml, Ac anti Ro/SSA: 10,5 U/ml, Complement fraction C3: 63 mg/dl (84-193), C4: 5 mg/dl (20-40), Latex RF: 7, CRP: 29,55 mg/l. Lupus inhibitor present. Ac anti Beta 2 IgG glycoprotein: 6,0 U/ml, Ac anti Beta 2 IgM glycoprotein: 10,8 U/ml, Ac IgG anti-cardiolipins: 5,8 U/ml, Ac IgM anti-cardiolipins: 16,8 /ml. Skin biopsy: Thrombosing vasculopathy, without inflammatory infiltration in the vascular walls, compatible with antiphospholipid syndrome. Evolution: The patient presents rapid worsening of skin lesions with necrosis, formation of blisters that deroofed and sharpening of burning pain in the lower limbs. Treatment: Pulses of methylprednisolone, hydroxychloroquine, anti-aggregation and anticoagulation with LMWH (enoxaparin), with clinical improvement and subsequent surgical debridement of the lesions. Initially proposed differential diagnosis: primary antiphospholipid syndrome (APS), APS secondary to systemic lupus erythematosus (SLE), drug-induced lupus or drug-induced ANCA vasculitis (Methylmercaptoimidazole). Evolution: It was interpreted as compatible with antiphospholipid syndrome associated with SLE with first stage pregnancy. The treatment of hyperthyroidism is discarded to be the cause of the condition, excluding drug-induced Lupus and drug-induced Vasculitis. The patient displayed adequate evolution of the lesions after surgical debridement, completing her pregnancy without obstetric complications.
Keywords: Systemic lupus erythematosus, antiphospholipid syndrome, skin, pregnancy.

0142

CRITICAL LOWER LIMB ISCHEMIA AT THE ONSET OF ANTIPHOSPHOLIPID SYNDROME-RELATED ABDOMINAL AORTIC THROMBOSIS: A CASE REPORT

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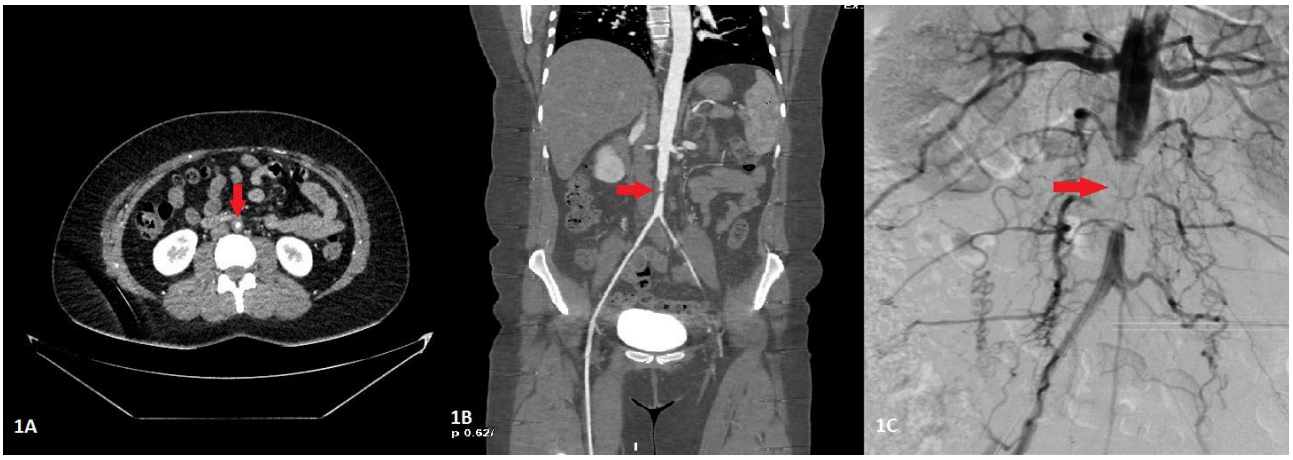
The antiphospholipid syndrome (APS) is characterized by clinical manifestations associated with venous and/or arterial thrombotic events in the presence of antiphospholipid antibodies (aPL). Thrombosis of the aorta is very unusual. Therefore, we report an unusual presentation of APS manifested by thrombosis of the abdominal aorta (AA).
Case report: A 28-year-old Mestizo non-pregnant woman, previously healthy and without any cardiovascular risk referred the onset of progressive claudication of the lower limbs associated with burning pain on her feet of seven months in duration. Three days before seeking help, she noticed cyanosis of some of her toes associated with moderate pain. On physical examination: patient presented normal vital signs and was afebrile; she had cyanosis of the 1st to the 3rd toes of her left foot with an ulcer present on the 2nd toe; pallor of the right foot, decreased dorsalis pedis and posterior tibial pulses, bilaterally were demonstrated. Because of these findings, she was hospitalized, and images were obtained: Arterial Doppler showed posterior tibial artery monophasic flow and almost undetectable flow in both dorsalis pedis arteries. Computed tomography angiography (CTA) showed subacute arterial thrombosis of the AA with a decrease in its lumen of 30 to 80 % associated with stenosis by vasospasm in all arterial structures of both lower limbs (Figure). The patient requested to be discharged against medical advice before any intervention could have been done. One month later she presented to the emergency service with necrosis of the 2nd and 3rd toes of her left foot. Arteriography showed a decrease in the AA lumen of more than 95 %. Laboratory tests revealed: activated partial thromboplastin time 117 seconds which did not correct with plasma, positive lupus anticoagulant, anti-β2-glycoprotein I IgG 48 U/mL and anticardiolipin IgG 55 GPL/mL. These tests remained positive 12 weeks apart. Therefore, thrombotic APS was considered with involvement of the infrarenal AA. The patient was started on clopidogrel 75 mg/d, acetylsalicylic acid 100 mg/d and warfarin 10 mg/d; in addition, angioplasty and stenting were performed in the AA with a good revascularization. One week later, the patient showed improvement in the ischemia of her lower limbs; one month later improvement on the claudication was noted but she had already lost the 2nd and 3rd toes of her left foot.



Conclusions: This patient presented an unusual arterial thrombosis localization, AA, associated with the presence of aPL; this caused lower limb ischemia, which improved with stenting.
Keywords: Antiphospholipid syndrome, thrombosis, abdominal aorta.

0143

POLYAUTOIMMUNITY IN SYSTEMIC LUPUS ERYTHEMATOSUS: HIGH FREQUENCY OF ANTIPHOSPHOLIPID SYNDROME AND THROMBOTIC COMPLICATIONS

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The presence of more than one autoimmune disease (AD) in a single patient it´s defined as Polyautoimmunity (PolyA). One of the most frequently AD presenting this phenomenon is Systemic Lupus Erythematosus (SLE). The aim of this study was to describe the frequency of PolyA in a Colombian-single center SLE cohort and to analyze the presumable associated factors.
Patients and methods: This is an observational, analytical, cross-sectional study in SLE patients attending a specialized rheumatology Colombian center and fulfilling SLICC/2012 criteria from January 2015 to December 2020.Univariate, bivariate and multivariate analyses methods were developed to identify the associated factors with PolyA. Ethics committee approved the study.
Results: A total of 463 patients fulfilled the SLICC/2012 criteria. (405 patients were females, mean age was 47.3±15.3 years and mean duration of disease was 10,6±10,1 years). There were 161/463 (34.7%) patients with PolyA. The most frequent PolyA was antiphospholipid syndrome (APS) (77 patients;16.6%), followed by Sjögren's syndrome (49 patients;10.5%) and systemic sclerosis (16 patients 3.6%). Antimalaric drugs, antiphospholipid antibody positivity as determined by SLICC criteria, pulmonary embolism and additional associated factors with PolyA were identified by simple logistic regression (See Table 1). After adjusting a multivariate model, PolyA patients were older, had sicca symptoms, thrombotic complications, and less renal compromise. Associated factor through simple logistic regression and multiple logistic regression are shown in Table 1.

Variable	PolyA n=161(%)	No PolyA n 302 (%)	SLR*	MLR**
Age(SD)	50.9 (13.7)	45.4 (15.7)	1.02 (1.01-0.03)	1.01 (1.00-1.03)
Lupus nephritis (SLICC Criteria)	46 (28.6)	137 (45.4)	0.48 (0.31-0.72)	0.61 (0.38-0.96)
Deep venous Thrombosis	28 (17.4)	11 (3.6)	5.56 (2.69-11.52)	5.98 (2.79-12.8)
SNC occlusion	11 (6.8)	2 (0.7)	11 (2.40-50.26)	10.23 (2.11-49.46)
Xerophthalmia	29 (18)	16 (5.3)	3.92 (2.06-7.48)	3.64 (1.84-7.22)
Corticosteroids	109 (67.7)	192 (63.6)	1.2 (0.80-1.80)	1.24 (0.79-1.93)
Pulmonary embolism	13 (8.1)	5 (1.7)	5.21 (1.82-14.9)	
Antimalaric drugs	111 (68.9)	241 (79.8)	0.56 (0.36-0.86)	
Osteoporosis	29 (18)	30 (9.9)	1.99 (1.14-3.45)	
Thrombocytopenia SLICC	45 (28)	40 (13.2)	2.54 (1.07-3.20)	
ANAS SLICC	141 (87.6)	239 (79.1)	1.85 (1.07-3.20)	
Antiphospholipid SLICC	72 (44.7)	56 (18.5)	3.55 (2.32-5.43)	

**SLR: Simple Logistic Regression OR (95% CI); MLR: **Multiple Logistic Regression OR (95% CI). R2 Nagelkerke:0.25; ANAS: antinuclear antibodies; SLICC: Systemic Lupus Erythematosus International Collaborating Clinics Criteria; SNC: Central Nervous System*

Conclusions: PolyA is a frequent sub phenotype in SLE (Nearly one in three patients). The most frequent Polyautoimmunity is APS. The use of antimalaric drugs might be considered as a protective factor for PolyA. Thrombotic complications were significantly associated with PolyA in a simple logistic regression and in a multivariate model, and an inverse association with lupus nephritis was found. Likewise, studies should continue to evaluate the behavior of PolyA in SLE patients, to understand its potential associations and implications.
Keywords: SLE, APS, thrombosis

0145

ASSOCIATION BETWEEN THE ADJUSTED GLOBAL ANTIPHOSPHOLIPID SYNDROME SCORE (AGAPSS) AND EXTRA-CRITERIA MANIFESTATION, ON PRIMARY OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (POAPS) PATIENTS

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The aim of this study is to evaluate the association between the aGAPSS and the extra-criteria manifestation on Primary Obstetric antiphospholipid syndrome (POAPS) patients.
Patients and methods: This retrospective multicenter study included 169 consecutive POAPS patients who attended in 6 centers (these centers are tertiary referral hospitals and are responsible for the management of severe APS patients). At the time of diagnosis, clinical and laboratory variables were evaluated, and the aGAPSS was calculated. The cut-off point was chosen considering the Youden Index, which was calculated for every possible value of the score. The value 7 was the most suitable for predicting events in our cohort. Based on this result, we classified POAPS patients into 2 groups according to the aGAPSS: a high aGAPSS, X=7, and a low aGAPSS, X<7. We evaluated the distribution of extra-criteria manifestation according to aGAPSS.
Results: Among the 169 POAPS patients (median age: 32 years; interquartile range: 28-37 years), we found that the presence of an aGAPSS=7 was associated with the possibility of presenting any extra-criteria manifestations OD: 6,081 (2,585 – 14,01), p=<.0001; especially: livedo reticularis OD: 4.224 (1,714 – 10,412), p=0.001 and Thrombocytopenia OD: 6,644 (1,364 – 32,34), p=0.01.
Conclusions: Our study, we suggest that POAPS patients with a higher risk profile A high aGAPSS (=7), might be at higher risk for developing extra criteria manifestations.
Keywords: Antiphospholipid syndrome.

0146

NEUROLOGICAL AFFECTATION BY ANTIPHOSPHOLIPID SYNDROME

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Our aim is to present 3 clinical cases of neurological involvement as a manifestation of antiphospholipid syndrome.
Case reports: Case 1: 44-year-old woman, urban area, housewife. Consultation for reticular livedo of spontaneous appearance throughout the body, not related to exposure to low temperatures. She denies abortion, thrombotic events. High blood pressure for 3 years without treatment. Laboratory: Platelets: 130,000; aPTT: 42 sec; VDRL: 1:4 fTA Abs: Negative. ANA/AntiDNA: Negative. Lupus anticoagulant, Anticardiolipin IgM positive. During her hospitalization, she presented generalized tonic/clonic seizures. MRI was performed: lacunar ischemic lesions. It is interpreted with primary APS and anticoagulation is started. Case 2: 53-year-old male, rural area, farmer. Consultation due to swelling of the left arm extended from the shoulder to the wrist, followed by intense pain on compression, with local erythema without change in temperature in the area. Diagnosed with schizophrenia 5 years ago in follow-up by psychiatry. On physical examination: erythematous indurated area throughout the left upper limb, presence of pulses. Doppler ultrasound is performed and thrombosis of the subclavian vein on the left side is confirmed. Laboratory: prolonged aPTT, thrombocytopenia, and nonreactive VDRL. Lupic antibody is requested: positive, Ab Anticardiolipin IgG and IgM negative. ANA/AntiDNA: negative. MRI is performed, reporting multiple ischemic lesions in the frontal region. It is interpreted with primary APS and anticoagulation is started. CASE 3: 57-year-old woman, urban area, housewife. Consultation due to generalized tonic-clonic seizure lasting 5 min and loss of muscle strength in the right side of the body. Epilepsy for 20 years under treatment with carbamazepine. DM2, hypertension in regular treatment. She denies abortions and thrombotic events. Physical examination: right brachiocrural hemiplegia. Reflexes exalted. Skull CT: old ischemic lesion and cerebral edema. Laboratory: Thrombocytopenia. Non-reactive VDRL. Positive lupus antibody. MRI of the brain is performed: ischemic lacunar lesions. In the 3 patients; the tests were repeated 12 weeks after admission and remained positive.
Conclusions: Vascular thrombotic phenomen are recurrent, and the symptoms vary in relation to the affected territory. The diagnosis can be established when there are unexplained signs of arterial or venous thrombosis, as well as repeated spontaneous abortions associated with thrombocytopenia, in which the positivity of specific antibodies can be demonstrated.
Keywords: Antiphospholipid syndrome, antiphospholipid antibodies, thrombosis.

0150

ANTIPHOSPHOLIPID SYNDROME. CHARACTERIZATION OF PATIENTS IN A REFERRAL HOSPITAL

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The aim of this study is to describe the sociodemographic, clinical and laboratory characteristics of patients with antiphospholipid syndrome who attended the National Hospital of Itaugua from January 2017 to February 2022.
Patients and methods: Observational, retrospective, cross-sectional, descriptive study. Sixty-six patients were included. Non-probabilistic sampling of consecutive cases. Quantitative variables were expressed as mean and SD (normal variables) and medians and RIQ (non-normal data). Qualitative variables were expressed as absolute values and percentages. The protocol was approved by the Ethics Committee of the National Hospital. The authors have no conflicts of interest.
Results: Of the 66 patients diagnosed with PFS, 53 (80%) were women. The median age was 34 years (RIQ 58). 57.6% were from the Central department. Secondary PFS was the most frequent form (72%), as 39 subjects (59%) had the diagnosis of SLE. Of the total patients, 59% had some risk factor for developing a thrombotic manifestation. The most common type of manifestation was cerebral ischemia present in 15 patients (22%). Twenty-two percent of patients had more than one aPLs. APTT was prolonged in 83% of the subjects. No case of catastrophic antiphospholipid antibody syndrome was found. Mortality was 4.5%. The most frequent cause of death was infections.
Conclusions: Most of the patients were young adult women from urban areas. PFS secondary to SLE was the most frequent form of presentation. Most of them presented risk factors for thrombotic manifestations. The most frequent form of presentation was cerebral ischemia. The most frequent cause of death was infections.
Keywords: Antiphospholipid syndrome, antiphospholipid antibodies, systemic lupus erythematosus.

