ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 01 | January - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A CASE OF AFB NEGATIVE PURE NEURITIC LEPROSY : PRESENTED AS MONONEURITIS MULTIPLEX DIAGNOSED BY PCR - A CASE REPORT

Internal Medicine

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ABSTRACT

Pure Neuritic Leprosy, defined as a peripheral neuropathy in which the patient has no dermatological manifestation, is difficult to diagnose. Its diagnosis by bacteriological index and histopathology is not possible in the majority of the patient. Mononeuritis multiplex (MM) refers to involvement of several or many peripheral nerves at the same or different points in time by a disease process.This report describes a case of an atypical presentation of Hansen's disease (HD) as mononeuritis multiplex in the left lower limb and right upper limb with corresponding electrodiagnostic and molecular data that confirmed pure neuritic leprosy (PNL). The incidence of PNL is exceedingly low, still leprosy is the commonest cause of MM in the Indian subcontinent. It is important that the treating physician should also know the various neurological presentations, both mimics and chameleons, of this treatable disease to prevent permanent neuropathic injury and disability. Although Mononeuropathy is most common in PNL, the mononeuritis multiplex as the sole clinical presenting phenotype is quite uncommon. The case illustrated underscores the need to foster inter-speciality awareness because of the curable nature of the disease.

KEYWORDS

Hensen's disease, Pure Neuritic Leprosy, Mononeuritis Multiplex, Molecular Study - Nerve Biopsy

INTRODUCTION

Leprosy (also known as Hansen's disease) is an infectious disease caused by Mycobacterium leprae and Mycobacterium lepromatosis that involves the skin and peripheral nerves.

M. leprae and M. lepromatosis comprise "Mycobacterium leprae complex" . The DNA sequences of M. leprae and M. lepromatosis differ enough to distinguish them as separate species, but they share many similarities (both are obligate intracellular parasites with a tropism for nerves) and cause the same clinical disease .

Leprosy is an important global health concern. Contrary to popular folklore, leprosy is not highly contagious, and very effective treatment is available . Early diagnosis and treatment are necessary to minimize the likelihood of disability involving the eyes, hands, and feet due to neuropathy as these are often not reversible and may require lifelong care

Case Report

A 43 yeras old male laborer came with complaints of numbness of left lower limb since 2 years and right hand since 1 year. Over a span of two years , he noted sequential progression in his numbness to involve the lateral aspect and heel/calcaneal area of left sole, then the medial aspect of the left sole and finally the anterolateral aspect and shin area of his left leg. After 6 months he also noticed loss of temperature sensation and numbness in right hand. After 1 year he noticed slipping of his footwear from the left leg and left foot drop . These symptoms were not accompanied by trophic ulcers, painless wounds, skin changes, positive sensory neuropathic symptoms (tingling, paresthesia, dysesthesia) or evidence of cranial neuropathies. There was no history of skin lesions, contact with a person suffering from leprosy or a family history of neuropathy.

General physical and systemic examination proved unremarkable. Positive neurological findings were In the form of loss of pin prick sensation and temperature with preserved proprioception on the left side below the knee , right hand and motor weakness in the form of foot drop on the left side. There were no cutaneous lesions suggestive of leprosy, trophic ulcers or deformities.

Investigations were directed towards mononeuritis multiplex. Complete hemogram, ESR, C reactive protein, fasting and postprandial blood sugars, and serum biochemistry , CSF study were normal. Vasculitis workup that included antinuclear antibodies profile, perinuclear antineutrophil cytoplasmic antibodies (pANCA) were unremarkable. Virology screening for hepatitis virus and HIV ELISA were negative.

His slit skin smear (SSS) from multiple sites for AFB-Mycobacterium leprae was negative.

Nerve conduction study was remarkable as an asymmetric multiple sensory more than motor axonal mononeuropathy multiplex.

Sural nerve biopsy was done, which on histologic examination inconclusive with m.leprae. Sural Nerve biopsy PCR for mycobacterium leprae was sent which came to be positive. On basis of that finally patient was diagnosed as pure neuritic leprosy.With the sural nerve biopsy pcr establishing the diagnosis of Hansen's disease, and the clinical phenotype of PNL presenting as sensorimotor mononeuritis multiplex, he was initiated on multibacillary multidrug therapy consisting of Dapsone 100 mg daily, Clofazimine 50 mg daily and 300 mg monthly, and rifampicin 600 mg monthly for one year. On a 1 year follow up, the patient's condition improved with no reactions during treatment and a significant improvement in both motor and sensory deficit.

