Erythematous Plaque to Lower Leg After Tropical Injury

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Keywords. mycobacteria; tuberculosis.

A 70-year-old retired nurse presented with a 3-month history of an asymptomatic, nonhealing lesion of her left leg. It developed after she fell and scraped this specific location on her leg on a creek rock while hiking in the jungle during a vacation in Ecuador. She denies any other trauma at any time between the scraping and presentation. After the fall, she subsequently developed an enlarging erythematous plaque with an overlying hemorrhagic crust without drainage. This crust sloughed but soon thereafter reformed. She was treated with triple antibiotic ointment, an antifungal cream, and one week of trimethoprim-sulfamethoxazole prior to presenting to her dermatologist. She was otherwise asymptomatic with a negative review of systems. Past medical history included hypertension, hypercholesterolemia, and hypothyroidism, and her medications were levothyroxine, lovastatin, atenolol, and sodium bicarbonate. She was born in the United States and had not spent any significant time outside the country before this episode. Examination revealed a 2 cm erythematous crusted plaque with several smaller satellite papules on the left shin at the site of trauma (Figure 1A). A punch biopsy (Figure 1B and C) and tissue culture were performed. What is the diagnosis?

DIAGNOSIS

Cutaneous Tuberculosis

Biopsy revealed epidermal erosion with surrounding spongiosis. The dermis contained a granulomatous infiltrate with necrosis. Periodic acid-Schiff, Gomori methenamine silver, and Fite stains revealed no fungal or mycobacterial forms, and fungal culture was negative. After 4 weeks, acid-fast bacilli (AFB) culture was positive, and *Mycobacterium tuberculosis* (MTB) was identified by DNA probe using the Hologic AccuProbe system. The isolate was susceptible to streptomycin, isoniazid, rifampin, ethambutol, and pyrazinamide. The patient was referred to the local health department, where a full review of systems was also negative including tests for fevers, chills, night sweats, and shortness of breath. Sputum smears and chest x-ray were negative, as was the subsequent AFB culture. Human immunodeficiency virus (HIV) testing was negative. Of note, the patient later reported a history of a positive purified protein derivative (+PPD) test decades prior when working as a nurse; she was treated for latent tuberculosis (TB) with an unknown regimen for a short period of time secondary to pregnancy. Subsequent yearly chest x-rays were normal until she retired as a nurse in 1986. She has begun a 6-month course of isoniazid 300 mg, rifampin 600 mg, and pyrazinamide 1500 mg daily by mouth 5 days per week directly observed therapy with plans to change to rifampin and isoniazid only after 2 months. Her current chest x-rays have also remained normal.

Cutaneous TB is rare, occurring in only 1%–2% of cases of TB [1]. The classification system of cutaneous TB is organized by the mechanism of entry and the status of the host's immune system (Table 1). Although scrofuloderma and lupus vulgaris are the most common forms of cutaneous TB overall, TB chancre and TB verrucosa cutis (TVC) are the 2 most commonly encountered forms of cutaneous TB due to exogenous inoculation; the former is seen in those patients without previous TB exposure, the latter in nonnaive patients with an intact immune system [1, 2]. The other etiologies of cutaneous TB occur through direct extension from an underlying infection (eg, scrofuloderma), via hematogenous dissemination (eg, lupus vulgaris, acute miliary TB, tuberculous gumma) or through autoinoculation (orificial TB) [3].

Exogenous inoculation TB occurs after direct introduction of mycobacterium into the skin or mucosa via a penetrating injury or break through the skin [4]. It commonly presents in healthcare or laboratory workers that come into contact with diseased material [3] and individuals with exposure to a family member with TB [1]. Cases have been reported with surgical procedures, tattoos, circumcisions, and piercings [2, 3]. Two to four weeks after the exposure, a red-brown papule or nodule develops at the site of direct entry [3]. Tuberculosis chancre progresses to a firm asymptomatic ulcer with a granulomatous base usually <1 cm in diameter [2, 4, 5]. Tuberculosis verrucosa cutis

Received 16 December 2014; accepted 19 May 2015.

