

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 antiphospholipid glycolipid antibodies (ELISA) would make a leprosy diagnosis certain, probable or possible

- **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 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 was 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

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.....

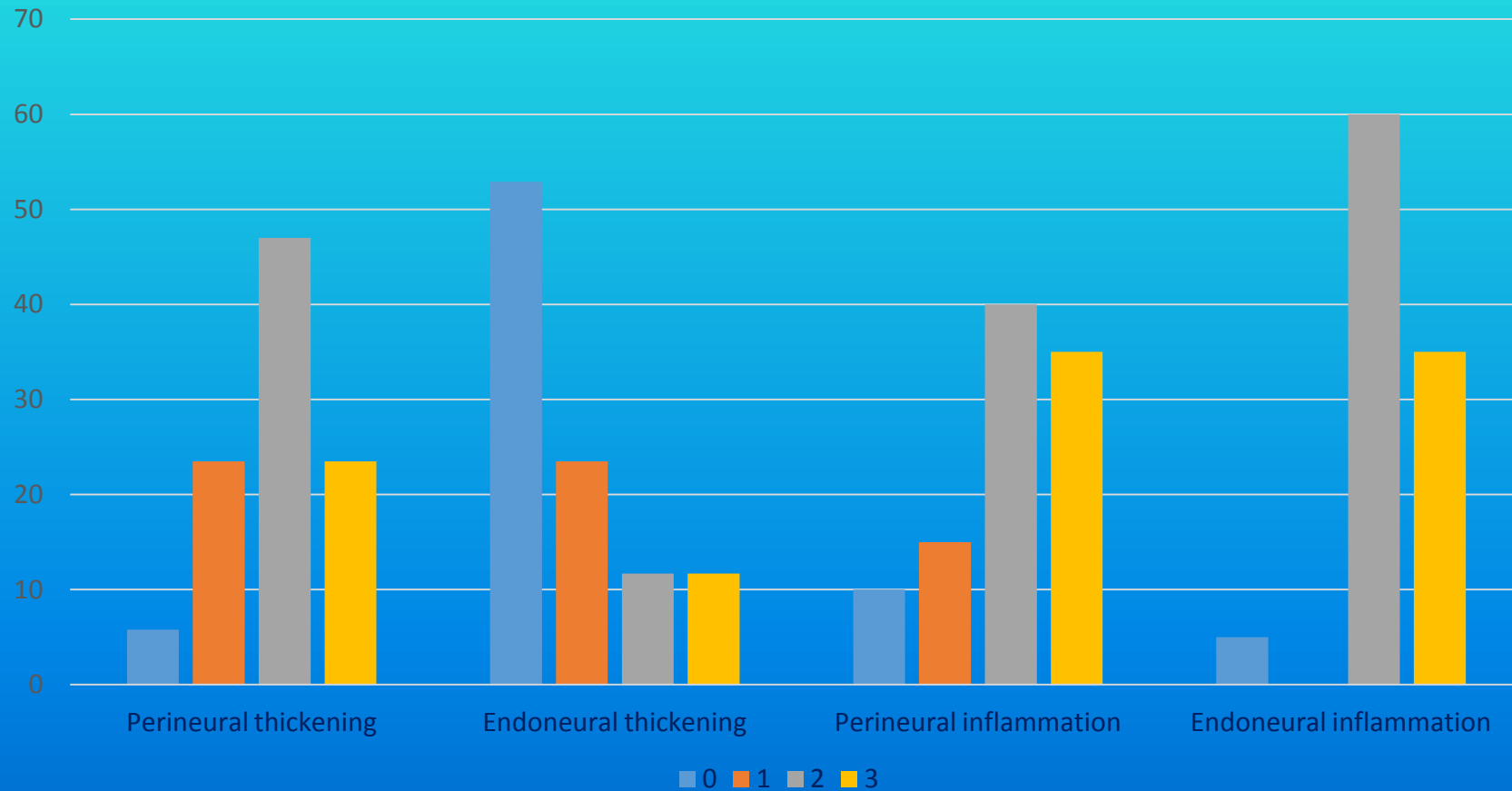
Most common nerve biopsied :

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

RESULTS....

