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Case Series

Pure Neuritic Leprosy : A Series of Three Cases

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Over the years, there has been significant decreasing trend in the prevalence of leprosy in India. Although the prevalence of leprosy in India is on a steady fall, the new case detection rate (NCDR) is not showing a parallel decline. The Leprosy Case Detection Campaign (LCDC), 2018 identified 363 hidden cases of leprosy in Mumbai. Polyneuritic Leprosy (PNL) has been considered relatively uncommon and reported only in 1.5% to 8.1% of leprosy patients. However, recent Indian studies have shown a greater incidence of PNL amongst all the leprosy cases diagnosed ranging from 5.5% to 18%. PNL does not present with skin lesions, hence many of them are likely to remain underdiagnosed for a long time. The patients usually visit Medicine and Neurology clinics for the symptoms and may be misinterpreted as neuropathies. The clinical suspicion of PNL is made in case of thickened peripheral nerve trunk associated with tenderness or sensory impairment and lack of skin lesions. Nerve biopsy is the gold standard for diagnosis of PNL followed by classification of cases as given by Indian Association of Leprologists (IAP 1982). We present here three cases of PNL diagnosed on nerve biopsy and discuss them in the context of review of literature.

Key words : Neuritic Leprosy, Nerve Biopsy, Fite Faraco Stain

Introduction

It is known that PNL is uncommon and has been reported only in 1.5% to 8.1% of leprosy patients. However, recent Indian studies have shown a greater incidence of PNL amongst the leprosy cases diagnosed ranging from 5.5% to 18% (Kolleri et al 2019). PNL is condition important for India and has been given due importance in Indian classification of leprosy (IAL 1982). As PNL does not present with skin lesions, many of such cases may remain underdiagnosed for a long time and may end up with disabilities. Most of the times they come to Medicine or Neurology department and are likely to be misinterpreted as demyelinating neuropathies. Since many institutes may not have experienced leprologist(s) such cases are likely to remain undiagnosed initially. Nerve biopsy is the gold standard for diagnosis of PNL. We here present three cases of PNL diagnosed on nerve biopsy.

Case Reports

We encountered these three patients who visited the outpatient of Medicine department over a span of 6 months with neurological symptoms

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only; as against 58 new cases of leprosy (with skin lesions) diagnosed during that period in the Dermatology department. The nerve biopsy was received in 10% buffered formalin. All the biopsy samples were linear membranous strips of 2.0 cm each. They were processed routinely and stained with Hematoxylin and Eosin stain. Further sections were stained with Toluidine Blue and Fite Faraco stain.

First case was a 48 year male who presented with lower limb weakness and numbness. Bladder bowel habits were normal. Sural nerve was palpable and thickened and the biopsy showed dense lymphocytic infiltration and granulomas (Fig. 1).

Our second patient was a 28-year female presenting with loss of sensation over fingers of both the hands from 15 days. No skin lesions were noted. Ulnar nerve examination did not reveal anything significant. Although sural nerve was tender. Nerve conduction study (NCS) of sural nerve suggested motor-sensory neuropathy.

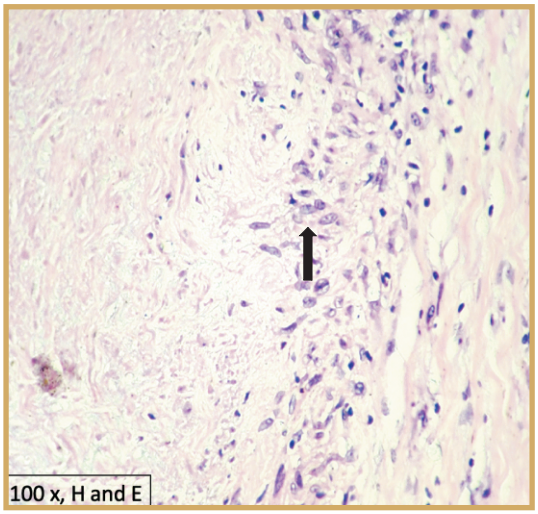

Fig. 1 : Nerve biopsy showing lymphocytic inflammation and granuloma (epithelioid cells: black arrow) in Case No. 01, (100 X, H & E)

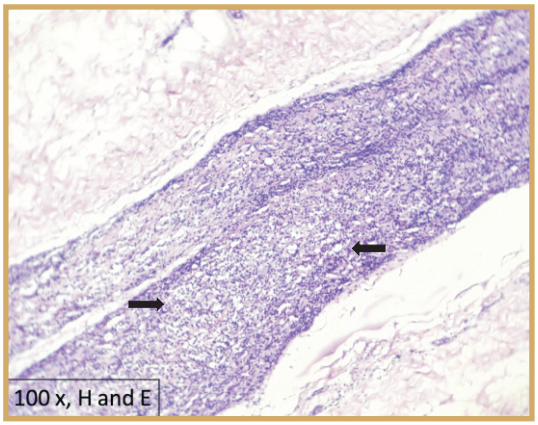

Fig. 2: Sural nerve biopsy shows dense lympho-histiocytic infiltrate within and around the nerve fibres, (100X, H&E).

