Juvenile dermatomyositis with anti-signal recognition particle antibodies: a case report

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ABSTRACT

Serologic investigation has been explored in inflammatory myopathies in order to define subgroups that can help us predict clinical course, treatment and prognosis. The level of similarity between juvenile and adult myopathies regarding the presence of myositis-specific autoantibodies has not been fully elucidated.

We report the case of a 8-year-old girl who presented with a rapid progression of muscle weakness and cutaneous signs consistent with the diagnosis of juvenile dermatomyositis and whose serologic testing revealed the presence of anti-signal recognition particle (SRP) antibodies. So far these antibodies have been described mostly in adult subsets, frequently associated with poorer outcomes and rarely related to cutaneous manifestations. The knowledge of the degree of overlap between paediatric and adult SRP positive myopathies may improve the medical care we provide to these children.

Keywords: Juvenile dermatomyositis; Anti-signal recognition particle antibody

INTRODUCTION

Juvenile dermatomyositis (JDM) is a rare autoimmune myopathy. United States population-based studies report estimated annual incidence rates that ranges from 2.5 to 5.5 new cases per million children[1,2], with a female predominance two-fold greater[1,3]. The mean age at diagnosis is usually around 7 years old[3–6].

Clinically, it is characterized by symmetric, proximal muscle weakness, and typical skin involvement[5,6]. The diagnosis based on criteria first proposed by Bohan and Peter included raised muscle enzymes, typical electromyography and muscle biopsy changes[7]. However, magnetic resonance imaging (MRI) has increasingly gain importance, obviating the need for invasive procedures in many situations.

Over the past decades, the diagnostic and prognostic utility of serologic investigation in inflammatory myopathies has been explored. Subgroups defined by the presence of different myositis-specific autoantibodies (MSA) have been recognized in adult patients and associated with distinct clinical phenotypes[8,9]. Although they have been described in juvenile subsets[10,11], the existence of distinct subgroups and similarity with the adults have not been fully elucidated in large studies.

We present the case of a child with JDM positive for anti-SRP antibodies, which so far has not been described in the literature.

CASE REPORT

A 8-year-old girl presented to our institution with a 3--month history of a rapid progressive proximal muscle weakness, along with a rash and papular lesions.

On examination the cutaneous signs were consistent with heliotrope dermatitis and Gottron's papules, affecting mainly the face, elbows, hands and feets (Figures 1 and 2).

She presented no symptoms or signs of systemic involvement, namely pulmonary or cardiac disease.

Initial strength testing using Manual Muscular Testing 8 (MMT8) resulted on a score of 57 out of 80. The blood analysis showed an elevation of muscle enzymes levels (creatine kinase of 1309 IU/L, aspartate aminotransferase of 123 IU/L, lactate dehydrogenase of 922 IU/L) and MRI presented with diffuse oedema of the thigh and shoulder girdle muscles. The muscular

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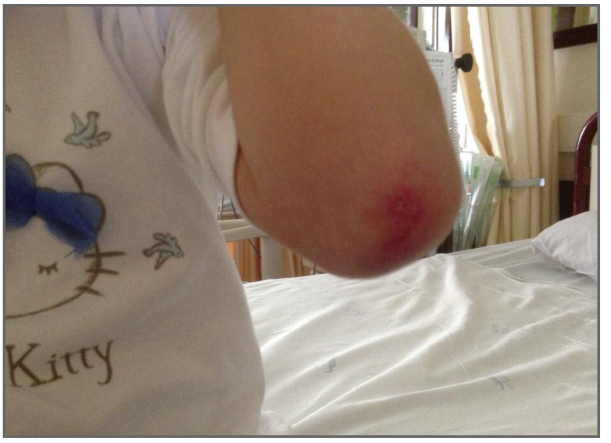

FIGURA 1. Gottron's papules affecting the elbows

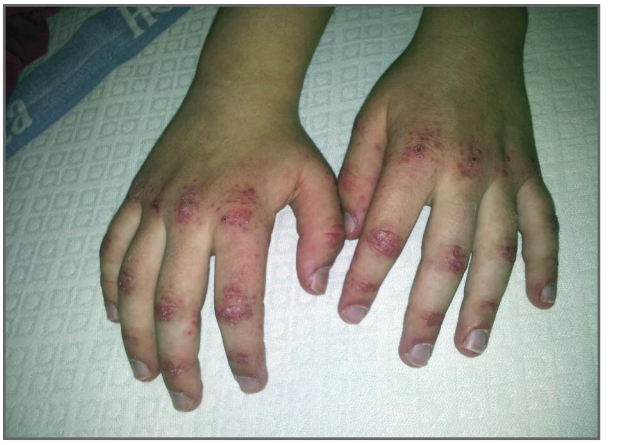

FIGURA 2. Gottron's papules affecting the hands

biopsy confirmed the diagnosis of JDM.

