A 5-Year-Old Girl with Fatigue, Diffuse Edema, and Weakness

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A 5-year-old previously healthy girl presented to our hospital with 10 days of periorbital edema, abdominal pain, muscle weakness, and progressive fatigue. Four days prior to admission, her pediatrician prescribed diphenhydramine and fexofenadine for a possible allergic reaction, and polyethylene glycol 3,350 for constipation, but the patient showed no signs of improvement. She became progressively more fatigued, and 1 day prior to admission mild extremity edema was noted. The patient denied fever, vomiting, diarrhea, cough, joint pain or stiffness, recent rash, or trauma. She had visited Mexico 1 month prior. There was no significant family history. Outpatient testing revealed a negative urinalysis.

In the emergency department, the patient was noted to be tachycardic (heart rate of 132 beats per minute) but otherwise well-appearing. Physical examination was significant for mild hepatomegaly, mild non-pitting edema of the bilateral upper and lower extremities, mild periorbital edema, and bilateral erythematous patches (2 cm × 2 cm) on her knees (Figure 1). Initial emergency department testing was significant for hypoalbuminemia (2.9 g/dL), transaminitis (aspartate aminotransferase [AST] of 231 units/L, alanine aminotransferase [ALT] of 139 units/L), and a mildly elevated erythrocyte sedimentation rate (24 mm/h).

Initial differential diagnosis included autoimmune hepatitis, viral hepatitis, protein-losing enteropathy, and viral myocarditis. Coagulation studies and glucose challenge test were normal (suggesting normal synthetic liver function), hepatitis panel was negative, and the AST to ALT ratio of 231:139 made a primary hepatic etiology less likely. Sustained tachycardia prompted further cardiology testing; however, electrocardiogram and echocardiogram revealed normal cardiac function.

Generalized fatigue and subjective muscle weakness remained a prominent symptom, and on further questioning the family then disclosed a history of intermittent facial rash and erythema above her eyelids (Figure 2). Therefore, a systemic inflammatory etiology was explored.
Further testing revealed elevated creatinine kinase (4,142 units/L), lactate dehydrogenase (729 units/L), aldolase (24.7 units/L), and an antinuclear antibody titer of 1:160. Rheumatology evaluation noted positive nail-fold capillaryoscopy (suggesting peripheral microangiopathy), and suspected the knee lesions to be Gottron’s sign.

A magnetic resonance imaging (MRI) scan of the hips and pelvis revealed extensive inflammatory myositis.

Therapy was initiated with high-dose intravenous methylprednisolone and intravenous immunoglobulin. The patient improved and was discharged home with a long-term steroid therapy plan, physiotherapy, and rheumatology follow-up.

**DISCUSSION**

Juvenile dermatomyositis (JDM) is a rare, multisystemic autoimmune vasculopathy. It is the most common inflammatory myopathy of childhood, with an annual prevalence in the United States of 3.2 per 1 million children. It is characterized by pathognomonic cutaneous skin manifestations and proximal muscle weakness. The well-recognized skin findings of JDM include a heliotrope rash over the eyelids, periorbital edema, and Gottron’s papules (an erythematous papulosquamous eruption over the dorsal surface of the knuckles). Other common findings include myalgia, arthralgia, and nail-fold changes. JDM can also have gastrointestinal tract, pulmonary, and cardiac involvement. The average age at onset is 7 years, and JDM has a female predominance of 2:1. There appears to be no ethnic or racial propensity. The literature suggests a multifactorial inheritance as there is both a genetic predisposition and likely an environmental trigger.

The widely accepted Bohan and Peter diagnostic criteria for JDM include typical skin rash and at least three of the following: (1) muscle weakness, (2) elevation of muscle enzymes, (3) abnormal electromyography suggestive of inflammatory myopathy, (4) abnormal muscle biopsy sample suggestive of inflammatory myopathy, and (5) MRI evidence of myositis. In our patient, Gottron’s papules, periorbital edema, proximal muscle weakness, elevated muscle enzymes, and MRI evidence of myositis met the criteria for JDM. MRI is the most common diagnostic modality used in the pediatric population, as it is more likely to show abnormalities consistent with JDM compared to electromyography or muscle biopsy.

Our patient exhibited a rare presentation of JDM, as the predominant clinical feature prompting her to seek medical evaluation was diffuse subcutaneous edema. Although localized edema is common in JDM, generalized edema has been reported rarely in the literature. The generalized edema of JDM can be initially mistaken to be nephrotic syndrome, but a lack of proteinuria, normal albumin levels, and other skin manifestations are usually present.

The pathogenesis of the subcutaneous edema remains unknown. It is thought that increased vascular permeability, immune complex deposition, and complement activation may all contribute to the generalized edema. This theory implies that generalized edema is a result of severe inflammation and may be an indicator of a more aggressive disease course. Another hypothesis suggests that microischemia-producing microinfarction may play a role in the pathophysiology of the generalized edema. Interestingly, in adults with dermatomyositis with generalized edema, symptoms evolve much quicker (2-8 weeks) than typical dermatomyositis cases. This is similar to our patient, as her symptoms evolved over a period of only 2 weeks.

The mainstay of treatment for JDM is a long and aggressive course of corticosteroids. The addition of an immunosuppressive agent, such as methotrexate, has been noted to improve muscle strength, decrease enzyme levels, and reduce the dosage of corticosteroids needed. Intravenous gamma globulin use ranges from 17% to 39% of cohorts and is typically used for more severe presentations of JDM or in symptomatic patients refractory to standard treatment. Once the myositis improves and enzyme levels normalize, corticosteroid treatment can be slowly tapered.

With early initiation and aggressive treatment plans, the prognosis for JDM has significantly improved; the lifetime mortality rate is less than 2% today, as compared to 30% approximately 40 years ago. Nevertheless, mortality still exists, and JDM patients can have significant disability from complications such as calcinosis, lipodystrophy, and severe muscle atrophy. Even with an aggressive treatment plan, more than half of JDM patients have continuous...
disease activity and/or continued need for medications 3 years after initiation of therapy. JDM has a largely unpredictable course, as one-third of patients recover spontaneously, one-third develop moderate to severe disability, and the remaining one-third die from the illness.

This case highlights a unique presentation of JDM with fatigue and diffuse edema as the prominent features rather than the classic skin manifestations. It should be noted that generalized subcutaneous edema might be the first presenting feature of JDM and may indicate a more rapid onset and more aggressive disease course. It is essential to get a full dermatologic history from parents and appreciate that the characteristic rash of JDM may be faint or difficult to recognize.

REFERENCES