Chapter 10
A 33-Year-Old Woman with Pain and Swelling in the Right Calf and Persistent Fever

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History

A 33-year-old woman presented with 3 weeks of pain and swelling in the right calf and persistent fever despite completing 10 days of oral antibiotics cephalexin for possible cellulitis. Lower extremity Doppler was negative for deep vein thrombosis. The patient was started on empiric broad-spectrum antibiotics with intravenous (IV) vancomycin and zosyn for presumed cellulitis. With ongoing fevers 1 week after the presentation, the antibiotics coverage was broadened and changed to Imipenem. The patient continued to have high-grade fevers, right calf pain and swelling despite being treated with broad spectrum IV antibiotics. She did not have cough or urinary pain. She had a past medical history of lupus on Prednisone 10 mg once daily and Plaquenil 200 mg once daily.

Physical Examination

The patient appeared ill with body temperature 100.8 °C. Heart rate, blood pressure, and breathing were normal. There was remarkable edema, skin red discoloration, and tenderness in the right calf. Mental status and cranial nerves were intact. There was no weakness or numbness, although the movement of the right distal leg and foot was limited due to the pain.

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Investigations

Computer tomography (CT) scan of the right lower extremity demonstrated focal skin thickening along the posterior-lateral aspect of the mid-distal right calf, subcutaneous fat stranding, and inflammatory changes suggestive of cellulitis. Gallium scan was also suggestive of cellulitis localized to the medial proximal tibia below the knee. Right distal leg magnetic resonance imaging (MRI) demonstrated extensive signal abnormalities of the medial gastrocenemius and soleus muscles, and small crecentric fluid collections along these muscles. Due to the concern of a focal myositis, two weeks after the presentation, the patient underwent a right gastrocnemius biopsy and washout.

Muscle Biopsy Findings

The right gastrocnemius muscle biopsy revealed necrotizing granulomatous fasciitis and myositis with the presence of many acid-fast bacilli (AFB) positive micro-organisms (Fig. 10.1). Gram stain and Grocott's methenamine silver (GMS) stain showed no Gram positive or negative bacterial or fungal organisms (data not shown). The findings are consistent with mycobacterial infection.

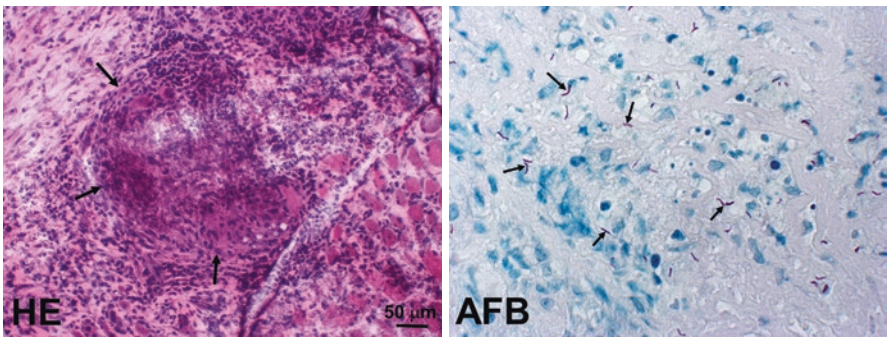

Fig. 10.1 Necrotizing granulomatous fasciitis and myositis with the presence of AFB positive micro-organisms. Muscle cross sections with hematoxylin and eosin (HE) and acid fact bacilli (AFB) stains show necrotizing granulomatous inflammation involving fascia and adjacent muscle tissue (HE, arrows) with the presence of many AFB positive bacteria in the necrotic tissue (AFB, arrows)

Final Diagnosis

Mycobacterial fasciitis and myositis

Patient Follow-up

The patient was isolated and started on rifampin, isoniazid, pyrazinamide, and ethambutol to cover mycobacterium tuberculosis (TB) infection. Approximately 1 week after the muscle biopsy, the patient developed right ankle and hip pain as well as cervical lymphadenopathy. CT scan of the neck showed necrotic internal jugular lymphadenopathy consistent with scrofula. CT of the chest, abdomen, and pelvis demonstrated multiple bibasilar pulmonary nodules, necrotic mesenteric lymph nodes, and fluid collections of the right iliacus and psoas muscles. The patient was subsequently found to have positive TB cultures in sputum, bone lesions, and cervical lymph nodes. She underwent drainage of multiple fluid collections. The patient's 6-month hospital course was complicated by drug rash, immune reconstitution syndrome, failure to thrive, worsening renal function and isoniazid-induced hepatotoxicity. Throughout the prolonged hospital course, she never demonstrated respiratory symptoms. She eventually showed significant improvement with the TB therapy and was discharged home with a plan to complete eleven total months of TB therapy.

Discussion

It is well known that patients with systemic lupus erythematosus are at increased risk for TB and other opportunistic infections because of the immunosuppression these patients require. Multiple studies have demonstrated that serious infections and extra-pulmonary manifestations are more common in this patient population [1, 2]. While approximately 3% of patients with TB have musculoskeletal involvement, the incidence of the even more uncommon manifestation of myositis is unknown [3]. It has been speculated that skeletal muscle is highly resistant to tuberculosis infection, based on its low oxygen and high lactate levels, as well as the lack of reticulo-endothelial tissue [4, 5].

Of the rare cases of TB myositis in the literature, it has been most commonly described in immunosuppressed patients, including those with systemic lupus erythematosus, rheumatoid arthritis, and HIV infection [3–5]. In each of the described cases of TB myositis, the diagnosis was made with fluid culture, and patients presented similarly with ongoing fever, pain, and swelling. To our best knowledge,

this is the first reported case of TB fasciitis and myositis with the initially diagnosis suspected by muscle biopsy findings.

Granulomatous myositis is a rare muscle pathology diagnosis. It can be seen in association with sarcoidosis, infections, Churg-Strauss Syndrome, Crohn disease, and anti-PD1 therapy, among others [6–11]. Granuloma consists of epithelioid cells, multinucleated giant cells, lymphocytes and other inflammatory cells. Necrotizing granulomatous inflammation shows necrotic tissue with granular and cheese-like cellular debris in the areas with granulomas. It is mostly seen in mycobacterial and fungal infections. The necrotizing granulomatous fasciitis and myositis seen in our case is caused by TB infection.

Our case illustrates that febrile focal myositis should raise a strong clinical suspicion for infectious myositis. Infection work up should be done on muscle biopsy specimens. TB can infect muscle, and should be considered especially in immunocompromised patients even without pulmonary symptoms.

Pearls

Clinical Pearls

1. Although uncommon, TB can infect muscle in immunocompromised hosts. Disseminated mycobacterium tuberculosis infection may initially present with febrile focal myositis.
2. One should consider the possibility of TB as the etiologic infectious agent in an immunocompromised patient with febrile focal myositis even without pulmonary symptoms.

Pathology Pearls

1. Febrile focal myositis should raise a suspicion for infectious etiologies, and infection work up should be done on muscle biopsy specimens by special stains, including Gram, GMS, and AFB stains.
2. Necrotizing granulomatous myositis is mostly seen in mycobacterial and fungal infections, and AFB and GMS stains can help differentiate.

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