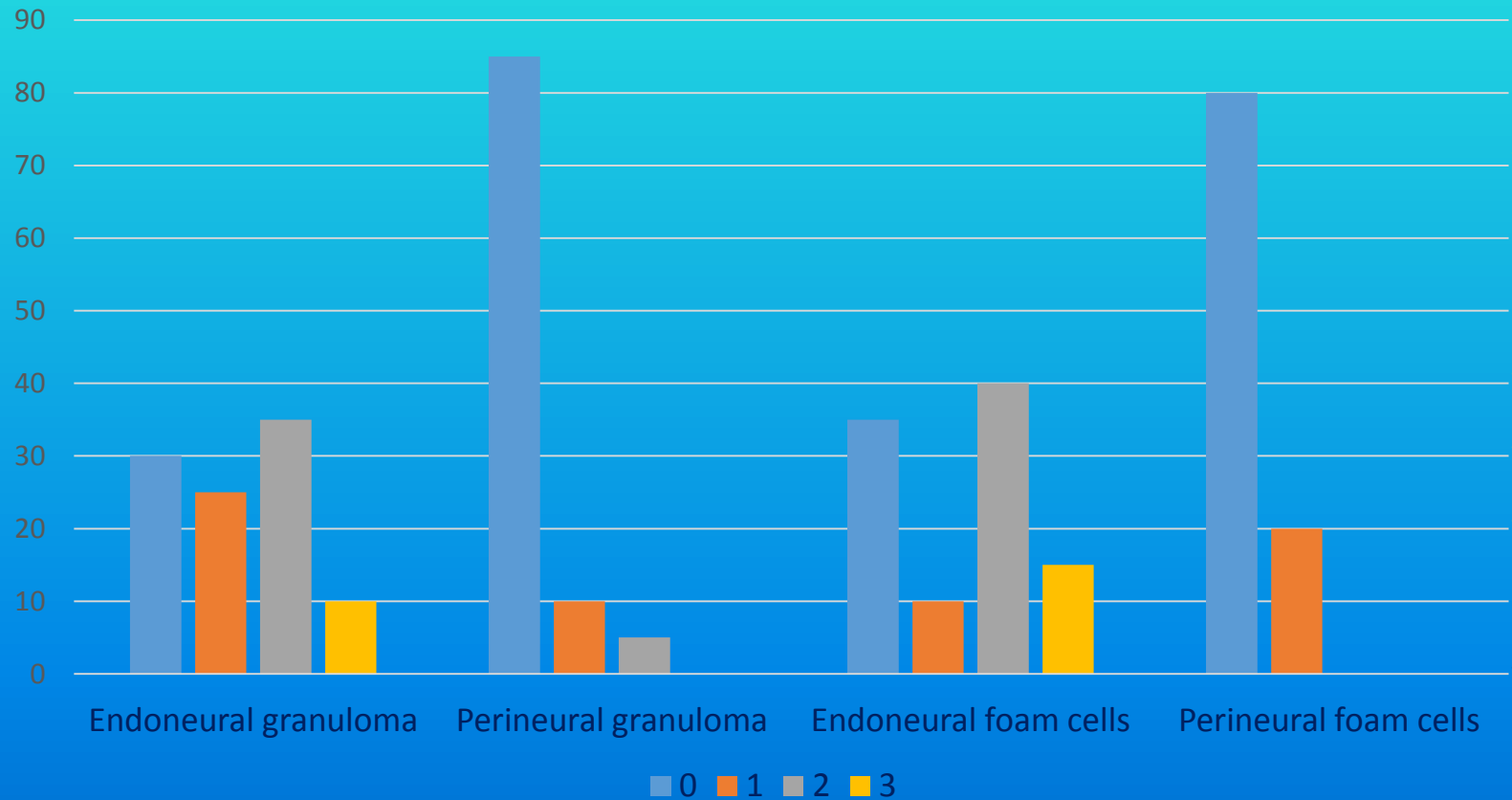
- Nerve biopsies in each case showed
 - Both Longitudinal and transverse section in 11 cases (55%);
 - Transverse Section only in 6 cases (30%) and
 - Longitudinal Section only in 3 cases (15%)
- Average fascicles : 5 , ranging from 3-9
- Skin biopsy in 6 patients- no e/o leprosy

