Cutaneous Gummatous Tuberculosis in a Kidney Transplant Patient

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PRACTICE **POINTS**

- Transplant patients are at increased risk for infection given their immunosuppressed state.
- Although rare, cutaneous tuberculosis should be considered in the differential for cutaneous lesions in an immunosuppressed patient.

Cutaneous gummatous tuberculosis (TB) is an uncommon subtype of cutaneous TB that can be seen in notably immunocompromised individuals. We report a case of cutaneous gummatous TB in an immunosuppressed kidney transplant patient. A 60-year-old Cambodian woman presented with fever attributed to recurrent pyelonephritis while on immunosuppressive medications 7 months after kidney transplant. She underwent a bilateral native nephrectomy and was found to have peritoneal nodules, which revealed caseating granulomas and acid-fast bacilli (AFB) consistent with kidney and peritoneal TB. Anti-TB therapy was initiated, resulting in symptom resolution. Subsequently, the Tuberculosis Control Program at the Department of Health (Philadelphia, Pennsylvania) discontinued her medications due to severe thrombocytopenia. During this time, she was closely monitored with blood draws. Approximately 10 weeks after treatment initiation, she noted recurrent fever and a painful, dull red, subcutaneous nodule on the right side of the flank. Biopsy showed an inflammatory infiltrate within the deep dermis indicative of suppurative granulomatous dermatitis. Ziehl-Neelsen stain demonstrated rare AFB within the cytoplasm of macrophages. The patient was restarted on anti-TB therapy resulting in the resolution of her fever and skin lesions. This case illustrates a noteworthy example of a rare form of cutaneous gummatous TB, which should be considered and included in the differential for cutaneous lesions in an immunosuppressed patient.

Cutis. 2019;103:E32-E35.

Case Report

A 60-year-old Cambodian woman presented with recurrent fever (temperature, up to 38.8°C) 7 months after receiving a kidney transplant secondary to polycystic kidney disease. Fever was attributed to recurrent pyelonephritis of the native kidneys while on mycophenolate mofetil, tacrolimus, and prednisone. As a result, she underwent a bilateral native nephrectomy and was found to have peritoneal nodules. Pathology of both native kidneys and peritoneal tissue revealed caseating granulomas and acid-fast bacilli (AFB) diagnostic for kidney and peritoneal tuberculosis (TB). She had no history of TB, and a TB skin test (purified protein derivative [PPD]) upon entering the United States from Cambodia a decade earlier was negative. Additionally, her pretransplantation PPD was negative.

Treatment with isoniazid, ethambutol, pyrazinamide, and levofloxacin was initiated immediately upon diagnosis, and all of her immunosuppressive medications—mycophenolate mofetil, tacrolimus, and prednisone—were discontinued. Her symptoms subsided within 1 week, and she was discharged from the hospital. Over the next 2 months, her immunosuppressive medications were restarted, and her TB medications were periodically discontinued by the Tuberculosis Control Program at the Department of Health (Philadelphia, Pennsylvania) due to severe thrombocytopenia. During this time, she was closely monitored twice weekly in the clinic with blood draws performed weekly.

Approximately 10 weeks after initiation of treatment, she noted recurrent subjective fever (temperature, up to 38.8°C) and painful lesions on the right side of the flank, left breast, and left arm of 3 days' duration. Physical

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The authors report no conflict of interest.

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examination revealed a warm, dull red, tender nodule on the right side of the flank (Figure 1) and subcutaneous nodules with no overlying skin changes on the left breast and left arm. A biopsy of the lesion on the right side of the flank was performed, which resulted in substantial purulent drainage. Histologic analysis showed an inflammatory infiltrate within the deep dermis composed of neutrophils, macrophages, and giant cells, indicative of suppurative granulomatous dermatitis (Figure 2). Ziehl-Neelsen stain demonstrated rare AFB within the cytoplasm of macrophages, suggestive of *Mycobacterium tuberculosis* infection (Figure 3). A repeat chest radiograph was normal.

