Pearls & Oy-sters: "Quiet Nerve Paralysis" due to Symmetrical Neuropathy in Pure Neuritic Leprosy

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Pearls

- Pure neuritic leprosy involves single or multiple nerves, often in different limbs (mononeuritis multiplex); however, it may rarely present with symmetrical distal neuropathy, referred to as "mononeuritis multiplex summation."
- Initial asymmetry and brisk deep tendon jerks, along with distal symmetrical motor weakness may indicate leprosy.

Oy-sters

- Nearly half of patients initially presenting with pure neuritic leprosy have paresis and deformities ("quiet nerve paralysis") due to the lack of telltale skin manifestations of leprosy.
- Absence of thickened nerves in pure neuritic leprosy may be due to lepromatous leprosy that shows the presence of numerous acid-fast bacilli but without any evidence of nerve inflammation on histopathology of nerve.
- In patients with distal polyneuritis, low threshold for nerve biopsy and use of special stains for *Mycobacterium leprae* may facilitate early diagnosis of quiet nerve paralysis.

A 27-year-old man from Uttar Pradesh (Northern India) presented with weakness and loss of sensation in 4 limbs for the past 10 months. He first noticed decreased sensation and pain in the dorsum of his right foot, which spread to his left foot within 1 month. He reported weakness in the right foot with foot drop that progressed to the entire leg within a month. Subsequently, he noticed similar weakness in the left foot with foot drop. After 3 months, the patient had lost sensation in both hands and legs and reported loss of grip strength. He did not have neck pain, girdle-like sensation, bowel or bladder incontinence, flexor spasm, diplopia, dysphagia, or dysarthria. There was no history of fever, joint pain, skin rashes, oral ulcers, sweating abnormality, palpitations, postural giddiness, or dryness of mouth or eyes. He denied a history of substance abuse or exposure to drugs or toxins. He was neither diabetic nor hypertensive.

On physical examination, the patient had clawing of both hands, wasting of thenar and hypothenar muscles, and bilateral foot drop. Deep tendon reflexes were brisk throughout. Sensory examination demonstrated stocking-glove loss of pinprick and hot/cold sensation to the midforearm and midcalf. However, there were no thickened or tender peripheral nerves or skin lesions.

Laboratory investigations for renal, liver, and thyroid function along with blood counts were in the normal range. Fasting, postprandial, and oral glucose tolerance tests to examine blood sugar profile were also normal. Glycosylated hemoglobin was 5.6% (normal 4%–5.6%). Laboratory investigation revealed normocytic normochromic red blood cells with no immature cells. Blood levels of vitamin B_{12} and folate were normal. Erythrocyte sedimentation rate was 50 mm within 1 hour of sampling. Testing was negative for antinuclear antibody and markers of systemic

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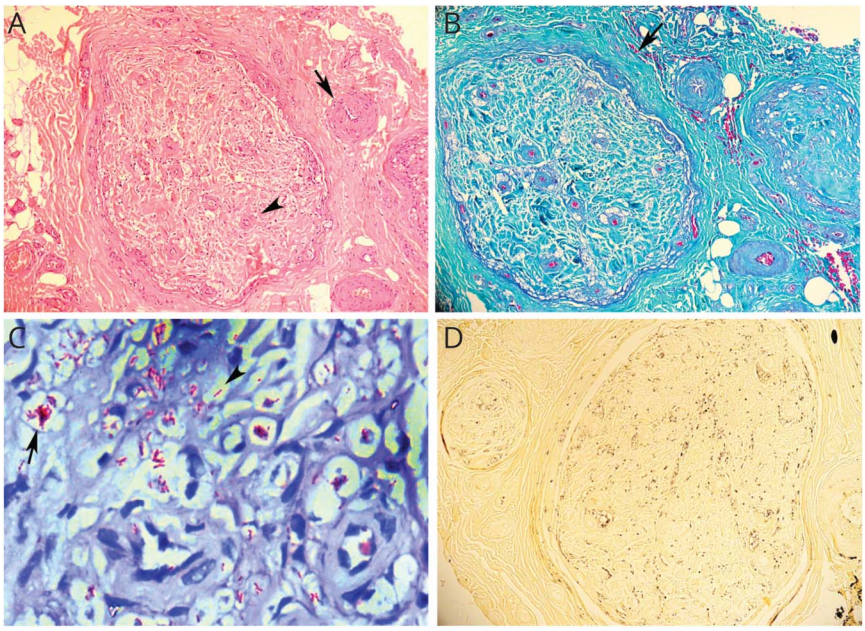
Figure Histopathology of Nerve Showing Features of Lepromatous Leprosy



(A) Nerve biopsy reveals maintained fascicular architecture with thickened endoneurial and perineurial vessels (arrow) and proliferation of Schwann cells (arrowhead; hematoxylin & eosin stain, 40×). (B) There is marked perineurial thickening and fibrosis (Masson trichrome stain, 40×). (C) Wade-Fite stain (oil immersion) reveals numerous acid-fast bacilli and foam cells filled with masses of bacilli (globi) (arrow). (D) K-Pal stain (20×) reveals reduction in myelinated nerve fibers.

