Disseminated Mycobacterium Tuberculosis with Ulceronecrotic Cutaneous Disease Presenting as Cellulitis

Kelly L. Reed, DO,* Rachel M. White, DO,** Nektarios Lountzis, MD***

*Dermatology Resident, Lehigh Valley Health Network, Allentown, PA
**Traditional Rotating Intern, Largo Medical Center, Largo, FL
***Attending Physician, Dermatology Residency, Lehigh Valley Health Network, Allentown, PA

Disclosures: None
Correspondence: Rachel M. White, DO; rachelwh@pcom.edu

Abstract

Cutaneous tuberculosis is a rare manifestation of infectious tuberculosis caused by invasion of the skin by Mycobacterium tuberculosis. Tuberculous cellulitis is a rare type of cutaneous tuberculosis with cellulitis-like symptoms. Only eight cases of tuberculous cellulitis have been reported in the literature. We report a case of tuberculous cellulitis in a patient taking chronic systemic steroids for polymyalgia rheumatica. Findings on all of the reported cases of tuberculous cellulitis are summarized.

Introduction

Tuberculosis (TB) is an infectious disease most commonly caused by *Mycobacterium tuberculosis* and primarily affecting the lungs. TB can affect organs in the central nervous system, lymphatic system and circulatory system, as well as the skin.[1] According to the World Health Organization (WHO), in 2013 there were 9.0 million cases of tuberculosis, and 0.8 million of the new cases were extrapulmonary.[2] Cutaneous TB is a rare manifestation of TB caused by invasion of the skin by *M. tuberculosis*.[3] Cutaneous TB occurs through direct infection of skin from an exogenous or endogenous source. It can also occur from an allergic response to tubercle bacilli or their metabolites, called tuberculid.[4] Only eight cases of TB cellulitis, a rare type of cutaneous TB with cellulitis-like symptoms, have been reported.[1] We present a case of tuberculous cellulitis in a patient with polymyalgia rheumatica (PMR) who was taking chronic systemic steroids.

Case Report

An 83-year-old Hispanic female with a past medical history of polymyalgia rheumatica (PMR) was treated at the hospital for a non-ST-segment elevation myocardial infarction and was noted to have redness and swelling of the right lower extremity, which the patient reported had been present for five months. She had been treated with multiple courses of antibiotics with no response. She denied fever, cough, night sweats, fatigue or other systemic symptoms. Additional past medical history included coronary artery disease, diabetes mellitus type 2, hypertension, atrial fibrillation, asthma, and hyperlipidemia. She had resided in Puerto Rico but recently moved to the United States. Her social history included > 100 pack years of smoking tobacco. The patient's pertinent medications included chronic low dose prednisone at 5 mg daily for many years to treat her PMR.

Physical exam revealed multiple red to purple, painful, indurated plaques associated with pitting edema extending along the right lower extremity and foot in a geographic distribution (**Figure 1**). Over the course of two weeks, the lesions became progressively necrotic and ulcerated (**Figure 2**). The left leg and remainder of her skin exam was unremarkable.

A chest X-ray showed well-circumscribed, opaque nodules in the left upper lobe. A biopsy of the right lateral upper leg revealed a neutrophilic and focally granulomatous dermatitis without acid-fast bacteria (**Figures 3, 4**). Tissue culture of the upper left lateral lower extremity and culture of bronchial lavage revealed *Mycobacterium tuberculosis* complex. The patient tested positive on QuantiFERON®-TB Gold and was diagnosed with disseminated *Mycobacterium tuberculosis* resulting in tuberculous cellulitis. Treatment included topical wound care and quadruple antibiotic therapy with rifampin, isoniazid, ethambutol, and pyrazinamide.

Discussion

Cutaneous tuberculosis manifests in a variety of clinical presentations and is caused by *Mycobacterium bovis*, bacillus Calmette-Guérin (BCG), or most commonly the acid-fast bacillus (AFB) *M. tuberculosis*.[3] Cutaneous tuberculosis accounts for less than 1% to 2% of all cases of TB.[6] Infection can occur through primary exogenous inoculation via direct implantation of mycobacterium into the skin.[3] Secondary spread occurs endogenously through hematogenous dissemination, proliferation via contiguous lymph nodes or direct extension to the skin from an internal source, most commonly lung infection.[3,4] Another manifestation of cutaneous TB, known as a tuberculid, occurs due to an allergic reaction to the bacteria or one of its metabolites.[3] Tuberculids are characterized by the absence of mycobacterium in the skin. Cutaneous tuberculosis is also classified depending on the quantity of acid-fast bacilli

