

caso clínico

A case of severe cutaneous involvement on initial clinical presentation of juvenile dermatomyositis

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ABSTRACT

Key words:
juvenile dermatomyositis,
clinical presentation.

Juvenile dermatomyositis is an autoimmune vasculopathy affecting children and adolescents, principally between the ages of four and 16 years. Its main clinical manifestations are symmetrical proximal muscle weakness, elevated serum muscle enzymes and the presence of cutaneous lesions, such as heliotrope and Gottron's papules. Herein we describe a case of juvenile dermatomyositis with a precocious time of onset at 18 months of age, notably presenting with severe ulcerative cutaneous lesions and vasculopathy likely due to gastrointestinal involvement, which required immediate treatment with immunosuppressants.

RESUMEN

Palabras clave:
dermatomiositis juvenil,
presentación inicial.

La dermatomiositis juvenil es una colagenopatía que afecta a niños y adolescentes, principalmente entre las edades de 4 y 16 años. Sus principales manifestaciones clínicas son la debilidad simétrica de músculos proximales, enzimas musculares elevadas y la presencia de lesiones cutáneas, como el heliotropo y las pápulas de Gottron. Aquí describimos un caso de dermatomiositis juvenil con un inicio precoz a los 18 meses de edad, presentando lesiones cutáneas ulcerativas severas y vasculopatía probablemente debido a la afectación gastrointestinal, que requirió tratamiento inmediato con inmunosupresores.

Introduction

Juvenile dermatomyositis (JMD) is an inflammatory muscular disease that, while rarely seen in a pediatric setting, is the most commonly occurring inflammatory myopathy during childhood. This disease has an incidence of 1-3 per 1,000,000 children per year, predominantly in females, with a mean age of onset of seven years^{1,2,3}.

JMD presents as a multisystemic vasculopathy of probable autoimmune etiology, and is thought to be triggered by environmental factors, such as viral or bacterial infection in a genetically predisposed individual¹. Recently, environmental exposure to pollutants has been described as a possible risk factor for the development of autoimmune diseases⁴. Orione et al. investigated the etiology of JDM and evaluated the influence of exposure to inhaled environmental factors during fetal development in pregnancy⁵.

The JDM diagnostic criteria initially proposed by Bohan and Peter considered clinical data, such as characteristic skin lesions, proximal and symmetrical muscle weakness, laboratorial parameters, including elevated muscle enzymes, electromyography suggestive of myopathy and the detection of inflammatory myositis via muscle biopsy. A definitive diagnosis is considered on the presentation of characteristic skin lesions in association with three criteria, while a probable diagnosis is considered in association with two criteria⁶.

The disease is characterized by myositis, classically represented by symmetrical proximal muscle weakness and cutaneous lesions typically seen in vasculitis, e.g. Gottron's papules and heliotrope rash⁷.

In addition to characteristic skin lesions, several other clinical manifestations involving the skin may be present on initial presentation and/or during the course of this disease, including ulcerative lesions, which can be associated with cutaneous vasculitis or vascular damage secondary to panniculitis⁷.

The present report aims to describe a case of dermatomyositis in a child of unusually young age (18 months) with regard to the time of disease onset, presenting with severe initial symptoms characterized by muscular involvement, as well as pronounced cutaneous and gastrointestinal tract lesions arising from vasculitis.

Case report

A 2-year-old male, previously healthy and with no family history of disease, born to healthy, non-consanguineous parents, whose mother, a rural agricultural worker, reported exposure to pesticides in her first trimester of gestation, was transferred to our hospital with complaints of papular lesions and cutaneous eruptions. The patient experienced drop attacks, frequent choking episodes and symmetrical progressive proximal muscular weakness, with a time of onset of 18 months of age.

During the six months preceding presentation at our institution, the patient was diagnosed with atopic dermatitis with no response to clinical treatment, which progressively evolved to worsening muscle weakness and cutaneous manifestations. He was admitted to our service with generalized muscle weakness (CMAS - childhood myositis assessment scale: 8; the maximum possible total score in a healthy child is 52; range 0-52) and severe cutaneous vasculitis (generalized livedo reticularis, disseminated painful ulcerated lesions of the oral mucosa, cephalic segment, thorax, axilla, abdomen, upper and lower limbs and buttocks) (Figures 1 A, B, C). On physical examination, he presented diffuse alopecia, periungual hyperemia, telangiectasia in the upper eyelids and heliotropic erythema, in addition to Gottron's papules on the surface of the elbow extensors as well as distal and proximal interphalangeal joints. No evidence of cardiopulmonary systemic involvement was detected and the child's parents denied the use of vaccines as well as the occurrence of any infections prior to his clinical presentation.