0151

RESOLUTION OF LIBMAN-SACKS ENDOCARDITIS WITH ANTICOAGULANT TREATMENT

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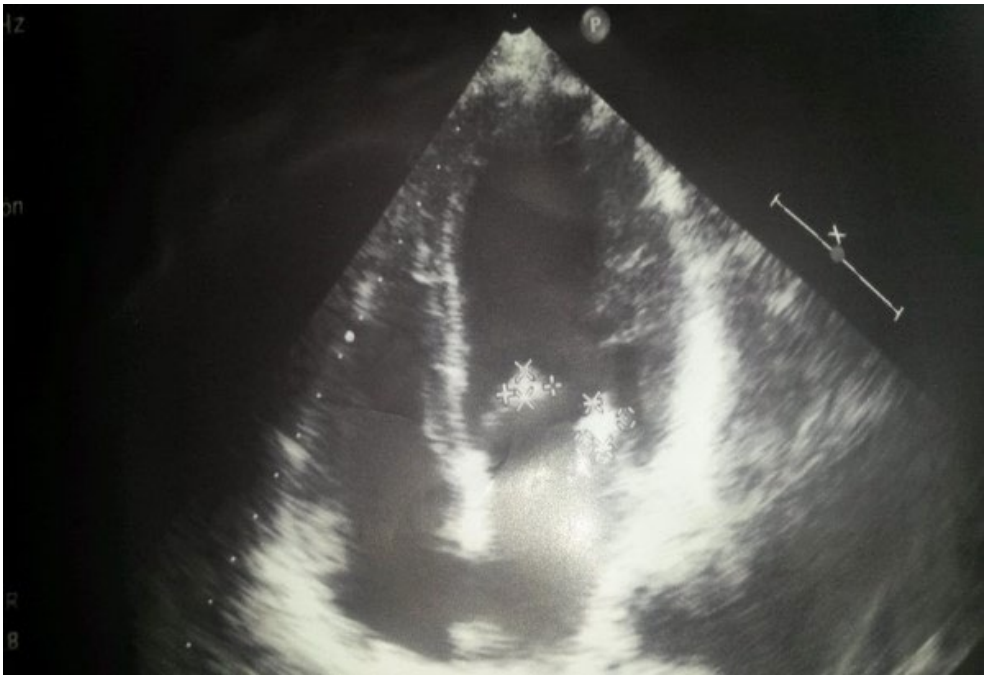
Libman-Sacks endocarditis is characterized by the presence of sterile valvular vegetations with a predilection for the mitral and aortic valves. It is associated with Systemic Lupus Erythematosus (SLE) activity and the presence of antiphospholipid antibodies (aPL). The treatment of Libman-Sacks (LS) endocarditis is controversial due to the scarcity of information on the risk-benefit of anticoagulation. The objective of this report is to describe the evolution of a patient with SLE and antiphospholipid syndrome (APS) secondary to LS endocarditis.
Case report: A 31-year-old female patient with a history disease of APS secondary to SLE in 2013. She presented as manifestations of retinal thrombosis, hemichorea in childhood, class IV lupus nephritis, ANAs 1/80, anti Sm, Positive RNP and hypocomplementemia. Presented fetal loss at 16 weeks of gestation; with strong positivity for lupus inhibitor and IgG anticardiolipins 56 GPL. "In 2014 she was hospitalized because of DVT, and started anticoagulation with acenocoumarol. She reported an episode of endocarditis in 2013, so a transthoracic echocardiogram (TTE) was requested, which reported calcium density vegetation on both mitral valve leaflets, of significant size on the free edge of the atrial side.
Results: A new TTE is performed 3 months later, and it shows that the vegetations disappear.



Conclusions: We present the case of a patient with APS secondary to SLE with LS endocarditis, whose vegetations disappeared after performing anticoagulant treatment. Echocardiographic evaluation should be considered in SLE patients with APS Antibodies, especially triple aPL positivity, even if they did not have specific symptoms of LS endocarditis. In addition to the clinical and laboratory characteristics of APS and LS Endocarditis, anticoagulation therapy should be considered to prevent thromboembolic complications, even in the absence of the clinical manifestations of APS.
Keywords: Libman-Sacks endocarditis, anticoagulation, antiphospholipid syndrome.

0152

SYSTEMIC LUPUS ERYTHEMATOSUS ASSOCIATED WITH ANTIPHOSPHOLIPIDIC SYNDROME

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The aim of this study is to determine sociodemographic, clinical and laboratory characteristics of patients with systemic lupus erythematosus associated with antiphospholipid syndrome who attended the Itauguá National Hospital between 2018 and 2020.
Patients and methods: Observational, descriptive, retrospective, cross-sectional study. 100 diagnosed with SLE from 2018 to 2021 were included. Non-probabilistic sampling of consecutive cases. Quantitative variables were expressed as Mean and SD. Qualitative variables in absolute values and percentages. The protocol was approved by the Ethics Committee of the National Hospital. The authors have no conflicts of interest.
Results: Of the 100 lupus patients, 67 were women with a mean age of 37 years ± 12 SD. 31% of patients with SLE had APS criteria. The most frequently positive antiphospholipid antibody (aPL) was anticardiolipin antibody (ACL) followed by lupus anticoagulant (LA). The most frequent clinical manifestation was thrombosis (55%). Of the 31 patients diagnosed with APS, 13 of them were inactive (SLEDAI). The most frequently established treatment was anticoagulation.
Conclusions: The antiphospholipid syndrome is frequently associated with SLE. In our study group, a little more than a third of the patients with SLE met the criteria for APS. Most of them were women over 30 years of age, the most frequent clinical manifestation was venous thrombosis followed by arterial thrombosis. The most frequently positive aPF was anticardiolipin antibody. Most patients had no or mild activity according to the SLEDAI scale. Keywords: antiphospholipid syndrome, systemic lupus erythematosus, anticardiolipins, antiβ2 glycoprotein1, lupus anticoagulant, thrombosis, anticoagulation.
Keywords: Antiphospholipid syndrome, systemic lupus erythematosus, anticardiolipins, antiβ2 glycoprotein1, lupus anticoagulant, thrombosis, anticoagulation.

0153

CLINICAL AND SEROLOGICAL CHARACTERISTICS OF ANA-POSITIVE VERSUS ANA-NEGATIVE ANTIPHOSPHOLIPID ANTIBODY-POSITIVE PATIENTS WITHOUT OTHER SYSTEMIC AUTOIMMUNE DISEASES: RESULTS FROM THE APS ACTION CLINICAL DATABASE AND REPOSITORY

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APS ACTION is an international Clinical Database and Repository of persistently antiphospholipid antibody (aPL)-positive subjects, collecting demographic, medical history, and aPL data. This study focused on the prevalence of antinuclear antibodies (ANA) in aPL positive patients without a defined concomitant autoimmune disease. The objective of this study was to evaluate potential differences when stratifying patients by ANA, and to better phenotype aPL positive patients.
Patients and methods: Data from aPL positive patients with or without APS classification criteria were retrieved from the APS ACTION Database. Patients with a diagnosis of systemic lupus erythematosus (SLE) or other connective tissue disease were excluded. Patients were divided in two groups (ANA+ and ANA-), based on ANA status at registry entry. Subsequently, demographic, clinical (including 1997 ACR SLE classification criteria), and serological data were compared between the two subgroups.
Results: 521 aPL-positive patients were included in the study (mean age 52.1±13 years, 70% female). Among them, 224 patients were ANA+ and 297 ANA-. Patients characteristics are displayed in Table 1. ANA positivity was significantly associated with previous history of hematological manifestations as a whole, including hemolytic anemia, thrombocytopenia, and leukopenia, (19.3% ANA+ vs. 8.4% ANA-, p <0.01) and livedo reticularis (15.1% ANA+ vs. 10% ANA-, p <0.05). A positive association with the number of unexplained fetal deaths beyond 10 weeks of gestation was also noted (p <0.05), and a trend was observed for lower platelet count, aPL-related nephropathy and arthritis, though these associations were not statistically significant. No significant association was found for extra-criteria manifestations such as hemolytic anemia and history of thrombocytopenia, when considered individually. When sub-analyzing the ANA- group, a significant association with any history of arterial thromboses (29.4% ANA+ vs. 38.8% ANA-, p <0.02) and the number of arterial events was observed (p

<0.01). When evaluating ANA positivity in aPL carriers and primary APS (PAPS) individually, the association between ANA+ and previous hematologic disorder remained significant for both groups, with stronger significance for PAPS patients. In addition, ANA positivity in PAPS patients was significantly associated with livedo reticularis and previous history of small vessel disease (p <0.05).

Patients' characteristics	Total patients (N.521)	ANA + (N.224)	ANA - (N.297)	P value
Demographics				
Age, mean years (±SD)	52.1 (13)	51.4 (13)	52.6 (13)	-
Gender, female, n(%)	365 (70)	162 (72)	203 (68)	n.s
Classification and Clinical manifestations				
aPL positive (aPL carriers), n (%)	98 (19)	51 (23)	47 (16)	0.045
PAPS, n (%)	423 (81)	173 (77)	250 (84)	0.045
Thrombotic PAPS, n (%)	306 (72)	128 (74)	178 (71)	n.s
Obstetric PAPS, n (%)	54 (13)	21 (12)	33 (13)	n.s
Thrombotic and obstetric PAPS, n (%)	63 (15)	24 (14)	39 (16)	n.s
Venous Thrombosis, n (%)	223 (60)	98 (64)	125 (58)	n.s
Arterial Thrombosis, n (%)	182 (50)	66 (43)	116 (53)	0.02

Conclusions: In this large international cohort, ANA positivity was associated with a higher rate of hematologic manifestations in aPL-positive patients without connective tissue disease. ANA+ patients, especially those with PAPS, showed a tendency toward a higher rate of microvascular manifestations and arthritis. ANA- subjects showed a significantly higher rate of arterial thrombosis, without any other significant association with clinical, serological or demographic data.
Keywords: Antinuclear antibodies, antiphospholipid antibodies, phenotyping.

0154

ANTIPHOSPHOLIPID ANTIBODIES LEVELS IN A COHORT OF PATIENTS WITH CONNECTIVE TISSUE DISEASES: CLINICAL-IMMUNOLOGICAL CORRELATE

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The current classification criteria for Antiphospholipid Syndrome (APS) determine levels of antiphospholipids (APLa) >=40 mg/dl (GPL/MPL) (activity of lupus inhibitor (LI), anticardiolipin (ACLa) IgG/IgM and anti B-2 glycoprotein 1 IgG/IgM (AB2GP1) although events can also occur with intermediate and low levels. Other clinical manifestations have been described, which at the moment are not considered within the clinical criteria (non-criteria manifestations - NCM). It can be primary or associated with another autoimmune disease (AIDA). Objectives: To describe the clinical manifestations associated with APS (criteria and NCM), to evaluate their relationship with APL titers (10 to <40 mg/dl and >=40 mg/dl) and the treatments used.
Patients and methods: retrospective, cross-sectional, descriptive study. Inclusion: >=18 years with at least one APL measurement >=10 mg/dl. Exclusion: primary thrombophilias, oncological or infectious disease.
Results: 105 patients were included, 80% with 2 APLa measurements (by 12 weeks apart). Female: 94.9%, median age 42 ys (IQ 25-75% 31-55), health insurance 67%, mean follow-up-months 33 (IQ 25-75% 17-58). Associated APS: 97.1%, systemic lupus erythematosus 81%, Sjögren's syndrome 24%, rheumatoid arthritis 7.6%, scleroderma 6.7% and others 10.5%. Treatments: oral contraceptives 8%, anticoagulant (ACO) 41%, aspirin (ASA) 62%, hydroxychloroquine 85%, corticosteroids 71.5%. Total Events: 114 in 105 patients (1.09 event: 1 patient). Total Obstetric Events (OEs): 80 (70%). Total Thrombotic Events (TEs): 34 (29.8%) Factors associated with a higher prevalence of events: smoking (TB) 25.5%, hypertension (HT) 30%, obesity 11.5%, sedentary lifestyle 25.9% and psychiatric illness 23% (depression). Analysis by groups: APLa >= 40 mg/dl: single (+0 47% (50), double (++) 26% (27), triple (+++) 22% (23) and APLa10 < 40 mg/dl: 5.25% (5). APLa >=40 mg/dl Group: 21 patients showed OEs: (40% OR 1.19 CI 0.3-3.8), total OEs was 66 (70%); 24 patients presented TEs (46% OR 2.63 CI 1-6), total TEs 28 (29.8%). APLa >=40mg/dl: 2.36 OEs:1 TEs. NCM 75% (OR 1.96, CI 0.8-4.6), thrombocytopenia 29% (OR 2.28 CI 1-7.2). CVRF: TB 29% (OR 1.53 CI 0.3-7.5), HT 23% (OR 0.94 CI 0.3-2.3), sedentary lifestyle 34% (OR 2.66 CI 1-6.7). Psychiatric illness 32% (OR 3.28 CI 1.2-8.8). AIDA: 84.5% (OR 2.82 CI 1.1-7.2). ACO 56% (OR 3,51 CI 1,54-7,9). Hospitalizations 57% (OR 3.62 CI 1.7-9.2), ASS 75% (OR 0,12 CI 0,01-1,2). APLa 10-<40 mg/dl Group: 7 patients had OEs 29% (OR 0.58 CI 0.20-1.56),

total of OEs 14 (58%). 4 patients showed TEs 17% (OR 0.29, CI: 0.09-0.9), a total of 6 TEs (25%). APLa 10-<40 mg/dl: 2.33 OEs:1 TEs. NCM 66% (OR 0.94 CI 0.36-2.5). AIDA 58% (OR 0.44 CI 0.16-1.18). Hospitalizations 16.6% (OR 0.28, CI: 0.08-0.091), ASA 41% (OR 7,3, CI: 1,1-50).
Conclusions: The greatest APLa titers were associated with the highest occurrence of OEs/TEs. In the APLa 10 at <40 mg/dl Group: OEs were predominant (population bias). A relevant percentage of patients had NCM in both groups. Psychiatric illness (depression) was associated with more risk of events in the group with high APLa titers.
Keywords: Antiphospholipid syndrome, associated with another autoimmune disease, non-criteria manifestations,

0155

HIGH TITER OF FALSE POSITIVE VENEREAL DISEASE RESEARCH LABORATORY (F+VDRL) TEST AMONG PATIENTS WITH OBSTETRIC ANTIPHOSPHOLIPID ANTIBODIES SYNDROME (OAPS) HAVING TRIPLE POSITIVITY PROFILE OF ANTIPHOSPHOLIPID ANTIBODIES (APL)

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The aim of our study was to explore the distribution of f+VDRL in OAPS patients.
Patients and methods: We studied 106 women with OAPS (International consensus classification criteria). Patients were classified according to the profile of aPL (lupus anticoagulant, anti-β2 glycoprotein I antibody and anticardiolipin antibodies) in triple positive (15.1%, n=16), double positive (15.1%, n=16) and single positive (69.8%, n=74). The median age was 32 years (28-37). All patients had negative treponemal test, absence of clinical or epidemiological evidence of syphilis and they had a history of pregnancy morbidity: 49 (46.2%) fetal loss, 75 (70.8%) early miscarriage, 36 (33.9%) late miscarriage, 45 (42.4%) premature birth, 17 (16.0%) preeclampsia and 17 (16.0%) low weight birth. All patients were treated with conventional therapy (aspirin plus Low Molecular Weight Heparin) during a new pregnancy. Patients with other thrombophilia diagnosis, metabolic or endocrine alterations, or patients receiving an additional treatment were excluded.
Results: Among all patients, 8.5% (9/106) presented f+VDRL, 44.4% (4/9) with titers≥1/8 (1/8-1/64) and with a triple positive aPL profile. Of these 9 patients with f+VDRL, 8/9 managed to have healthy newborns while only one had an early abortion.
Conclusions: In conclusion, among OAPS woman, f+VDRL is a common condition. Despite the common beliefs, almost half of the f+VDRL patients had high titers and presented a triple positive profile of aPL. It seems that f+VDRL would not affect pregnancy outcomes. Besides, it is important that physicians would acknowledge that high titers of VDRL could not be only due to syphilis and it seems to be related to triple positivity.
Keywords: VDRL, Obstetric APS.

