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## CLINICAL CASE OF THE MONTH

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# 3-Year-Old Boy Presenting with a Hand Rash

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Of the diseases within the spectrum of the juvenile idiopathic inflammatory myopathies, juvenile dermatomyositis (JDM) is the most common. As the name implies, JDM affects the muscles and skin most commonly, but can involve other organ systems as well. Dermatologic manifestations often precede other signs and symptoms by months or even years and frequently are the primary reason the patient seeks medical attention. In the case presented here, a 3-year-old boy initially developed a hand rash that brought him to his primary care physician. By the time muscle weakness had developed, the patient had already been evaluated for dermatomyositis and therapy had been initiated. An understanding of these early clinical findings will enable physicians to make a timely diagnosis and commence therapy promptly in order to prevent life-threatening sequelae of the disease.

**A** 3-year-old white boy was referred to the dermatology clinic with a 4-6-week history of a non-pruritic skin eruption over the dorsal surface of his fingers. He had previously been seen by his primary care physician and treated for a presumed bacterial infection with a 10-day course of cephalexin and later trimethoprim/sulfamethoxazole without improvement. He also failed to respond to a topical antifungal cream for possible tinea manuum.

The mother reported that he had a history of asthma and allergic rhinitis. He also had a recent "cold" with rhinorrhea, sneezing, cough, and low-grade fever, but no gastrointestinal or pulmonary complaints. He had no weight changes, arthritis, or arthralgias; however, the mother noticed he was somewhat more fatigued than

usual, spending more time sitting down or resting than previously. He attends pre-school and has achieved appropriate developmental milestones. No one in the family has had psoriasis or a similar skin eruption. There is a family history of connective tissue disease, including a paternal grandfather with rheumatoid arthritis and a maternal cousin with systemic lupus erythematosus. The mother has a history of hypothyroidism.

On exam, the patient was afebrile with normal blood pressure, heart rate, and respiratory rate. He appeared his stated age and was in no apparent distress. Cardiovascular and pulmonary exams were unremarkable. There was no hepatomegaly or splenomegaly. A musculoskeletal exam was unremarkable. His skin exam revealed erythematous papules and scaly plaques on the

### CME INFORMATION

#### TARGET AUDIENCE

The September/October Clinical Case of the Month is intended for family physicians, general practitioners, pediatricians, general internists, dermatologists, pathologists, emergency medicine physicians, radiologists, and medicine subspecialists.

#### EDUCATIONAL OBJECTIVES

The Clinical Case of the Month is a regular educational feature from the Department of Medicine at the LSU Health Sciences Center. Medical students, residents, postdoctoral fellows, and faculty collaborate in the preparation of these discussions. After reading this article, physicians should be better able to identify and to understand the clinical presentation, diagnosis, pathogenesis, and treatment of juvenile dermatomyositis.

#### CREDIT

The LSMS Educational and Research Foundation designates this educational activity for a maximum of one (1) category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

#### DISCLOSURE

Dr. Kendrick has nothing to disclose.  
Dr. Poole has nothing to disclose.  
Dr. Nicotri has nothing to disclose.  
Dr. Gedalia has nothing to disclose.  
Dr. Lopez discloses that he is a member of the LSMS *Journal* Board and the LSMS *Journal* Editorial Board.

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**Figure 1.** Right hand with Gottron's papules over 4<sup>th</sup> and 5<sup>th</sup> proximal interphalangeal joints and periungual erythema.

dorsum of his hands overlying the proximal interphalangeal joints. Distal erythema and swelling in a periungual distribution of all 10 fingernails, without distinct telangiectasias of the nail folds, was noted (Figure 1). There were no nail pits or other nail changes. The skin of his face revealed erythematous-to-violaceous discoloration of the periorbital area and nasal bridge with mild periorbital edema (Figure 2). The remainder of his skin, including the scalp and genital area, was clear with the exception of a few erythematous patches overlying his elbows and knees.

Initial laboratory testing included a complete blood count (CBC), erythrocyte sedimentation rate (ESR), anti-nuclear antibody (ANA), creatine phosphokinase (CPK), and aldolase. The CBC and ESR were normal, but the ANA test revealed a titer of 1:160 (normal <1:80) in a homogeneous pattern. The CPK was elevated at 1,320 U/L (normal 0-200 U/L). Aldolase was elevated at 17.7 U/L (normal 3-12 U/L).

