Diagnosis of Leprosy Using Sural Nerve Biopsy Findings: A Case Report

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ABSTRACT

Leprosy, also known as Hansen disease, is an uncommon chronic disease caused by the slowly growing acid-fast bacilli, Mycobacterium leprae. Leprosy has tropism for peripheral nerves and skin and can also be found in the upper respiratory tract, eyes, and nasal mucosa. When left untreated, there can be considerable nerve damage resulting in paralysis, blindness, and the crippling of hands and feet. Although infrequent in the United States, leprosy has been diagnosed in patients exposed to armadillos, an animal reservoir. We describe an 80-year-old man who presented with a 6-year history of chronic erythematous, macular rash, and progressive symmetric sensory motor neuropathy. Initially, it was thought that the patient had an eczematous rash; however, he was later diagnosed with polar lepromatous disease owing to findings from a sural nerve biopsy. When results of clinical examination and skin biopsy are inconclusive, use of a peripheral nerve biopsy may help confirm leprosy.

Keywords: Leprosy, Hansen Disease, Sural Nerve Biopsy

INTRODUCTION

Leprosy, also known as Hansen disease, is caused by the slowly growing acid-fast bacilli, Mycobacterium leprae, infecting the skin and peripheral nerves. Most leprosy cases occur in developing countries. Countries with high incidence rates include India, Brazil, Indonesia, Bangladesh, and Nigeria. In the United States (US), a few hundred new diagnoses are reported each year. About 75% of affected patients immigrated to the US or have traveled to endemic countries. It is suggested that leprosy is spread through the respiratory route, although the means of transmission are not fully understood. In the US, leprosy is also a zoonotic disease, passed between humans and armadillos. Other risk factors include old age, genetic predisposition, immunosuppression, and close contact with known cases.

Leprosy is classified into the following categories: tuberculoid, borderline tuberculoid, mid-borderline, borderline lepromatous, lepromatous, and indeterminate. Patients with a high degree of cell-mediated immunity and delayed hypersensitivity present as tuberculoid with relatively few well-demarcated lesions. Patients with no apparent resistance to Mycobacterium leprae present as lepromatous with many poorly demarcated lesions. Patients in the other categories can present with a spectrum of symptoms between tuberculoid and lepromatous. Early physical examination findings include: hypopigmented or reddish skin patches, diminished sensation or loss of sensation in involved areas, paresthesias, painless wounds or burns, and tender enlarged peripheral nerves. Neuropathy and ophthalmic injury can also occur. The diagnosis is established when at least one of these physical findings is present, and skin biopsy findings (obtained from the leading edge of the skin lesion) confirm the presence of acid-fast bacilli in a cutaneous nerve. Alternatively, sural nerve biopsy findings can confirm diagnosis.

When other diagnoses have been ruled out, leprosy should be in the differential for patients who present with skin manifestations and progressive neuropathy. Early diagnosis and a full course of treatment are critical for preventing lifelong neuropathy and disability. Often, diagnosis is delayed owing to potentially fragmented care and unfamiliarity with the rare disease in the US. We describe an older man who was diagnosed with leprosy 6 years after onset of symptoms.
CASE REPORT

An 80-year-old Hispanic man, born and residing in the US, presented for an assessment of hand contracture. His medical history included Parkinson disease. Before retirement, he had traveled for work in South America, including Brazil and Mexico. The patient did not recall any close contacts with individuals who may have had Hansen disease, and thus he was unsure about the source.

Six years before his current presentation, the patient developed an erythematous macular rash on his extremities, which progressed to his trunk and back. He did not recall if there was hypoesthesia associated with the lesions. His skin lesions were initially diagnosed as eczema. After 3 years of failed treatment, skin biopsies were performed revealing superficial and deep perivascular lymphohistiocytic infiltrates that were suggestive of infection. Immunohistochemical stains were negative for *Treponema pallidum* but showed rod-shaped microorganisms in areas containing histiocytes. Acid-fast bacilli smear and culture were negative for *mycobacterium*. Fungal and routine bacterial cultures were negative. *Treponema pallidum* antibody and QuantiFERON Gold were both nonreactive. Subsequently, the diagnosis of leprosy was not considered definitive at that time. The lesions did not resolve and continued to be nonpruritic and hypoesthetic.

The patient developed numbness (associated with tingling and paresthesias) in both upper and lower extremities. At that time, electromyography findings were normal. He was seen at multiple facilities during the next few years for treatment of progressive sensorimotor neuropathy in all extremities due to unclear causes before progressing to his current level of disability. Other symptoms included the chronic rash, mild left lagophthalmos, madarosis, and a nonobstructive lesion on the left vocal fold.