Histopathological Findings(n-20)



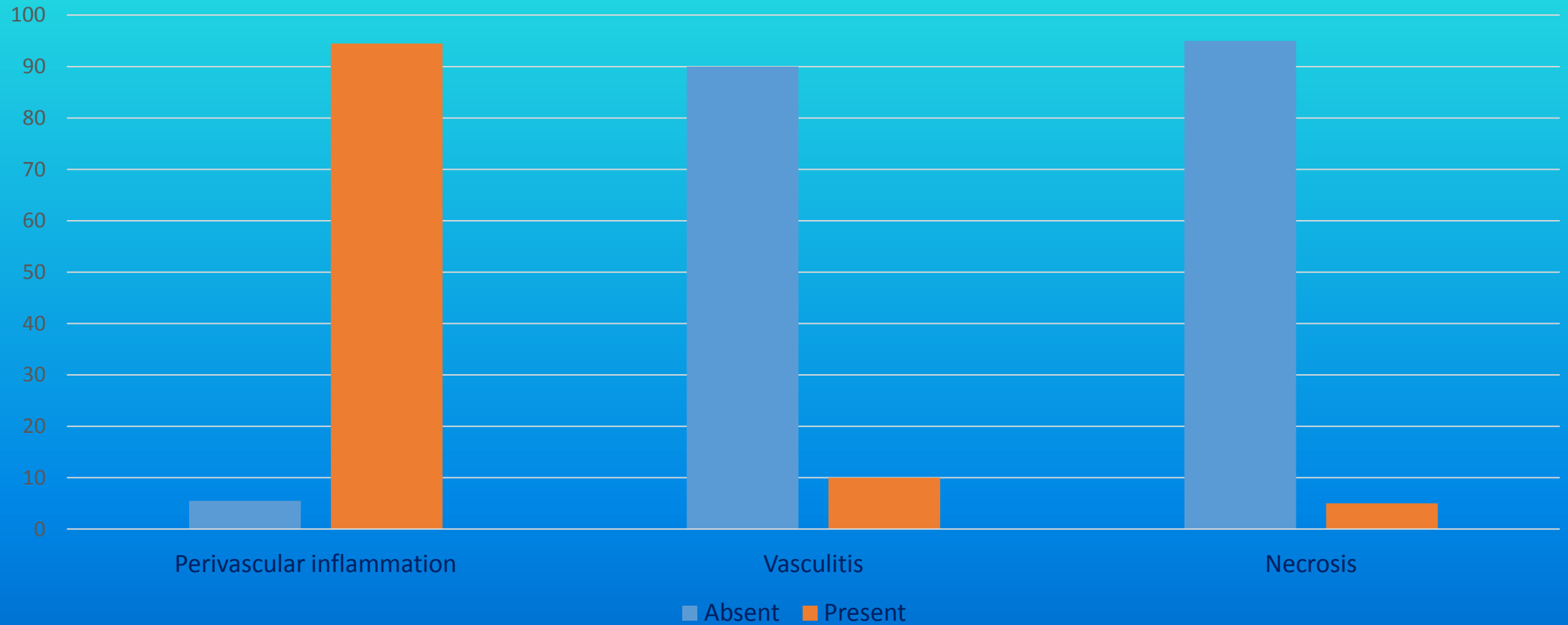
- Perineural thickening- 19 (95%)
- Endoneural thickening- 9 (45%)
- Endoneural LM inflammation- 19 (95%)
- Perineural LM inflammation- 18 (90%)