A skin biopsy of one of the papules on his index finger revealed dyskeratotic keratinocytes, a cell-poor lichenoid infiltrate of lymphocytes, and vascular dilatation (Figure 3). These findings were consistent with those seen in connective tissue diseases and, of all possibilities, were most representative of dermatomyositis (DM).

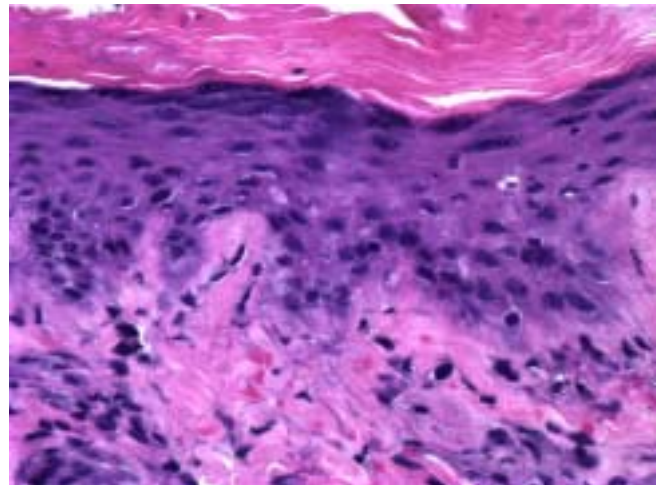
The patient had a follow-up visit with the dermatologist a few weeks later in order to review the lab and biopsy findings. At that time, he continued to have no objective muscle weakness. On strength testing, he could start with both hands and feet touching the ground and bring himself to a standing position without using his hands to push along his legs in order to get fully upright. In other words, he had a negative Gower sign. However, he was complaining of joint pain and tightness, particularly of the knees. Given the patient's clinical, laboratory, and histopathologic findings, JDM was considered the likely diagnosis. The patient was evaluated by a pediatric rheumatologist approximately one week after the



**Figure 2.** Heliotrope rash.

initial dermatology work-up and was found to have proximal muscle weakness, especially of his trunk and shoulder girdle bilaterally, in addition to the classic heliotrope rash and Gottron's papules. Laboratory testing at that time revealed a positive ANA of 1:320, this time in a speckled pattern; however, the double-stranded DNA antibody was negative. The von Willebrand factor antigen was mildly elevated to 140 percent (normal 60-100%). The aldolase level was 25 U/L, and the CPK was increased to 1,825 U/L. Aspartate aminotransferase (AST) was elevated to 124 IU/L (normal 2-50 IU/L). Alanine aminotransferase (ALT), complement levels, immunoglobulin levels, and serum chemistries were normal.

On the same day, magnetic resonance imaging of his thighs was performed and revealed diffuse areas of inflammation bilaterally. A muscle biopsy showed endomysial and perimysial inflammation that was suggestive of a diagnosis of DM, and he was then given a



**Figure 3.** Histopathology (Hematoxylin and eosin). High power view of skin, taken from index finger. Loss of clear boundary between the epidermis and dermis at basement membrane zone where autoantibody deposits.

definitive diagnosis of JDM. An initial treatment with prednisolone oral solution 15mg twice daily was instituted, and given the fact that ultraviolet exposure can exacerbate the disease, he was instructed to use photoprotective measures such as hats and sunscreen. In addition, he was scheduled for physical and occupational therapy. Due to the slow clinical improvement, methotrexate 15 mg once a week and hydroxychloroquine 100 mg once daily were added with a resultant good response.

Currently, 9 months after the initial diagnosis, the patient has continued to slowly taper off the oral corticosteroids while on methotrexate and hydroxychloroquine. His skin and muscle disease have improved significantly and he continues physical therapy and photoprotective measures.

## JUVENILE DERMATOMYOSITIS

Dermatomyositis is an inflammatory disease that most commonly affects skeletal muscle and skin. Patients can present with dermatologic features months-to-years before muscle symptoms develop.

