Leprosy in the Upper Midwest

Kathy Bach, MD; Molly A. Hinshaw, MD; Bridget E. Shields, MD

ABSTRACT

Introduction: Leprosy is a life-threatening infection caused by *Mycobacterium leprae* with an average 5-year long incubation period. It is curable when treated early. Early diagnosis requires knowledge of its myriad clinical features as risk factors may not be readily apparent.

Case Presentation: We report the case of a male patient from Wisconsin who tested positive for leprosy without a known exposure or recent travel to endemic areas.

Discussion: The clinical presentation of leprosy exists on a spectrum and correlates with cell immunity levels. The Ridley-Jopling and World Health Organization classifications are used to define leprosy subtypes and guide treatment. Histopathologic examination may aid in diagnosis of suspicious presentations.

Conclusions: Leprosy may present with nonspecific clinical features and elevated inflammatory markers leading to a misdiagnosis. It should be considered on the differential diagnosis for suspicious presentations and appropriately worked up with various diagnostic modalities. A multidisciplinary approach to treatment may prevent spread and permanent damage.

INTRODUCTION

Leprosy is a curable infectious disease that primarily affects the skin, peripheral nerves, upper respiratory tract, and eyes.[1] Endemic to over 140 countries, leprosy continues to spread through human transmission and travel.[1] In the United States, armadillos also serve as a reservoir for zoonotic transmission.[2-4] However, there have been reports of autochthonous leprosy (human-to-human transmission) in the United States between Americans with no history of foreign exposure.[5] With multiple variables affecting an individual's susceptibility for contracting the disease and a long incubation period of several years, leprosy can be difficult to diagnose in the absence of obvious risk factors for infection and classic clinical features. We present a case to highlight the diagnostic pathway that leads to leprosy in a patient without identifiable risk factors for infection.

CASE PRESENTATION

A Wisconsinite in his 70s was sent to dermatology in consultation for presumed connective tissue disease in the setting of a 3-month history of asymptomatic plaques and nodules on the trunk and extremities, an elevated rheumatoid factor (19), and antinuclear antibody (1:320). The lesions began on his arms and spread to involve his chest, abdomen, and back. He noted concomitant edema of the hands, feet, and lower legs; fatigue; arthralgias; nasal congestion; epistaxis; decreased visual acuity; increased cold sensitivity; anorexia; and acute onset left foot drop. Treatment with compression stockings, hydrochlorothiazide, and diclofenac sodium 1% cream had been ineffective.

Physical examination revealed numerous pink to violaceous indurated plaques without ulceration on the upper arms, chest, abdomen, flanks, and back (Figure 1). Punch biopsies of the right upper arm and left flank revealed a dermal and focally subcutaneous infiltrate of histiocytes arranged in multinucleate collections and sheets with minimal associated lymphocytic inflammation (Figure 2). Within histiocyte cytoplasms were innumerable acid-fast bacilli- and Fite-positive organisms diagnostic of an atypical mycobacterial infection (Figure 3). In

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Author Affiliations: University of Wisconsin School of Medicine and Public Health (UWSMPH), Madison, Wisconsin (Bach); Department of Dermatology, UWSMPH, Madison, Wis (Hinshaw, Shields).

Corresponding Author: Bridget E. Shields, MD, FAAD, Department of Dermatology, University of Wisconsin School of Medicine and Public Health, 600 Highland Ave, Madison, WI 53792; email bshields@dermatology.wisc.edu; ORCID ID 0000-0002-5734-0167

