

Juvenile Dermatomyositis–Associated Panniculitis

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PRACTICE POINTS

- Juvenile dermatomyositis is an autoimmune disorder with childhood onset that predominantly affects the muscles and skin.
- Juvenile dermatomyositis has a higher incidence of calcinosis cutis and is not associated with an increased risk for malignancy in contrast to the adult-onset variant, dermatomyositis (DM).
- Panniculitis is a rare but severe complication of DM, and this subset of DM may be challenging to treat, requiring aggressive therapy.

To the Editor:

Juvenile dermatomyositis (JDM) is an autoimmune disorder with childhood onset that predominantly affects the muscles and skin, among other organs. Since the recognition of dermatomyositis (DM) more than 100 years ago, a variety of clinical diagnostic criteria have been utilized. Classically, DM presents with muscle weakness and a pathognomonic cutaneous macular, violaceous, erythematous eruption. The juvenile variant is defined by onset prior to 16 years of age. Histologically, these entities are indistinguishable and demonstrate an interface dermatitis with epidermal atrophy. Clinically, JDM has a higher incidence of calcinosis cutis and is not associated with an increased risk for malignancy in

contrast to the adult-onset variant.¹ Panniculitis is a rare but serious complication in a subset of patients with DM and may represent a precursor to calcinosis cutis.² We describe a case of JDM-associated panniculitis that was difficult to control with prednisone and rituximab.

A 21-year-old woman with fever, fatigue, muscle pain, and new-onset swelling of 2 weeks' duration was admitted to the hospital. She had a 5-year history of intermittent muscle weakness and concomitant rash. Prior to presentation, she had been hospitalized twice for fever of unknown origin, and the source remained undetermined. Physical examination revealed prominent facial and periorbital edema. There was tender nonpitting edema present on all 4 extremities and hyperpigmented indurated nodules on the shins (Figure 1). A full laboratory and imaging workup was performed for autoantibodies and infectious etiologies. The complete blood cell count was notable for pancytopenia, and a thorough infectious workup was negative. Creatine kinase level was within reference range. A biopsy of the right shin was performed, and histopathology revealed a lobular panniculitis with fat necrosis and mixed inflammation with neutrophils with perieccrine involvement as well as an interface dermatitis (Figure 2). Periodic acid–Schiff, Grocott methenamine–silver, and Gram stains were negative. Myositis-specific antibody testing revealed anti-p155/140 autoantibodies, and magnetic resonance imaging did not reveal active myositis within the visualized muscles, consistent with stable nonprogressing DM. A diagnosis of JDM with

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FIGURE 1. A, Edema of the periorbital skin and cheeks, as well as pink scaly plaques on the cheeks and chin. B, Scattered hyperpigmented scaly plaques with indurated nodules on the legs.

panniculitis was made. The patient was started on oral prednisone. Subsequently, a trial of rituximab was initiated. Although the patient's symptoms initially improved, the response was not sustained on rituximab, and the patient was continued on systemic steroids with initiation of cyclosporine.

Juvenile dermatomyositis is an autoimmune disorder with childhood onset that involves systemic inflammation of the muscles, skin, and internal organs. It often can present diagnostic and therapeutic challenges.^{2,3} Bohan and Peter^{4,5} clinical criteria may help identify potential patients with JDM, but magnetic resonance imaging, electromyography, and muscle biopsy often are required to confirm the diagnosis.⁶ Skin manifestations include heliotrope rash; V sign; shawl sign; Gottron papules;