There is a bimodal age distribution for the onset of DM, with one small peak in childhood and one in the fifth to sixth decade of life. The childhood form of DM is much less common than the adult-onset form. Children present on average at 8 to 12 years of age, but there have been reports of patients presenting before age 2. The disease affects girls more frequently than boys. It is a relatively uncommon disease, with less than 5 cases per million children per year.<sup>1,2,3</sup>

## CLINICAL PRESENTATION

The most pathognomonic feature is seen on the dorsum of the hands as flat-topped violaceous papules overlying the metacarpal and interphalangeal joints. These are known as *Gottron's papules* and should be differentiated from the more macular erythema seen in some patients with systemic lupus erythematosus *between* the interphalangeal joints.<sup>4</sup> The hands can also manifest what has been termed "*mechanics' hands*," which are scaly, fissured, and cracked hands suggestive of manual labor.<sup>5</sup> The fingertips can even become ulcerated. In addition to the above hand changes, the fingernail folds can exhibit telangiectasias as well as thickened cuticles.<sup>6</sup>

Other skin manifestations include red-to-violaceous scaly patches and slightly raised plaques overlying joints such as the elbows, knees, and medial malleoli. These lesions are often mistaken for psoriasis and are known as *Gottron's sign*, not to be mistaken for the *Gottron's papules* mentioned previously.<sup>4</sup>

Another classic skin finding is the heliotrope rash, a pinkish-violet discoloration of the eyelids that may be accompanied by edema and tenderness of the underlying orbicularis oculi muscle. On the scalp, patients can

exhibit alopecia or erythematous scaly patches and plaques that can be pruritic.<sup>6,7</sup>

Poikiloderma, defined as skin exhibiting atrophy, hyperpigmentation / hypopigmentation and telangiectasias, can be seen on the face, V-neck area, or in a shawl-like distribution. With time, these findings can progress from the sun-exposed areas to more widespread skin involvement.<sup>4,7</sup> Calcinosis cutis, evidenced by tumorous soft-tissue calcium deposits, can also develop and is much more common in the juvenile form than in adults with the disease. Some studies have indicated that two-thirds of juveniles with dermatomyositis will eventually develop calcinosis. Although calcinosis can be limited and of cosmetic importance only, it often develops around joints and can severely limit mobility or lead to fixed joint contractures. Calcification of the muscles and soft tissue can lead to difficulty eating or breathing.<sup>8</sup>

The muscle disease often presents as proximal muscle weakness affecting the limb girdles and trunk. Patients can also have difficulty with dysphonia and/or dysphagia. Respiratory muscle weakness can develop, with aspiration pneumonia sometimes complicating the disease. Other potential pulmonary findings include interstitial fibrosis or interstitial pneumonitis. Cardiovascular complications may also develop and include cardiomyopathy or cardiac conduction defects. Polyneuropathy has been reported as a rare complication.<sup>9</sup> Of particular importance in juvenile patients with DM is the development of vasculopathy in the muscles and gastrointestinal tract, and very rarely in the brain. Life-threatening bowel necrosis or infarction can ensue. The rationale for why some of these systemic complications develop will be discussed later.

## DIAGNOSIS AND CLASSIFICATION

The classification of dermatomyositis was initially developed in the mid-1970s and was later revised to include amyopathic dermatomyositis, a subtype that represents less than 10% of patients with dermatomyositis. In order to have a *definitive* diagnosis of dermatomyositis, a patient must have a cutaneous eruption typical of dermatomyositis plus three of the four following findings: 1) proximal, symmetric muscle weakness progressing over weeks to months, 2) muscle biopsy evidence of an inflammatory myopathy, 3) elevation of serum muscle enzymes, and 4) electromyographic features of a myopathy.<sup>10,11</sup> Having cutaneous changes plus two of the four findings is referred to as *probable* dermatomyositis.

The distinction of JDM from the other juvenile idiopathic inflammatory myopathies is based in part upon the autoantibody profile exhibited by the patient. ANA positivity, primarily in the speckled pattern, is seen in more than half of JDM patients. The myositis-specific autoantibodies (MSAs), long described in adult patients with idiopathic inflammatory myopathies and present in over a fourth of these patients, are now recognized in

the various forms of juvenile idiopathic inflammatory myopathies, although they are not used in practice in following juvenile patients with this disease. The MSAs can be divided into three groups with different clinical features and responses to treatment: 1) anti-signal recognition particle (SRP) antibodies, 2) anti-synthetase antibodies (Jo-1, PL-7, PL-12, EJ and OJ), and 3) anti-Mi2 antibodies. Those with anti-SRP have the poorest response to treatment. Patients typically have an acute onset of weakness with severe polymyositis. Patients with anti-synthetase antibodies are generally thought of as having a moderate response to therapy with disease persistence. They have commonly been found to have interstitial lung disease, fever, and arthritis. Those patients with the best response to treatment are patients with anti-Mi2 antibodies. They more commonly have many skin manifestations of the disease and usually fall into the classification of dermatomyositis.<sup>12,13</sup>