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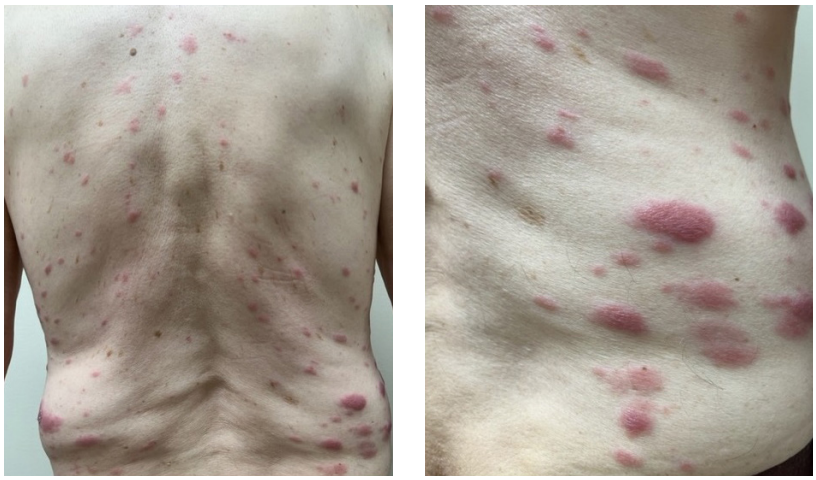
context of the clinical presentation, tissue was sent for nontuberculous mycobacterial testing by polymerase chain reaction (PCR), and *Mycobacterium leprae (M leprae)* was detected using 16s and rpoB primer sets. These combined clinical and pathologic features correspond to the diagnosis of borderline lepromatous leprosy. Recommendations were given by the National Hansen's Disease Program (NHDP) to initiate prednisone, methotrexate, folic acid, vitamin D, rifampin, moxifloxacin, and minocycline.

On further history taking, the patient denied a history of immunodeficiency, prior unusual infections, or known exposure to leprosy. He denied pet or animal exposures, including to armadillos. He had an extensive travel history over the preceding 20 years, including to Central America, Caribbean islands, South America, the Mediterranean, and Eastern Europe. His travel in the southern United States included the Carolinas and New Orleans within the last 5 years.

The source of our patient's *M leprae* is unclear, but he is improving slowly with treatment co-managed by dermatology and infectious disease.

Figure 1. Skin Lesions



Numerous pink to violaceous indurated plaques without ulceration on the back and flanks.

DISCUSSION

The highest incidence of leprosy in 2016 was recorded in Southeast Asia at 75% of the global total; however, the Americas recorded a significant 15% of the global total.[1] In 2020, there were 159 new cases of leprosy reported in the United States.[6] Most cases in the United States occur in Arkansas, California, Florida, Hawaii, Louisiana, and New York.[1]

M leprae is an obligate intracellular organism with low pathogenicity that requires a genetically or immunologically susceptible host to have prolonged contact with an untreated carrier of leprosy, especially with multibacillary lepromatous leprosy.[1] Risk factors for infection include armadillo exposure and ages 5 to 15 years or over 30 years at time of exposure.[1] An average incubation period of 5 years makes it difficult to find the source of infection. The skin, peripheral nerves, upper respiratory tract, and eyes are most affected. The Ridley-Jopling and World Health Organization (WHO) classifications are used to define leprosy subtypes and guide treatment.[1]

Clinical presentation exists on a spectrum—when cell-mediated immunity is high, tuberculoid leprosy exhibits one to a few well-defined, anesthetic, paucibacillary plaques. When cell-mediated immunity is low, lepromatous leprosy exhibits innumerable infiltrative, multibacillary papules and nodules. Borderline tuberculoid leprosy presents clinically as a few, less-defined anesthetic macules and plaques, while borderline lepromatous leprosy presents clinically as numerous macules, plaques, and nodules with sensation mostly intact.[1] Accompanying features may include painless ulcerations, madarosis, and early nerve damage.[1]

Immunologic reactions may occur at any time during the disease course regardless of multidrug therapy and include reversal reaction (type 1), erythema nodosum leprosum (ENL) (type 2), and Lucio phenomenon.[7] Reversal reactions may cause significant nerve damage, ENL may cause inflammation to multiple organ systems, and Lucio phenomenon may cause necrotic ulcers.[7] Between 30% and 50% of patients with leprosy develop immunologic reactions, most commonly in patients with lepromatous and borderline subtypes.[8] As these are the most common subtypes occurring in the United States, it is important to identify these reactions early and to treat emergently to prevent further morbidity.[8]

Our patient's presentation emphasizes that leprosy may present with nonspecific findings of elevated inflammatory markers and with features suggesting a rheumatologic disorder. The diagnosis of leprosy relies on exposure identification, travel history, and clinical features, including anesthetic, hypopigmented skin lesions and motor neuropathy.[1] Our patient did not have a recent travel history, which emphasizes the indolent nature of this infection. It is important to include leprosy on the differential diagnosis when one or more of these risk factors and findings are noted.