Based on the patient's history and clinical presentation, she was continued on isoniazid, ethambutol, and levofloxacin, with complete resolution of symptoms and cutaneous lesions. Over the subsequent 2 months, the therapy was modified to rifabutin, pyrazinamide, and levofloxacin, and subsequently pyrazinamide was stopped. A subsequent biopsy of the left breast and histologic analysis indicated that the specimen was benign; stains for AFB were negative. Currently, both the fever and skin lesions have completely resolved, and she remains on anti-TB therapy.

Comment

Clinical Presentation—Cutaneous TB is an uncommon manifestation of TB that can occur either exogenously or endogenously.[1] It tends to occur primarily in previously infected TB patients through hematogenous, lymphatic, or contiguous spread.[2] Due to their immunocompromised state, solid organ transplant recipients have an increased incidence of primary and reactivated latent TB reported to be 20 to 74 times greater than the general population.[3,4] One report stated the total incidence of posttransplant TB as 0.48% in the West and 11.8% in endemic regions such as India.[5] The occurrence of cutaneous TB is rare among solid organ transplant recipients.[1] On average, a diagnosis of latent TB is made 9 months after transplantation because of the opportunistic nature of *M tuberculosis* in an immunosuppressed environment.[6]

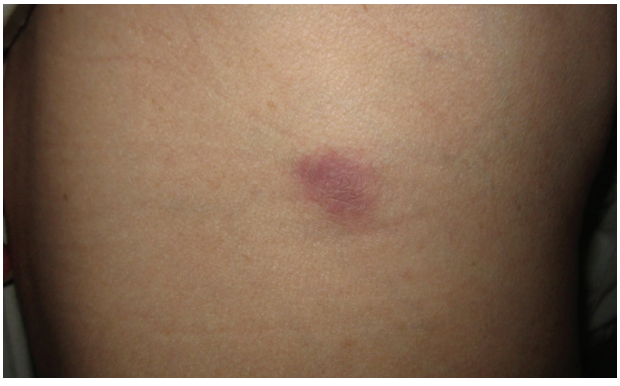

FIGURE 1. Dull red and tender nodule on the right side of the flank.

TB Subtypes—Cutaneous TB can be in the form of localized disease (eg, primary tuberculous chancre, TB verrucosa cutis, lupus vulgaris, smear-negative scrofuloderma), disseminated disease (eg, disseminated TB, TB gumma, orificial TB, miliary cutaneous TB), or tuberculids (eg, papulonecrotic tuberculid, lichen scrofulosorum,