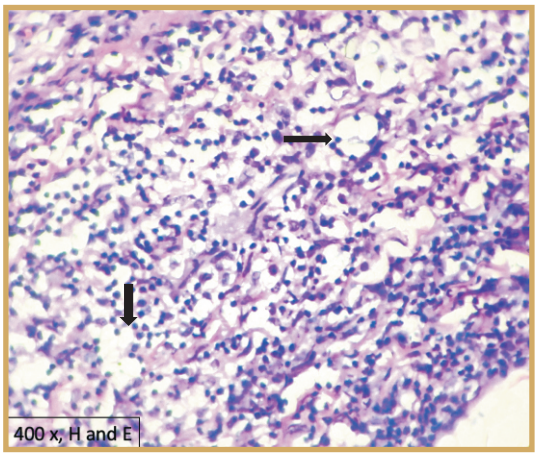

Fig. 3 : High power (400 X) view of HE staining of sural nerve biopsy showing foamy macrophages (black arrow), no granuloma in this case (seen in case 02, 03) .

Common etiological factors for peripheral neuropathy like alcoholism, toxins, trauma were ruled out. Hematological examination ruled out megaloblastic anemia. Thus, nerve biopsy was done which revealed dense lympho-histiocytic infiltrate within and around the nerve (Fig. 2). Fite

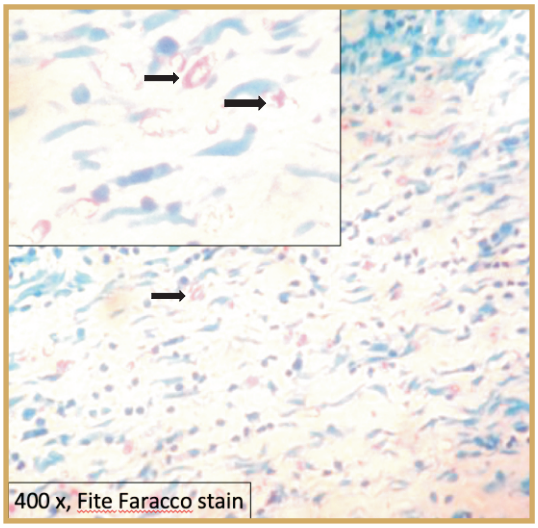

Fig. 4 : Fite Faraco staining to demonstrate AFB positivity (bacilli : black arrow) (400 X)

Faraco stain for acid fast bacilli was strongly positive (3+).

Third case was a 14 years old male with loss of sensation below knee and difficulty in squatting in the past 1 year. No skin lesions were present and there was no evidence of shiny skin or loss of hair. Clinical suspicion was leprosy v/s inflammatory polyneuropathy. Microscopic examination of thickened sural nerve showed dense lymphocytic aggregates and foamy histiocytes (Fig. 3). Fite Faraco stain revealed strong positivity (3+) for AFB/ *M. leprae* (Fig. 4).

According to the modified five-group classification by Indian Association of Leprologists (IAL 1982), all our three cases belonged to the Pure Neuritic Leprosy group (Table 1). On examination there was no evidence of skin lesions. They presented with only neurological complaints. Thus, these three cases were labelled as multibacillary type for treatment purposes according to NLEP Classification.

Discussion

Neuritic form was accepted as a subtype of leprosy in the International Leprosy Congress, Madrid in 1953 (Rao & Suneetha 2016). The definition of PNL approved by Indian Association of Leprologists IAL (1982) is, "in this type of leprosy, there are no skin lesions. Larger nerve trunks or their branches are enlarged. There is a sensory loss in the areas of distribution of the nerves. Single or multiple nerves may be involved. Skin smears are negative. Lepromin reaction is generally positive, but sometimes may be doubtful or negative. The histology could be of tuberculoid, borderline or non-specific type."

An earlier Indian study reported that PNL constituted 8.2% of the leprosy cases (Noorden 1985). A large database was studied by Dongre et al (1976) in 1976 at the Acworth Leprosy Hospital Clinic. Out of 11,581 leprosy patients, 494 (5.5%) had primary polyneuritic leprosy. Garbino (2007) from Brazil in 2007 identified 34 PNL cases in 162 leprosy patients. A retrospective study was done in Mangalore, Karnataka by Jaiswal et al (2018), out of 453 nerve biopsies received, Hansen's was diagnosed in 18 cases. A recently published study from a Tertiary care Centre in Kerala indicated PNL as an important type of leprosy (Thyyalappill et al 2019).