Approximately one-third of patients with JDM have an acute course with complete resolution in less than 2 years. The other two-thirds have a chronic course, which can consist of persistently active disease or can be marked by episodes of exacerbations and remissions.<sup>14</sup>

## ETIOLOGY AND PATHOGENESIS

The etiology of dermatomyositis remains uncertain, but the development of autoimmune complexes and complement deposition by the membrane attack complex (MAC) within the capillaries of involved tissues appears to play a pivotal role.<sup>15</sup> The tissue edema and problems with tissue perfusion to vital muscles and nerves that develops after deposition of the MAC in vessel walls can explain many of the clinical manifestations of this disease.<sup>9,16</sup>

One particularly intriguing theory of the pathogenesis of JDM is related to the concept of chimeric cells, or non-self cells. It has previously been shown that fetal cells can persist in the circulation of many healthy women and those with autoimmune disease for years after pregnancy.<sup>17</sup> This has been used to explain the higher incidence of some autoimmune diseases in women than men and the fact that the peak onset of autoimmune disease in women is during and after their childbearing years. The reverse may also be true. Researchers have shown that the passage of cells from the mother to the fetus can persist in the child's circulation.<sup>18</sup> These chimeric cells induce immunologic activity. A study of 72 JDM patients revealed that children with JDM are more likely to exhibit chimerism than their siblings or healthy controls.<sup>19</sup> In addition, the mother's HLA genotype may play a role in the transfer and/or persistence of these cells in the child's circulation.<sup>19</sup>

Epidemiologic studies show that certain infectious illnesses have been seen with increased rates in the three months prior to the onset of juvenile dermatomyositis. Antigens produced by an infectious agent that share homology with self antigens could be responsible for

driving this disease. Viruses,<sup>6</sup> such as coxsackie B, influenza, parainfluenza, and hepatitis B, have been most strongly implicated; however, bacterial (*Streptococcus pyogenes*)<sup>20</sup> and parasitic (*Toxoplasma gondii*)<sup>21</sup> infections have also been associated with disease onset.

## TREATMENT

In general, children with JDM fare better than adults with this disease. Prior to the use of systemic corticosteroids, almost half of children with this disease died, most notably from cardiopulmonary events, gastrointestinal hemorrhage, or sepsis.<sup>22</sup> With modern medical therapy and early diagnosis, this number has been reduced to less than 10%.<sup>4</sup>

The mainstay of initial medical treatment is high-dose corticosteroid therapy. In comparison to adults who are typically given a dose of 1mg/kg/day of Prednisone, children may need 1.5 to 2.0 mg/kg/day. Although daily corticosteroid therapy has certainly decreased the mortality associated with JDM, it is unclear whether the morbidities of long-standing disease or of side effects and complications from therapy have been reduced. It does appear that early diagnosis and initiation of treatment is associated with a decreased likelihood of developing calcinosis, a major cause of morbidity in these patients.<sup>23</sup> The use of pulse-dosed methylprednisolone in patients with rapidly deteriorating muscle function may help to prevent irreversible muscle damage.<sup>24</sup>

Another cornerstone of therapy is rehabilitation. Physical and occupational therapy are utilized in order to preserve muscle function and prevent contractures. In times of active myositis, passive range of motion exercises are implemented. Once senescence of the disease occurs, resistive exercises are suggested. Speech therapy can be utilized for dysphonia and dysphagia.<sup>13</sup>

Treatment of calcinosis can be difficult. Those with localized forms may wish to have the lesions surgically removed. The calcium channel blocker diltiazem has gradually decreased calcinosis in a small number of cases.<sup>25</sup> The use of the bisphosphonate alendronate has coincided with resolution of calcinosis and improvement in range of motion.<sup>8</sup>

Due to the rarity of JDM, randomized, prospective trials looking at therapeutic options are lacking. However, some other therapeutic options which have been utilized for the treatment of systemic disease include methotrexate,<sup>2,26</sup> intravenous immunoglobulin,<sup>27</sup> hydroxychloroquine,<sup>28</sup> cyclosporine,<sup>29</sup> and azathioprine.<sup>2,30</sup> These options are helpful when side effects from corticosteroids have become unacceptable, when patients have chronic disease, or when patients are refractory to treatment. Another potentially important treatment is anticytokine therapy,<sup>31,32</sup> especially with the recent introduction of new biologics to treat rheumatoid arthritis and juvenile rheumatoid arthritis. Current research in this area may uncover useful treatment options.

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