0156

ASPIRIN TRIGGERED LIPOXINS MODULATE ENDOTHELIAL NITRIC OXIDE SYNTHASE PHOSPHORYLATION AND NITROSATIVE STRESS INDUCED BY ANTIPHOSPHOLIPID ANTIBODIES

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Antiphospholipid syndrome (APS) is an autoimmune disease characterized by the clinical manifestation of vascular thrombosis (VT) or pregnancy morbidity (PM) and persistent antiphospholipid antibodies (aPL). aPL can bind to endothelial cells and induce endothelial activation and dysfunction. In endothelial dysfunction, endothelial nitric oxide synthase (eNOS) phosphorylation and nitric oxide production are altered. Low-dose aspirin is used to prevent and treat diverse alterations of pregnancy. One of the mechanisms of action of aspirin is to induce the production of aspirin-triggered-lipoxins (ATL), which have anti-inflammatory and antioxidant effects. ATL could modulate endothelial function in APS. The objective of this study was to evaluate the modulatory effect of ATL over the activation of eNOS and nitrosative stress induced by aPL.
Patients and methods: We included women with the presence of aPL and clinical criteria of PM/VT or VT only; women with pregnancy morbidity only and positive for non-criteria aPL (SN-OAPS). In sera from patients, nitrosative stress was assessed. The protein expression of nitrotyrosine and the phosphorylation of eNOS (at Ser1177) were estimated in human umbilical vein endothelial cells (HUVECs) stimulated with polyclonal IgG with or without ATL
Results: Women with SN-OAPS had increased circulating levels of nitrites and nitrotyrosine. Likewise, polyclonal IgG from

either SN-OAPS or VT patients stimulated nitrotyrosine expression in HUVECs. ATL decreased the nitrotyrosine expression induced by polyclonal IgG from the SN-OAPS group. ATL also recovered the reduced eNOS phosphorylation at Ser1177 in HUVECs stimulated with polyclonal IgG from women with PM/VT or SN-OAPS. Therefore, increased nitrosative stress present in the serum of women with pregnancy morbidity only and positive for non-criteria aPL could be associated with IgG-mediated impaired endothelial nitric oxide synthesis in endothelial cells. ATL prevents these cellular changes.
Conclusions: Increased nitrosative stress present in the serum of women with pregnancy morbidity only and positive for non-criteria aPL could be associated with IgG-mediated impaired endothelial nitric oxide synthesis in endothelial cells. ATL prevents these cellular changes.
Keywords: Endothelial nitric oxide synthase, aspirin-triggered-lipoxins, nitrosative stress, endothelial cells and antiphospholipid antibodies.

0158

ANTIPHOSPOLIPID SYNDROME ASSOCIATED TO SEVERE HIDRADENITIS SUPPURATIVA

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The aim of this report is to present the rarely notified association of antiphospholipid syndrome and hidradenitis suppurativa
Case report: A 27 years old female patient, with medical history of hypothyroidism, recreational use of marihuana and no records of abortions or pregnancy, referred that during the pandemic confinement in 2020 she noticed enlargement and pain of her left leg. Due to the social context, she waited a month before any consult, when she was diagnosed with acute thrombosis of the femoral plexus and the great saphenous vein, chronic anemia and hepatic enzyme alteration. She was started on anticoagulants and underwent laboratory and imaging studies that proved absence of neoplastic processes, but confirmed positive lupus anticoagulant and anticardiolipins Ig G and M in two controls more than 12 weeks apart, thus confirming antiphospholipid syndrome (APS). During her sonographic follow up, furuncles and fistulae of the groin were observed by the physician, who referred her to the dermatology consult based on the sonographic classification stage ECO SOS-HS III. The patient informed to have recurrent boils and flares since adolescence. The dermatologic diagnosis was severe Hidradenitis Suppurativa (HS) Hurley stage IIc-III, inflammatory phenotype, with bilateral clinical compromise of axillae, groin and vulva with dermohypodermic fistulae in all regions. She is currently expected to begin biologic therapy with adalimumab prior surgical conduct.
Results: Our patient had an autoinflammatory undiagnosed disease (HS) with increased TNF activity, which added to the lack of movement during confinement and the serum antibodies of APS, may be the explanation for the cause of acute deep vein thrombosis. This development eventually led to the diagnosis of both diseases and allowed the patient to receive proper assistance.
Conclusions: The association of APS and HS has been rarely described in the literature and presents a challenge for treatment, prognosis and follow up considering the pathophysiology of both diseases.
Keywords: Antiphospholipid syndrome, hidradenitis suppurativa, adalimumab.

0159

REAL-LIFE APPLICATION OF 2019 EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF ANTIPHOSPHOLIPID SYNDROME

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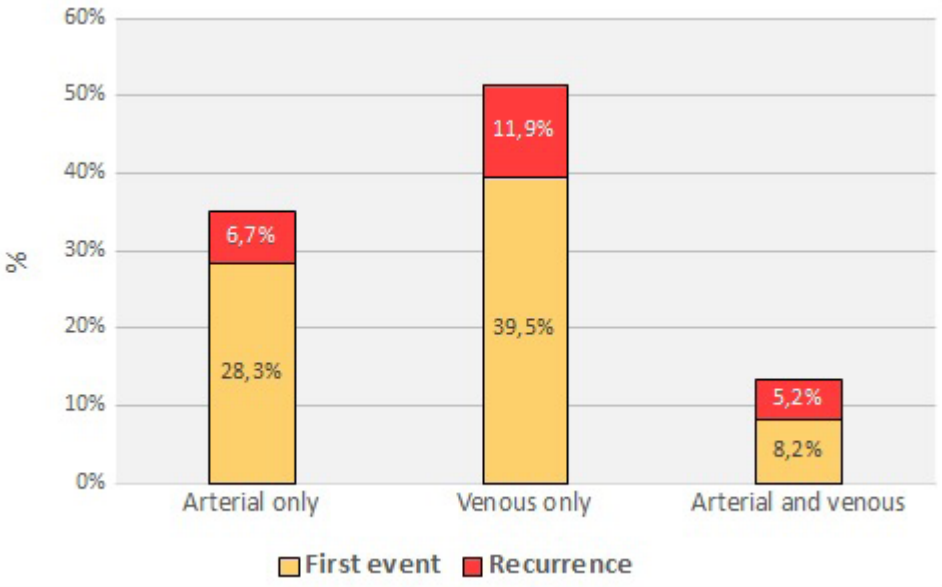
Antiphospholipid syndrome (APS) is a systemic autoimmune disease associated with thrombotic and obstetric morbidity, and the presence of antiphospholipid antibodies (aPL). In 2019, EULAR published a new set of recommendations for the management of primary and secondary APS prophylaxis according to aPL risk profile and type of event.

Patients and methods: An observational cross sectional multicentric study was performed using data from the APS Registry of the Argentinian Society of Rheumatology. Adult men and women with primary or secondary thrombotic-APS diagnosis (Sydney criteria) were included. Patients with positive aPL without criteria manifestations or asymptomatic were also included (aPL carriers) and classified into high or low risk profiles according 2019 EULAR guidelines definitions.

Results: Two hundred four patients were included (78.9% were female, 65.7% had thrombotic APS and 34.3% were aPL carriers). Thrombotic patients were older at the time of inclusion in the registry and had more arterial hypertension and dyslipidemia compared to aPL carriers (p<0.001 for all comparisons), 55.7% of aPL carriers fulfilled high risk profile definition; 56.1% of patients with definite APS and 69.6% of aPL carriers had other autoimmune disease associated (systemic lupus was the most frequent). Venous thrombosis was the most frequent type, and single thrombotic events were more frequent than recurrent (Graphic 1). Regarding pharmacologic treatment, 59% of aPL carriers with high risk profile matched EULAR recommendations for primary prophylaxis, and 72.3% (arterial thrombosis only), 66.7% (venous thrombosis only), and 88.9% (arterial and venous thrombosis) matched the recommendations for secondary prophylaxis (Table). Hydroxychloroquine and statins were used in 56% and 27% of thromboses, respectively.



Graphic 1: Distribution of thrombotic events.

Primary Prophylaxis for thrombotic	Events (high risk profile), n=39	Match recommendations
Antiplatelet drugs	6,15.4% (5.9-30.5)	23,59.0% (42.1-74.4)
HCQ*	12,30.8% (17.0-47.6)	
Antiplatelet +HCQ	17,43.6% (27.8-50.4)	
Without treatment	4,10.2% (2.9-24.2)	
Secondary prophylaxis for thrombotic	**Events , n=134**	**Match recommendations**
Arterial, n=47		
Antiplatelet drugs	11,23.4% (12.3-28.0)	34,72.3% (57.4-84.4)
Anticoagulation (VKA** or heparin)	20,42.5% (28.3-57.8)	
Anticoagulation + antiplatelet drugs	14,29.8% (17.3-449)	
Without treatment	2,4.2% (0.5-14.5)	

Venous , n=69		
Antiplatelet drugs	13,18.8% (10.4-30.1)	46,66.7% (54.3-77.6)
Anticoagulation (VKA** or heparin)	38,55.1% (42.6-67.1)	
Anticoagulation + antiplatelet drugs	8,11.6% (5.1-21.6)	
Without treatment	9,13%0 (6.1-23.3)	
Arterial and venous, n=18		
Antiplatelet drugs	2,11.1% (1.4-34.7)	16,88.9% (65.3-98.6)
Anticoagulation (VKA** or heparin)	7,38.9% (17.3-64.2)	
Anticoagulation + antiplatelet drugs	9,50.0% (26.0-74.0)	
Without treatment	0	

Conclusions: The 2019 EULAR recommendations were moderately applied for primary and secondary prophylaxis, with better execution in groups with arterial events
Keywords: Primary and secondary prophylaxis, APS, EULAR recommendations.

0160

A RARE CASE OF CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME (CAPS)

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Case report: 31-year-old Hispanic woman with a history of Hashimoto's Thyroiditis under control and treatment, primary Raynaud's syndrome diagnosed 3 years ago and two surgeries in the last two years (breast implants and abdominal liposuction) without complications and no obstetric history. Scheduled bilateral mammary pexy surgery was performed, she presented ASA I pre-surgery risk with normal lab values. Forty-eight hours later, she presented nausea, vomiting and watery diarrhea with a post-surgical wound without complications. She assisted for a consult on the 4th postoperative day and an astringent diet was indicated. Two days later, asthenia, marked adynamia and febrile syndrome were reported, she was admitted to the Intensive Care Unit, with an initial diagnosis of enterocolitis, dehydration and acute renal failure, progressive deterioration of renal function with subsequent uremic encephalopathy and request of emergency hemodialysis. In the following 48 hours subject presented severe anemia, generalized edema, ascites, bilateral pleural effusion with acute respiratory failure and she was intubated. She presented generalized tonic clonic seizures and Computed Axial Tomography was performed. On the 5th day of her admission she died of cardiorespiratory arrest secondary to multiple organ failure. Laboratory received after death showed: positive antiphospholipid tests, Anticardiolipin IG 15.7 U/ml and B2 Glycoprotein IG 13.4 U/ml, Anticardiolipin IM, B2 Glycoprotein IM, lupus anticoagulant, ANA and Anti DNA negative and normocomplementemia. Autopsy reported the following macroscopic diagnoses: breasts with necrotic crusted lesions, pale kidneys with hemorrhagic areas, indurated heterogeneous pancreas, lungs with bilateral focal interstitial hemorrhages, edematous brain with pale ischemic appearance and generalized hemorrhagic. Abundant fluid in abdomen, both pleurae and pericardium. Microscopic founding: hemorrhagic exudative acute pancreatitis, renal acute tubular necrosis, and glomerulonephritis with bilateral acute thrombotic microangiopathy in arteries, arterioles, and glomeruli. Brain parenchyma and both lungs with multiple generalized thrombotic microangiopathy.
Conclusions: Diagnosis of CAPS was made in the young woman, with two possible precipitating factors, acute, diffuse and fatal involvement with multiple clinical manifestations, a determination in high titers of two types of antiphospholipid antibodies, histopathological confirmation and death due to multi-organ failure.
Keywords: CAPS, Pexy surgery.

0162

CLINICAL CHARACTERISTICS OF "SINGLE" ANTIPHOSPHOLIPID ANTIBODY (APL) POSITIVE THROMBOTIC APS PATIENTS: RETROSPECTIVE RESULTS FROM THE APS ACTION CLINICAL DATABASE AND REPOSITORY ("REGISTRY")

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APS ACTION is a network collecting and analyzing data of aPL positive patients recruited by international centers. Based on the assumption that triple aPL-positive (LA, aCL IgG/M, and aß2GPI IgG/M) patients are at higher risk for thrombosis, we investigated the clinical phenotype of single aPL-positive (LA, aCL IgG/M, or aß2GPI IgG/M) patients in a large cohort of primary thrombotic APS subjects.

Patients and methods: APS ACTION Registry includes persistently aPL positive patients with or without other systemic autoimmune diseases. We screened the registry for primary thrombotic APS patients with persistent single aPL positivity (defined as LA, aCL, and aß2GPI results [from local laboratories] all available at registry entry with two consecutive results and only one aPL test being persistently positive in accordance to the revised Sapporo Criteria). For each patient, we assessed the site of the event, the type and isotype of aPL, and the number of retrospective documented recurrences. Single aPL-positive patients, with no history of thrombotic or obstetric APS, were used as a control group for comparing the prevalence of different isotypes. Basic statistical analysis was performed using SPSS 26.0.

Results: Of 427 primary APS patients collected in the registry, 233 triple aPL-tested patients were included in the analysis and 63/233 (27%) had persistent single aPL positivity (66% women, 77% white): 45(71%) single LA positive, 9 (14.5%) single aCL (8 IgG,1 IgM) and 9 (14.5%) single aß2GPI (7 IgG, 2 IgM). As a comparison, of 66 triple aPL-tested patients with no thrombotic or obstetric APS, 22 had persistent single aPL-positivity (68% women, 90% white): nine (41%) single LA positive, eight (36%) single aCL (3 IgG, 5 IgM), and five (23%) single aß2GPI (2 IgG, 3 IgM). Single LA positivity was significantly more common in the thrombotic APS cohort compared to aPL carriers (71% Vs 41%, p:0.021). Associations between different aPL tests and clinical manifestations are shown in Table 1. Among single aPL-positive patients with history of arterial or venous thrombosis, 68% and 75% had single LA-positivity, respectively. Based on small numbers, a trend for a higher frequency was observed: a) for arterial thrombosis in single aCL-positive patients (aCL+ 7/9 [78%] Vs. aCL- 2/9 [22%]); and b) for venous thrombosis in single aB2GPI-positive patients (aß2GPI+ 8/9 [89%] Vs aß2GPI- [1/9] 11%). A history of thrombosis recurrence was observed in 18(28%) patients. However, no significant difference was detected between aPL profile and recurrences (both for number and type of events).

	Total (63)	La(45)	aCL(9)	aB2GpI(9)
Arterial Thrombosis (History)				
Any 28	28	19 (68%)	7 (25%)	2 (7%)
Stroke (anterior circulation)	6	4	1	1
Stroke (posterior circulation)	6	2	2	2
Stroke (cortex)	2	0	2	0
Stroke (small vessels or lacunae)	5	3	2	0
Myocardial infarction	3	2	1	0
Venous Thrombosis (history)				
Any	40	30 (75%)	2 (5)	80 (20)
Distal leg thrombosis	11	10	0	1
Proximal leg thrombosis	12	9	0	3
Pulmonary embolism	8	5	0	3
Central venous sinus thrombosis	5	2	1	2

Retinal vein thrombosis	4	3	0	1
Extra criteria				
Transient ischemic attack	3	1	1	1
Livedo recatularis	9	6	2	1
Persistent thrombocytopenia	5	4	1	0
Skin ulcer	2	2	0	0
aLP associated nephropathy	1	0	0	1
Cognitive dysfunction	4	4	0	0
Seizure	4	1	1	2
White matter lesions	14	8	5	1

Conclusions: Based on the analysis of an international persistently aPL-positive cohort with no other systemic autoimmune diseases: a) approximately 30% of patients have "single" aPL positivity b) the majority of "single" aPL-positive manifest LA-positivity (64%), which is more frequent among those with thrombotic APS (71%), compared to those without APS classification (41%); and c) approximately one-third of "single" aPL-positive patients have history of recurrent thrombosis.
Keywords: Antiphospholipid antibodies, single aPL positivity, thrombotic APS.

0163

LIBMAN-SACKS ENDOCARDITIS IN THE CONTEXT OF ANTIPHOSPHOLIPID SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS

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Case report: Woman, 49 years old, urban area, housewife. Fever of 3 weeks of evolution, accompanied by progressive dyspnea and edema of the lower limbs, in addition to arthromialgia. As personal background he presented hypertension, regular treatment, Epilepsy, treatment with lamotrigine. Systemic lupus erythematosus treated with hydroxychloroquine. Two abortions, third pregnancy interrupted by preeclampsia. Physical examination: First hear sound low intensity, second heart sound normophonetic, GIII/VI holosystolic murmur in high frequency mitral focus radiating to the neck and left armpit, Laboratory: Hypochromic microcytic anemia. Platelets: 168000; ESR: 132mm; PCR: 13.45 mg/dL TTPA: 90seg; six blood cultures: Negative; ANA: 1/80; AC. Lupico, IgM anticardiolipin: Positive. Echocardiogram: 6 x 8 mitral valve posterior leaflet vegetations. Treatment with corticosteroids, antiplatelet agents, was initiated. Valve replacement surgery is scheduled, operative part is sent to anatomy pathology that concludes: Vegetation constituted by fibrinoid material, with few leukocytes and bacterial colonies absence. Findings suggestive of ELS.
Conclusions: The acute form of presentation can mimic that of infectious endocarditis and complicate both differential diagnosis and treatment. The diagnosis is based on high clinical suspicion and the presence of laboratory criteria.
Keywords: Antiphospholipid syndrome, aseptic endocarditis, Libman Sacks endocarditis.

