BRIEF ARTICLES

Lepromatous leprosy: an elusive mimicker mistaken for polyarteritis nodosa and disseminated tuberculosis

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ABSTRACT

Leprosy is a chronic infectious disease caused by the obligate intracellular microorganism, *Mycobacterium leprae* and presents as skin lesions and peripheral neuropathies with upper respiratory mucosa involvement. We present a case of a 36-year-old immunocompromised female whom was recently diagnosed polyarteritis nodosa vasculitis (PAN) in Trinidad and returned back to the US with a two-week history of pleuritic chest pain, fever, chills, fatigue, nausea, vomiting, epistaxis and cough. Physical examination revealed a diffuse rash. Pancytopenia prompted a bone marrow biopsy, which revealed acid-fast bacteria, suspicious for disseminated tuberculosis. Histologic examination of the skin lesions revealed disseminated acid-fast, Fite-positive microorganisms within the dermis and nerves. She developed anuric renal failure and purpura fulminans with disseminated intravascular coagulation (DIC). PCR results from the skin sample shortly thereafter revealed the presence of *M. leprae* DNA. *Mycobacterium tuberculosis* complex DNA was not identified. This case demonstrates an unusual presentation of leprosy with bone marrow involvement and highlights the importance of utilizing histologic examination together with molecular diagnostic techniques to aid in establishing the correct diagnosis and treatment. This case also cautions that leprosy can be misdiagnosed as a vasculitis, specifically PAN, as there is overlap in the clinical presentation of each disease and that clinicopathologic correlation is essential.

INTRODUCTION

Leprosy or Hansen's disease refers to an infection caused by the obligate-intracellular organism *Mycobacterium leprae* or less commonly *Mycobacterium lepromatosis*. It affects fewer than 250 individuals in the United States per year (1), although epidemiologic data is based on voluntary reporting and likely underestimates its true incidence. Most cases occur in immigrants from other countries. The average incubation time is 5 years. It primarily affects the skin, peripheral nerves, upper respiratory tract, eyes and reticuloendothelial system (1). Clinically, the disease may initially present as hypopigmented macules, sometimes mistaken for tinea versicolor or vitiligo. The Ridley-Jopling classification system classifies cases along a spectrum with a tuberculoid

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pole and a lepromatous pole (tuberculoid, borderline tuberculoid, mid-borderline, borderline lepromatous, lepromatous and indeterminate) depending on the integrity of the individual's immune response (2). The tuberculoid pole is characterized by a robust host immune response with few organisms and typical clinical findings of one to three hypopigmented, hypoesthetic, well-demarcated patches. The lepromatous pole is typified by an ineffective host immune response with numerous organisms and widely distributed, raised skin lesions forming coalescing plaques (2). Histologically, the disease is diverse on a spectrum and may demonstrate dermal granulomas with or without abundant Langerhans cells, lymphocytes and foamy macrophages with blue-gray cytoplasm; however, clinicopathological correlation is essential for properly assigning a specific diagnosis among the various clinical forms of the disease. Leprosy is a curable disease with treatment consisting of a multidrug regimen administered for 24-months with the aim of preventing resistance and relapse. A combination of dapsone and rifampin is generally used for tuberculoid leprosy with clofazamine added for lepromatous disease (1, 10).

CASE REPORT

A 36-year-old woman from Trinidad and Tobago presented with localized skin nodules on the right foot and leg, lower extremity paresthesia, progressive difficulty walking, fatigue and low-grade fevers. She was diagnosed with polyarteritis nodosa (PAN) by her doctor in Trinidad and Tobago and initiated on prednisone (1 mg/kg, tapered over months). Four months later, azathioprine was added for persistent fever, malaise and skin lesions. Three weeks later, after returning to the U.S., she presented with fever, chills, fatigue, nausea, vomiting, epistaxis and cough. Examination revealed numerous erythematous-violaceous papules on the trunk and extremities as well as livedoid erythema of the lower extremities (Figure 1).