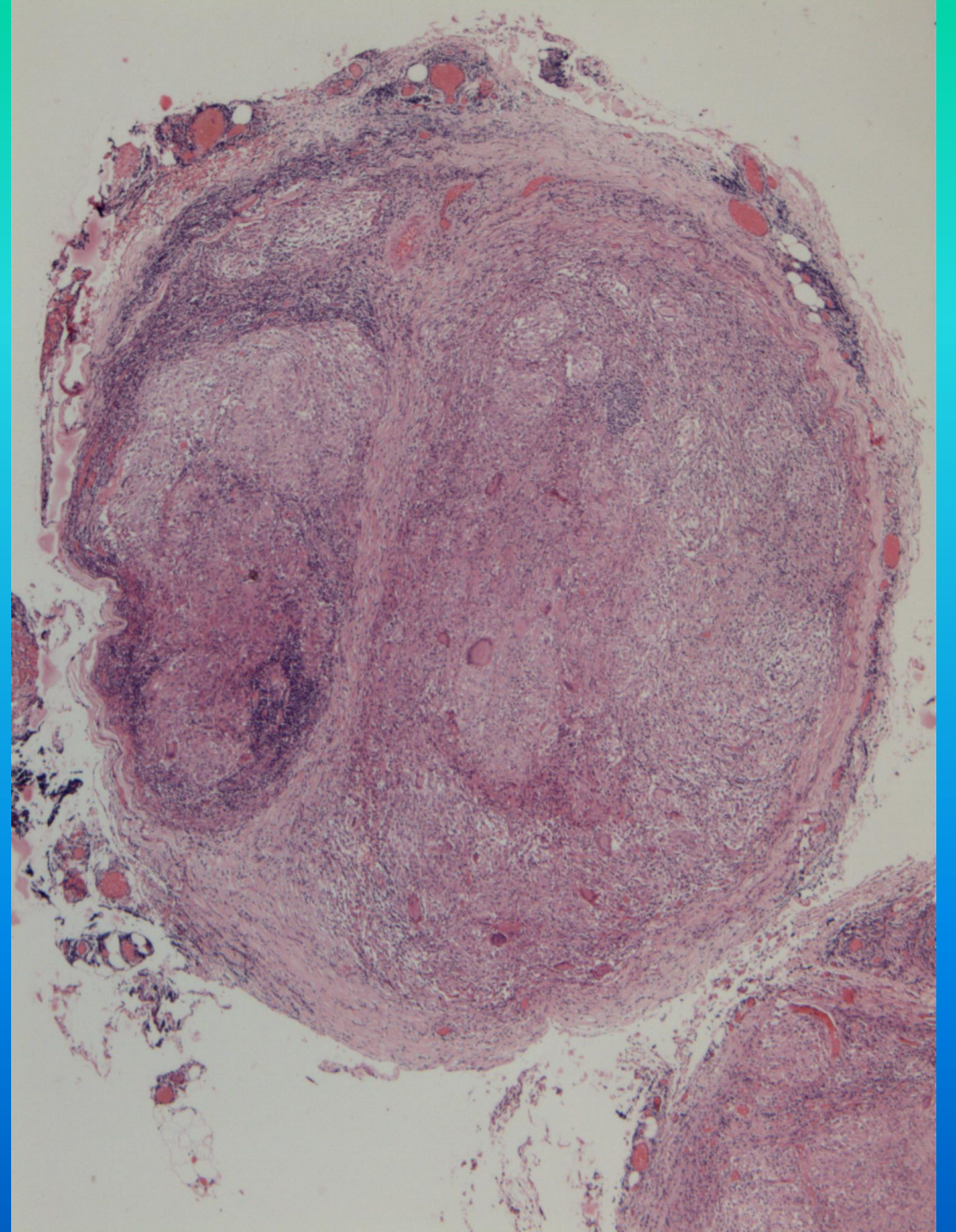