vasculitis (i.e., antinuclear antibody, anti-double-stranded DNA, extractable nuclear antigen, antineutrophil cytoplasmic antibodies, rheumatoid factor). Furthermore, serum protein electrophoresis did not reveal monoclonal bands. Serologic testing for HIV and hepatitis B and C were negative. Split-skin smear test did not show acid-fast bacilli. A nerve conduction study could not record ulnar, radial, common peroneal, posterior tibial, or left median nerve compound muscle action potentials (CMAPs). Right median nerve showed reduced CMAP along with normal distal latency and conduction velocity. Sensory nerve action potentials were unrecordable in the upper and lower limbs. Biopsy of the left sural nerve was examined due to concern for nonsystemic vasculitic neuropathy. Histopathology examination revealed foam cell infiltrates in endoneurial and perineurial spaces with numerous lepra bacilli and globi (figure). Diagnosis of lepromatous neuritis was confirmed and the patient was treated with multidrug therapy (multibacillary regimen) including dapsone 100 mg daily, rifampicin 600 mg once monthly, and clofazimine 300 mg once monthly. Clofazimine 50 mg daily along with oral prednisolone 40 mg daily was also started. After 2 months, there was 50% improvement in handgrip. However, there was no improvement in the sensation in the hands and no improvement in sensations and motor weakness of the legs.

Discussion

According to the WHO, the global prevalence of leprosy in 2018 was 0.2 cases per 10,000 people (208,619 new cases). In 2018, India and the United States registered 8.89 and 0.05 new cases per 100,000 population, respectively.[1]

Pure neuritic leprosy (PNL) is manifested in around 4%–18% of patients with leprosy.[2] PNL commonly involves a single nerve trunk (mononeuritis); however, in some cases, more than 1 nerve is involved in the same or a different limb (mononeuritis multiplex). PNL is characterized by sensory loss, motor weakness (mixed nerves), absence of skin lesions, and variably thickened and tender nerves. Lack of acid-fast bacilli on split skin smear and a positive lepromin test are also important features. Symmetrical polyneuritis is uncommon in PNL. However, if a polyneuritis pattern is observed, a diagnosis of "mononeuritis multiplex summation" is used.[3-5] Symmetrical neuropathy in leprosy is not due to axonal dying-back phenomenon, as seen in most metabolic neuropathies. Instead, this is likely due to sequential summation of involved nerve trunks, leading to a symmetrical pattern of neuropathy. Early asymmetry points towards a preceding mononeuritis multiplex neuropathy. Preserved or brisk deep tendon reflexes in advanced disease with foot drop and claw hands also indicate progression towards leprosy.[6] It has been reported that the involved nerve trunks becomes irritable in advanced disease, resulting in lively deep tendon jerks.[5] Recent reports suggest involvement of spinal cord in leprosy.[7,8] *Mycobacterium leprae* resides in the dorsal root ganglia and may cause subclinical involvement of the spinal cord that might explain the occurrence of brisk deep tendon jerks despite distal paresis.

The initial diagnosis of PNL is difficult due to the absence of skin lesions. Most patients seek attention only after sustaining sensory loss or motor weakness. A variable proportion of cases may have intermittent type 1 lepra reaction that causes increased nerve pain, tenderness, and exacerbation of deficits, but without the appearance of skin lesions.[2] However, many

patients may have only a low-grade nerve inflammation, leading to incessant nerve damage and silent paresis and deformities (quiet nerve paralysis).[3,9] Nearly half of all patients with PNL present with deformities as an early sign.[2] The absence of thickened nerves in the present case might be due to a lepromatous pattern of nerve involvement and relative absence of inflammation.

The histopathologic spectrum of PNL varies from tuberculoid changes that are characterized by numerous epithelioid cell granulomas and giant cells to lepromatous changes. The latter is characterized by large numbers of acid-fast bacilli. For therapeutic purposes, the widely used WHO classification divides leprosy into paucibacillary and multibacillary leprosy based on the number of skin lesions and findings of split skin smear. In PNL, neither finding is seen, and therefore WHO classification is not applicable for determining a treatment regimen in such cases. Most patients with PNL have tuberculoid or borderline pathology, which is compatible with the classification of paucibacillary leprosy. However, nerve biopsy must be performed in order to make this determination.

The current patient had lepromatous pathology and was managed with treatment regimen for multibacillary leprosy. Intermittent acute neuritis is treated with corticosteroids in dosage and duration similar to type 1 lepra reaction due to lack of clear guidelines for treating this condition. Therefore, during treatment, paralysis should be monitored for the appearance of quiet nerve paralysis. Most physicians consider tapering the doses of corticosteroids as a treatment strategy.[10] Residual sensory, motor, and sudomotor changes secondary to nerve fibrosis are seen in 38%–79% of all patients with PNL despite adequate treatment.

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Disclosure

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Pratishtha Sengar, DNB	Department of Pathology, SGPGIMS, Lucknow, India	Collected clinical and pathologic data and wrote the rough draft
Ritu Verma, MD	Department of Pathology, SGPGIMS, Lucknow, India	Conception and drafting of manuscript
Varun Kumar Singh, DM	Department of Neurology, SGPGIMS, Lucknow, India	Drafted clinical details of the patient
Vimal Kumar Paliwal, DM	Department of Neurology, SGPGIMS, Lucknow, India	Drafting of manuscript

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