Labs were notable for pancytopenia: WBC of 3.0 x 10^9/L (absolute neutrophil count of 0), platelets of 80 x 10^9/L and a hemoglobin of 8.3 g/dL. Blood cultures were positive for *Streptococcus mitas/oralis*. A T2 candida antigen was positive, consistent with candida fungemia. A bone marrow biopsy revealed hypocellular marrow with abundant foamy macrophages and acid-fast bacilli (Figure 2). Treatment was initiated for presumed tuberculosis with rifampin 600 mg/d, isoniazid 300mg/d, pyrazinamide 1500 mg/d and ethambutol 1370 mg/d (RIPE) in addition to piperacillin/tazobactam and amphotericin B for treatment of bacterial and fungal sepsis. A skin biopsy of the lesions revealed abundant acid-fast, Fite-positive bacilli throughout the dermis and within nerves, foamy macrophages with blue-grey cytoplasm as well as an extensive thrombotic vasculopathy (Figure 3). The patient developed anuric renal failure, purpura fulminans and disseminated intravascular coagulation (DIC) and died within 2 weeks of presentation and initiation of RIPE therapy. A skin biopsy sent for PCR revealed *Mycobacterium leprae* DNA. *Mycobacterium tuberculosis* complex DNA was not identified.

Figure 1. Skin examination revealed livedoid erythema of the bilateral lower extremities (A) and widely scattered annular, raised, 0.5-2 cm, dusky, erythematous-violaceous papules on the trunk and extremities (B)

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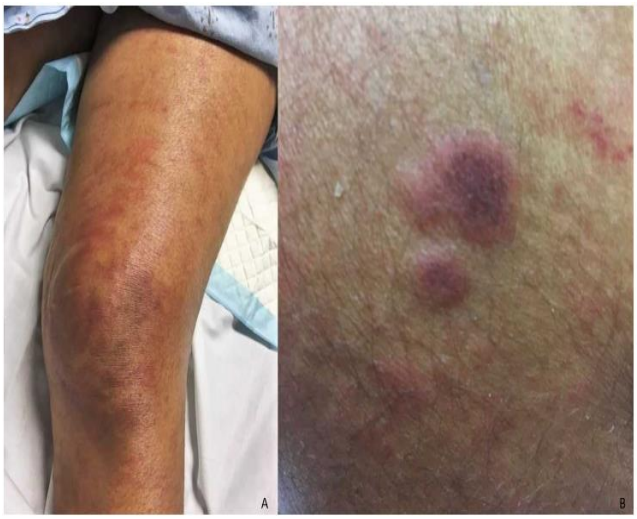


Figure 2. Bone marrow biopsy (20x) showing markedly hypocellular marrow with abundant foamy macrophages (A). Additional AFB stain (100x) demonstrates rare acid-fast bacilli within the bone marrow (B).

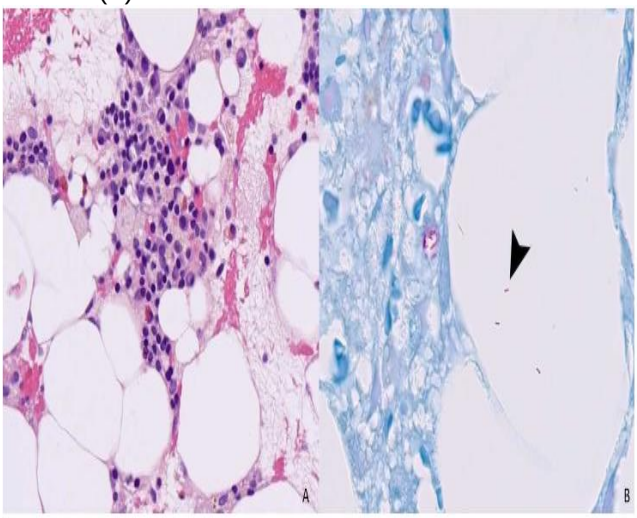
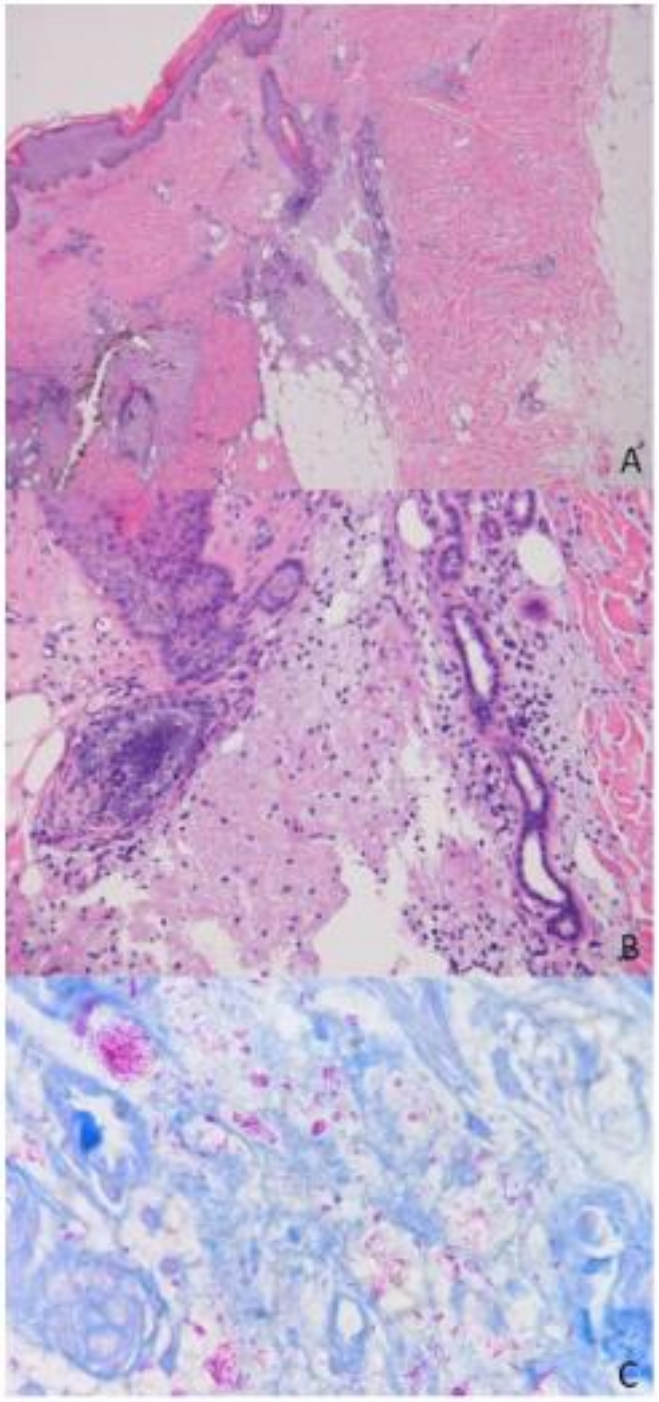


