An evolving presentation of cutaneous tuberculosis

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Abstract

Tuberculosis is a fairly common disease in the United States and around the world, newly infecting ten million people throughout the world per year. Despite the pervasiveness of tuberculosis, cutaneous tuberculosis (CTB) rarely manifests worldwide. Tuberculous infections of the skin arise in several distinct variants that can be classified as either multibacillary or paucibacillary; each subtype within these categories presents with its own morphological and histological findings. The diagnosis of CTB can prove clinically challenging as its variants mimic many conditions dermatologist encounter on a daily basis. Additionally, tissue confirmation is difficult. We report a case of CTB which evolved from a lupus vulgaris presentation to the metastatic tuberculous abscess variant.

Keywords: cutaneous tuberculosis, mycobacterium tuberculosis, tuberculum, tuberculous infection

Introduction

Cutaneous tuberculosis (CTB) is an uncommon manifestation of tuberculosis (TB). Although TB is becoming increasingly common in the United States with 9,029 cases reported in 2017, CTB is reported in 1-2% of infections [1-3]. CTB has many different morphologies including tuberculous chancre, tuberculosis verrucosa cutis (TVC), lupus vulgaris (LV), scrofuloderma, and metastatic tuberculous abscess [4]. The varied clinical presentation of CTB can make the diagnosis difficult. Furthermore, tissue diagnosis can be difficult as acid-fast bacilli staining and mycobacterial cultures often are often negative [3].

Case Synopsis

A 78-year-old woman with a history of non-Hodgkin lymphoma in remission presented to a dermatology clinic for an asymptomatic eruption for one year. Clinical examination demonstrated clustered erythematous and violaceous crusted papules on the ventral side of her right wrist (**Figure 1**). Differential diagnosis included granuloma annulare, verruca, or tinea corporis. Punch biopsy demonstrated granulomatous and suppurative dermatitis (**Figure 2**). Bacterial and fungal stains at that time were negative. No acid-fast bacilli stain was performed. The patient was started on topical steroid creams with minimal improvement. On follow-up, she was noted to have swelling, warmth, and tenderness of the subcutaneous tissue in the ventral forearm with

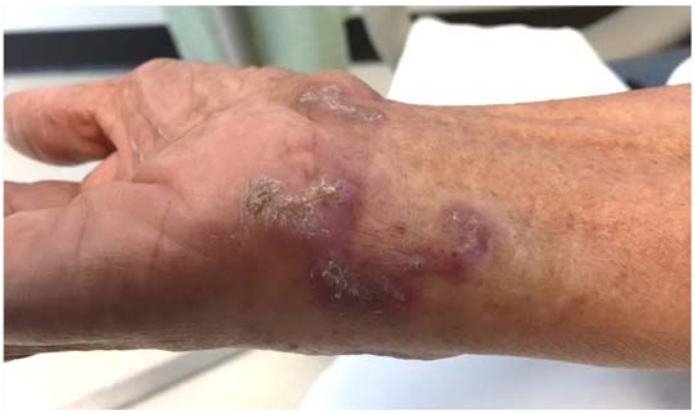

Figure 1. *Clustered violaceous papules on right wrist.*

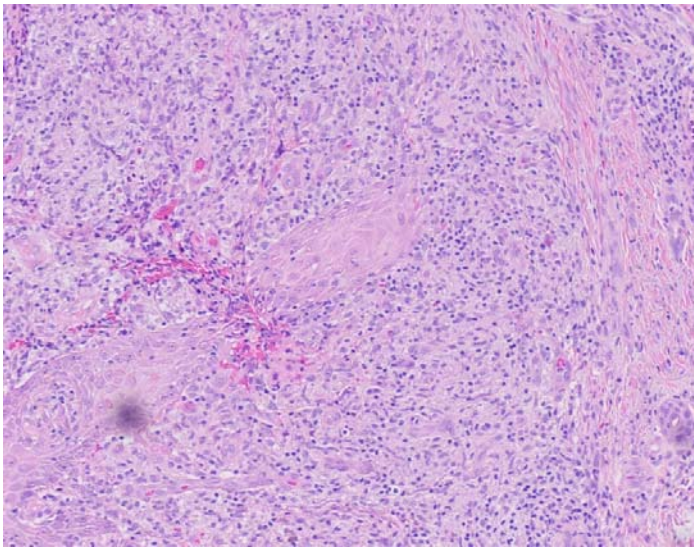

Figure 2. *Punch biopsy showing perivascular, interstitial, and focally lichenoid lymphohistiocytic infiltrate with occasional palisading of histiocytes around collagen bundles and sparse mucin. H&E, 10x.*

subjective fevers and chills (**Figure 3**). She was also noted to have new sporotrichoid erythematous nodules on the right arm. She was admitted to the hospital for work-up and was found to have a 5.9cm abscess confirmed by MRI (**Figure 4**). Culture via fine needle aspiration confirmed *Mycobacterium tuberculosis*.

