Erythematos Plaque to Lower Leg After Tropical Injury

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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, tuberculosis 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
progresses to a 1–5 cm [2] single purple-brown [4] painless verrucous plaque that may express keratinous material from a non-ulcerated 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

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.
### Table 1. Types of Cutaneous Tuberculosis

| Transmission | Tuberculosis Chance | Tuberculosis Verrucosa Cutis | Scrofuloderma | Orificial Tuberculosis | Lupus Vulgaris | Acute Miliary Tuberculosis | Tuberculosis Gumma (Metastatic TB Abscesses) |
|--------------|---------------------|-----------------------------|---------------|-----------------------|---------------|--------------------------|-------------------------------------------|
| Exogenous    | Exogenous           | Endogenous, contiguous      | Endogenous, contagious; autoinoculation | Endogenous, or endogenous, hematogenous or lymphatic | Endogenous, hematogenous | Endogenous, hematogenous | Massively skin necrosis, abscesses formation, abundant bacilli |

#### Presentation
- Painless inflammatory papule or 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
- Variable, often negative
- Positive
- Variable, often negative
- Variable, often negative

#### Culture
- Positive
- Usually negative
- 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 abscesses formation, abundant bacilli

#### Transmission
- Exogenous
- Endogenous, contiguous
- Endogenous, hematogenous

#### Transmission
- Exogenous
- Endogenous, contagious
- Endogenous, hematogenous

#### Tuberculosis Chance
- Exogenous
- Endogenous, contagious
- Endogenous, hematogenous

#### Tuberculosis Verrucosa Cutis
- Exogenous
- Endogenous, contagious
- Endogenous, hematogenous

#### Scrofuloderma
- Exogenous, contagious
- Endogenous, hematogenous

#### Orificial Tuberculosis
- Endogenous, contagious
- Endogenous, hematogenous

#### Lupus Vulgaris
- Endogenous, contiguous
- Endogenous, hematogenous

#### Acute Miliary Tuberculosis
- Endogenous, hematogenous

#### Tuberculosis Gumma (Metastatic TB Abscesses)
- Massively skin necrosis and abscesses formation, abundant bacilli
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].

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