Skin biopsy in leprosy is a readily accessible piece of diagnostic information that should be utilized when this infection is suspected. Histopathologic examination and PCR testing are the most used diagnostic modalities in the United States.[9] While expensive and labor-intensive in most endemic countries, PCR is free of charge at the NHDP and, therefore, commonly used in

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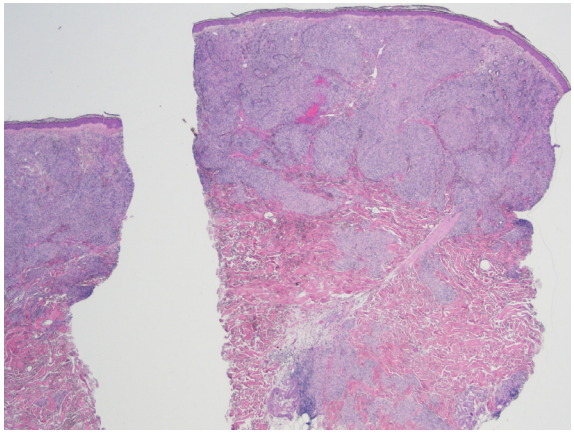
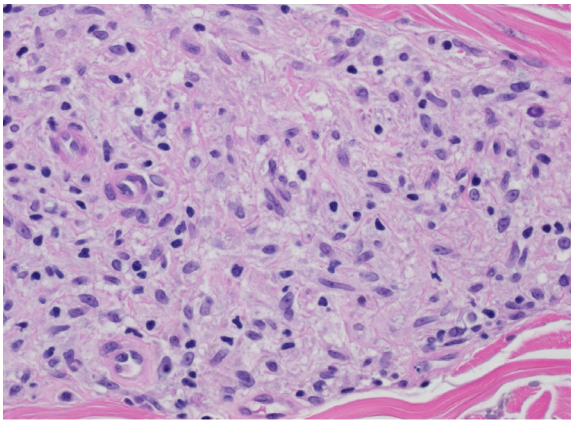
Figure 2. Dermatopathology



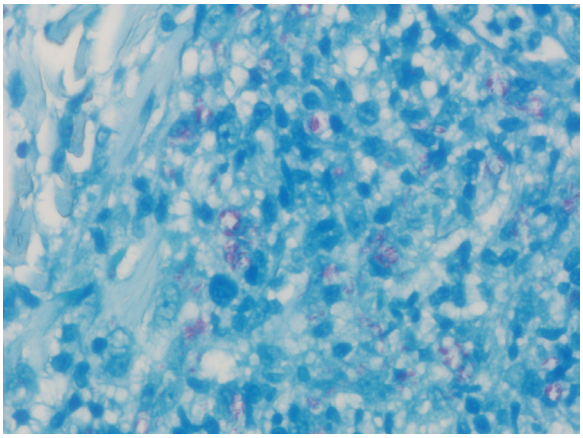
x20 hematoxylin and eosin stain



x400 hematoxylin and eosin stain

Throughout the dermis is a nodular, vaguely linear, and sheet-like infiltrate of histiocytes forming multinucleated collections with minimal associated lymphocytic inflammation.

Figure 3. Fite Stain, x600



Special staining, with appropriate controls, shows innumerable Fite-positive acid-fast bacilli.

the United States to support a leprosy diagnosis. Treatment with multidrug therapy is subtype dependent, and the WHO and the NHDP provide separate recommendations on specific antibiotics and treatment durations.[1,3,8,9]

CONCLUSIONS

Cases of leprosy in developed countries remain low but still persist, including in the United States. We present this case of leprosy in a Wisconsinite with remote history of risk factors to highlight the key clinical, histologic, current molecular, and therapeutic features of this rare but life-threatening infection to aid clinicians and patients in its early diagnosis.

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