Biopsy at this time showed fibrous tissue with acute and necrotizing granulomatous inflammation (**Figure 5**). The patient was started on rifampin 600mg, 300mg isoniazid, pyrazinamide 1000mg, and ethambutol 800mg for two months, at which point she was found to have pyrazinamide-resistant TB. Based on this development, she was transitioned to rifampin and isoniazid for seven months. Lesions

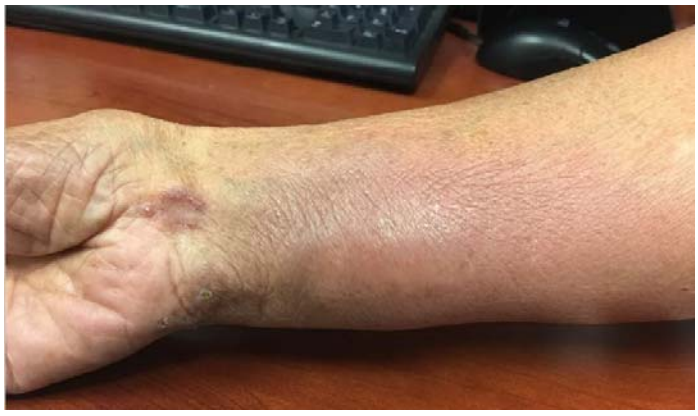

Figure 3. *Swelling and erythema of the wrist.*

Figure 4. *2.1×3.5×5.9cm (AP×TV×CC) oval-shaped T1 isointense T2 hyperintense partially enhancing mass is seen within the volar distal forearm centered around the flexor carpi ulnaris tendon.*

resolved after five months of treatment. Four years have passed without recurrence of the disease.

After the diagnosis of cutaneous tuberculosis, a retrospective chart review was performed. She was seen in the hematologic oncology clinic earlier in the year because of reports of night-sweats once a month. A CT-scan taken for lymphoma surveillance found interval development of a few right lower lobe multifocal nodules and airspace disease.

Case Discussion

Diagnosing cutaneous tuberculosis can prove challenging to clinicians as it causes a range of skin morphologies that cannot easily be confirmed by acid-fast testing for mycobacteria. Additionally, the diagnosis itself is rare, reported in less than 1-2% of

TB infections [2,3]. These morphologies include tuberculous chancre, TVC, LV, scrofuloderma, and metastatic tuberculous abscess [4]. Mode of transmission partially dictates the morphologic type that manifests. This is worth considering in the context of the patient case presented above. The case presented above exhibits an especially difficult situation as it does not adhere to one single CTB variant. During the initial visit, the papule form most closely fit with TVC morphologically. However, it most likely represents LV mimicking TVC given the mode of transmission. As the infection progressed it assumed the morphology of metastatic tuberculous abscess. Although there have been a handful of cases reporting two concurrent manifestations of CTB this is the first case to the author's knowledge to shift manifestations during the disease course [5,6].

Tuberculosis verrucosa cutis lesions result from exogenous inoculation of TB directly into the skin of a susceptible individual [5]. These lesions present as slowly growing, asymptomatic violaceous or brownish red plaques [4]. Histology shows noncaseating granulomas without mycobacteria being detected via acid-fast bacilli or culture [3]. Acid-fast bacilli staining and mycobacterial culture are often negative [7]. Although our patient's original lesion morphologically resembled TVC, given the lack of exogenous inoculation it is more consistent with LV. Neither TVC nor LV is known to produce an abscess. As a result, the later variant more closely matched metastatic tuberculous abscess, also known as TB gumma.

Lupus vulgaris lesions are sharply emarginated red brown papules that have a gelatinous consistency, giving them the description "apple jelly nodules." These lesions slowly change via peripheral extension and central atrophy into large plaques. Lupus vulgaris may arise as a result of direct inoculation in a sensitive individual or hematogenous spread from a primary infection. Histology shows noncaseating granulomas and mononuclear cell infiltrate [3]. Acid-fast bacilli staining and mycobacterial culture are often negative [4]. Lupus vulgaris can manifest in a sporotrichoid form, with lesions having a linear pattern along lymphatics spreading from a primary focus.