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DOI: 10.1093/ofid/ofv072

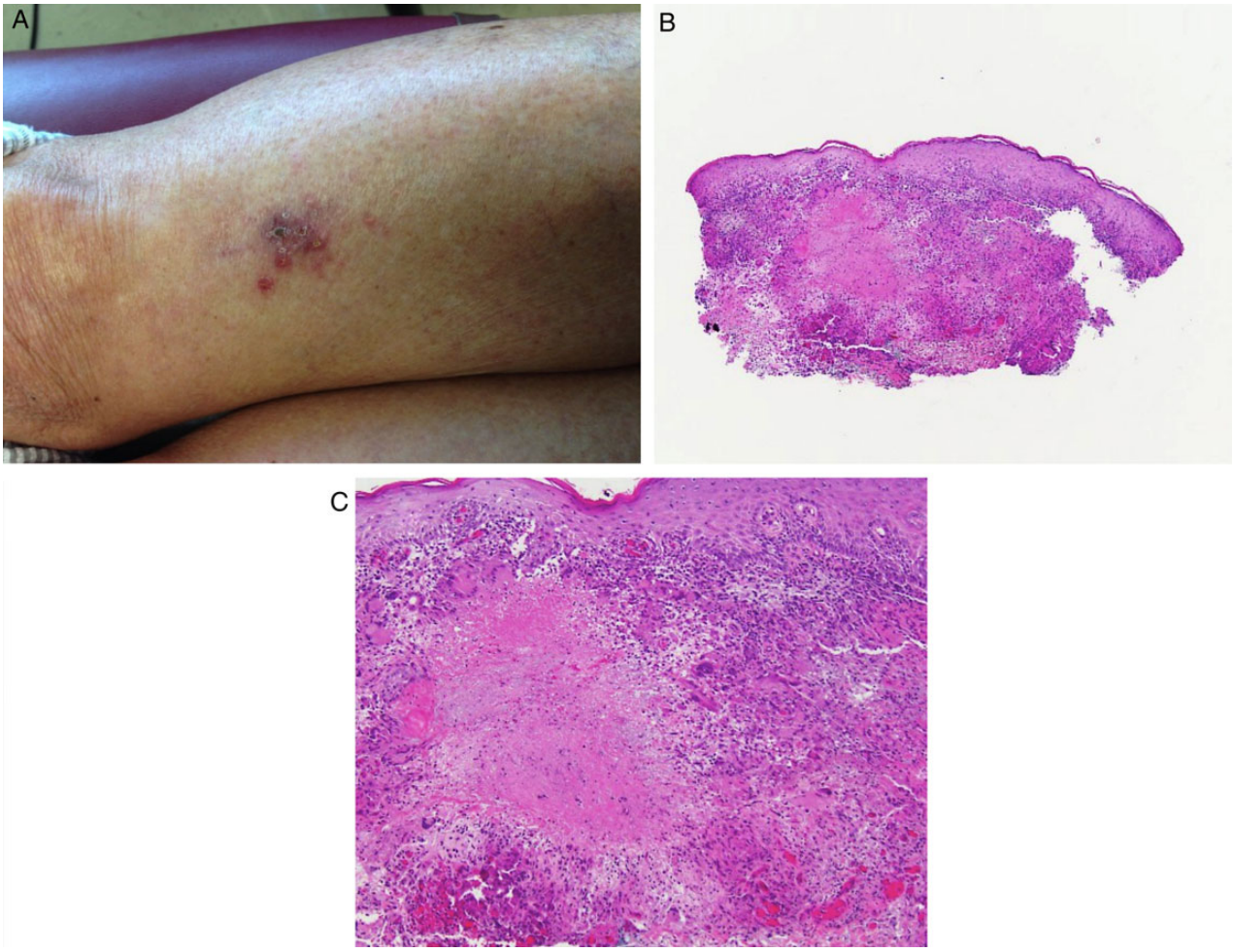

Figure 1. (A) Erythematous eroded plaque with satellite papules on left shin. (B) A 40× magnification demonstrating granulomatous infiltrate. (C) A 100× magnification demonstrating a dermal granuloma with caseous necrosis.

progresses to a 1–5 cm [2] single purple-brown [4] painless verrucous plaque that may express keratinous material from a nonulcerated atrophic center [3, 5]. The face and the extremities are the most common lesion sites [1]. Painless regional lymphadenopathy may be present [4].

Histological examination of TVC shows hyperkeratosis and pseudocarcinomatous hyperplasia with acute inflammation and dermal granulomas [1, 5]. Mycobacteria are rarely seen on microscopy [4]. Early histologic examination of TB chancre reveals acute inflammation and necrosis with multiple *Mycobacterium* bacilli and becomes more granulomatous with very few bacilli 3–6 weeks later [3, 5].

A complete history and physical examination are required for diagnosis. Early in disease presentation in those without previous exposure, tuberculin PPD tests are negative [3]. They become positive through the disease course and remain positive after resolution of the lesion [5]. In cases of TVC, PPD tests are markedly positive from the beginning. Skin biopsy with histological analysis and special staining for AFB should be done [4]. Early AFB smears of TB chancre are likely to be positive, but later in the disease, the number of MTB in the lesion decreases, corresponding to (+) PPD conversion [3]. This varies from diagnostic findings in TVC, which consistently has few or no bacilli on AFB smear [3]. A positive mycobacterial culture confirms the diagnosis and is the most reliable diagnostic method. Growth may take weeks and results are low yield, with a culture rarely becoming positive in TVC [4]. A newer method for diagnosis of cutaneous TB is polymerase chain reaction (PCR) for MTB, gaining popularity with its rapidity and increased sensitivity and specificity [6]. Company-provided information cite a sensitivity and specificity of >99%; however, other reports have shown a wide span of values in cutaneous or extrapulmonary TB, ranging from 25% to 88% for sensitivity and 74% to 100% for specificity [7–9]. These figures are likely affected by the scarcity of organisms seen in extrapulmonary sites and differences in PCR techniques. The most prudent evaluation still favors the use of PCR in conjunction with local tissue culture, which should be interpreted in light of clinical and histopathological