0164

ASSOCIATION BETWEEN ANTIPHOSPHOLIPID SYNDROME, ACCRUAL DAMAGE AND PREGNANCY IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Antiphospholipid antibodies (aPL) are present in 40% of systemic lupus erythematosus (SLE) patients. aPL and antiphospholipid syndrome (APS) may impact pregnancy outcome in SLE patients. There is few information about accrual damage in pregnancy women with SLE with aPL or APS.

Patients and methods: A multicenter, cross-sectional, study from the RELESSAR – trans registry was performed. SLE patients with one or more pregnancies were included. Sociodemographic data, clinical data, autoantibody, aPL profile, accrual damage and APS were analyzed. Accrual damage was evaluated by SLICC-SDI index, and it was present when scoring was more or equal than 1. Pregnancy outcome was defined as complicated if any of these complications were present: preeclampsia, eclampsia, fetal death, preterm delivery, and miscarriage.

Results: 892 patients with at least one pregnancy with AD and without NoAD were analyzed. Sociodemographic and clinical data are shown in Table 1. The age at the diagnosis was 31.9 in AD group and 32 in NoAD (p0.776). There was not relationship between accrual damage and ethnicity, socioeconomic status, education, but smoking was associated to AD P 0.012. After multivariate analysis disease duration had an OR 1.004 (CI 1.002 – 1.006), Charlson index OR 1.319 (CI 1.143 – 1.532), hypertension OR 1.834 (CI 1.176 - 2.889), Stroke 7.095 (CI 1.352 -130.9), no APS and aPL -(ve) vs APS OR 0.492 (CI 0.286 – 0.829), no APS and aPL +(ve) vs APS 0.588 (CI 0.309. 1.105), corticosteroids <= 10 mg/d vs MP Pulses IV OR 1.072 (CI 0.620 - 1.854); corticosteroids 10-30 mg/d vs MP Pulses IV OR 1.992 (CI 1.226 – 3258); corticosteroids >30-60 mg/d vs MP Pulses IV OR 2.348 (CI 1.366 – 4.079)

Table 1: Demographic and clinical data of SLE women comparing accrual damage versus no accrual damage.

	Accrual damage (N=486)	No Accrual damage (N=406)	P - value	Total (N=892)
Age at last visit , Median [Q1 , Q3]	43.5 [35.5, 54.0]	39.4 [31.7.48.5]	<0.001	41.2 [33.7,51.3]
Disease duration (*9) Median [Q1 , Q3]	108 [41.2, 202]	65.5 [28.9, 117]	<0.001	84.0 [34.1,161]
Corticosteroids use, n(%) (*131)				
Bolus	67 (15.7)	89 (26.6)	<0.001	156 (20.5)
< - 10 mg/d prednisone	76 (17.8)	83 (24.8)		159 (20.9)
10-30 mg/d	159 (37.3)	107 (31.9)		266 (35.0)
>30-60 mg/d	124 (29.1)	56 (16.7)		180 (23.7)
Antimalarial, n(%)(*67)	59 (13.2)	25 (6.6)	0.004	84 (10.2)
Pregnancy complications, n(%)(*19)				
With complications	143 (30.1)	98 (24.6)	0.083	241 (27.6%)
Without complications	332 (69.9)	300 (75.4)		632 (72.4%)
aPL[1][2] **and APS, n(%)**(*174)				
No APS y aPL +	78 (19.3)	54 (17.2)	0.007	132 (18.4)
APS	76 (18.8)	35 (11.1)		111 (15.5)

Conclusions: The presence of aPL and APS has a negative impact in AD in pregnant SLE patients.

Keywords: Systemic lupus erythematosus, antiphospholipid syndrome pregnancy accrual damage.

0170

REAL-LIFE ANTICOAGULATION IN ANTIPHOSPHOLIPID SYNDROME

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Our objectives were to evaluate percentage of achievement of anticoagulation (ACO) target in a cohort of patients with antiphospholipid syndrome (APS), to estimate rates of new thrombotic events and their relationship with the adjusted Global Antiphospholipid Syndrome Score (aGAPSS) and the damage index in antiphospholipid syndrome (DIAPS). An additional objective was to describe the non-criterion manifestations found in our population.

Patients and methods: Retrospective cohort of APS patients seen at a university hospital with at least one venous or arterial thrombotic event were included. The diagnosis of APS was carried out by their doctors based on clinical and laboratory characteristics. These data were obtained from electronic medical records. Percentage of times that INR was in range according to recommended target was calculated and descriptive statistics was performed.

Results: 87 APS patients were revised, 71 patients with thrombotic APS and 16 with obstetric APS. 71 APS patients with thrombotic events were included in the analysis (59.2%, primary APS and 40.8%, secondary APS), 66.2% females, 49.7 years old (SD 19.4) at time of thrombotic event and with 8.5 years (IQR 2.6-13.3) of follow-up thereafter. First event was venous in 51 (71.8%) and arterial in 20 (28.2%). Those with venous events were treated with dicumarinics (76.5%), direct oral anticoagulants (3.9%) and combination of dicumarinics and aspirin (19.6%). Patients with arterial events with dicumarinics (80.0%), aspirin alone (10.0%) and combination (10.0%). Other characteristics of the cohort are described in Table 1. In total 67 patients (94.4%) required INR controls. INR data could be collected from 62 patients, with a follow up of 546.5 patient-years (PY) (95% CI 442.6-650.3). They had in average 7.5 INR controls per year (95% CI 5.8-9.3) and 62.6% (SD 19.6) of times INR was in target range. 20 patients (28.2%) stopped anticoagulation: 17 indicated by doctors, 2 because of patient decision and 1 because of adverse event. 15 patients (21.1%, 95% CI 13.0-32.4) had a second thrombotic events (8 venous and 7 arterial), 4 patients had no anticoagulation treatment at that time and 11 were on treatment (10 with vitamin K antagonist and 1 with heparin); of these patients' previous percentage of INR in range was 65.6% (SD 21.4). The characteristics for type of event (venous or arterial) are described in Table 2. The aGAPSS at first episode was significantly higher is patients with a second event than in those without re-thrombosis (median 10.5, IQR 8-13, versus 7, IQR 4-9, p=0.01). Median damage index (DIAPS) at the end of follow-up was 0 (IQR 0-1). 38 patients (53.5%) presented one non-criterion manifestation. The most frequent were superficial venous thrombosis (9 patients, 11.2%), amaurosis fugax (6 patients, 8.4%) and livedo reticularis (5 patients, 5.6%). Of these 38 patients, 14 (19.7%) presented two non-criterion manifestations, the most frequent in this group being white matter lesions on brain MRI (3 patients, 4.2%) and Raynaud's phenomenon (3 patients, 4.2%).

Table 1: Patient characteristics, demographic data, and comorbidities.

Variable	Total population (N=71)
Female sex, n (%, 95% CI)	47 (66.2, 54.2-76.2)
Age at thrombotic event, years, media (SD)	49.7 (19.4)
Follow-time after thrombotic first event, years, median (IQR)	8.5 (2.6-13.3)
Complete fulfillment of Sapporo criteria, n (%, 95% CI)	49 (69.0, 57.1-78.8)
Type of APS: - Primary APS, n (%, 95% CI) - Secondary APS, n (%, 95% CI)	 42 (59.2, 47.2-70.1) 29 (40.8, 29.9-52.8)
Antiphospholipid antibodies profile *: - Positive Lupus Anticoagulant, n (%, 95% CI) - Positive anticardiolipin antibodies (IgG and/or IgM), n (%, 95% CI) - Positive antibeta2glycoprotein I antibodies (IgG and/or IgM), n (%, 95% CI)	46 (64.7, 53.6-75.8) 45 (63.4, 51.4-73.9) 8/23 (34.7, 15.3-54.2)
Type of first event: - Venous event, n (%, 95% CI) - Arterial event, n (%, 95% CI)	 51 (71.8, 60.0-81.2) 20 (28.2, 18.8-39.9)
Vascular risk factors: - Arterial hypertension, n (%, 95% CI) - Dyslipidemia, n (%, 95% CI) - Diabetes, n (%, 95% CI) - Obesity, n (%, 95% CI) - Current or past smoker, n (%, 95% CI)	 28 (39.4, 28.6-51.4) 11 (15.5, 8.7-26.1) 3 (4.2, 1.3-12.6) 8 (11.3, 5.6-21.2) 24 (33.8, 23.6-45.8)
aGAPSS at thrombotic first event, median (IQR)	8 (4-9)
Mortality, n (%, 95% CI)	7 (9.8%, 2.9-16.7)

**At least two positive determinations separated by 12 weeks*

Table 2: Patients with venous or arterial event with available INR data (n=62)

	Venous event with INR data (44 patients)	Arterial event with INR data (18 patients)	p
Total Follow up in patients with INR controls, PY (95% CI)	394.6 (300.2-488.9)	151.9 (102.7-201.1)	–
Number of INR controls per year (95% CI)	6.9 (20.7)	8.9 (4.6-13.1)	–
Percentage of INR times in range (SD)	63.3 (20.7)	60.7 (17.1)	0.630
2nd thrombotic event (n,%): - Venous event (n,%) - Arterial event (n,%)	9 (20.4) 5 (56%) 4 (44%)	4 (22.2) 1 (25%) 3 (75%)	0.480

Conclusions: After a first thrombotic episode in APS patients, INR was in target range 62.6% of times measured. Anticoagulation was stopped in 28.2% of patients. 21.1% had a second thrombotic event. More than half of the patients presented non-criterion manifestations.
Keywords: Antiphospholipid syndrome, anticoagulation, Non-criteria manifestations.

0171

USE OF ROMIPLOSTIM IN A PREGNANT PATIENT WITH ITP AND ANTICOAGULATED DUE TO THROMBOTIC DISEASE IN THE CONTEXT OF APS AND SLE

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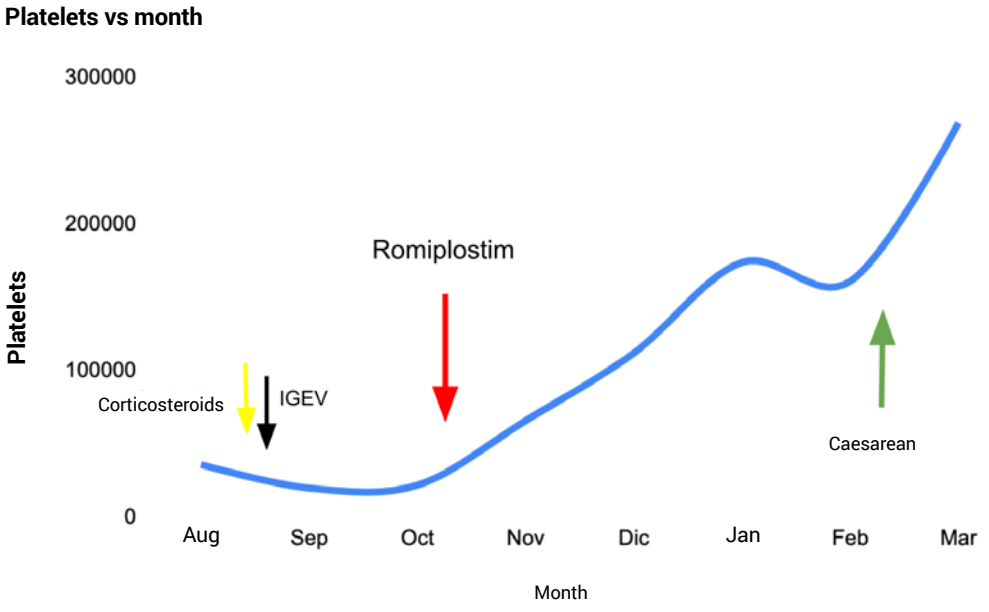
The purpose of the clinical case, given the limited bibliography available, is to report the use of Romisplostim in ITP in pregnancy.
Case report: A 28-year-old patient with a history of SLE (Systemic Lupus Erythematosus) and APS (Antiphospholipid Syndrome), diagnosed from recurrent PE (Pulmonary Thromboembolism), had been anticoagulated with warfarin since the last thrombotic event, and initially received treatment with deflazacort 60 mg daily. and then with hydroxychloroquine 100 mg daily. She was in an 11-week pregnancy, asymptomatic, which in a control laboratory setting revealed anemia of chronic disorders and moderate thrombocytopenia (36,000 mm^3). It was decided to suspend oral anticoagulation and start oral corticosteroid therapy with meprednisone 40 mg daily and weekly control with platelet count. 48 hours after starting corticosteroids, she progressed with anterior epistaxis, platelets 16,000 mm^3, without major bleeding, and was hospitalized. During hospitalization, transfusion support was started (negative immunohematology), human gamma globulin 1g/kg/day for 48 hours and methylprednisolone 500 mg daily for 3 days. During her stay, she underwent close follow-up by obstetrics and rheumatology. In the laboratory controls, the platelet count was not greater than 30,000 mm^3 and she had recurrent epistaxis and ecchymosis. Complementary bone marrow studies did not find relevant data, viral serologies were negative and rheumatological studies were repeated. It was interpreted as ITP (Idiopathic Thrombocytopenic Purpura). In a multidisciplinary meeting (Clinical, Hematology and Obstetrics) ILE (Legal Interruption of Pregnancy) was proposed, to which the patient refused, and given the bibliography available at the time, it was decided to start treatment with Romiplostim with the consent of the patient.
Results: Two weeks after treatment, the platelet count was higher than 50,000 mm^3 in a sustained manner, without evidence of fetal involvement, anticoagulation with low molecular weight heparin 1mg/kg every 12 hours adjusted to antixa was restarted, hospital discharge and hematological and obstetric follow-up. On an outpatient basis, laboratory controls were performed with no drop in platelet count and no bleeding. The pregnancy was terminated by scheduled cesarean section at 40 weeks without obstetric complications and the newborn did not show signs of bleeding or thrombocytopenia.

Table 1: Controls, treatment and pregnancy progression.

Weeks of pregnancy	12	16	20	24	26	32	36	Postpartum
Month follow-ups	Aug	Sep	Oct	Nov	Dic	Jan	Feb	Mar
Hb (g/dl)	8.5	9.4	8.7	10.3	10.6	10.7	11.3	12
GB (mm^3/dl)	7600	8400	8300	9000	9900	8400	9700	9000
Platelets (mm^3/dl)	36000	20000	22000	66000	112000	174000	161000	269000
Fe Ev (ferinject)								
Corticosteroids								
Romiplostim (240 mcg weekly)								
Hydroxychloroquine								
Enoxaparin 1mg/kg c12								



Conclusions: We report an ITP in pregnancy in an anticoagulated patient, with APS and SLE, without response to first-line therapy, and given the lack of knowledge and the scarce bibliography available on the use and teratogenic effects of thrombo-mimetics in pregnancy, we decided to treat with romiplostim obtaining good results and ending the pregnancy without obstetric and neonatal complications.

Keywords: ITP in pregnancy without response to corticosteroids, aPL, SLE and ITP, romiplostim in pregnancy.