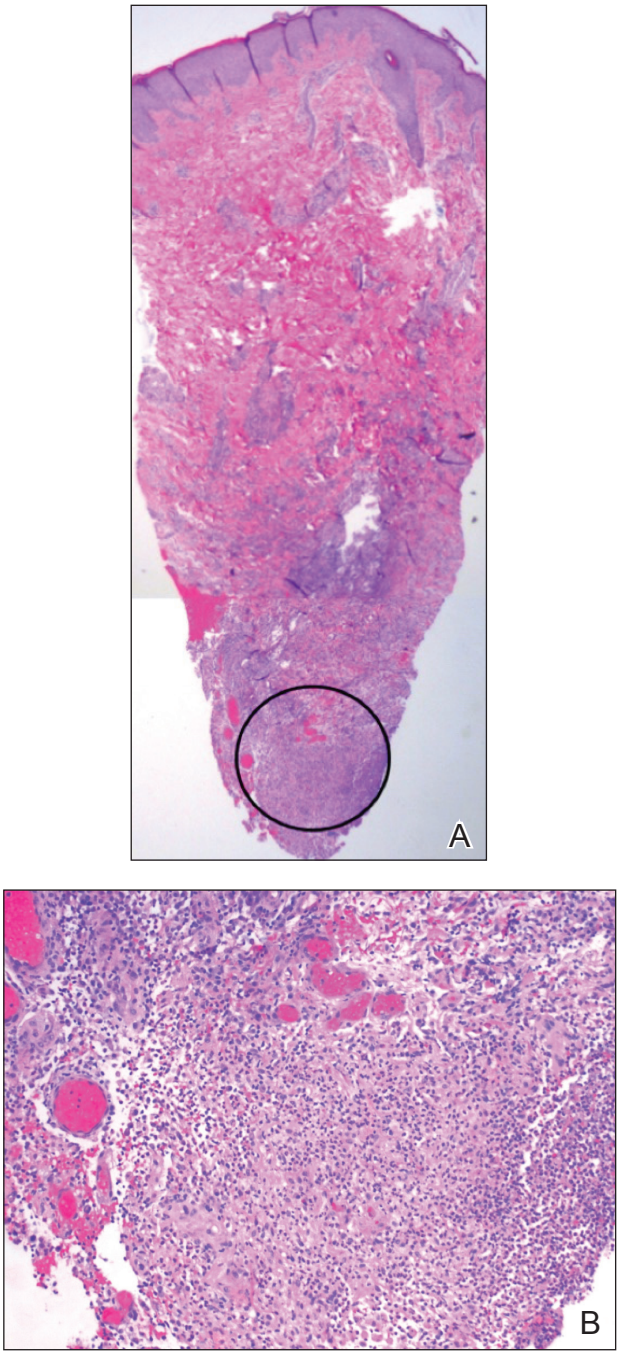

FIGURE 2. A, Marked inflammatory infiltrate within the deep dermis (H&E, original magnification ×2). B, Infiltrate composed of neutrophils, macrophages, and giant cells, indicative of suppurative granulomatous dermatitis (H&E, original magnification ×10).

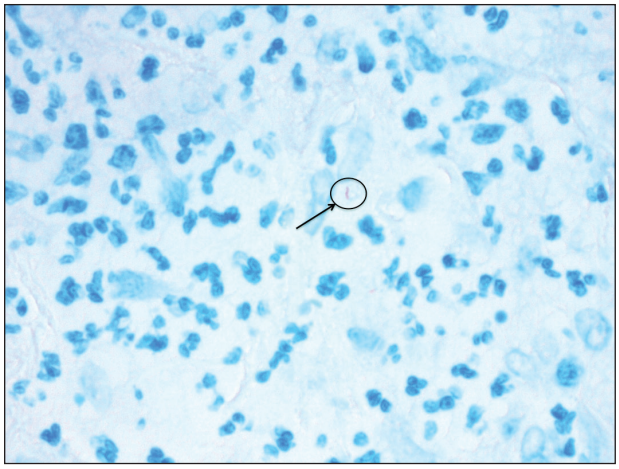

FIGURE 3. Rare acid-fast bacilli (circle and arrow) within the cytoplasm of macrophages (Ziehl-Neelsen, original magnification ×63).

erythema induratum).[7] Due to the pustular epithelioid cell granulomas and AFB positivity of the involved cutaneous lesions, our patient's TB can be classified as a metastatic TB abscess or gummatous TB.[7]

Metastatic TB abscess, an uncommon subtype of cutaneous TB, generally is only seen in malnourished children and notably immunocompromised individuals.[2,8,9] In these individuals, systemic failure of cell-mediated immunity enables *M tuberculosis* to hematogenously infect various organs of the body, resulting in alternative forms of TB, such as gummatous-type TB.[10] One study reported that of the 0.1% of dermatology patients presenting with cutaneous TB, only 5.4% of these individuals had the rarer gummatous form.[7] These metastatic TB abscesses begin as a single or multiple nontender subcutaneous nodule(s), which breaks down and softens to form a draining sinus abscess.[2,8,9] Abscesses are most commonly seen on the trunk and extremities; however, they can be found nearly anywhere on the body.[8] The pathology of cutaneous TB lesions demonstrates caseating necrosis with epithelioid and giant cells forming a surrounding rim.[9]