He was referred to an orthopaedic surgeon (EAM) and noted the following concerns: lack of sensation in his lower extremities distal to his knees, minimal sensation in his hands to his elbows, contractures of both of his hands, and left foot drop. Findings of sural nerve biopsy using Fite staining revealed many acid-fast organisms, severe intraneural mononuclear inflammation, destruction of axon and myelin, and involvement of the blood vessel wall with luminal narrowing but without fibrinoid necrosis. Findings of 16S ribosomal molecular testing were positive for *Mycobacterium leprae* complex; however, no *Mycobacterium tuberculosis* was detected. There were no distinct granulomas on nerve biopsy findings. Biopsy results were consistent with polar lepromatous disease (Figures 1A through 1D).

It was determined that the hand contractures were likely caused by considerable imbalance.

![Figure 1. Various stains of the sural nerve biopsy. A) Haemotoxylin and eosin stain shows axonal and myelin destruction and blood vessel wall involvement with luminal narrowing but without fibrinoid necrosis. Axons, light blue; blood vessels, light pink; and epithelium enclosing pink-red stained lumen. B) Cluster of differentiation 68 (CD68) immunohistochemical stain shows dark brown CD68 staining of intracellular granules in monocytes, representing intraneural mononuclear inflammation. C) Sevier-Munger silver stain shows differentiation of histological features within the nerve tissue. Axons, black; myelin sheath, light brown; and collagen and muscle, brown. D) Fite acid-fast stain, revealing *Mycobacterium leprae* as indicated by pink clusters of bacilli.](image-url)
involving severe weakness of his intrinsic muscles. At presentation to our clinic, the patient had developed contractures of multiple fingers. After discussing treatment options with the patient, surgical treatment was not recommended because of uncertainty that the benefits would outweigh the risks. He was subsequently referred to physical therapy. Recommendations were considered for immunosuppressive therapy to prevent further nerve damage.

Shortly after definitive diagnosis, the patient was prescribed antibiotics by the infectious disease specialist (KSS). After consultation with the National Hansen’s Disease Program in Louisiana, the oral regimen was started and included 500 mg of clarithromycin extended-release tablets daily, 100 mg of minocycline daily, and 600 mg of rifampin monthly to be taken for at least 1 year. The patient was not a risk to infect others, thus he did not require decreased contact with the public.

**DISCUSSION**

Leprosy should be considered as a diagnosis in patients with skin lesions, enlarged nerves, and sensory loss. Loss of sensory perception occurs in the early stages of leprosy. Preventing or minimizing injury to peripheral nerves is a major goal of treatment; therefore, assessment of peripheral nerves is essential. In a prospective study of early neuropathy diagnosis in leprosy, sensory nerve conduction and warmth perception were the earliest and most frequently affected tests. Nerve trunks involved include the ulnar and median nerves, common peroneal nerve, posterior tibial nerve, facial nerve, radial cutaneous nerve, and great auricular nerve. Deficits associated with the involved nerve trunks include claw hand, foot drop, claw toes, plantar insensitivity, and lagophthalmos. Nerve biopsy findings are important in confirming the diagnosis of leprosy, usually from the sural, superficial radial, or dorsal branch of the cubital nerves. Histopathological features of leprosy lesions in the skin and peripheral nerve may have discrepancies. Biopsy is also useful for evaluating the effectiveness of treatment.

On sural nerve biopsy, polar lepromatous leprosy is characterized by firm, cord-like thickening of the peripheral nerves, which is the result of extensive fibrosis. There is extensive loss of nerve fiber and an increase in endoneurial collagen. Infiltration with foamy macrophages and an absence of lymphocytes are prominent. The perineurium may be thick and extensively multilayered. The subperineurial area may contain a granular proteinaceous matrix and pockets of collagen. Numerous bacilli are seen in the foamy macrophages, and Schwann cells are frequently packed in clusters or bundles. In the absence of any infiltrating cells, it is common to find Schwann cells loaded with bacilli in a clinically cord-like nerve from an untreated polar lepromatous case (Figures 2). Although fibrosis in our patient’s specimen was mild to moderate and CD8 positive lymphocytes were present in numbers nearly equivalent to those of macrophages, the quantity of organisms was quite high and the histologic appearance appeared more consistent with a less inflammatory category of disease.

Our patient presented with symptoms of chronic lepromatous leprosy. He had notable physical deficits because of the delay in diagnosis due to fragmented care and the rareness of this disease. His skin lesions and neuropathy did not have a conclusive diagnosis until the findings of a sural nerve biopsy. Although risks of sural nerve biopsies include infection and increased pain, the biopsy is recommended in patients with considerably progressive symptoms, dense sensory loss in the associated nerve territory, and inconclusive findings from less invasive testing such as skin biopsies. Notably, obtaining a skin biopsy presents minimal risk to the patient and should thus be obtained early. However, findings of sural nerve biopsy can prove helpful when skin biopsy results are inconclusive in patients with progressive neurological deficits.

![Figure 2](image-url)
REFERENCES