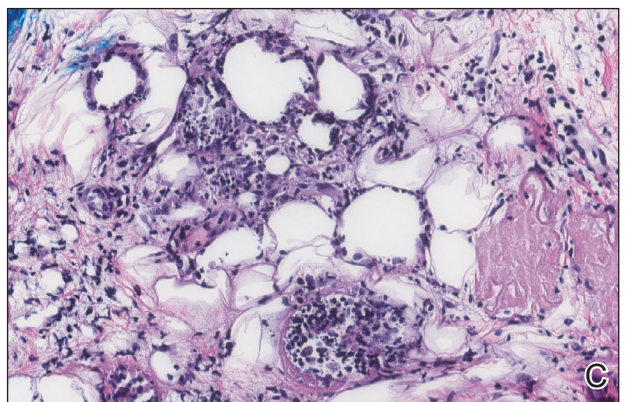
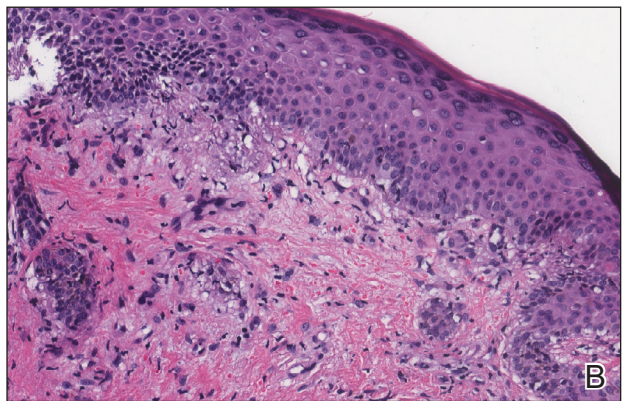
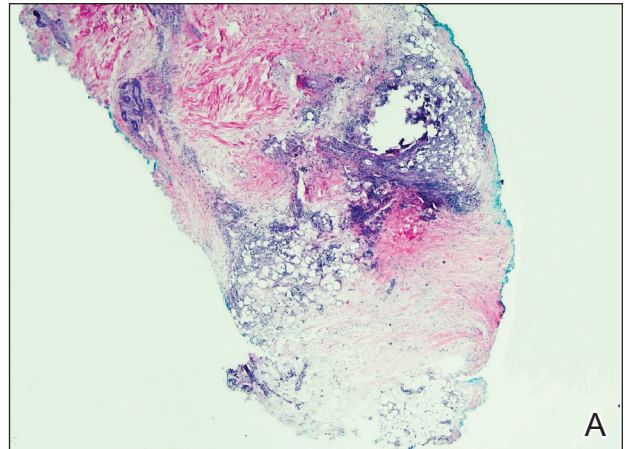


FIGURE 2. A, Histopathology showed superficial and deep lobular panniculitis with perieccrine inflammation (H&E, original magnification $\times 40$). B, Interface dermatitis with mixed infiltrate, including neutrophils, lymphocytes, and giant cells, was present (H&E, original magnification $\times 200$). C, Panniculitis with fat necrosis was shown (H&E, original magnification $\times 200$).

periorbital edema; and infrequently panniculitis, the subcutaneous inflammation of adipose tissue.^{3,7}

Although panniculitis is found in approximately 10% of skin biopsies in patients with DM, our patient presented with anti-p155/140 antibodies.⁸⁻¹⁰ Fat involvement in these patients traditionally manifests as lipodystrophy. Panniculitis also may precede calcinosis

cutis, a debilitating skin change that may occur in approximately 46% of patients with JDM and can cause severe morbidity.^{2,6,9}

Subcutaneous edema rarely is described in DM-panniculitis, present in only 6% of 86 DM patients in one study.⁷ The pathophysiology of DM may be due to antibodies that target endothelial cells and activate complement, resulting in the membranolytic attack complex. This leads to microischemia, and microinfarction of the muscle fibers has been suggested to result in edema of the subcutaneous tissue in severe cases.^{7,11} Microinfarction has been found to be present 2.3 times more often in edematous DM compared with nonedematous DM.⁷ Subcutaneous edema may be an isolated presentation of DM that arises more quickly with severe disease activity. As such, recommendations have been made to consider edema in future classification schemes.⁷

Because of the severity of edematous and/or subcutaneous DM, aggressive therapy may be required. First-line therapy consists of corticosteroids with additional immunosuppressants and immunomodulatory agents if adequate response is not achieved.^{3,12} The effectiveness of rituximab in DM has been suggested.^{2,12,13} The Rituximab in Myositis (RIM) trial (N=200) was the first double-blind, placebo-controlled, phase 3 clinical trial to assess rituximab's efficacy in refractory compared with early-onset inflammatory myopathies. Although outcomes were similar in both groups, 83% of patients overall, including the JDM subset, met the definition of improvement.¹² In re-examining the RIM trial data and other cases using rituximab to treat inflammatory myopathies, an overall response rate of 78.3% was observed, with 52.1% of patients with DM reporting improvement in skin lesions (N=458, pooled from 48 studies).¹³ Further analysis of the RIM data revealed that panniculitis affected 10.4% of patients with JDM at baseline, which decreased to 6.8% at 36 weeks of rituximab therapy (N=48).¹²

As exhibited in our patient, subcutaneous tissue involvement, including calcinosis cutis and panniculitis,

is seen more often in JDM than adult DM.^{2,6} However, panniculitis in anti-p155/140 patients is rare. Our patient also had antibody positivity, which likely predisposed her to a more severe course. Despite not having sustained improvement on rituximab, initiating aggressive therapy earlier in the disease course may be beneficial, and our patient continues with alternative therapies.

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