Diagnosis—Diagnosis may be difficult because of the vast number of dermatologic conditions that resemble cutaneous TB, including mycoses, sarcoidosis, leishmaniasis, leprosy, syphilis, other non-TB mycobacteria, and Wegener granulomatosis.[9] Thus, confirmatory diagnosis is made via clinical presentation, detailed history and physical examination, and laboratory tests.[11] These tests include the Mantoux tuberculin skin test (PPD or TST) or IFN-γ release assays (QuantiFERON-TB Gold test), identification of AFB on skin biopsy, and isolation of *M tuberculosis* from tissue culture or polymerase chain reaction.[11] Given our patient's history, clinical presentation, and the identification of mycobacteria with AFB stain, the diagnosis of cutaneous gummatous TB was confirmed.

At-Risk Populations—The recommendation for the identification of at-risk populations for latent TB testing and treatment have been clearly defined by the World Health Organization (Table).[12] Our patient met 2 of these criteria: she had been preparing for organ transplantation and was from a country with high TB burden. Such at-risk patients should be tested for a latent TB infection with either IFN-γ release assays or PPD.[12] These recommendations are supported by the American Thoracic Society, which specifies that a positive PPD test in a solid organ transplant recipient is defined as having induration greater than 5 mm.[13] However, even with a high index of suspicion, it has been reported that as many as 75% to 80% of organ recipients who developed TB had a false-negative pretransplantation PPD due to anergy from immunosuppression.[14] Given the notable risk for TB in organ transplant recipients on immunosuppressive medications, these patients should receive screening tests with high sensitivity and specificity, while controlling for

Identification of At-Risk Populations for Latent TB Testing and Treatment[a]

Strong Recommendation	Conditional Recommendation
Individuals living with human immunodeficiency virus	Prisoners
Patients initiating anti–tumor necrosis factor treatment	Health care workers
Patients receiving dialysis	Immigrants from countries with high TB burden
Patients preparing for organ or hematologic transplantation	Homeless individuals
Patients with silicosis	Illicit drug users

Abbreviation: TB, tuberculosis.

[a]Strong recommendations based on the likelihood of progression to active TB disease and the benefits of treatment outweighing the potential harms. Conditional recommendations are limited by the weak quality of evidence and are determined based on specific patient considerations.

Data from the World Health Organization.[12]

possible anergy. Unfortunately, the role of anergy testing in the diagnosis of latent TB is not well defined, and thus not recommended at this time.[13,15] It is recommended to repeat PPD testing 7 to 10 days after the first test as a booster effect to rule out false-negative results.[15]

Treatment—The recommended treatment of active TB in transplant recipients is based on randomized trials in immunocompetent hosts, and thus the same as that used by the general population.[16] This anti-TB regimen includes the use of 4 drugs—typically rifampicin, isoniazid, ethambutol, and pyrazinamide—for a 6-month duration.[11] Unfortunately, the management of TB in an immunocompromised patient is more challenging due to the potential side effects and drug interactions.

Finally, thrombocytopenia is an infrequent, life-threatening complication that can be acquired by immunocompromised patients on anti-TB therapy.[17] Drug-induced thrombocytopenia can be caused by a variety of medications, including rifampicin, isoniazid, ethambutol, and pyrazinamide. Diagnosis of drug-induced thrombocytopenia can be confirmed only after discontinuation of the suspected drug and subsequent resolution of the thrombocytopenia.[17] Our patient initially became thrombocytopenic while taking isoniazid, ethambutol, pyrazinamide, and levofloxacin. However, her platelet levels improved once the pyrazinamide was discontinued, thereby suggesting pyrazinamide-induced thrombocytopenia.

Conclusion

The risk for infectious disease reactivation in an immunocompromised patient undergoing transplant surgery is notable. Our findings emphasize the value of a comprehensive pretransplant evaluation, vigilance even when test results appear negative, and treatment of latent TB within this population.[16,18,19] Furthermore, this case illustrates a noteworthy example of a rare form of cutaneous TB, which should be considered and included in the differential for cutaneous lesions in an immunosuppressed patient.

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