Figure 1: A- Deep cutaneous vasculitis in the abdomen; B- severe cutaneous vasculitis in lower limbs; C- cutaneous vasculitis with associated ulcers.

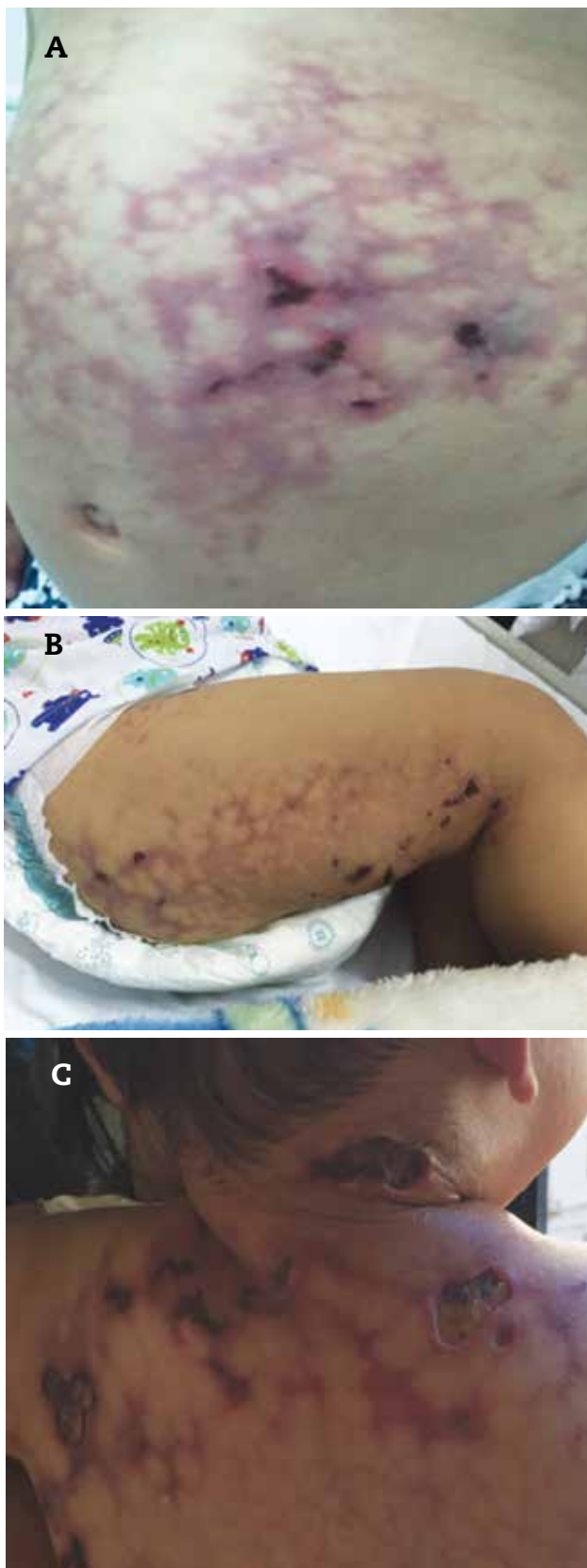


Figure 2: A-Vasculitis and ulcers with improvement after starting treatment; B- vasculitis and ulcers with improvement after initiation of treatment; C- healed cutaneous ulcers.



Laboratory parameters upon admission: lactic dehydrogenase: 867 [Reference value (VR) 120 to 300 U/L]; Creatine kinase (CK): 875 U/L (VR <200U/L); Aldolase 14.6 (VR <7.6 U/L); C-reactive protein 26 (VR <6); Antinuclear antibody (ANA) 1:160, dense fine speckled (DFS) pattern; Anti-SM, anti-DNA, anti-SSa, anti-SSb, smooth anti-tumor, anticardiolipin, IgG, IgM and lupus anticoagulant antibodies all negative. C3, C4 and Ch50 serum complements normal. Other laboratory tests were normal (thyroid function, viral serologies, glucose, hepatic and renal function cholesterol and triglycerides). Electromyography compatible with inflammatory myopathy; upper gastrointestinal endoscopy: non-erosive duodenitis; abdominal ultrasonography showed discrete hepatomegaly; radiological examination (with contrast) of the esophagus: normal stomach and duodenum; echocardiogram, chest CT scan and chest x-ray were all normal.