0172

EVALUATION OF ADJUSTED GLOBAL ANTIPHOSPHOLIPID SYNDROME SCORE (AGAPSS) IN PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME (APS)

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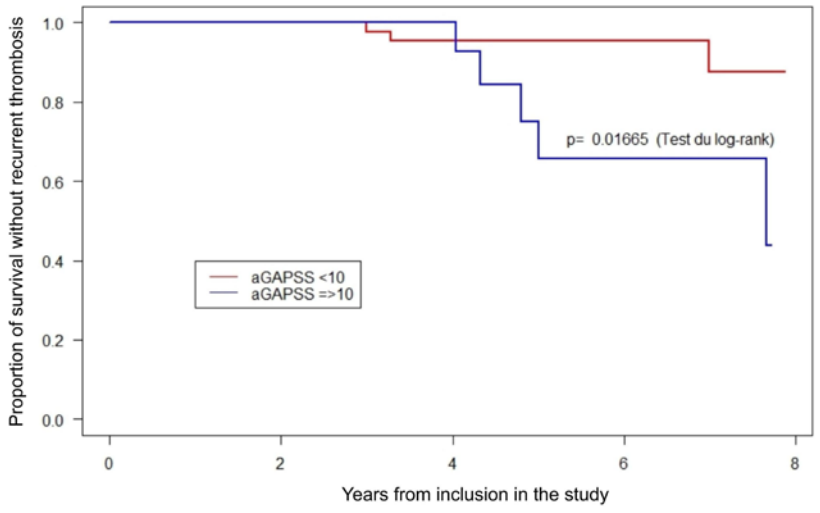
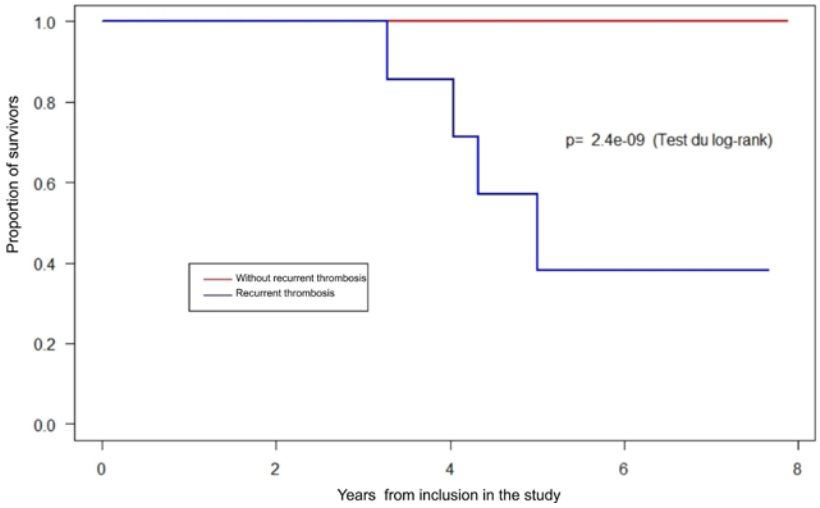
Assessment of risk both for pregnancy morbidity and thrombosis in APS is still a challenge. Score systems have been developed to assess thrombotic risk in APS. One of them, "The Global Antiphospholipid Syndrome Score" (GAPSS) contains the antiphospholipid antibodies (aPL) profile (criteria and non-criteria aPL) and the conventional cardiovascular risk factors. aGAPSS (adjusted Global Antiphospholipid Syndrome Score) is a simplified version of GAPPS that excludes anti-phosphatidylserine/Prothrombin (aPS/PT), and both were validated in cohorts of patients with APS and SLE/APS. Objective: to evaluate aGAPSS in the risk of vascular thrombosis and its associations with both criteria and non-criteria manifestations in a single center cohort of patients with APS.

Patients and methods: We studied patients with APS according to Sydney Criteria at Rheumatology Unit in Córdoba Hospital from May 2013 to March 2020. Clinical and demographic characteristics as arterial and venous thrombosis (tAPS), obstetrical morbidity(oAPS), non-criteria manifestations (NCM) were evaluated. aGAPSS was performed in basal visit in tAPS and oAPS and it was considered high >= 10. A new thrombotic event and mortality were evaluated in the last follow up. Fisher's test, Wilcoxon test and survival curves were performed. p<0.05 was considered statistically significant.

Results: 85 patients were included and 74,11% completed the follow-up. 87,1% were women with mean age of 36 years (32,75-40,25), and disease duration of 53 months (25-114). 62,35% had oAPS, 24,5% tAPS and 12,94% both. 18 patients had arterial thrombosis, 11 venous thrombosis and 3 in both sites. tAPS patients had more disease duration (p=0,04), and more presence of aB2GP1 antibodies (p=<0,001) and triple positivity aPL (p=0,0003). The mean aGAPSS was 9 (5-12) in all groups and it was 9 (8,75-13) in tAPS and 9 in oAPS 9 (5-9) (p=0,008) There was no difference between patients with criteria and NCM. 12,69% had new thrombotic event in tAPS and the mean time to it was 26 months (15-49). 4 patients developed arterial thrombosis, 2 venous thrombosis and 2 in both sites. The mean aGAPSS in patients with recurrent thrombosis (RT) was 13 (9-13), 62,50% had aGAPSS >=10; and 87% had NCM. 4 (6,34%) patients died, all of them with RT. aGAPSS >=10 was associated with new thrombotic events (p=0,016, Graphic 1). Patients with RT had a worse survival (p= 0,000, Graphic 2).



Graphic 1: Recurrent thrombosis according to AGAPSS.



Graphic 2: Survival according to recurrent thrombosis.

Conclusions: aGAPSS is a useful risk assessment tool which may identify a population at greater risk for developing thrombosis. High aGAPPS was associated with aPL high risk profile, RT and mortality in our APS patients.
Keywords: primary antiphospholipid syndrome, adjusted global antiphospholipid syndrome score, recurrent thrombosis.

0173

OBSTETRIC ANTIPHOSPHOLIPID SYNDROME: BEYOND THE SIDNEY CRITERIA

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The aim of this work is to study the prevalence of aPL in a population of women with and without a history of Obstetric Complications (OC).
Patients and methods: We retrospectively evaluated patients with and without a history of OC. We determined Lupus Anticoagulant (LA) according to ISTH criteria and Anticardiolipin (aCL) IgG and IgM antibodies and aB2GPI screen all by ELISA. For objective 2, we classified patients according to clinical manifestations into 3 groups: Group O: without OC, Group I (GI): IVF failure, 1 abortion, and 2 abortions; Group II (GII): 3 or more abortions, intrauterine fetal death, intrauterine growth retardation, pre-eclampsia and preterm delivery. Statistical analysis InfoStat 2011 UNC.
Results: The prevalence of aPL positive observed was: Group O (n=50): 4%, Group I (n=118): 56%, Group II (n=66): 58% ($p > 0.005$). We observed no difference in the profile of the antibodies found in the 3 groups.
Conclusions: In our patients we observed a high % aPL+. These antibodies had the same prevalence in GI (not included in SC) as in GII. These results support the concept of "diagnostic criteria" considered in the Obstetric Antiphospholipid Syndrome
Keywords: Antiphospholipids, obstetric complications.

0174

ACUTE PROMYELOCITIC LEUKEMIA IN ANTIPHOSPHOLIPID SYNDROME: A DIAGNOSIS AND TREATMENT CHALLENGE

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Acute promyelocitic leukemia (APL) is a subtype of leukemia which is associated with unique and distinctive coagulopathy. In the absence of treatment, it is rapidly fatal and even after initiation of therapy the major cause of early mortality is related to hemorrhagic complications. Antiphospholipid syndrome (APS) is a multisystem autoimmune disease associated with recurrent arterial and venous thrombosis and pregnancy loss. Recurrent thrombosis is the leading cause of mortality and long term anticoagulation therapy is required. Patients with antiphospholipid antibodies have an increased risk of developing hematological neoplasms and the risk of thrombosis. We report a case of APL who developed after years of diagnosis of thrombotic APS.

Case report: A 51 year old man was referred for hematology and rheumatology evaluation to our hospital. He had a medical history of primary APS diagnosed 20 years ago. He had 2 episodes of Myocardial infarction (when he was 30 and 40 years old respectively) with triple positivity of antiphospholipid antibodies (LA, aCL Ig G and B2GPI Ig G) and he has been treated with oral anticoagulation with warfarin plus aspirin with INR of 3, statins and hydroxycloroquine. He developed dyspnea and tiredness. Laboratory findings showed pancytopenia: Hot 32.1%, HB 8.4 grs%, WBC 1400, platelets 20.000. Antinuclear, ds-DNA, Sm, RNP, Ro and la antibodies were negative. Hepatitis B, C, HIV and syphilis serology was negative and complement levels were normal. CRP Sars-Cov2 was negative. Iron and folic acid levels were normal. BMP. 79% promyelocytes infiltration. Flow cytometry; 85% abnormal cells with immunophenotype of APL (CD34 -, HLA Dr -, CD117+, CD33 ++ (homogenous), CD13 ++ (heterogeneous), CD15 +/-, CD123 +, CD56 partial expression.). PML RAR ALFA (T 15,17): presence of PML RAR ALFA band. He started treatment with ATRA and he completed induction and seven cycles of consolidation therapy. He required platelets transfusions and Low weight molecular heparin bridge therapy for short periods. He had no hemorrhage neither thrombotic complications. 50 days after BM examination showed remission.

Conclusions: The association of APL and APS is extremely rare and a diagnostic and therapeutic challenge. The onset of cytopenia in APS require a clinical and laboratory workup and bone marrow (BM) examination to determine the cause and for appropriate patient management. Common causes should be exclude including development of SLE, infection, iron and folic deficiency or effect of medications

Keywords: Acute promyelocitic leukemia, antiphospholipid syndrome.

0175

ANTIPHOSPHOLIPID ANTIBODY PROFILE IN PATIENTS WITH LEVAMISOLE-ADULTERATED COCAINE VASCULOPATHY (LACIV): A 60-CASE SERIES

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Up to 88% of cocaine is tainted with levamisole, anthelmintic withdrawn from the market due to toxicity. Since 2010 LACIV patients, characterized by retiform purpura, ear necrosis, multisystemic compromise, and positivity for multiple autoantibodies have been reported. The purpose of this investigation was to describe the positivity of antiphospholipid antibody (aPL) profile in patients with LACIV and to analyze its association with thrombotic events.

Patients and methods: We describe the aPL profile of a 60-case series with LACIV admitted in four high complexity institutions in Colombia from December 2010 to January 2022.

Results: All patients were mestizos, with a mean age of 33.3 years (SD ±8.0). The male: female ratio was 4.4:1. Eighty-three percent of the patients presented with retiform purpura and 66.6% with necrosis in the ears. Thrombocytosis was found in 16.6% with an average platelet count of 615000/mm^3 (SD ±147561). Regarding the aPL profile, 45 patients had positive confirmatory tests for lupus anticoagulant (LA). The rest of the findings are described in Table 1. The mean value of IgM and

IgG anticardiolipin antibodies (aCL) was 50.1 MPL (SD ±30.8) and 41.1 GPL (SD ±19.6), respectively. Among 36 patients with a skin biopsy, 36.1% presented thrombotic vasculopathy: five of them (13.8%) isolated, all these five patients were positive for LA, three for IgM aCL, and one for anti-beta2 glycoprotein I antibodies (anti-B2GPI). Concerning clinical and laboratory findings in patients with macrovascular thrombosis (the details about the thrombotic events are described in table 1), the median of erythrocyte sedimentation rate was 79 mm/H (IQR 53 – 99.5), the median of C-reactive protein was 12.1 mg/dL (IQR 9.2-6.2), and one had significant organ involvement (membranous nephropathy; 24-hour urine protein 9.6 g). Two cases had leukocytoclastic vasculitis on skin biopsy and positive LA. Finally, during the following 3/60 patients died, two of them were positive for LA.

Variable	LACIV patients (%)
aPL profile	
AL (n=60)	75%
IgM aCL (n=57)	24.5%
IgG aCL (n=57)	10.5%
IgG/IgM anti-B2GP1 (n=36)	13.8%
Thrombotic events	**Number of LACIV patients**
Lower leg deep venous thrombosis	2
Axillo-subclavian and humeral vein thrombosis	1

Conclusions: In LACIV, despite a high positive aPL rate (mainly LA), macrovascular thrombosis prevalence is low (5%). The evidence of leukocytoclastic vasculitis, high acute phase reactants, cocaine-induced hypercoagulability state, and the nephrotic proteinuria in one of the patients proposes a multifactorial origin of thrombotic phenomena.
Keywords: Cocaine, thrombosis, antiphospholipid antibodies.

0176

WHICH IS THE UTILITY OF NEW ANTIPHOSPHOLIPID ANTIBODIES IN PLACENTAL INSUFFICIENCY MANAGEMENT? A PRELIMINARY REPORT.

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The clinical utility of some new antiphospholipid antibodies in cases of adverse obstetric outcomes is not well known. We aimed to assess the performance of antibodies against the phosphatidylserine prothrombin complex (IgM and IgG), onwards "anti-PS/PT" in preeclampsia or foetal growth restriction.
Patients and methods: A case control study was performed in a maternal care unit. Cases were patients with preeclampsia or foetal growth restriction developed before the 37th weeks of gestation. The full sample was calculated in 100 cases and 200 controls. Controls were patients who were hospitalized in the third trimester of gestation, with age +/- 5 years old respect to the controls, without known autoimmune diseases or history of adverse obstetric outcomes. All patients were studied with general laboratory, doppler, classical antiphospholipid antibodies and anti-PS/PT IgG and IgM. We present demographic characteristics and media comparisons which were performed with T test. Categorical variables were compared with Chi square test or Fisher test if applicable. The statistical significance was established in 5% ($p<0.05$). Informed consent from the participants as well as approval from the institutional ethics committee were obtained.
Results: A hundred and fifty pregnant women were included in this preliminary report (50 cases and 100 controls). Demographic data are presented in Table 1. All anti-PS/PT IgG test were negative, the mean (SD) value was 5.9 (3.4) GPL U/ml in cases and 5.9 (3.3) GPL U/ml in controls. Regarding to anti-PS/PT IgM test, 3 (6%) were positive into the cases and 3 (3%) into the controls, no statistically significant difference, OR 1.3 (95%CI: 0.6-2.9); the mean (SD) value was 15.2 (19.1) MPL U/ml in cases and 15.2 (32) MPL U/ml in controls.

	Case (n=50)	Controls (n=100)	p value
Maternal age (years) (means, SD)	28.9 (6.1)	28.9 (6.1)	NS
Gestational age at inclusion (weeks) (mean, SD)	34.7 (3.3)	37.7 (3.7)	<0.001
Systolic blood pressure at inclusion (mmHg) (mean,SD)	130.5 (20.2)	116.14 (12.9)	<0.001
Systolic blood pressure at inclusion (mmHg) (mean,SD)	78.5 (15.1)	78.5 (15.1)	<0.001
Weight of newborn (grams) (means,SD)	2256.7 (683.2)	3420.4 (468.5)	<0.001

Conclusions: In this preliminary report, we did not find association between ant-PS/PT both IgG or IgM in cases of foetal growth restriction or preeclampsia. It is worth to note that this is not the final analysis, in which the sample size is going to double this number. Further analysis may show the utility of this biomarkers in obstetric adverse pregnancy outcomes management.
Keywords: Adverse obstetric outcomes, antibodies against phosphatidylserine prothrombin complex.

0178

DIFFICULT TO TREAT: RECURRENT THROMBOSIS IN PRIMARY ANTIPHOSPHOLIPID, SYNDROME (APS)

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Antiplatelet and anticoagulant agents currently provide the mainstay of APS treatment. However, the debate is still open: controversies involve the intensity and the duration of anticoagulation and the treatment of recurrent and refractory cases. Unfortunately, the literature cannot provide definite answers to these controversial issues and much work is still to be done to unravel these issues about APS management. We present the case of a patient with primary APS who had a recurrence of thrombotic event while on treatment with Vitamin K antagonist (VKa).
Case report: We report the case of a women, aged 39, recently diagnosed with primary APS and recurrent thrombotic episodes. She was first admitted to the hospital for an episode of deep venous thrombosis (DVT) in two territories: left common femoral and popliteal vein. Oncological screening was performed with negative results. Thrombophilia profile test developed and the positive results were: IgG Beta 2 Glicoprotein 1 antibodies and Antinuclear Antibody: 1/1280. Treatment with low molecular weight heparin was started for 5 days and on the third day acenocumarol was added. She evolved in good health and was discharged in therapeutic range. After four weeks, she was readmitted to hospital for progressively worsening shortness of breath and pulmonary thromboembolism was confirmed in a computed tomography (CT) angiography of the chest. The International Normalized ratio (INR) was: 1.4. The therapeutic management was low molecular weight heparin and new strategic administration of acenocumarol. The patient was discharged after one week, with strict out-patient follow-up. Finally, after Two months, she was hospitalized with a recurrent pulmonary thromboembolism. Lupus anticoagulant was positive in this third testing. She was switched to warfarin, aspirin and hidroxycloroquine were added.
Results: Her clinical condition markedly improved, her INR reached 2.5 and she was discharged. No recurrent or new thromboembolic events were reported.
Conclusions: Recurrent thrombotic events are common, with an estimated annual recurrence rate of 5% to 12%, while on Vitamin K antagonist (VKa). Risk stratification in aPL-positive individuals, should include determining the presence of high risk aPL-profile, history of thrombotic and /or obstetric APS, coexistence of other autoimmune diseases, such as SLE, and the presence of traditional cardiovascular risk factors. But still, many clinical issues remain unresolved: Are there newer therapeutic strategies that might lead to safer and more efficacious treatment modalities? In this patient, was the combination of warfarin and hydroxicloroquine the reason for his good response to treatment? We consider that primary APS should be tailored cautiously when using vitamin k antagonist, especially in high-risk profiles.
Keywords: Antiphospholipid syndrome, difficult treatment, recurrent thrombosis.