We proceeded to the laboratory testing of MSAs by immunoblot (EUROLINES test provided by EUROIMMUN® company), including anti-Mi2, Ku, PM-Scl100, PMScl75, Jo1, SRP, PL7, PL12, EJ and anti-OJ, which revealed the presence of anti-SRP antibodies.

Regarding therapeutic approaches, it was first tried corticosteroids but she developed an anaphylactic reaction to intravenous (IV) administration of methylprednisolone. Oral prednisolone and dexamethasone were also poorly tolerated, so the medical team decided to initiate a cyclophosphamide regimen (6 administrations of 250 mg/m^2: 3 fortnightly pulses followed by 3 monthly pulses), complemented with daily deflazacort (at an initial dosing of 1.5 mg/kg) and 3 pulses of 2g/kg immunoglobulin (IVIg). This lead to a significant progress of muscular strength, presenting a MMT8 score of 77 (out of 80) and a CK value normalized to 45 IU/L. Although sustaining discrete papular lesions on the elbows and hands, cutaneous manifestations also presented a reasonable improvement.

She was then maintained on treatment with progressively lower doses of daily deflazacort along with weakly 15 mg/m^2 oral methotrexate, but in less than 2 months began to show signs of relapse with deterioration of both cutaneous signs and muscular strength, with a MMT8 score decreasing to 68 (out of 80). Parenteral methotrexate, IVIg and 3 more cyclophosphamide administrations yielded minimal improvements.

Treatment with 575/m^2 rituximab was recently established (500 mg twice), followed by combined therapy of azathioprine and corticosteroids. Two months have passed after the institution of this treatment and so far the patient shows a remarkable improvement of cutaneous lesions and strength (MMT8 score of 74 out of 80 in the last appointment), allowing for a progressive reduction of corticosteroids dose. Blood analysis reveal normal levels of muscle enzymes and negative anti-SRP antibodies. The patient remains on close medical observation.

DISCUSSION

We describe the case of a child with inflammatory myopathy diagnosed by the age of 8 years old. She presented with rapidly developing proximal muscle weakness and severe skin lesions typical of JDM. The findings on MRI and on muscle biopsy were also strongly suggestive of this diagnosis. Interestingly, the patient showed anti-SRP antibodies in her serum. Her response to treatment has been so far rather instable. After an apparently good response to the first cycle of cyclophosphamide, she presented a quite rapid decline of her health status leading to a second immunosuppressive cycle. Following several combined therapies with no remarkable results, she is now showing improvements with rituximab.

MSAs have been identified in small subsets of juvenile idiopathic inflammatory myopathies. Rider et al[12] describes one of the largest samples so far, including 374 children, from witch 63% had at least one MSA. Anti-SRP were present in only 1.4% of the cases and all had juvenile polymyositis and presented with severe course of disease (with higher frequency of distal weakness, muscle atrophy, falling episodes and higher

levels of CK levels). Those descriptions are similar with the ones in adult patients[13].

Recently, Hengstman et al[13] described myopathy associated with antibodies anti-SRP as an immune-mediated necrotizing myopathy based on histological findings; clinically characterized by rapidly progressive muscle weakness resulting in marked disability. Several other reports also in adult subsets display a similar clinical pattern of severity, with association to cutaneous rashes being very uncommon[14–16].

Anti-SRP myopathy also seems to differ from other immune-mediated myopathies by its characteristically poor responsiveness to steroid monotherapy and conventional immunosuppressive therapies. In this regard, there is evidence of the potential benefits of B cell depletion therapy using rituximab, especially on the refractory cases[17,18].

To our knowledge there are no reports in the literature of JDM with anti-SRP identified in serum. Our clinical case shows obvious correlations with the descriptions of myositis associated with these antibodies in adults, namely the rapid progression of muscle weakness, poor response to first-line therapeutics and an apparently good reaction to treatment with rituximab. On the contrary, dermatomyositis typical cutaneous signs are not frequently reported, which highlights one of the points of interest of this case.

This report emphasizes the need for additional studies with larger samples including JDM and juvenile polymyositis myopathy patients to substantiate the existence of different serological phenotypes that can help us predict clinical course, treatment and prognosis.

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