Metastatic tuberculous abscess is typically the result of hematogenous spread from a primary focus during periods of lowered resistance such as in an immunocompromised state [3].These nodules do not demonstrate predilection for any particular anatomic location. Inverse sporotrichoid spread of abscesses, as seen in this patient, has been reported previously [8]. Abscesses begin as single or multiple nodules that form draining sinus abscesses unless surgically incised and drained [4]. Histology shows suppurative granulomata with nonspecific infiltrates and necrosis [3]. Pus drained from the abscess usually demonstrates mycobacteria. Given the pathophysiology of LV and metastatic tuberculous abscess both rely on hematogenous spread, the progression of this patient's clinical cutaneous findings could represent evolution of TB infection from a superficial-to-deep infection originating from the pulmonary lesions.

Detection of mycobacteria within the suspected lesion can aid in determining the variant of CTB. The multibacillary forms (TB chancre, scrofuloderma, TB orificialis, military TB, metastatic TB abscess, and some forms of LV) are more likely to be acid-fast bacilli positive whereas the paucibacillary forms (TVC and acral forms of LV) are usually acid-fast bacilli negative [4]. The presence of paucibacillary forms renders CTB a difficult diagnosis to clinch. As a consequence, the differential diagnosis list widens

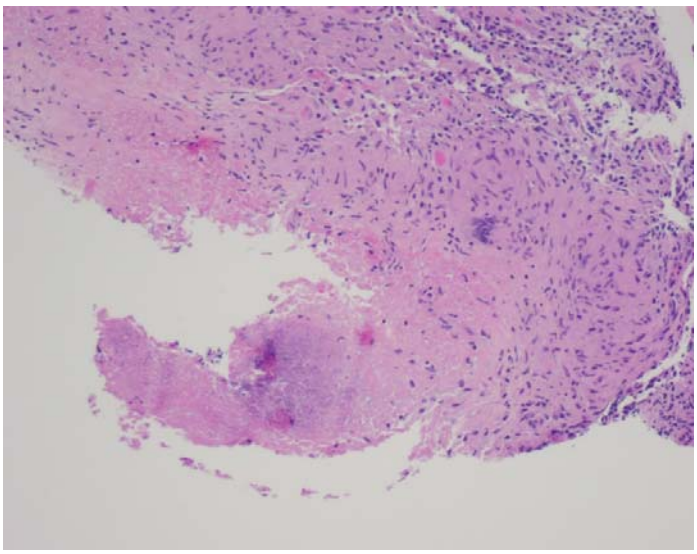

Figure 5. *Re-biopsy exhibiting fibrous tissue with chronic lymphohistiocytic inflammation, focal necrosis, and foreign body giant cells. H&E, 10x.*

considerably in this context, as CTB to appear similar to a host of other diseases with cutaneous manifestations. Diseases such as leishmaniasis, leprosy, actinomyces, and deep fungal infection must be considered in this setting [3]. The diagnosis of CTB requires a thorough history and physical examination. A high degree of suspicion should be entertained for immunocompromised or high-risk patients with atypical lesions. Additional tests that could aid diagnosis are PCR for mycobacterium, tuberculin skin test, and serum QuantiFERON-TB gold testing. QuantiFERON-TB gold exposes the patient's serum to *Mycobacterium* proteins and quantifies interferon production by the patient's white blood cells, which indicates infection by the pathogen [4]. In our case, a rheumatologist who had seen the patient one year before presentation to dermatology had ordered QuantiFERON-TB gold testing; however, the test was not completed.

Treatment for cutaneous TB is the same as treatment for pulmonary or systemic TB with a multi-drug approach that typically utilizes rifampin, isoniazid, pyrazinamide, and either ethambutol or streptomycin [9]. The treatment scheme is divided into two phases: the intensive phase and the maintenance phase. The intensive phase lasts eight weeks and is bactericidal; during this time, rifampin, isoniazid, pyrazinamide, and streptomycin can be used. The maintenance phase maintains sterility by utilizing rifampin and isoniazid over the course of two months; ethambutol may be used in place if isoniazid if resistance is suspected. Two percent lactic acid and local anesthesia may be applied if lesions manifest near orifices. Surgery can be utilized but it is typically reserved for treatment of LV, TVC, and scrofuloderma [10].

Cutaneous TB, if caused by atypical mycobacteria, cannot be treated by anti-TB drugs. For this reason, treatment proves to be difficult. Treatment must be tailored to the exact organism but can involve doxycycline, minocycline, amikacin, ciprofloxacin, or trimethoprim-sulfamethoxazole depending on the organism [10].

Conclusion

This case was challenging to diagnose owing to its presentation which was complicated by the evolving clinical manifestations of CTB. This case shows CTB can have fluid morphology that can confuse or delay the diagnosis if clinical suspicion is not high.

Potential conflicts of interest

The authors declare no conflicts of interests.

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