Figure 3. Skin biopsy of lesion (4x) showing abundant foamy macrophages within the dermis and subcutaneous tissue (A). Foamy macrophages with blue-grey cytoplasm (20x) surrounding adnexal structures (B). Accompanying Fite stain (100x) demonstrating numerous positive staining microorganisms within macrophages in dermis (C).



DISCUSSION

Leprosy should be considered in the differential of skin lesions on the extremities, especially those occurring on the hands and

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feet with associated sensory loss. In the United States, most cases are acquired abroad, so foreign birth or a history of international travel increase the probability of the diagnosis (2). In this case, the patients presenting symptoms were attributed to PAN. Other authors have cautioned about leprosy being misdiagnosed as a vasculitis, specifically PAN (3, 4). Both diseases can present with nodules on the skin of the lower legs with associated numbness and weakness (in the case of PAN this is due to mononeuritis multiplex). A biopsy generally allows for a clear distinction. This avoidable error has important consequences as immunosuppressive therapy further impairs the host response to M. leprae and may lead to a worse prognosis.

M. tuberculosis and Mycobacterium avium complex are more frequently encountered in bone marrow biopsies than *M. leprae*. All of these organisms are acid-fast and PAS-positive (6). A Fite stain should routinely be done as it has higher specificity in the skin and helps to avoid missing this diagnosis. In this case, the patient was initially presumed to have disseminated tuberculosis based on a positive acid-fast stain in the bone marrow.

Because bone marrow evaluation is not routinely done in leprosy care (6) the frequency of bone marrow involvement is unknown. The histologic features have been described in case series (8, 9). Pancytopenia has been reported (6, 10) in association with bone marrow involvement. The pancytopenia observed in this case may have been due to lepromatous infiltration of bone marrow, azathioprine toxicity or sepsis.

Catastrophic immunologic reactions may occur in the course of leprosy, bacterial and fungal sepsis or as a consequence of initiation of rifampin for disseminated mycobacterial disease (11, 12). In this case, the patient developed DIC and purpura fulminans within 11 days of diagnosis, despite treatment for disseminated mycobacterial, fungal and bacterial infections. While her labs later in the admission supported the diagnosis of DIC (including elevated PT/PTT and D-dimer), we also considered the possibility of Lucio phenomenon to explain the livedoid erythema on her legs that we noted on our initial examination.

In summary, this case highlights the importance of combining clinical presentation and histologic examination with further ancillary testing including appropriate immunohistochemistry and molecular testing to aid in a definitive diagnosis and subsequent proper treatment. This case further demonstrates the importance of considering an infectious disease such as leprosy in the clinical setting of cutaneous vasculitis such as PAN or autoimmune disease and under immunosuppressive therapy.

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