Histological Spectrum of Pure Neuritic Leprosy: Experience at Tertiary Care Centre

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INTRODUCTION

• Leprosy is still an important public health problem in India with

• Nerve involvement being a rare complication.

• Despite stringent control measures established by WHO and a consequent decrease worldwide, rate of newly detected leprosy cases remains epidemiologically high in endemic countries (WHO 2010).
INTRODUCTION

• Leprosy patients may present with peripheral neuropathy (simple or multiple mononeuropathies and/or polyneuropathy) in absence of any verifiable cutaneous lesions.

• The clinical features of leprotic nerve involvement include nerve enlargement, tenderness, pain and sensory motor impairment.

• These are not specific and not always present.

• The most commonly affected nerves: posterior tibial, peroneal, ulnar and median nerves.
DEFINITION

• Pure neuritic leprosy (PNL):
  Neural involvement by leprosy in absence of skin involvement.
• Accounts for 5-17.7% of all leprosy cases.
• Responsible for the disabilities and deformities.
• Confirmation of a PNL diagnosis requires the demonstrated presence of *Mycobacterium leprae* in a biopsy of any affected sensory nerve.
Diagnosis

• Most of the cases are diagnosed based on clinical findings.

• Nerve biopsy is required only in doubtful or challenging cases.

• *Nerve biopsy examination is an important auxiliary procedure for diagnosing pure neural leprosy (PNL)*

• Elevated levels of serum antiphenolic glycolipid antibodies (ELISA) would make a leprosy diagnosis certain, probable or possible

Jardim et al. 2005
• The gold standard: Histopathological examination of a peripheral nerve biopsy.

• It is important for a histopathologist to recognise the histological spectrum of PNL.

• Value of nerve biopsy examination increases when the results are interpreted in the context of pertinent clinical, epidemiological, electroneuromyographical and laboratory data [i.e., *M. leprae* DNA determined with polymerase chain reaction (PCR)]

AIM

To assess the histological spectrum of Pure Neuritic Leprosy
Material and Methods

• Retrospective study (January 2000 to June 2016)
• All histologically diagnosed cases of PNL were analysed.
• Biopsies were retrieved from the archives from the department of Histopathology.
• All biopsies were reviewed by 3 histopathologists.
Material and Methods.....

• Detailed demographic profiles and clinical findings were noted from the histopathology requisition proforma:
  - Duration of symptoms
  - Nerve thickness
  - Loss of sensation
  - Associated features
Material and Methods.....

- The nerve samples were fixed in 4% paraformaldehyde
- Routinely processed and embedded in paraffin for routine histopathological examination
- Haematoxylin-eosin stain to evaluate inflammatory infiltrate and cellularity
- Masson’s trichrome to assess fibrosis and nerve structure
- Ziehl Nelsen stain to detect AFB
- Luxol fast blue stain for Myelin
- IHC for Neurofilament protein
Material and Methods-Histopathology

- Detailed histopathological examination was done including special stains
  - Modified Ziehl-Neelsen
  - Luxol Fast Blue for myelin
  - IHC for neurofilament protein (NFP)

- Various histological parameters were graded from scale 0 to 3
  - 0-absent
  - 1-mild
  - 2-moderate
  - 3-marked
RESULTS

Total PNL cases during 2000-2016 (16 year) period was 20 cases.

Clinical demography

• Average age: 40.8 yrs (Range 22-82 yrs)
• Male preponderance (5.7:1)
• The suspected clinical diagnosis:
  - Hansen in 15 cases (75%)
  - Mononeuritis multiplex in 3 cases (15%)
  - Demyelination in 1 case (5%)
  - Vasculitis in 1 case (5%)
RESULTS....

Most common nerve biopsied:

- Sural nerve (14 cases, 70%)
- Ulnar nerve (3 cases, 15%)
- Radial
- Lateral cutaneous and
- Dorsal cutaneous (1 each, 5%)
RESULTS....