Pulse therapy with methylprednisolone (30 mg/kg/day, 3 days) was initiated, with unsatisfactory muscular and cutaneous response. Following pulse therapy, the child evolved to a diagnosis of sepsis (Extended spectrum β -lactamase-producing-EBSL *Klebsiella pneumoniae*), treated by initial administration of cefepime and vancomycin, subsequently modified to imipenem, with satisfactory resolution. Following the clinical stabilization of the child's infectious condition, he began to present intense abdominal pain, with suspected visceral vasculitis involving the mucosa of the digestive tract corroborated by a positive fecal occult blood test. At this time, the child continued to present severe cutaneous

ulcerative lesions. High doses of corticosteroids were maintained in association with the introduction of weekly administrations of subcutaneous methotrexate for six months (increasing up to 1 mg/kg), followed by oral administration until present (currently tapered to 0.8 mg/kg/weekly); hydroxychloroquine (5 mg/kg/day; still being administered); prednisone (2 mg/kg/day, slowly tapered to 0.3 mg/kg/day); immunoglobulin (2 g/kg/day, three biweekly doses, followed by monthly doses for one year) and monthly cy-

clophosphamide (500 mg/m², for 6 months).

A progressive return of muscle strength was observed with complete resolution of abdominal pain and partial improvement in cutaneous lesions (Figures 2 A, B, C). Initial healing of ulcerations was obtained following the third dose of cyclophosphamide (total of six doses) and after the sixth dose of immunoglobulin, and the patient was subsequently discharged with recommendation of follow-up on an outpatient basis. Monthly immunoglobulin infusions were maintained until the completion of one year of treatment. This patient is currently being followed on an outpatient basis, with the obtainment of healed ulcerative lesions, persistent discrete livedo reticularis accompanied by periods of improvement and worsening, facial rash and eyelid erythema, residual Gottron's papules and preserved muscle strength (DAS-Disease Activity Score: 5), allowing for a progressive reduction in corticosteroid dosage, with current administration of methotrexate and prednisone. Laboratory parameters reveal normal levels of muscle enzymes.

Considering the age of the patient (<2 years), the instruments used to evaluate activity, muscle strength and functionality are difficult to apply. The scores obtained by applying 14 physical maneuvers of CMAS evidenced a global improvement (initial clinical presentation: 8; six and twelve months after starting treatment: 29 and 43, respectively; currently: 48).

Discussion

Juvenile dermatomyositis, a rare, chronic autoimmune disease typically occurring in childhood, is a systemic vasculopathy characterized by symmetrical proximal muscle weakness, increased muscle enzymes and pathognomonic skin lesions, including heliotrope rash and Gottron's papules on extensor surfaces⁸.

A range of etiological factors may be potentially involved in individuals genetically susceptible to this disease. In the present case, there were no reports of likely exposure or apparent infectious manifestations during the child's first two years of life, which does not rule out the possibility of silent exposure.

There was reported occupational maternal exposure to pesticides occurring during the first trimester of gestation. While the role of adult exposure to pesticides in the development of autoimmune diseases, such as rheumatoid arthritis and systemic lupus erythematosus, remains controversial, some reports have taken this into consideration^{9,10,11}. The literature contains no studies evaluating the influence of pesticide exposure during gestation with regard to the development of autoimmune disease in children.

JDM presents as a broad spectrum of cutaneous manifestations of variable clinical course and severity. Cutaneous ulcerations are the pathological result of the deposition of the complement in association with occlusive endarteropathy of dermal vessels¹². These occur in less than 10% of patients with dermatomyositis, and are generally related to a more aggressive course of disease¹³.

The vasculopathy seen in JDM compromises the skeletal muscle, skin, gastrointestinal tract and other tissues, including the lungs, eyes and heart. Both humoral and cellular immunity contribute to the pathogenesis of this disease. Evidence suggests that innate immunity may play an important role in this disease^{14,15}.

A study by Gitiaux et al. highlights that JDM can be divided into distinct subgroups, and that severe forms of presentation, as well as poor prognosis, are linked to vasculopathy¹⁶. Gastrointestinal involvement, although infrequently found in JDM, especially in young children^{17,18}, yet consistent with the present case, is associated with inflammatory vasculopathy and the complete narrowing of the vascular lumen or multiple occlusion of small and medium arteries, resulting in ulceration and perforation¹⁹.