In our case two of the three cases studied were male patients. This corelates with the male predilection in PNL as stated in the literature (Dongre et al 1976, Rao & Suneetha 2016). Our youngest patient was 14-year male and oldest was 48-year male. Most commonly (60%) of PNL present as mononeuritis (Kumar 2016). In our cases, one patient showed neurological symptoms in bilateral upper limbs, suggestive of mononeuritis multiplex. The other two showed single nerve involvement.

Table 1 : Summary details, clinical features and histopathology of three cases studied

Age	Case 01	Case 02	Case 03
Gender	48 year	28 year	14 year
Address	Male	Female	Male
Chief complaints	Dharavi Lower Limb weakness Lower Limb numbness	Govandi Loss of sensation (touch, pain, temperature) over left ring finger, right ring finger, right little finger and bilateral ulnar side of forearm.	Dharavi Loss of sensation below knee. Difficulty in squatting.
On clinical examination	Palpable, thickened sural nerve No skin lesions	Deep peroneal nerve and bilateral anterior tibial nerve Palpable. No evidence of skin lesions.	No evidence of skin lesions
Other investigations	Advised nerve conduction studies (NCS). Lost follow-up	NCS: Asymmetric Sensory - motor mononeuropathy in Upper limb and inflammatory pathology.	Advised NCS. Lost follow-up.
Clinical suspicion	? neuritic leprosy ? demyelinating neuropathy	Pure Neuritic Hansen's (based on NCS report)	? Leprosy ? Inflammatory polyneuropathy
M/microscopic Examination	Dense lymphocytes, nerve thickening, Granuloma noted.	Lymphocytic and histiocytic infiltrate within and around the nerve. No evidence of granuloma.	Dense Lymphoplasmacytic infiltrate in endoneurium and perineurium and foamy histiocytes forming aggregates. No evidence of granuloma.
Ridley – Jopling Classification	Tuberculoid leprosy	Lepromatous leprosy	Lepromatous leprosy
IAL 1982 Special Stain	Pure Neuritic Leprosy (PNL)	Pure Neuritic Leprosy	Pure Neuritic Leprosy
(Fite Faraco : FF)	FF: occasionally positive	FF: strongly positive	FF: Strongly positive 3 +++

A recent study by Narang et al (2016) used mandatory and auxiliary for the diagnosis of PNL. Mandatory criteria included residence in endemic area, history of contact, presence of thickened nerve with sensory loss, clinical absence of skin lesions and negative slit skin smears whereas auxiliary criteria included nerve biopsy and reduced amplitude on nerve conduction. Nerve

biopsy was studied in all our patients. Nerve conduction studies were performed only in one of the patients which revealed neuropathy.

Hui et al (2015) studied in detail the histopathology findings in patients with PNL and compared it with other non-lepromatous neuropathies. They concluded that in the absence of lepra bacilli, endoneurial inflammation, endoneurial fibrosis and reduction in the number of myelinated nerves fibres are supportive indicators for probable diagnosis of PNL. In the present study we tried to evaluate the myelination by using toluidine blue the results, however, were unsatisfactory. Lepra bacilli were not identified in one case but granuloma was identified, suggestive of tuberculoid leprosy. Kulshreshtha et al (2018) in their article have emphasized a need of nerve biopsy in cases of PNL. The ability to classify patients has a significant impact on the management of the patient. NLEP guidelines advocates a categorization of cases as paucibacillary and multibacillary for treatment regimens.

There is a significant decreasing trend in the prevalence of leprosy (per 10,000 population) in India from 57.6 in 1931, 3.74 in 2002 to 0.66 in 2017, yet the new case detection rate (NCDR) is not showing a parallel decline (NLEP 2007, NLEP 2017). In this scenario, PNL has to be given special attention so as to treat these cases in time and avoid disabilities. Diagnosis of PNL is challenging as it needs a high level of suspicion by the clinicians. The possibility of missing out the cases is high due to absence of skin lesions. Thus, patients with neurological symptoms and thickened peripheral nerves should be promptly evaluated with a nerve biopsy and an accurate histopathological diagnosis. In such cases, the thickening of nerves is to be actively looked for and if feasible, should be evaluated with a nerve biopsy followed by special stain to look for acid fast bacilli. Considering the field realities, an amalgamation of clinical and histological approach would be most useful.

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