0179

EVALUATION OF THE EFFECT OF UCB4470 (ANTI-MOUSE FCRN) ON AMELIORATION OF THROMBOSIS IN A MOUSE MODEL OF ANTIPHOSPHOLIPID (APL)-INDUCED THROMBOSIS

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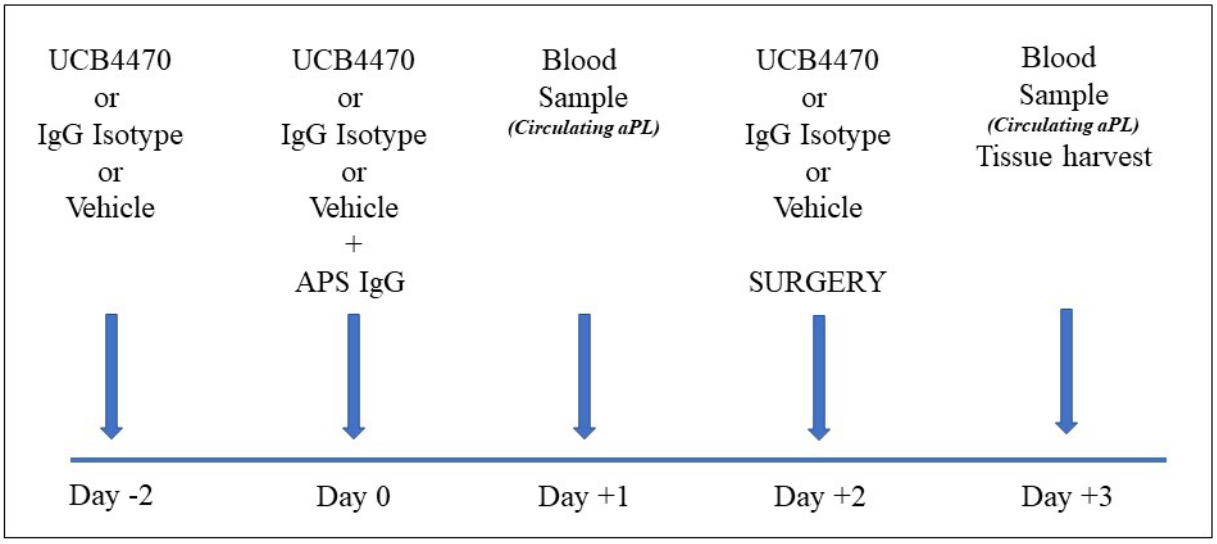
FcRn (the neonatal Fc receptor) is a receptor expressed by antigen-presenting cells, such as monocytes, macrophages, and dendritic cells, as well as on neutrophils. Its function is to "rescue" IgG and albumin from degradation. UCB4470 is an anti-mouse FcRn antibody that specifically blocks the interaction between FcRn and IgG without interfering with FcRn-albumin interactions. In this study, we evaluate the effect of UCB4470 on circulating aPL and aPL-induced thrombus formation.
Material and methods: Balb/c mice were treated with either UCB4470 (30mg/kg), isotype control (30mg/kg) or vehicle by intravenous injection. This was repeated 2 days later, along with an intraperitoneal administration of human purified IgG (500µg/animal) pooled from 17 patients positive for IgG aCL and anti-ß2GPI, and lupus anticoagulant (LA). Thrombus was induced 2 days after the aPL+UCB4470 or isotype or vehicle injection using the stenosis model in the inferior vena cava (IVC) in adult male BALB/C mice. A further dose of UCB4470, isotype control, or vehicle was administered immediately after thrombus induction. Thrombus and surrounding vein wall were excised 24hrs after surgery. Thrombi were separated from the IVC wall and weighted. Blood samples were obtained at day 1 and day 3 to measure total human IgG and IgG aCL and anti-ß2GPI by commercial ELISA. Protocol is shown in Figure 1.
Figure: Protocol for treatment of thrombosis model with UCB4470.



Results: Thrombi from UCB4470-treated animals were lighter than those treated with aPL only (22±1mg (n=21) vs. 27±1mg (n=17), respectively; P=0.034). There were no differences in thrombus weight between UCB4470-treated animals and control animals (22±1mg vs. 21±2mg (n=12), respectively; P=0.6); or between animals treated with isotype control and aPL only (26±1mg (n=20) vs. 27±1mg, respectively; P=0.5). UCB4470 treatment reduced total IgG levels between day 1 and day 3 (11.6±1.6µg/ml (n=26) vs. 3.7±0.5µg/ml (n=24), respectively, P<0.0001), while there was no difference found for the isotype control (20.7±2.6µg/ml (n=24) vs. 20.2±2.7µg/ml (n=22), P=0.68), or the aPL only treated group (21.6±3.5µg/ml (n=24) vs. 18.9±2.1µg/ml (n=22), P=0.05) between these time points. On day 3, titres of IgG aCL were significantly lower in the UCB4470-treated group when compared with the isotype control group (8.97±0.02GPL vs. 9.6±0.11GPL, P<0.0001) and aPL only treated group (9.29±0.06GPL, P<0.0001). Titres of IgG anti-ß2GPI were significantly lower in the UCB4470-treated group when compared with the isotype control group (6.98±0.02GPL vs. 7.7±0.15GPL, P<0.0001) and aPL only treated group (7.5±0.09GPL, P<0.0001). A good correlation between IgG aCL and anti-ß2GPI was seen in mouse blood (R2 0.8487, P<0.0001).
Conclusions: Blocking FcRn ameliorates thrombus formation in a mouse model of aPL-induced thrombosis. Blocking FcRn also decreased the concentration of IgG aCL and anti-ß2GPI in this model. These data indicate that therapeutic inhibition of FcRn may be beneficial in APS.
Acknowledgement: This study was funded by UCB Pharma.
Keywords: animal model, thrombosis, IgG, treatment.

0180

HYDROXYCHLOROQUINE AFFECTS THE FLUCTUATION OF ANTI-DOMAIN 1 ANTIBODIES OVER TIME IN PATIENTS WITH PERSISTENTLY POSITIVE ANTIPHOSPHOLIPID ANTIBODIES: RESULTS FROM THE APS ACTION CLINICAL DATABASE AND REPOSITORY ("REGISTRY")

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Data on fluctuation of antibodies directed against domain 1 (anti-D1) of ß2-glycoprotein I (ß2GPI) are scarce. Patients with antiphospholipid syndrome (APS) and all three criteria tests for antiphospholipid antibodies (aPL) display higher titers of anti-D1. This project evaluates predictors of the variation of anti-D1 titers over time in a large international cohort of persistently aPL positive patients.

Patients and methods: Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking (APS ACTION) Registry studies the course of persistently aPL-positive patients with or without autoimmune disorders over at least 10 years. Inclusion criteria are positive aPL by Updated Sapporo Criteria tested within one year prior to enrolment. Patients with available blood samples from at least three time points were included in this analysis. Anti-ß2GPI and anti-D1 IgG were tested by chemiluminescence (BioFlash, INOVA Diagnostics) at APS ACTION core laboratories. Positive results were >20 CU. Anti-D1 titers within the same subject were compared by Friedman's test. A mixed linear model was built to identify predictors of the fluctuation of anti-D1 antibody titers over time.

Results: In this longitudinal study, 230 patients with anti-D1 tested at 4 time points were included. Among 135 patients with at least one anti-D1 positive result, anti-D1 titers varied significantly over time (Friedman statistics: 508.5, p<0.0001; anti-D1 geometric mean at baseline 189.0; T1 132.3 [-15%]; T2 113.8 [-17%]; T3 109.2 [-6% versus T2, -38% versus T1]. Anti-D1 titers were significantly higher at baseline compared to T3 (p=0.029). At 4 years follow-up, 18 new thrombotic events occurred. Patients with double/triple aPL positivity displayed 12.5-fold increase [95%CI 7.4-20.0] in baseline anti-D1 titers. After adjustment for age, gender and number of positive aPL tests, the fluctuation of anti-D1 titers was associated with treatment with hydroxychloroquine (HCQ) at each time-point. HCQ, but not conventional immunosuppressors, was associated with a 1.3-fold decrease in anti-D1 titers [95%CI 1.1-1.5]. In the same model, incident vascular events were associated with a 1.5-fold increase of anti-D1 titers. A concomitant diagnosis of SLE did not affect anti-D1 titers.

Conclusions: Treatment with HCQ and vascular events during follow-up were identified as significant predictors of the fluctuation of anti-D1 antibody titers over time.

Keywords: Anti-domain 1 antibodies, Antibody titers, Hydroxychloroquine.

0181

ANTI-DOMAIN1 AND ANTI-ß2GPI ANTIBODY TITERS DROP AT THE TIME OF VASCULAR THROMBOSIS IN PATIENTS WITH PERSISTENTLY POSITIVE ANTIPHOSPHOLIPID ANTIBODIES: RESULTS FROM THE APS ACTION CLINICAL DATABASE AND REPOSITORY ("REGISTRY")

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This project aims at clarifying whether anti-D1 and anti-ß2GPI antibody titers fluctuate around the time of thrombosis in patients persistently positive for antiphospholipid antibodies (aPL).

Patients and methods: Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking (APS ACTION) Registry include patients with positivity for aPL by Updated Sapporo Criteria tested within one year prior to enrolment. Patients with blood samples from at least four time points were included in this analysis. Anti-ß2GPI and anti-D1 IgG were tested by chemiluminescence (BioFlash, Werfen) at APS ACTION core laboratories. Anti-D1/anti-ß2GPI titers within the same subject were compared by Friedman's test. The exposure to anti-D1 and anti-ß2GPI titers during the case window (blood sampling close to the thrombotic event) was compared to the titer exposure during the control window in anti-D1/anti-ß2GPI positive patients who had developed thrombosis during follow up (case-crossover design). Conditional logistic regression was applied to estimate matched odds ratio (OR) and 95% confidence interval; there were no relevant time-dependent confounder variables.

Results: 230 patients with anti-D1 and anti-ß2GPI tested at 4 time points were included. Anti-D1 titers varied significantly over time (p<0.0001). Anti-ß2GPI titers significantly reduced at T3 compared to baseline (p=0.010). Patients with previous thrombotic events had significantly higher anti-D1 and anti-ß2GPI titers. Incident vascular events developed during 4-year follow-up in 7 patients with at least one positive anti-D1 test. The median time from thrombosis to blood sampling was 61 days. A mean 1.6-fold decrease in anti-D1 titers conferred an OR for incident thrombosis of 6.0 (95%CI 0.62-59.3), which only approached statistical significance due to the small sample size (Figure 1A). Incident vascular events developed in 10 patients with at least one positive anti-ß2GPI IgG test. The median time from thrombosis to blood sampling was 64.5 days (IQR 28-115.5). A mean 2-fold decrease in anti-ß2GPI titers conferred an OR for incident thrombosis of 9.4 (95%CI 1.1-80.2, p=0.01, Figure 1B).

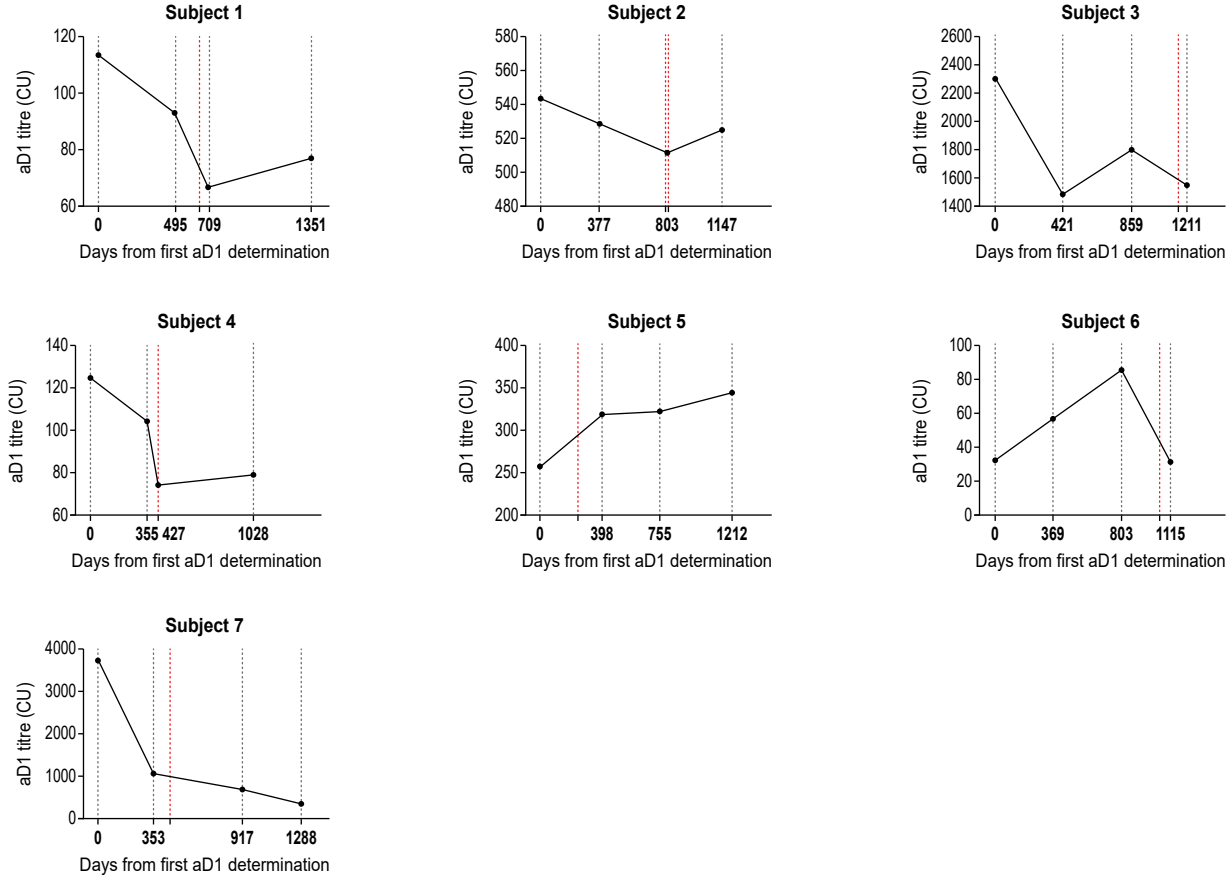

Figure 1A) Anti-D1 antibody titers in patients with incident thrombosis.

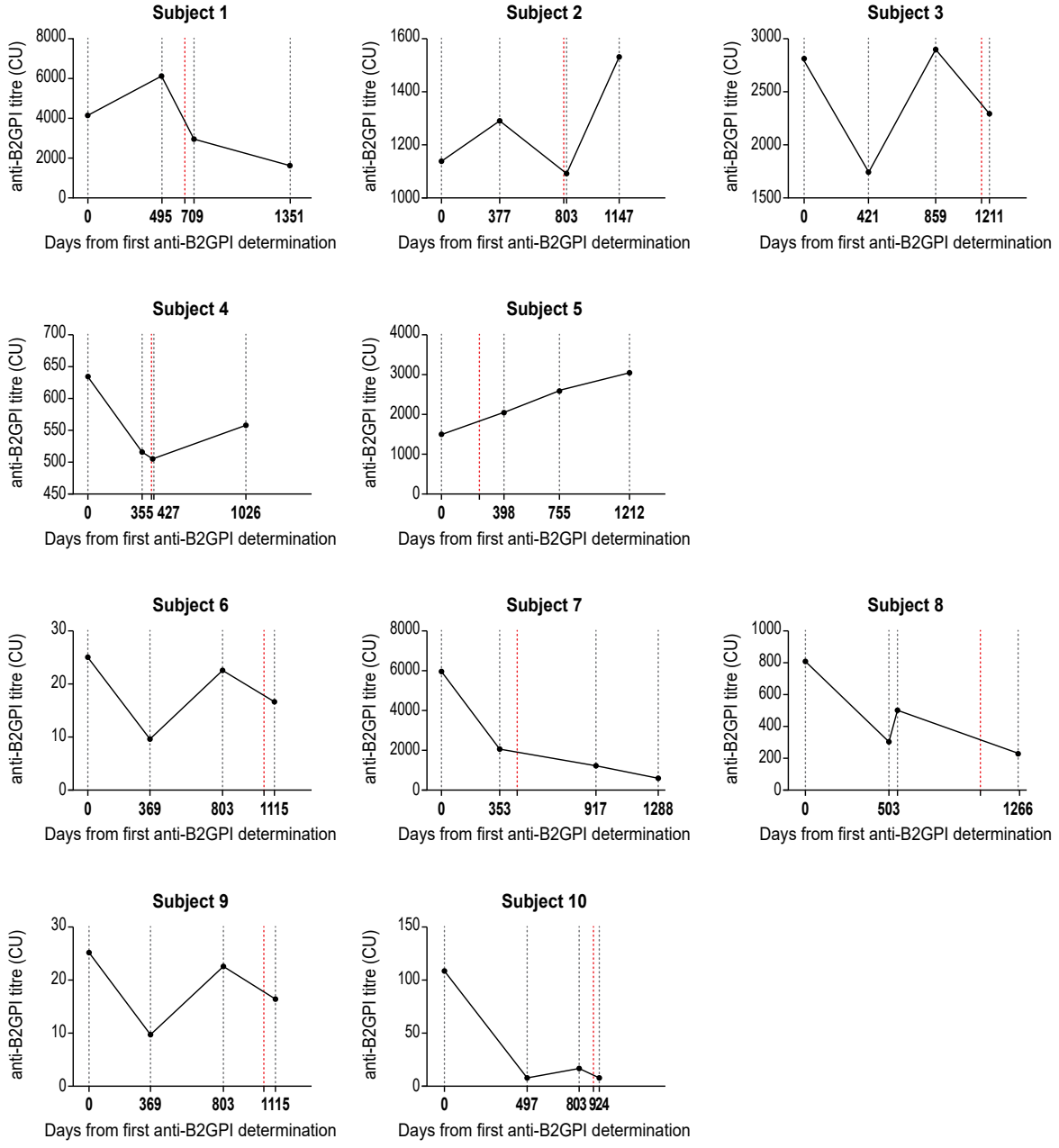

Figure 1B) Anti-β2GPI antibody titers in patients with incident thrombosis.