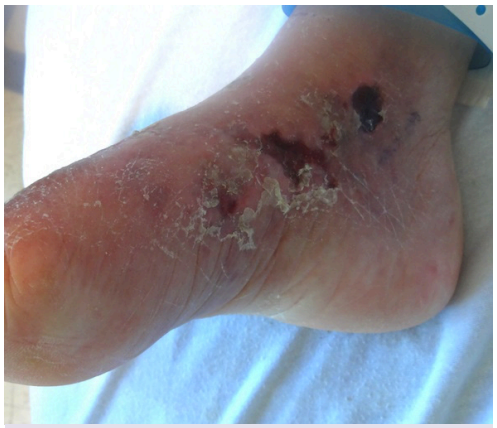

Figure 1. Right medial foot with erythematous plaque and central stellate purpura and necrosis.

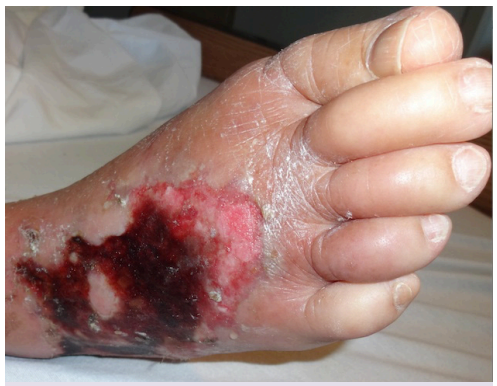

Figure 2. Right dorsal foot with necrotic ulcerated plaque.

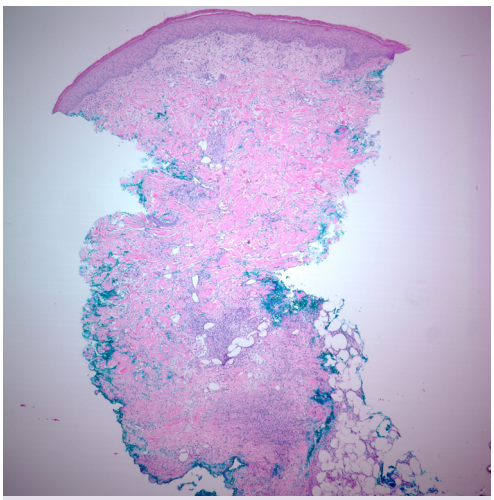

Figure 3. Punch biopsy (4x) of right lateral thigh showing neutrophilic and granulomatous dermatitis.

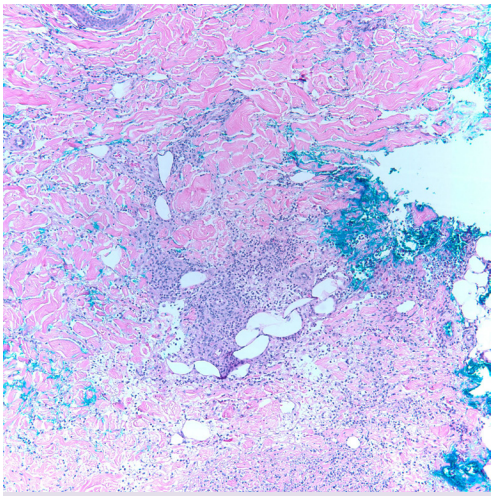

Figure 4. H&E (10x): Clear view of histiocytic epithelioid granuloma.

present in skin lesions. Lesions with many AFB are classified as multibacillary, and infections with few AFB are termed paucibacillary.

Clinical presentation of cutaneous tuberculosis is extremely variable and dependent upon both the route of infection and the bacterial load present in lesions.[3] It most often affects elderly, immunocompromised hosts, such as those with HIV or taking immunosuppressive medications like corticosteroids.[4] Clinically, exogenous inoculation causes tuberculous chancre, TB verrucosa cutis, and some cases of lupus vulgaris.[3] Endogenous spread results in scrofuloderma, miliary TB, orificial tuberculosis, and most cases of lupus vulgaris. Tuberculids are reactive conditions that include papulonecrotic lesions, lichen scrofulosorum and erythema induratum. Tuberculous cellulitis, as our patient developed, is an uncommon presentation and does not fit neatly into the aforementioned categories.