Table 1. Types of Cutaneous Tuberculosis

	Tuberculosis Chance	Tuberculosis Verruscosa Cutis	Scrofuloderma	Orificial Tuberculosis	Lupus Vulgaris	Acute Miliary Tuberculosis	Tuberculosis Gumma (Metastatic TB Abscesses)
Transmission	Exogenous	Exogenous	Endogenous, contiguous	Endogenous, contiguous; autoinoculation	Exogenous or endogenous, hematogenous or lymphatic	Endogenous, hematogenous	Endogenous, hematogenous
Presentation	Painless inflammatory papule → granulomatous ulcer with adenopathy in nonsensitized individual	Painless purple-red verrucous plaque in previously infected person	Subcutaneous, painless red-brown nodules with purulent sinus tracts and ulcers over an active focus of tuberculosis	Yellow red nodules → ulcers on oral, nasal, anal or vulvar mucosa	Small, nodular red-brown lesions with "apple-jelly" consistency	Small papules and pustules with hemorrhagic necrosis	Nontender fluctuant nodules with draining sinus tracts and abscesses
Tuberculin Skin Test	Negative early, then becomes positive	Positive	Positive	Variable, often negative	Positive	Variable, often negative	Variable, often negative
Culture	Positive	Usually negative	Positive	Positive	Usually negative	Positive	Positive
Histology	Initially, neutrophillic inflammatory cells and necrosis with bacilli. Later, caseating granulomas with disappearance of bacilli.	Acute inflammation, pseudo-carcinomatous hyperplasia, dermal micro-abscesses, few bacilli	Caseating granulomas surrounding necrosis in dermal tissue, bacilli present	Nonspecific inflammation and necrosis, bacilli present	Tubercles with some caseation without bacilli, nonspecific inflammatory infiltrate	Nonspecific inflammation with necrosis and micro-abscesses, abundant bacilli	Massive skin necrosis and abscess formation, abundant bacilli

findings. A full work-up for other foci of TB disease is required through sputum culture and chest x-ray [4].

In immunocompetent hosts, exogenous inoculation TB may resolve spontaneously [1], leaving an atrophic scar [3] and, in the case of primary inoculation TB, calcified regional lymph nodes [5]. However, cutaneous TB should be treated with the same multidrug regimen as systemic TB [4], even in the absence of obvious internal disease [6]. The Centers for Disease Control and Prevention recommend a 2-phase treatment regimen. The initial intensive phase consists of 8 weeks of daily multidrug therapy with isoniazid, rifampicin, pyrazinamide, and either ethambutol or streptomycin, with streptomycin being considered the second-line agent [3, 6]. In some cases, the ethambutol or streptomycin can be removed, as in the regimen chosen by the Infectious Disease specialist for our patient. This therapy is chosen in areas of low isoniazid resistance if the mycobacterium is susceptible to both isoniazid and rifampin, as was the case with our patient [6]. The continuation phase follows and consists of a 2-drug regimen of either daily or 2 or 3 times weekly isoniazid and rifampicin for 16 weeks [4, 6]. Surgical intervention may also be considered in cases of TVC [6].

The patient described likely has TVC based upon her past PPD positivity and the paucity of bacilli seen on histology. Late-stage TB chancre can also have a paucity of bacilli, but this patient's PPD positivity predated her presentation by several decades. Other forms of cutaneous TB were considered, and, in fact, the diagnosis of cutaneous TB was doubted by one of the patient's physicians due to her lack of other symptoms and the low likelihood of bacilli surviving in an environment such as the Ecuadorian jungle. Hematogenous spread of pulmonary TB to the skin is far more common than external implantation via trauma. The patient's workup, including chest x-ray and sputum culture, were negative, making an underlying focus of infection very low. In addition, this patient received latent TB infection therapy, reducing the chance of her developing endogenous reactivation disease. Therefore, although the mechanism of pathogenesis remains uncertain, the most plausible explanation of our patient's case would be exogenous inoculation. Although the habitat for mycobacteria in this case is unusual, it is not without precedent because cases of cutaneous TB have been described in individuals from merely walking barefoot with minimal trauma [10–12] in endemic countries. A specific case was published in 2005 in which a 13-year-old boy from the Colombian Amazon was diagnosed with cutaneous TB by PCR and culture. Although the authors state it is not possible to know whether route of infection was endogenous or exogenous, the patient's immunocompetency, negative chest x-ray, and lack of systemic systems led the authors to believe that exogenous inoculation at the site of a previous trauma (insect bite) was possible, as in our case [13]. Although Ecuador is not considered a country with endemic TB per the World Health Organization, the country still has an incidence rate of

56 cases per 100 000 population compared to 3.3 per 100 000 in the United States [14].

CONCLUSIONS

We find this case to be illustrative of the importance of an increasingly mobile society on the incidence of esoteric or rare diagnoses in populations in which these diseases are not classically found. It underscores the importance for the clinician to gather a travel history from patients and to ensure adequate specimens are sent to microbiology and pathology for atypical cases such as these [3, 4, 15].

Acknowledgments

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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