Conclusions: This observation might shed light into the pathogenic mechanisms of aPL-induced vascular events and exert prognostic implications.

Keywords: Anti-domain 1, antibodies anti-ß2GPI, antibodies thrombosis.

0183

REPORTING AND ESTABLISHMENT OF REFERENCE INTERVALS FOR ANTIPHOSPHOLIPID ANTIBODY IMMUNOASSAYS: A SURVEY OF PARTICIPANTS IN THE COLLEGE OF AMERICAN PATHOLOGISTS PROFICIENCY TESTING PROGRAM

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The lack of international calibrators, absence of harmonized reference intervals and use of diverse immunologic methods for testing antiphospholipid (aPL) antibodies can all contribute to missed or delayed diagnosis of antiphospholipid syndrome (APS). The aim of this study was to survey laboratory practices regarding reporting and establishing reference intervals for assays quantifying IgG and IgM antibodies to cardiolipin (aCL) and beta 2 glycoprotein I (anti-β2GPI).
Patients and methods: Supplemental questions related to reporting and establishing reference ranges for aCL and anti-β2GPI IgG and IgM and methods for assessment were sent to laboratories participating in the College of American Pathologists proficiency testing program as part of the ACL-B 2019 Survey. At the completion of the survey, the response rate for each analyte including the methods for their detection and quantification, reference intervals, units, qualitative and quantitative interpretations for all participants was determined.
Results: The number of participants reporting results for aCL and anti-β2GPI antibodies varied based on the analyte and antibody type (aCL IgG: n=495, aCL IgM: n=479; anti-β2GPI IgG: n=352 and anti-β2GPI IgM: n=330). Kits from 18 different manufacturers were identified and ELISA was the most commonly utilized method (255/448); others included BioPlex (87/448), FEIA (70/448), CIA (31/448), and unknown (5/448) based on data for quantitative determination of aCL IgG. More respondents returned quantitative than qualitative results and manufacturer cut-off ranges were used by 92.2% and 94.0% of respondents for the aCL and anti-β2GPI kits respectively. Most respondents only reported a simple negative to positive cut-off, while for IgG aCL: 42.2% also reported equivocal range cut-offs and 41.6% reported weak/low-positive cut-offs. This was similar for IgM aCL (42.2% and 40.9% respectively) but much lower for IgG anti-β2GPI (27.5% and 5.8%) and IgM anti-β2GPI (25.9% and 5.8%). The consensus for most frequently reported negative cut-offs varied widely by kit manufacturer to a high of 100% but a low of 71.4% for IgG aCL, 40.9% for IgM aCL, 60% for IgG anti-β2GPI and 60% for IgM anti-β2GPI depending on the assay.
Conclusions: ELISA remains the most commonly used method for detecting aPL antibodies with most laboratories reporting quantitative results based on manufacturers' suggested reference ranges. Qualitative categorization of results as equivocal, weak positive, positive, or strong positive for responders using kits from the same manufacturer was variable.
Keywords: Reference, ranges, proficiency, testing, survey, immunoassay.

0184

CATASTROPHIC SERONEGATIVE ANTIPHOSPHOLIPID SYNDROME

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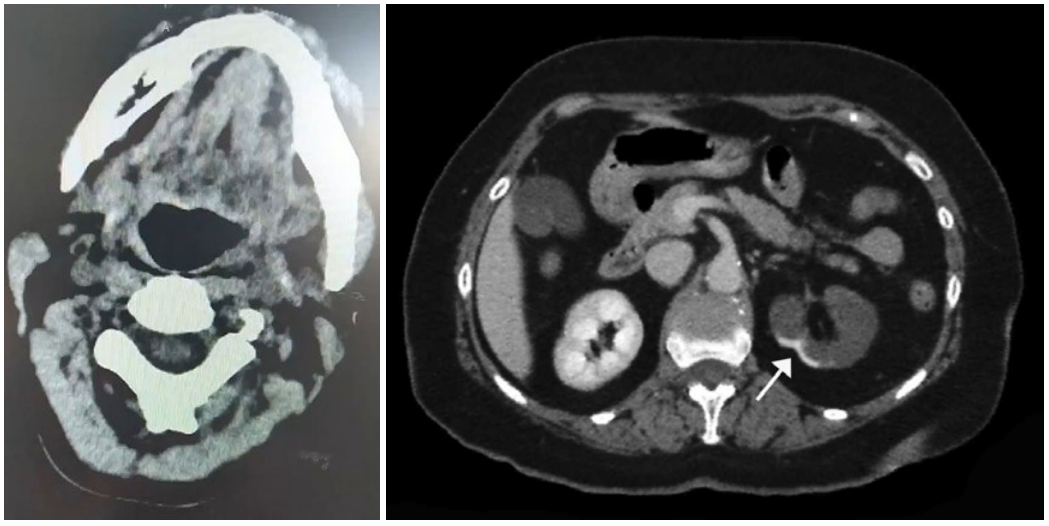
Catastrophic antiphospholipid syndrome (CAPS) is a life-threatening variant of antiphospholipid syndrome (APS) characterized by the development of multiple thrombosis in a short period of time related to a prothrombotic situation or a precipitating factor. It generally affects small vessels leading to a disseminated microangiopathic syndrome that resembles thrombotic thrombocytopenic purpura. It has been shown that some patients may present clinical features of APS with negative antibodies persistently or transiently.
Case report: 37-year-old patient with no medical history, in the postpartum period 15 days after her third pregnancy. Suddenly developed aphasia, right brachial paralysis, right lower limb paresis associated with ascites, livedo reticularis and ischemic lesions in the right foot. There were no symptoms or images related to neoplasia or infection. She had no history of obstetric complications or traditional cardiovascular risk factors and denied alcohol or drug use. Tomography (CT) showed hypodensity in the left cerebral hemisphere (Figure 1), bilateral pulmonary infarction, portal vein, hepatic veins, superior mesenteric vein and splenic vein thrombosis (Budd-Chiari syndrome) with left renal ischemia (Figure 2). Doppler ultrasound of the lower limbs showed right popliteal arterial thrombosis and left femoral and popliteal deep vein thrombosis. The laboratory presented a coagulopathy characterized by Quick Time 20%, KPTT 39, correction with normal plasma, fibrinogen 90 mg/dl, thrombocytopenia (60,000/mm3), Hb 9.8 g, slightly elevated transaminases and bilirubin, D-dimer 800 ng/dl, LDH 1400 IU/l, Factor V 16%, normal renal function and signs of thrombotic microangiopathy with schistocytes in the peripheral blood

smear. COVID PCR negative. He reported no history of previous SARS-Cov2 infection and had not received any vaccinations. Antiphospholipid antibodies (aPL) were requested and three pulses of methylprednisolone, IV immunoglobulin 400 mg/kg for 5 days, enoxaparin 60 mg every 12 hours, cryoprecipitate concentrate, furosemide, and spironolactone were indicated. The patient presented clinical and analytical improvement however, 10 days later, she developed neurological deterioration and multiple hypodense areas on brain CT, suggestive of subacute infarction. Laboratory tests showed normal hepatic and kidney function, Quick time 40%, normal KPTT, platelets 64,000/mm^3, Hb 9 g, fibrinogen 200 mg and schistocytes. ANA and aPL were negative in two determinations during the acute episode (anticardiolipin antibodies, anti- β 2 glycoprotein-I and lupus anticoagulant). She was referred to our hospital for plasmapheresis and she was admitted hemodynamically stable, afebrile with digital ischemia in the right foot, ascites, Glasgow scale 8/15, reactive pupils, right hemiplegia and left paresis. Despite triple therapy with anticoagulation, corticosteroids, and plasmapheresis, progressed the neurological condition, hemodynamic instability requiring inotropic and ischemia in the territory of the middle cerebral artery with compression of the lateral ventricles and midline deviation >5mm, multiorgan failure and death.



Conclusions: The diagnosis of seronegative APS is usually made by exclusion, but its recognition is important to adopt the most appropriate therapeutic strategy to reduce the rate of thrombotic recurrences and mortality. Nevertheless, the negativity to classic aPL criteria does not imply that other antibodies may be involved in the onset of thrombosis.
Keywords: Catastrophic antiphospholipid syndrome.

0185

IMPACT OF TESTING METHOD AND ANALYTE ON THE DIAGNOSIS OF ANTIPHOSPHOLIPID SYNDROME: A SURVEY BY THE ASSOCIATION OF MEDICAL LABORATORY IMMUNOLOGISTS

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Methods other than ELISA are increasingly being used for the detection and quantification anticardiolipin (aCL) and anti-β glycoproteinI (aβ GPI) antibodies for the diagnosis of antiphospholipid syndrome (APS) and/or systemic lupus erythematosus (SLE). This study evaluates the correlations between methods for the detection of these antiphospholipid (aPL) antibodies and the impact of immunoassay diversity in disease assessment.
Patients and methods: Aliquoted specimens from 100 patients (57 female); 56 with clinical disease (n=12 APS, n=18 APS/SLE, n=26 diverse autoimmune diseases including 7 with SLE), and 44 healthy controls were evaluated in 9 clinical laboratories. All specimens were tested for aCL and aβ GPI IgG, IgM, IgA antibodies using four different methods [ELISA, chemiluminescence immunoassay (CIA), fluoro-enzyme (FEIA), and multiplexed bead immunoassay] from 7 manufacturers. Quantitative (Spearman) and qualitative (kappa) inter-assay agreement and various analytical measures of assay performance, including sensitivity and specificity with respect to APS diagnosis were evaluated. An exploratory principal component analysis (PCA) evaluated binding patterns among qualitative and quantitative testing results from all centers.
Results: All aCL and aβ GPI tests showed good clinical sensitivities (73-87% and 63-83%) and specificities (70-89% and

70-86%) for APS diagnosis. Quantitative and qualitative agreement among IgG aCL assays ranged from 0.41-0.84 and 0.45-0.96 respectively. A broader range of agreement was seen for IgM aCL (0.19-0.82/0.11-1.00), IgA aCL (0.05-0.81/0.20-0.92), IgG aβ GPI (0.57-0.79/0.55-0.96), IgM aβ GPI (0.31-0.83/0.18-0.84) and IgA aβ GPI (0.27-0.88/0.17-0.96). Assays tended to cluster together according to similar methodology in relation to the first 2 PCA axes that explained the majority of variation in the dataset. Distinct APS patient clusters were noted along the PCA axes defined by binding in all assays versus partial binding in noted patterns, particularly among IgG aCL and aβ GPI assays. Patients within these 'binding clusters' shared similarities with regards to arterial vs venous thrombosis, pregnancy related morbidity and the presence or absence of a secondary autoimmune disease.

Conclusions: APL assays of varying methodology demonstrate comparable analytical performance in identifying APS diagnosis despite variable levels of agreement. PCA analysis has identified interesting binding patterns among the full dataset of varying aPL testing methods with a suggestive link to certain clinical features, but requires confirmation in large, well-defined patient cohorts.

Keywords: Immunoassay, Inter-assay agreement, aPL binding.

0186

CLINICAL PERFORMANCE OF A NOVEL MULTI-ANALYTE ASSAY FOR THE DETECTION OF AUTOANTIBODIES IN THE DIAGNOSIS OF ANTIPHOSPHOLIPID SYNDROME (APS)

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Antiphospholipid antibodies (aPL) are the hallmark in the diagnosis of antiphospholipid syndrome (APS). Recently, a particle-based multi-analyte technology (PMAT) system has been developed, allowing the simultaneous detection of anti-cardiolipin (aCL) and anti-β2glycoprotein I (aβ2GPI) antibodies. This study aimed to evaluate the diagnostic performance of the APS reagent on the PMAT system on specimens from both patients meeting the APS classification criteria and those with clinically diagnosed APS, but not meeting APS classification criteria.

Patients and methods: A total of 333 serum samples collected from diagnosed APS patients (n=125) and from various disease controls (n=208) were tested for anti-CL and anti-ß2GPI antibodies (IgG, IgM and IgA) by PMAT (research use only, Inova Diagnostics, San Diego, USA). A subset of patient samples was also tested by chemiluminescent immunoassay (CIA) and ELISA methodology for comparison (Inova Diagnostics, San Diego, USA). The diagnostic performance of all biomarkers was evaluated considering the clinically diagnosed APS samples and the samples included in the APS classification criteria separately. In addition, accumulative APS detection has been evaluated on both diagnosed and classified APS samples.

Results: Moderate to good agreement between platforms (PMAT vs. ELISA and CIA) was found for all assays and isotypes (Cohen's kappa: 0.46-0.82). The clinical performance of the PMAT assays is outlined in the Table below. Interestingly, non-criteria biomarkers like aCL IgA and ß2GPI IgA showed good clinical performance with a sensitivity of 35.2% and 44.8% and a specificity of 98.8% and 95.2%, respectively. Additionally, inclusion of non-criteria biomarkers increased total PMAT APS sensitivity on clinically diagnosed samples by 11.2%.

Characteristic	aCL IgG PMAT	aβ2GPI IgG PMAT	aCL IgM PMAT	aβ2GPI IgM PMAT	aCL IgA PMAT	β2-GPI IgA PMAT
	51.2 (42.5-59.8)	44.0 (35.6-52.8)	14.4 (9.3-21.6)	12.8 (8.0-19.8)	35.2 (27.4-43.9)	44.8 (36.4-53.5)
Sensibility on classified APS % (95% CI)	82.1 (72.1-89.0)	70.5 (59.6-79.5)	23.1 (15.1-3.6)	20.5 (13.0-30.8)	42.3 (32.0-53.4)	56.4 (45.4-66.9)
Specificity % (95% CI)	94.7 (90.8-97.0)	99.5 (97.3-99.9)	95.2 (91.4-97.4)	95.7 (92.0-97.7)	96.6 (93.2-98.4)	95.2 (91.4-97.4)
LR+ (95% CI)	15.5 (8.8-27.8)	146.7 (26.3-833.4)	4.8 (2.3-9.8)	4.7 (2.2-10.1)	10.4 (5.0-22.2)	9.3 (5.0-17.5)
LR- (95% CI)	0.2 (0.1-0.3)	0.3 (0.2-0.4)	0.8 (0.7-0.9)	0.8 (0.7-0.9)	0.7 (0.6-0.7)	0.6 (0.5-0.6)
Odds ratio (95% CI)	81.9 (35.3-188.5)	495.0 (81.5-2948.4)	5.9 (2.6-13.4)	5.7 (2.4-13.3)	15.6 (6.9-35.4)	16.1 (7.8-32.9)
Youden's index	0.77	0.70	0.18	0.16	0.32	0.40
Accumulative diagnosed APS detection %	51.2%	51.2%	54.4%	54.4%	64.8%	65.6%
Accumulative classified APS detection %	82.1%	82.1%	87.2%	87.2%	89.7%	89.7%

Conclusions: The new PMAT APS reagents show excellent diagnostic performance as well as moderate to good correlation to the reference methods. The addition of non-criteria IgA biomarkers into the testing algorithm holds promise in closing the seronegative gap in APS, reducing diagnostic and treatment delay, and enabling additional patient stratification.
Keywords: Diagnostics, automated assay, seronegative gap.

