The Wide Range of Clinical Manifestations in Leprous Neuropathy: Two Case Reports

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Abstract

The present report describes two patients with leprous neuropathy diagnosed in Japan and manifesting with different clinical features. A 78-year-old Japanese man presented with a 3-year history of numbness and weakness affecting the upper and lower extremities. Although he did not have skin eruptions, nerve biopsy revealed acid-fast bacilli. Another patient, a 41-year-old Japanese-Brazilian man, presented with a 1-month history of numbness in the right fourth and fifth fingers and whole-body erythema. These cases highlight the fact that, as a result of worldwide travel and immigration, leprosy should still be considered in the differential diagnosis of neuropathy in developed countries.

Key words: leprosy, neuropathy, perineuritis


Introduction

Leprosy, a chronic infectious disease caused by Mycobacterium leprae, predominantly affects the skin and peripheral nerves (1, 2). Because the disease causes significant social, economic and psychologic problems due to physical incapacity, early diagnosis and treatment is important. The course and clinical manifestations of the disease are largely dependent on the degree of cell-mediated immune response of the host (3, 4). The clinical features of leprosy are variable and can be roughly classified according to tuberculoid, borderline, and lepromatous forms (2, 3). Multiple-drug therapy has facilitated the treatment of this disease, and physicians should be aware of its variable manifestations (5).

Due to the effort to integrate leprosy services into existing general health services in most endemic countries, the prevalence of the disease has decreased to less than 1 per 10,000 people in many regions (6). However, higher prevalences persist in some areas; for example, the prevalence exceeds 2 per 10,000 people in Brazil (6). The recent increase of worldwide travel and immigration may increase the chance of spread of the disease.

In this report, we describe two patients with leprous neuropathy in Japan that manifested with different clinical features.

Case Report

Case 1

A 78-year-old Japanese man noted numbness in the distal portions of the lower extremities beginning 3 years prior to admission to our hospital. Numbness in the distal portions of the upper extremities appeared 2 years later, followed by weakness in the distal portions of the extremities. Symptoms grew worse, and he was seen by a consulting neurologist and then admitted to our hospital.

The patient had no significant past medical history or family history of disease. Neurological examination revealed severe weakness in the distal portion of the upper extremities. Muscle atrophy was evident in both hands (Fig. 1A and B). Atrophy of interossei and lumbrical muscles was especially prominent, and claw hand deformity was observed. Mild muscle weakness was present in the distal portion of the lower extremities. Strength of the muscle in the proximal portions of the limbs was normal. Loss of all-modality of sensation was observed in the extremities dis-
Figure 1. Representative photographs from Case 1 (A to D) and Case 2 (E and F). Atrophy of interossei and lumbral muscles was prominent, and claw hand deformity was observed in both hands (A and B). A sural nerve biopsy specimen revealed massive perineurial mononuclear cellular infiltration (arrowheads) (C). Epithelioid cells were abundant and sometimes formed granulomas in the endoneurium (D). Erythematous macules were observed. Skin smear from the erythematous lesion showed acid-fast bacilli by Fite’s stain (Fig. 1F).

Laboratory examination showed slightly elevated erythrocyte sedimentation rate (35 mm/hr) and C-reactive protein (1.1 mg/dL) with a normal white blood cell count (5,000/mm$^3$). Cerebrospinal fluid examination revealed 1 cell/mm$^3$ with a protein content of 49 mg/dL. A nerve conduction study in the right median nerve revealed motor conduction velocity of 34 m/s and compound muscle action potential of 6.5 mV. Compound muscle action potentials in the left median, bilateral ulnar, and right tibial nerves were not elicited. Sensory nerve action potentials in the bilateral median, bilateral ulnar, and right sural nerves were not elicited.

A sural nerve biopsy specimen revealed prominent hypertrophy of nerve trunk with massive perineurial mononuclear cellular infiltration (Fig. 1C). Destruction of endoneurial structures was prominent, and myelinated fibers were almost completely lost. Epithelioid cells were abundant, sometimes forming granulomas in the endoneurium (Fig. 1D). Fite’s acid fast stain revealed rare acid-fast bacilli. Myelinated fiber loss was confirmed in epoxy resin-embedded transverse sections stained with toluidine blue.
The patient was diagnosed with a paucibacillary, tuberculous form of leprosy, and combination therapy with diaphenylsulfone and rifampicin was initiated. Erythrocyte sedimentation rate and C-reactive protein were normalized after 1 month of therapy. Although there was mild improvement in sensory function, subjective numbness and muscle strength did not change.