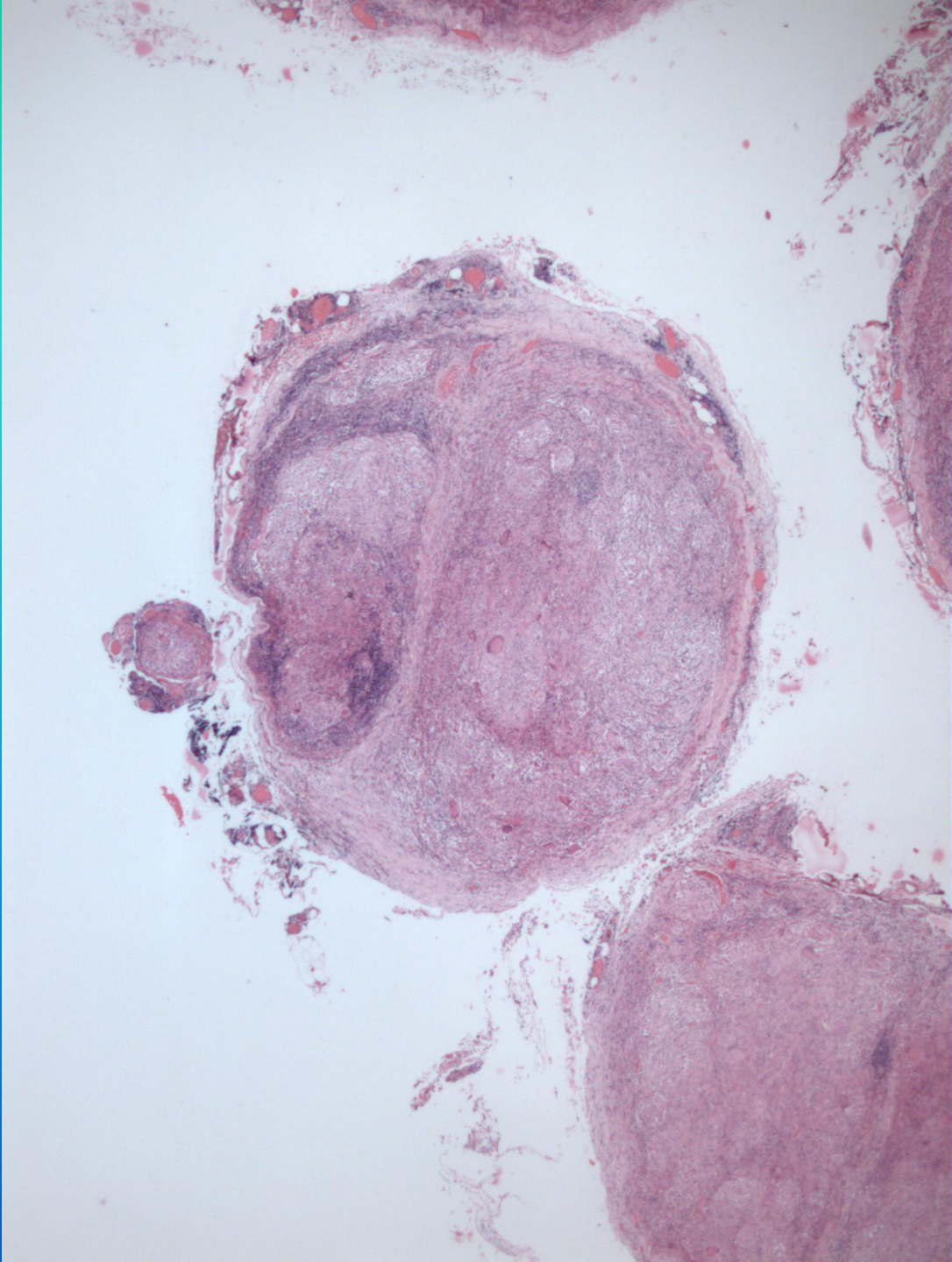
Histopathological Findings (n-20)