Histopathological findings vary depending on the type of infection; however, cutaneous TB characteristically manifests as a mixed inflammatory reaction of the dermis and subcutis comprised of neutrophils, multinucleate giant cells and epithelioid histiocytic granulomas that may display caseation necrosis.[3] The biopsy of our patient's cellulitis was congruent with these findings, revealing mixed inflammatory infiltrate with granulomatous changes. Diagnosis of cutaneous TB is multifaceted and often includes a combination of purified protein derivative (PPD), interferon-γ release assay, tissue culture, polymerase chain reaction (PCR) for mycobacterial DNA, and tissue culture and/or biopsy with special staining techniques, such as Auramine-Rhodamine, Ziehl-Neelsen or Wade-Fite stain.[3] Our patient's lesions were positive in tissue culture, Ziehl-Neelsen stain, PCR and interferon-γ release assay.

Our patient's cutaneous tuberculosis resulted from endogenous spread and presented as a recalcitrant "cellulitis" that deteriorated to an uncommon ulceronecrotic form of the disease. Typically, ulceronecrotic cases are due to tuberculid reactions; however, in this case, the isolation of bacilli on tissue culture favors an active cutaneous infection from hematogenous spread.

With the addition of this report, there are only nine cases of tuberculous cellulitis in the literature.[1] In eight of those cases, the patients were on corticosteroid therapy when they developed tuberculous cellulitis.[1,4,6-10] In one case, the patient was an adolescent recently treated for lymphadenitis TB using triple antibiotic therapy.[5] Therefore, immunosuppression most likely plays an important role in the etiology of the disease.[1] Three out of nine cases had prior infection with different forms of TB. Additionally, one third of tuberculous cellulitis cases have been identified as skin manifestations of miliary tuberculosis.[4] Miliary tuberculosis usually involves diffuse, minute nodules in the bilateral lungs, which our patient did not exhibit.[6,8,10] In two reported cases, including this one, chest X-rays showed signs of pulmonary TB.[4] The likelihood of detecting tubercle bacilli in tuberculous cellulitis is high, as demonstrated by 88% of cases being PCR positive, 88% culture positive, and 89% Ziehl-Neelsen stain positive.

Treatment of cutaneous TB is primarily antibiotic therapy with triple or quadruple coverage, based on the culture and sensitivities of the isolated strain of *M. tuberculosis*.[3] All nine reported cases of tuberculous cellulitis were treated with triple or quadruple therapy including rifampin, isoniazid, pyrazinamide, and ethambutol. All prior reported cases of tuberculous cellulitis drastically improved and eventually resolved with antibiotics.

Conclusion

This case is relevant to clinicians because it increases awareness of cutaneous TB as the presenting symptom of disseminated tuberculosis infections in immunocompromised patients. It also serves as a reminder to maintain a high index of suspicion for such opportunistic infections, specifically in cases of resistant cellulitides, and to complete a thorough patient work-up.

References

1. Taguchi R, Nakanishi T, Imanishi H, Ozawa T, Tsuruta D. A case of tuberculous cellulitis. Clin Med Insights Case Rep. 2015;8:11-2.

2. WHO: Global tuberculosis report 2014 [Internet]. Switzerland: World Health Organization; 2014 [cited 2015 Sep 28]. Available from: http://www.who.int/tb/publications/global_report/gtbr14_main_text.pdf?ua=1.

3. Dias M, Bernardes FF, Quaresma M, Nascimento LV, Nery JA, Azulay DR. Update on cutaneous tuberculosis. An Bras Dermatol. 2014;89:925-38.

4. Daido-Horiuchi Y, Kikuchi Y, Kobayashi S, Fujii T, Oshima S, Kondo T. Tuberculous cellulitis in a patient with chronic kidney disease and polymyalgia rheumatica. Intern Med. 2012;51:3203-6.

5. Rosenfeldt V, Jensen KE, Valerius NH. Tuberculous cellulitis in a child demonstrated by magnetic resonance imaging. Scand J Infect Dis. 1999;31:417-9.

6. Koba S, Okawa T, Misago N, et al. A case of tuberculous cellulitis lacking epithelioid granuloma. Acta Derm Venereol. 2013;93:596-7.

7. Lee NH, Choi EH, Lee WS, Ahn SK. Tuberculous cellulitis. Clin Exp Dermatol. 2000; 25:222-3.

8. Seyahi N, Apaydin S, Kahveci A, Mert A, Sariyar M, Erek E. Cellulitis as a manifestation of miliary tuberculosis in a renal transplant recipient. Transpl Infect Dis. 2005;7:80-5.

9. Chin PW, Koh CK, Wong KT. Cutaneous tuberculosis mimicking cellulitis in an immunosuppressed patient. Singapore Med J. 1999;40:44-5.

10. Kim JE, Ko JY, Bae SC, Ro YS. Tuberculous cellulitis as a manifestation of miliary tuberculosis in a patient with dermatomyositis. J Am Acad Dermatol. 2011;65:450-2.