Subcutaneous Immunoglobulin in Refractory Juvenile Dermatomyositis

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Juvenile dermatomyositis (JDM) is the most common idiopathic inflammatory myopathy in childhood.1 Over the last few years, several consensus treatment plans have been published that address the initial treatment of the disease2 and its therapy beyond the first 2 months.3 These recommendations include the use of corticosteroids and methotrexate with or without intravenous immunoglobulin (IVIG),2 and with the addition of an immunosuppressant such as mycophenolate mofetil, azathioprine, or a biologic agent when the disease worsens despite appropriate initial therapy.3 Cyclosporine A used in combination with prednisone has shown similar efficacy but with higher rates of adverse effects than methotrexate.4 In addition, hydroxychloroquine is commonly used for cutaneous disease.5

CASE REPORT

A 4-year-old girl was referred to our center in May 2008 with a 1-month history of malar rash, heliotrope, Gottron’s papules, proximal muscular weakness, and knee arthralgia. She did not have fever, dysphagia, dysphonia, or cutaneous ulcerations at the time of hospital admission. Her childhood myositis assessment scale score was 35 (of 52). Her initial workup revealed normal blood counts, acute-phase reactants and biochemistry, elevated serum levels of muscle enzymes (alanine aminotransferase 150 U/L [reference value 5–40 U/L], aspartate aminotransferase 203 U/L [reference value 5–40 U/L], lactic dehydrogenase 836 U/L [reference value 120–300 U/L], creatine kinase 2210 U/L [reference value 34–170 U/L]), and negative antinuclear, myositis-specific (anti-Jo1, anti-SRP, anti-Mi-2) and myositis-associated (anti-U1-RNP, anti-Ro, anti-PM-Scl, anti-Ku) antibodies. An electromyographic study revealed a myopathic pattern. She was diagnosed with JDM and started on intravenous methylprednisolone followed by high-dose oral prednisone (2 mg/kg/day) with an excellent clinical response. In July, her serum muscle enzymes were normal (alanine aminotransferase 40 U/L; aspartate aminotransferase 31 U/L, lactic dehydrogenase 230 U/L, creatine kinase 33 U/L).

In July, prednisone was tapered to 1.5 mg/kg/day. After 6 weeks, the dose was decreased to 1 mg/kg, tapering

abstract

Juvenile dermatomyositis (JDM) is the most common form of juvenile idiopathic inflammatory myopathy. We report a child with steroid-dependent JDM refractory to hydroxychloroquine and subcutaneous methotrexate who experienced systemic reactions to intravenous immunoglobulin and was successfully treated with subcutaneous immunoglobulin. This form of therapy has been shown to be safe, has a very low rate of adverse effects, does not require hospital admission, reduces the number of missed school days, and decreases the costs associated with treatment.

Dr de Inocencio drafted the initial manuscript; Drs de Inocencio and González-Granado conceptualized and designed the study; Drs Enríquez-Merayo and Casado collected the data and performed the literature review; Drs Enríquez-Merayo, Casado, and González-Granado critically revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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by 2.5 mg/month from then on. In February 2009, she was receiving 0.5 mg/kg/day when she presented with erythroderma and Gottron’s papules without accompanying muscle weakness or serum muscle enzyme elevation. The dose of prednisone was slightly increased, and hydroxychloroquine (6 mg/kg/day) was added to her therapy, with cutaneous improvement. In September, her cutaneous disease flared up again, coinciding with another reduction in the dose of prednisone. She was started on subcutaneous methotrexate (MTX), 15 mg/m²/week, with clinical improvement. In April 2010, she had a new flare-up while on prednisone at 0.3 mg/kg/day and MTX, so IVIG was started at a dose of 2 g/kg/month. Twenty-four hours after its administration, she required hospital admission due to aseptic meningitis. In May, a second dose of IVIG was administered at a very low infusion rate with a postinfusion headache that did not require admission. Considering the side effects of IVIG and that cutaneous lesions had resolved completely, IVIG was interrupted and she continued on a low dose of prednisone (<0.2 mg/kg/day) and subcutaneous MTX (15 mg/m²/week).

In January 2011, she presented with a new cutaneous flare-up (Fig 1). A new infusion of IVIG had to be discontinued because of a severe headache and nausea.

In February 2011, she was started on subcutaneous immunoglobulin (SCIG) at a dose of 240 mg/kg/week (Vivaglobin, 16% IgG) with rapid clinical improvement and excellent tolerance. The mother underwent training at the Primary Immunodeficiencies Unit of our center to learn how to administer SCIG, and she administered the therapy at home. Seven weeks later (Fig 2), prednisone was discontinued and shortly thereafter, in May 2011,
MTX was interrupted. Therapy with SCIG was de-escalated to every 2 weeks in October 2012 without disease flare-ups and discontinued in September 2013. Two years later, she remained in complete clinical remission off medication.

**DISCUSSION**

SCIG is extensively used in children with primary immunodeficiencies. Multiple studies have confirmed its efficacy, safety, and very low rate of complications or adverse effects. SCIG can be administered at home, avoiding hospital admissions and reducing the number of lost work and school days, thus becoming more cost-effective than IVIG. SCIG can be administered by rapid push or by infusion pump; the first method may be very useful in areas with limited access to medical technology, further reducing the costs of the therapy.

SCIG is administered weekly, so its dose, pharmacokinetics, and bioequivalence differ from monthly IVIG. SCIG results in lower peaks and higher trough levels of serum IgG, more stable steady-state IgG levels. In immunodeficient patients, SCIG dose can be adjusted according to the trough IgG concentration obtained. The dose required to treat inflammatory myopathies, however, is unknown. A study published in January 2011 showed that SCIG was effective in treating adults with polymyositis and dermatomyositis at a dose of 0.8 g/kg/month. For our patient, we used a similar dose (1 g/kg/month) with excellent results. More recently, Gelardi et al reported long-term stable remission in 3 adults with polymyositis and 3 with dermatomyositis, using lower maintenance doses (0.2–0.8 g/kg/month) of 20% subcutaneous IgG. Our data using maintenance doses of 0.4–0.5 g/kg/month support their observation.

This report represents, to the best of our knowledge, the first patient with refractory JDM successfully treated with SCIG, suggesting that it may also be an effective therapy in children. The treatment improves tolerability among patients who had experienced systemic reactions to IVIG and can be administered at home, resulting not only in greater convenience to the family and the patient, but also reducing the number of missed school days. In addition, SCIG may reduce the cost of therapy up to 33%.

**ABBREVIATIONS**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>IVIG</td>
<td>intravenous immunoglobulin</td>
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<td>JDM</td>
<td>juvenile dermatomyositis</td>
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<td>MTX</td>
<td>methotrexate</td>
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<td>SCIG</td>
<td>subcutaneous immunoglobulin</td>
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