0187

THROMBOTIC AND OBSTETRIC ASSOCIATIONS OF IGA NON-CRITERIA ANTIPHOSPHOLIPID IMMUNOASSAYS THAT DETECT ANTIBODIES TO NEUTRAL AND NEGATIVELY-CHARGED PHOSPHOLIPIDS

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This study evaluates the performance characteristics of non-criteria IgA aCL, anti-ß2GPI, anti-phosphatidylserine (anti-PS), anti-phosphatidylinositol (anti-PI), anti-phosphatidic acid (anti-PA), anti-phosphatidylglycerol (anti-PG) and anti-phosphatidylethanolamine (anti-PE) assays in identifying APS related clinical manifestations compared to criteria aPL assays in a large group of patients with aPL-related diseases.
Patients and methods: Serum samples from 516 patients from the Hopkins (n=342) and Jamaican SLE cohorts (n=41), the PROMISSE cohort (n=76), as well as APS patients (n=29) and healthy control (n=28) from the Antiphospholipid Standardization Laboratory were examined for IgG/IgM/IgA positivity in aCL, anti-ß2GPI and IgA positivity in anti-PS, anti-PI, anti-PA, anti-PG and anti-PE ELISA assays. Correlation of assay positivity with clinical manifestations, quantitative and qualitative inter-assay agreement; and various analytical measures of assay performance including sensitivity, specificity, positive (PPV) and negative (NPV) predictive values were evaluated.
Results: The prevalence of IgA anti-PS positivity was 3.5%, anti-PI was 6.2%, anti-PA was 4.3%, anti-PG was 5.6%, anti-PE was 8.5%, aCL was 3.7% and anti-ß2GPI was 12.2%. The prevalence of IgG/IgM aCL and anti-ß2GPI was 24.4% and 18.4% respectively. Criteria assays, particularly IgG assays demonstrated the highest strength and most consistent correlation with APS diagnosis and thrombotic or obstetric (PRM) manifestations. IgA aCL, anti-ß2GPI, anti-PA and anti-PE were associated with APS diagnosis and at least one thrombotic or obstetric manifestation. IgA anti-PS and anti-PG were associated with thrombosis only while there were no significant associations with IgA anti-PI. While the quantitative and qualitative correlation between IgA aCL or anti-ß2GPI with other IgA non-criteria PLs was poor to moderate (0.10-0.50), there was moderate to excellent agreement among other non-criteria IgA anti-PL assays (0.40-0.80) assays. Overall, sensitivity (2.1-12.0%) and specificity (92.3-98.6%) for thrombosis, PRM or APS diagnosis were relatively similar among IgA aCL and non-criteria PL assays, while IgA anti-ß2GPI demonstrated higher sensitivity (12.5-22.0%) and lower specificity (86.3-98.6%). PPV and NPV values were similar among all assays.
Conclusions: While IgG criteria assays had the strongest and most consistent associations with APS clinical manifestations, IgA aCL, anti-β2GPI, anti-PA and anti-PE were associated with APS diagnosis and at least one thrombotic or obstetric manifestation. IgA anti-PI had less robust performance in this respect. The clinical utility of IgA aPL is not fully understood but this study provides evidence that certain non-criteria IgA aPL can be used to identify patients with thrombotic or obstetric APS manifestations in patients with autoimmune disease.
Keywords: Non-criteria aPL, IgA aPL, APS Diagnosis.

0189

DIFFUSE ALVEOLAR HEMORRHAGE IN CATASTROPHIC ANTIPHOSPHOLIPIDIC SYNDROME. CASE REPORT

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Case report: A 49-year-old female patient with a history of deep vein thrombosis and obstetric antiphospholipid syndrome (APS) diagnosed 23 years ago, treated with acenocoumarol, was admitted to the emergency department due to an acute respiratory failure associated with massive hemoptysis. She adds neurological deterioration, requiring respiratory assistance and admission to the intensive care unit. Our patient had been diagnosed with APS and remained stable for 23 years. Three months before admission to emergency department, a high aPL risk profile was found, with high titers of antibodies (anticardiolipin and B2glycoprotein IgG/M) Admission laboratory: hematocrit 26%; hemoglobin 8.6 mg/dl,

platelets 13000 /mm^3, PT 19 sec.; KPTT 60 sec., anticardiolipin IgG/M negative, anti B2 glycoprotein IgG/M negative, lupus anticoagulant negative, ANA negative, ANCA C and P negative, complement normal, antiplatelet antibodies negative, PCR for SARS COV 2 negative, HIV negative, extended peripheral blood where schistocytes were observed. A chest tomography was performed, which revealed bilateral and diffuse ground-glass infiltrate that was interpreted as DAH. Pulses of methylprednisolone 500 mg/24 hours for 3 days were indicated, and 48 hours later plasmapheresis was performed (overall 5). Due to persistent severe thrombocytopenia and adding hemorrhagic cystitis, metrorrhagia and persistent fever with positive blood cultures for Staphylococcus aureus, she received IV immunoglobulin (IVIg), romiplostim and broad-spectrum antibiotic treatment with negative blood cultures at 72 hours. Despite treatment, the patient envolved unfavorably with persistent hemoptysis, so rituximab 1gr IV was indicated. Without treatment response, the patient added hemodynamic instability and died on the 23rd day of hospitalization.
Discussion: The diagnosis of CAPS is determined by clinical criteria: 1Clinical evidence of involvement of more than 3 organs; 2Development of symptoms in less than one week; 3Pathological confirmation of vascular occlusion; 4Analytical confirmation of antiphospholipid antibodies(aPL). All 4 criteria are confirmatory. Since our patient had neurological, pulmonary and urogynecological involvement, which developed within 48 hours, it was considered a probable case of CAPS. Anticoagulation is an essential part of treatment but should be discontinued in the event of major bleeding. Immunosuppressive drugs should be considered early. Treatment usually combines corticosteroids, plasmapheresis and/or IVIg infusion, the latter particularly when an infection is identified, rituximab could be considered as an effective treatment for refractory CAPS or when anticoagulation is contraindicated. Despite the quickly established treatment, the evolution was unfavorable with persistent low platelets, hemorrhagic foci persisted and added infectious complications. From this we ask ourselves: What clinical manifestations or aPL profile can predict the development of CAPS? Could the development of CAPS have been prevented in this patient?
Conclusions: CAPS-associated DAH can be a fatal complication since patients develop symptoms in less than 72 hours, and must be treated with aggressive immunosuppression. Rituximab is a good option in refractory cases or when anticoagulation is contraindicated and should be started immediately. It is essential to emphasize the vital importance of clinical suspicion to establish early treatment, with a multidisciplinary team.
Keywords: Diffuse alveolar hemorrhage, catastrophic, antiphospholipidic syndrome.

0190

RENAL THROMBOTIC MICROANGIOPATHY AS ONSET OF ANTIPHOSPHOLIPID SYNDROME IN HIV PATIENT

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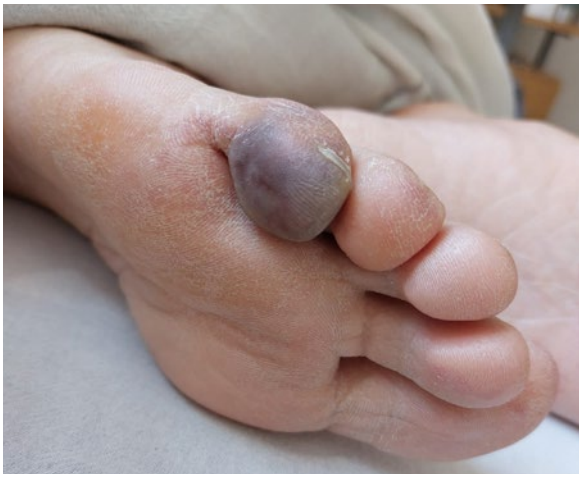
Antiphospholipid syndrome (APS) is a multisystemic autoimmune disease associated with recurrent arterial and venous thrombosis and pregnancy loss. Renal manifestations of APS conform a wide spectrum of renal syndromes. Hypertension is one of the most frequent and less recognized renal alteration. APS nephropathy is a vascular disease that affects glomerular tuft, interstitial vessels and peritubular vessels and the classic histopathologic finding is thrombotic microangiopathy (TMA). The existing studies have showed that HIV infected patients have increased risk of developing thrombosis. However, the mechanism of the presence of coexisting APS and HIV infection affecting thrombosis has not been well studied. We report a case of renal involvement as first manifestation of APS in an asymptomatic HIV patient.
Case report: A 48 year old man was referred for arterial hypertension and hyperkalemia who required haemodialysis treatment only for 2 weeks and was treated with diuretics, carvedilol and amlodipine. He also had a history of HIV infection diagnosed in 2017 under treatment with undetectable viral load and CD4 count 711 cells/mm^3. He also had history of smoking and cocaine and alcohol consumption in the past. He developed dyspnea, weight loss and ulcers lesions in both ankles and violet and blue changes in 5th finger of right foot. (Images 1, 2) Laboratory findings showed creatinine level 4,29mg/dl, urea 1.44 mg/dl, hemoglobin level 11 g/dl, normal liver function, urine sediment showed red and white casts, Hepatitis B, C and syphilis serology was negative. Complement levels were normal and ANCA, crioglobulin, anti-ds.DNA, anti-Sm were negative. Antinuclear antibody was positive in speckled pattern and anticardiolipin IgG and antiBGPI IgG were positive, and Lupus anticoagulant and anticardiolipin IgM were negative. Skin biopsy showed thrombotic vasculopathy. Renal Biopsy showed Mesangial glomerulonephritis with thrombotic microangiopathy and Focal interstitial nephritis. Immunofluorescence and EM were negative. Anticoagulation treatment was prescribed with fully recover of renal function and skin lesions.



Conclusions: Conclusion; APS is one of the main causes of renal TMA, especially if it coexists with HIV, it should be considered. HIV may induce the occurrence of APS and promote thrombotic events. The autoantibodies levels should be routinely tested to look for thrombotic events in HIV patients.
Keywords: Antiphospholipid Syndrome, renal disease, HIV

0191

CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME SECONDARY TO CHANGES IN THE TYPE AND INTENSITY OF ANTICOAGULATION.

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Catastrophic antiphospholipid syndrome (CAPS) has a mortality close to 50%. It has been possible to identify "trigger" factors that. An inadequate anticoagulation is a key element in the beginning and development of CAPS. We present four clinical scenarios in which this mechanism represents a crucial piece in the occurrence of CAPS.
Case reports: Case 1: 47-year-old woman with a history of SLE / APS. In the context of an application of botulinum toxin, an anticoagulation change of a vitamin K antagonist to LMWH is performed. Two days after the change presented acute myocarditis and systemic inflammatory process. Progresses with rapidly progressive renal failure and probable lung sub segmental embolism. The case was interpreted as CAPS. Case 2: A 59-year-old woman, diagnosed with APS and SLE at the age of 23. Due to anemic symptoms, it was decided to perform a video colonoscopy with suspension of anticoagulation. Following this, she developed acute respiratory distress syndrome (ARDS) and was admitted to the intensive care unit with pulmonary arterial hypertension, circulatory collapse, renal failure, and alveolar hemorrhage. Case 3: 44-year-old woman. He has a history of SLE with APS. Diagnosis of APS performed by DVT. It was decided to replace AVK with Rivaroxaban. After one month, he presented episode of aphasia, digraphism and right upper limb apraxia with thrombocytopenia. Evolves with endocarditis of Libman-Sacks. is interpreted as probable CAPS. Case 4: 48-year-old female with history of SLE and APS. In current treatment with AVK. She presents with meningeal syndrome with left subdural hematoma with a mass effect, so anticoagulation was suspended. After a period of observation, she remained stable and was discharged with Rivaroxaban. After these change of anticoagulation, present chest pain. It evolves with abdominal pain with adrenal ischemia. Given the suspicion of CAPS, effective anticoagulation is initiated.
Results: In the four cases in which AVK changed, different organ compromises occurred in less than a week (heart, brain, pulmonary embolism and adrenal glands) with persistently positive antiphospholipid antibodies, which are hallmarks of CAPS. In case I and II, the substitution by LMWH or directly the suspension of AVK seems to have been the triggering factor. On the other hand, in cases III and IV the AVK were replaced by Rivaroxaban, oral direct inhibitors of thrombin and factor Xa (DOAC).
Conclusions: In patients with APS anticoagulation should only be interrupted if absolutely necessary. Surgical procedures that are not strictly necessary should be avoided. Given the need to change AVK by a DOAC, the decision must be made in conjunction with all the specialists linked to the follow-up of the patient and is not being recommended for those patients with high risk characteristics. For the moment, the best tool we have to avoid or effectively treat this entity, is the judicious and interdisciplinary medical evaluation.
Keywords: Catastrophic antiphospholipid, syndrome Triggers Anticoagulation.

0192

COEXISTENCE BETWEEN PRIMARY BILIARY CIRRHOSIS AND OBSTETRIC ANTIPHOSPHOLIPID SYNDROME IN A WOMAN UNDER ASSISTED REPRODUCTIVE TREATMENT: CASE REPORT

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The association between Primary Biliary Cirrhosis (PBC) and antiphospholipid (aPL) antibodies was previously described but we found only one case report that associate Obstetric Antiphospholipid Syndrome (APS) and PBC in the literature. Objective: To describe a female patient under fertility treatment with new diagnosis of concomitant PBC and APS.
Case report: A 42 years-old woman was referred to Rheumatology department because false positive VDRL. She is undergoing fertility treatment with 4 pregnancy attempts, the last one with ovo-donation but without success. The patient had not personal and familial background of autoimmune diseases neither any thrombosis. The physical examination showed livedo reticularis in both legs and Raynaud´s Phenomenon in her hands. Antiphospholipid Syndrome (APS) was suspected and Anti-phospholipid antibodies (aFL) were requested: ACL IgG (+27.4 CU), B2GPI IgG (+47.7 CU) and LAC were positive. After 12 weeks, aFL were repeated and only LAC remained positive. Antinuclear antibodies (ANA) were positive: 1/1280 with centromeric and AC-21 reticular cytoplasmatic patterns. Also, the patient presented altered hepatogram: AST 79 U/L, ALT 115 U/L, ALP 318 U/L and GGT 45 U/L but with normal bilirubin, normal magnetic resonance cholangiography, abdominal ultrasound without gallstones and negative hepatic viruses. Celiac Disease was ruled out. The videocapilaroscopy was normal. Primary biliary cirrhosis (PBC) was suspected and other antibodies were requested: anti-mitochondrial (AMA) anti SP-100 were positive (+ >1/320, + 29 U respectively), and anti-GP 210, anti-SLA/LP, anti-LKM-1 and anti-LC1 were negative. The patient started the treatment with ursodeoxycholic acid and aspirin and in the next fertilization treatment she will receive enoxaparin.
Conclusions: The coexistence of PBC and APS is rare and the liver test could help to do the diagnosis. In women under fertility treatment with false positive VDRL test should be studied to rule out the presence of aFL. Obstetric APS is a potentially treatable cause of pregnancy failure that could improve assisted reproductive outcomes.
Keywords: APS, PBC, false positive VDRL.

0193

CARDIAC MANIFESTATIONS IN ANTIPHOSPHOLIPID SYNDROME

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Antiphospholipid syndrome (APS) is a multisystem autoimmune disease associated with recurrent arterial and venous thrombosis and pregnancy loss. Cardiac manifestations include valve abnormalities, coronary artery disease, myocardial dysfunction, pulmonary hypertension and intracardiac thrombi. Objective: to investigate cardiac manifestations of primary APS and their relationship with clinical and antiphospholipid profile in a cohort of a single center
Patients and methods: We retrospectively studied patients with primary APS according to Sydney Criteria at Rheumatology Unit in Córdoba Hospital from May 2013 to March 2020. Clinical and demographic characteristics as arterial and venous thrombosis (tAPS), obstetrical morbidity(oAPS), non-criteria manifestations (NCM) and antiphospholipid profile (Lupus anticoagulant (LA), aCL Ig G and Ig M and anti-BGPI) were evaluated.
Results: 85 patients were included, 74 were women and 11 men. 11.63% of patients had cardiac manifestations (CM) and 55,5% were men. Mean age was 43.22 +/- 11.87 in CM patients vs 36.24+/-8.30 in non CM and disease duration was 113.38+/- 67.36 months in CM patients vs 64.56 +/- 61.87 in non CM. Regarding cardiac manifestations, 80% (n=8) had valve disease, 30% (n=3) myocardial infarction, 30% (n=3) pulmonary hypertension, 10% (n=1) intracardiac thrombi and 10% (n=1) chronic myocardiopathy. 50% of CM patients had triple positivity of antiphospholipid antibodies, 77.7% LA, 88.8% aCL, and 55.5% antiBGPI antibodies. All CM patients had tAPS.
Conclusions: CM were associated to older age, longer disease, tAPS and high risk antibody profile. Preventive measures against cardiovascular risk factors and proper therapy are essential in these group of patients.
Keywords: Cardiac manifestations, antiphospholipid syndrome.