Case 2

A 41-year-old Japanese-Brazilian man noted numbness in the fourth and fifth fingers of the right hand 1 month before consultation at our hospital. An erythematous macule arose on his forehead 1 week prior to onset of numbness (Fig. 1E). The patient then experienced onset of progressive cutaneous erythema, and, after being seen by a dermatologist, he was admitted to our hospital. Neurologic consultation was obtained at that time.

The patient had no significant past medical history or family history of disease. Upon examination, mild ulnar palsy was present in the right hand, and prominent erythematous macules were observed throughout the body. Pain and thermal sensations were decreased on areas of erythematous macules and in the ulnar side of the fourth finger and fifth finger of the right hand. Otherwise, vibration, joint, pain, and thermal sensations were preserved in the distal portions of the upper and lower extremities. Although muscle atrophy was not evident, strength of adductor pollicis muscle, abductor digiti minimi muscle, and interossei dorsales muscle were mildly decreased. Deep tendon reflexes were preserved in the upper and lower limbs. Plantar responses were flexor on both sides. Consciousness was intact, and cranial nerve function was normal except for decreased sensation in the erythematous lesions.

Routine blood and urine analyses, including inflammatory indices, revealed no abnormalities. On nerve conduction studies, sensory nerve action potentials could not be evoked in the right ulnar nerve. Other indices of nerve conduction studies were preserved in the upper and lower extremities. Skin smear from an erythematous lesion showed acid-fast bacilli by Fite’s stain (Fig. 1F).

The patient was diagnosed with a multibacillary, lepromatous form of leprosy, and combination therapy with diaphenylsulfone, rifampicin, and clofazimine was initiated. Three days after initiation of treatment, reduction of erythema was observed. Symptoms of ulnar nerve palsy were subsequently decreased.

Discussion

The two cases in the present study presented with different clinical manifestations. Leprosy can be classified into three major clinical subtypes based on the extent of cell-mediated immune response of the host: lepromatous, tuberculoid, and borderline leprosy (2, 3). In the tuberculoid form, bacilli induce a cell-mediated inflammatory response so that few bacilli are found in the affected tissue. This scenario is consistent with that observed in Case 1 in the present study. By contrast, the inflammatory response in the host is attenuated in the lepromatous form, which is consistent with the massive presence of bacilli in skin lesions in Case 2. Borderline leprosy, as its name implies, has features that lie somewhere between the two other extremes of this disease.

Leprosy is uncommon in Japan. However, due to increasing travel and immigration, physicians should still be aware of the variable clinical features of leprosy and consider this diagnosis when patients present with suggestive symptoms. Indeed, leprosy must be considered in the differential diagnosis of peripheral neuropathy, even in the absence of skin lesion (as illustrated by Case 1) and especially when present in a patient from an endemic country (5, 7). Tissue analysis is helpful and is often necessary to confirm and classify the disease. Histological diagnosis can be made on tissue from skin lesions in some cases (as in Case 2), but nerve biopsy is often required and can reveal this diagnosis in an apparently idiopathic peripheral neuropathy (8, 9). Indeed, nerve biopsy is requisite to confirm the diagnosis of leprosy in patients without skin lesion as in Case 1. Because tuberculoid leprosy is characterized by granulomas and few bacilli, sarcoidosis should also be considered in the differential diagnosis (10). In fact, sarcoid neuropathy was initially suspected after nerve biopsy in Case 1. However, the absence of corroborative signs of sarcoidosis on laboratory and radiological examinations led to Fite’s staining to detect acid-fast bacilli. The distribution of granulomas can assist in the differentiation of sarcoid neuropathy from leprous neuropathy; granulomas tend to be found in the epineurium in sarcoid neuropathy and in the endoneurium in leprous neuropathy (10).

Diagnosis of leprous neuropathy is difficult without a high index of clinical suspicion, particularly in countries with a low prevalence. Since leprosy is a disease that can lead to severe functional impairment and physical disfigurement, clinicians should consider this potential diagnosis in order to facilitate early diagnosis and treatment.

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