DISCUSSION

Patients with leprosy, 4–8% (up to 18% in some Indian series) may present with PNL characterized by evidence of nerve deficit or thickening, with or without tenderness in the absence of skin involvement. Our patient had involvement of peripheral nerves without any skin lesions, and a split skin biopsy not revealed any evidence of leprosy. His sural nerve biopsy histologic examination also didn't show presence of AFB. On sural nerve PCR for M.leprae came positive this clinical features with nerve biopsy pcr report consistent with diagnosis of PNL.

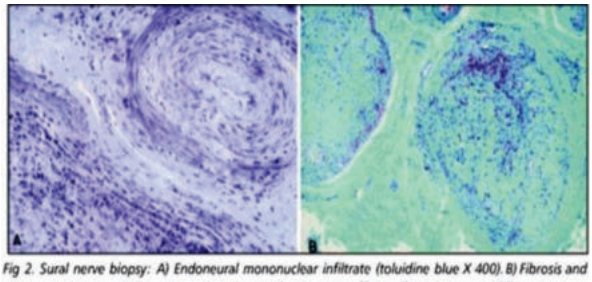

Fig 2. Sural nerve biopsy: A) Endoneural mononuclear infiltrate (toluidine blue X 400). B) Fibrosis and thickness of the endoneurium, perineurium and epineurium (Gomori's trichrome X 100).

Mycobacterium leprae infects Schwann cells and axons, causing a subacute demyelination involving larger peripheral nerve trunks and cutaneous nerves. M.laprae preferentially invades non myelin - producing Schwann cells (attaching via phenolic glycolipid 1, an *M. leprae*–specific antigen) where the organisms multiply in large numbers. After attachment of the organism, myelin-producing Schwann cells also undergo significant loss of myelination by an immune-dependent mechanism. The Schwann cells are also changed by infection, producing metabolic and functional changes that trigger the immune system in recruiting cytotoxic cells, T lymphocytes, and macrophages. The end result is unrestrained multiplication of the organism within Schwann cells, demyelination, inflammatory changes leading to axonal injury, and secondary destruction of the nerve structure .

The diagnosis of PNL can often be difficult and delayed, resulting in the presence of disability at the time of presentation. Jardim et al. assessed 67 patients with PNL and found the most common presentation was mono-neuritis multiplex, occurring in 61% of the patients, followed by mononeuropathy in 33% and polyneuropathy in only 6%. Sensory impairment occurred in 89% of all cases and motor dysfunction in 81%. Axonal neuropathy as was present in our patient was the predominant electrophysiological finding. Acid-fast bacilli were only found in 16%, and PCR for *M. leprae* was positive in 47% of the nerve biopsy samples. In a prospective study of 317 new cases of PNL in Brazil, the combined evaluation of all diagnostic tools, including PCR of the skin, EMG, symptoms and neural thickening, and ELISA anti-pepsinogen 1, demonstrated a highly variable presentation with 8.6% negative in all tests. This study reinforces the need for nerve biopsy in many cases and pcr testing from nerve biopsy sample.

Any nerve may be involved in PNL. The dorsal ulnar cutaneous, the medial/lateral antebrachial, or the superficial radial or sural nerves are most suitable for biopsy. A nerve biopsy may be limited by sampling error because most PNL patients fall into the tuberculoid or borderline tuberculoid portions of the spectrum with low bacillary load. Nerve ultrasounds may be able to reduce the sampling error because they can identify and direct the biopsy to abnormal nerves that may be subclinical. High-resolution ultrasonography is an inexpensive tool that can be used to obtain information that is static (size of the nerve, echo texture, nerve abscess) and dynamic (Doppler studies of neural blood supply). It can be used on multiple nerves and can detect focal nerve thickening (not picked up clinically), and sequential studies can be used to follow increased vascularity in leprosy reactional states. Studies have shown close correlation between abnormalities on ultrasound and nerve conduction studies in leprosy. In contrast, MRI allows a more detailed but expensive evaluation of peripheral nerves, limiting its use in leprosy, where its use is not usually necessary. Leprotic peripheral nerve involvement ranges from nerve thickening on T1- and T2-weighted images, with preserved fascicular architecture to disruption of this architecture and formation of micro-abscesses. Magnetic resonance imaging has also allowed detection of plexopathies and lesions in the spinal cord and brain. This was not used in our patient because of the multiple nerves involved and the clinical decision that his diagnosis required a nerve biopsy.