In the differential diagnosis of conditions characterized by intense cutaneous involvement and erythematous rashes on the face or extremities in the absence of physical weakness, e.g. atopic dermatitis, allergies, eczema or psoriasis, juvenile dermato-

myositis should be considered. Physicians must take measures to avoid delays in diagnosis and therapy initiation, which could result in well-documented implications regarding disease evolution and prognosis. Robinson et al. demonstrated that the delayed onset of treatment in patients with over two years of symptomatology was associated with higher CMAS (Childhood Myositis Assessment Scale) scores, low CHAQ (Childhood Health Assessment Questionnaire) scores, as well as impacts on both physician and patient global assessments¹⁸.

Other conditions may present similarly and must be considered in the differential diagnosis: **diseases presenting with weakness alone**, e.g. muscular dystrophies, metabolic and endocrine myopathies, drug-induced myopathy or neuromuscular transmission disorders; **diseases with weakness with or without rash**, e.g. viral, bacterial or parasitic myositis; **other rheumatic conditions**, e.g. systemic lupus erythematosus, scleroderma, juvenile idiopathic arthritis, mixed connective-tissue disease, idiopathic vasculitis or other inflammatory conditions. In many of these conditions, the diagnosis is facilitated by muscle biopsy^{6,8}.

The diagnosis presented in the present case was compatible with JDM, in accordance with the 1975 criteria by Bohan and Peter, despite the inability to conduct a muscle biopsy, which did not represent a basis for invalidation. It is important to note that, concomitant to myopathy as evidenced by alterations in muscle strength, muscle enzymes and EMG, the patient presented cutaneous manifestations suggestive of JDM. According to records from the Juvenile Dermatomyositis National Registry and Repository (UK and Ireland) and the European and Latin American registry, muscle biopsy has been used as a diagnostic tool for myopathy in 36% and 55% of these patients, respectively^{20,21,22}. A study showed that just 56% of pediatric rheumatologists surveyed internationally employed electromyography, and only 61% used muscle biopsy to diagnose juvenile dermatomyositis²³. In the present case, the evaluation of the patient's clinical history and laboratory examinations influenced the determination of our diagnostic hypothesis.

It is important to note that had a muscle biopsy been carried out, complementary information regarding prognosis could have been obtained. Gitiaux et al. evaluated two distinct homogeneous subgroups of JDM patients, categorized according to clinical disease severity and pathological findings, and reported that the best predictors of poor treatment response were CMAS <34 with gastrointestinal involvement, or the presence of fibrosis in the endomysium at the onset of disease¹⁶.

According to the consensus-based recommendations for the management of juvenile dermatomyositis, the patient described herein could be considered at high risk, since he presented at least four of 10 consensus criteria, specifically: severe weakness, as he was bedridden; CMAS <15; the need for admission in an intensive care unit; gastrointestinal vasculitis; and the presence of cutaneous ulcerations²².

The high degree of risk presented by this patient's condition, characterized by severe ulcerative lesions, together with the diagnosis of JDM in a child at such a young age, greatly influenced the course of therapeutic intervention. JDM treatment is largely based on the experience of the treating pediatric rheumatologist. The mainstay of therapy is an initial high-dose of corticosteroid in combination with disease-modifying drugs, such as MTX or ciclosporin A (CsA). The addition of MTX or CsA leads to better disease control than prednisolone alone; safety profiles favor the combination of methotrexate and prednisolone (evidential level 1B, strength of recommendation A)²².

Ruperto et al. in a randomized controlled trial, compared three commonly used protocols (prednisone alone vs. a combination of prednisone with either MTX or CsA). The combination of steroids and MTX was found to offer the best outcome in terms of efficacy and safety²³.

In this case, despite the use of high doses of corticosteroids at the onset of therapy, including via the parenteral route in conjunction with MTX, the patient evolved with intense abdominal pain and severe ulcerative lesions, after which we administered

cyclophosphamide and immunoglobulin (evidence level 2B-4, force of recommendation C)²².

Cyclophosphamide has been used to treat JDM patients faced with a high risk of morbidity and mortality, in which case high-risk markers must be carefully evaluated, including ulcerative cutaneous disease, gastrointestinal and respiratory tract involvement, cardiac and central nervous system involvement, CMAS score <15, or MMT8 score <30^{24,25,26}. Despite this child's young age, he exhibited remarkable tolerance to immunosuppressant medication.

On average, 40 to 60% of JDM cases are chronic in nature, requiring long-term immunosuppressant medication, often in association with multiple therapeutic treatments¹⁶.

In sum, the herein described case of JDM with severe initial presentation in a 2-year-old child is notable with regard to the presence of gastrointestinal vasculopathy and, above all, the aggressiveness of cutaneous vasculitis in this remarkably vulnerable case, especially considering the patient's age, disease severity and established course of treatment.

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