• Nerve biopsies in each case showed
  • Both Longitudinal and transverse section in 11 cases (55%);
  • Transverse Section only in 6 cases (30%) and
  • Longitudinal Section only in 3 cases (15%)
• Average fascicles : 5 , ranging from 3-9
• Skin biopsy in 6 patients- no e/o leprosy
Histopathological Findings (n=20)

- Perineural thickening - 19 (95%)
- Endoneural thickening - 9 (45%)
- Endoneural LM inflammation - 19 (95%)
- Perineural LM inflammation - 18 (90%)
Histopathological Findings (n=20)

- **Granuloma (n=14)**:
  - Endoneural: 14 (70%)
  - Perineural: 3 (15%)

- **Foam cells (n=13)**:
  - Endoneural: 13 (65%)
  - Perineural: 4 (20%)
  - Granuloma only: 4 (20%)
  - Foam cells only: 3 (15%)
  - Both granuloma and foam cells: 10 (50%)

- None of them: 3 (15%)
Histopathological Findings (n=20)

- **Perivascular inflammation**: Present
- **Vasculitis**: Present
- **Necrosis**: Present

Legend:
- Absent
- Present
• Lepra stain for acid fast bacilli was positive in 11 cases (55%) and negative in 9 cases (45%).

• One case showed normal histology with lepra bacilli positivity.

• There was no significant histological difference between lepra bacilli positive and negative cases.

• Myelin and Axonal loss:
  • Absent in only 1 case (5%)
  • Moderate in 4 cases (20%)
  • Severe in 15 cases (75%)
Atypical Histopathological Findings

- Vasculitis (2/20, 10%)
- Necrosis (1/20, 5%)
- Plasma cell rich inflammatory infiltrate (1/20, 5%)
- Normal morphology with Lepra positivity (1/20, 5%)
<table>
<thead>
<tr>
<th>Histological Parameters</th>
<th>AFB positive cases (11)</th>
<th>AFB negative cases (9)</th>
</tr>
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<tbody>
<tr>
<td>Perineural thickening</td>
<td>10 (90.9%)</td>
<td>9 (100%)</td>
</tr>
<tr>
<td>Endoneural thickening</td>
<td>4 (36.3%)</td>
<td>4 (44.4%)</td>
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<tr>
<td>Perineural inflammation</td>
<td>10 (90.9%)</td>
<td>9 (100%)</td>
</tr>
<tr>
<td>Endoneural inflammation</td>
<td>10 (90.9%)</td>
<td>9 (100%)</td>
</tr>
<tr>
<td>Perineural granuloma</td>
<td>2 (18.1%)</td>
<td>1 (11.1%)</td>
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<tr>
<td>Endoneural granuloma</td>
<td>9 (81.8%)</td>
<td>7 (77.7%)</td>
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<tr>
<td>Perineural foam cells</td>
<td>2 (18.1%)</td>
<td>2 (22.2%)</td>
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<tr>
<td>Endoneural Foam cells</td>
<td>8 (72.7%)</td>
<td>6 (66.6%)</td>
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<tr>
<td>Perivascular inflammation</td>
<td>10 (90.9%)</td>
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</tr>
<tr>
<td>Vasculitis</td>
<td>1 (9%)</td>
<td>1 (11.1%)</td>
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<tr>
<td>Necrosis</td>
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<tr>
<td>Myelin loss</td>
<td>10 (90.9%)</td>
<td>9 (100%)</td>
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<tr>
<td>Axonal loss</td>
<td>10 (90.9%)</td>
<td>9 (100%)</td>
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</tbody>
</table>
CONCLUSION

• Endoneural inflammation, granuloma and foam cell infiltrate are common features of PNL.
• Inflammation and granulomas can be seen in perineural space as well.
• There may be variable epineural and perineural thickening, depending on the duration of the disease.
• Myelin and axonal loss are almost universal
• Myelin stain and IHC for NFP should be performed in all cases.
CONCLUSION

• Necrosis and vasculitis can be rarely found in PNL
• Even if morphologically biopsy is normal, lepra stain should be performed in all suspected cases of PNL
• Anti-PGL1 antibodies in patient’s sera can be helpful in early diagnosis
• PCR may be done in cases with negative Lepra stain
Summary: Flowchart for the investigation of pure neuritic leprosy

1. Possible case of pure neuritic leprosy
2. Clinical and neurophysiological classification
   - Polyneuropathy
   - Mononeuritis multiplex
3. Biopsy
   - Single or multiple skin punch biopsies over skin region with altered sensation
   - Nerve biopsy of a sensory nerve in or near an area of altered sensation or an enlarged nerve
   - Nasal mucosa
4. Histological outcomes:
   - Positive Histology: Macrophage/epithelioid granulomas, +/- acid-fast bacilli, nerve inflammation. Likely pure neuritic leprosy
   - Negative Histology: Clinical follow up or consider for trial of Prednisone
THANK YOU