Fine needle aspiration of affected nerves for cytology, Fite staining, and PCR for *M. leprae* DNA in nerves have all been helpful. The histopathology of PNL reveals a spectrum ranging from tuberculoid to borderline lepromatous type. In lepromatous leprosy, there is extensive nerve fiber loss with a concomitant increase in endoneurial collagen, and numerous bacilli are seen in foamy macrophages.

Our patient illustrates the difficulty in making a diagnosis of PNL when there are atypical features present, despite a high index of suspicion, given his country of origin. Given the diffuse nature of his neurological involvement, it was surmised that his clinical picture would be most consistent with lepromatous leprosy, which rarely presents as PNL. In addition, he had no skin lesions or any evidence of palpable nerve trunks based on the examination by two experienced clinicians. In retrospect, it would have been helpful for him to have had an earlier nerve biopsy in addition to a blind split skin biopsy for PCR,from which nerve biopsy pcr came positive for leprosy. Biopsies of apparently normal skin from the areas of sensory change in cases of PNL have revealed microscopic evidence of nerve involvement in deep dermal tissue. There are many reports of patients with PNL developing visible skin lesions during follow-up of months and years (with and without MDT), including progression to classical borderline tuberculoid leprosy in typical patients with mononeuropathy. These findings suggest that, in leprosy, a neuritic phase precedes the development of visible cutaneous lesions.

Multidrug therapy alone is aimed at treating the infection but is insufficient in preventing the nerve damage. Unlike WHO guidelines, in India (where PNL is most common), when five or less nerve trunk is involved, it is considered paucibacillary, and when six or more than six nerve trunk is involved, it is considered multibacillary for therapeutic purposes. Prednisone remains the drug of choice for neuritis due to its ability to reduce nerve edema, act as an immunosuppressant, and decrease post inflammatory scar formation, which are all important for improving nerve function. A prospective longitudinal trial in Brazil studied 24 PNL patients who were treated with MDT (dapsone, clofazimine, and rifampin) and prednisone (1 mg/kg) tapered over the 6-month treatment period. Most of the clinical parameters showed significant improvement; EMG evidence of nerve conduction block was reduced in 42% of the patients. contributing to the prevention of further neurological damage. Cyclosporine, azathioprine, and methotrexate have all been tried as steroid sparing agents in leprous neuritis. Physical therapy and education about self-care may be required in those who have residual permanent nerve function impairment. Mutations associated with resistance to rifampin, ofloxacin, or dapsone have been identified in 7.8% specimens of PNL17 but have yet to be found to be clinically significant.

CONCLUSION

Nerve biopsy is an efficient tool to diagnose PNL and differentiate it from other causes of non-leprosy neuropathies presenting as mononeuropathy multiplex.

PCR helps in diagnosing PNL in doubtful cases. A positive PCR increases the sensitivity of detection of *M. leprae* especially in cases of probable PNL group where AFB cannot be demonstrated on histopathology.

This case is of considerable practical importance to the clinician confronted with diagnosing leprosy neuropathy without the typical dermal involvement.

REFERENCES

1) Jaiswal N, Chakraborti S, Nayak K, Pai S, Shelley BP, Sreeram S, *et al*. Hansen's neuritis revisited- A clinicopathological study. J Neurosci Rural Pract 2018;9:42-55
2) Rao PN, Suneetha S. Pure neuritic leprosy: Current status and relevance. Indian J Dermatol VenereolLeprol 2016;82:252-61
3) Mauermann ML, Burns TM. Pearls and Oy-sters: Evaluation of peripheral neuropathies Neurology 2009;72:e28-31.
4) Kumar B, Kaur I, Dogra S, Kumaran MS. Pure polyneuritic leprosy in India: An appraisal. Int J Lepr2004;72:284-90.
5) Narang T, Vinay K, Kumar S, Dogra S. A critical appraisal on pure neuritic leprosy from India after achieving WHO global target of leprosy elimination. Lepr Rev 2016;87:45663
6) Mendiratta V, Khan A, Jain A. Primary neuritic leprosy: A reappraisal at a tertiary care hospital. Indian J Lepr2006;78:261-7.
7) Kolleri JJ, Sasidharanpillai S, Vadakkayil B, Chathoth AT. A 10-year retrospective descriptive study on pure neuritic leprosy from a tertiary referral centre. Indian Dermatol Online J 2019;10:13-8.
8) Shelley BP, Shenoy MM. Revisiting Hansen's disease: Recognizing the many neurodermatologic faces and its diagnostic challenges. Arch Med Health Sci 2018;6:157-70.
9) Kumar B. Pure or primary neuritic leprosy (PNL). Lepr Rev 2016;87:450-5.