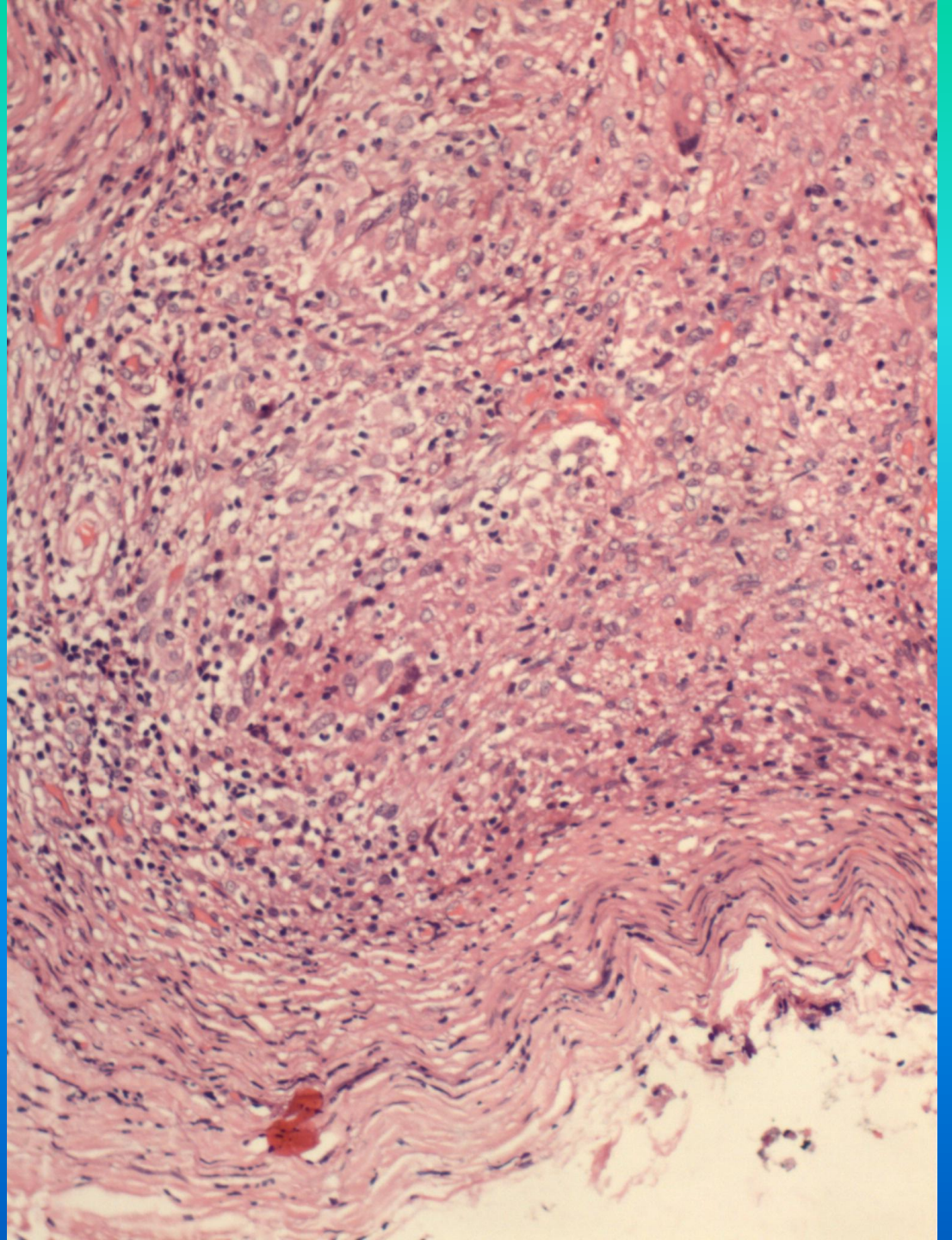
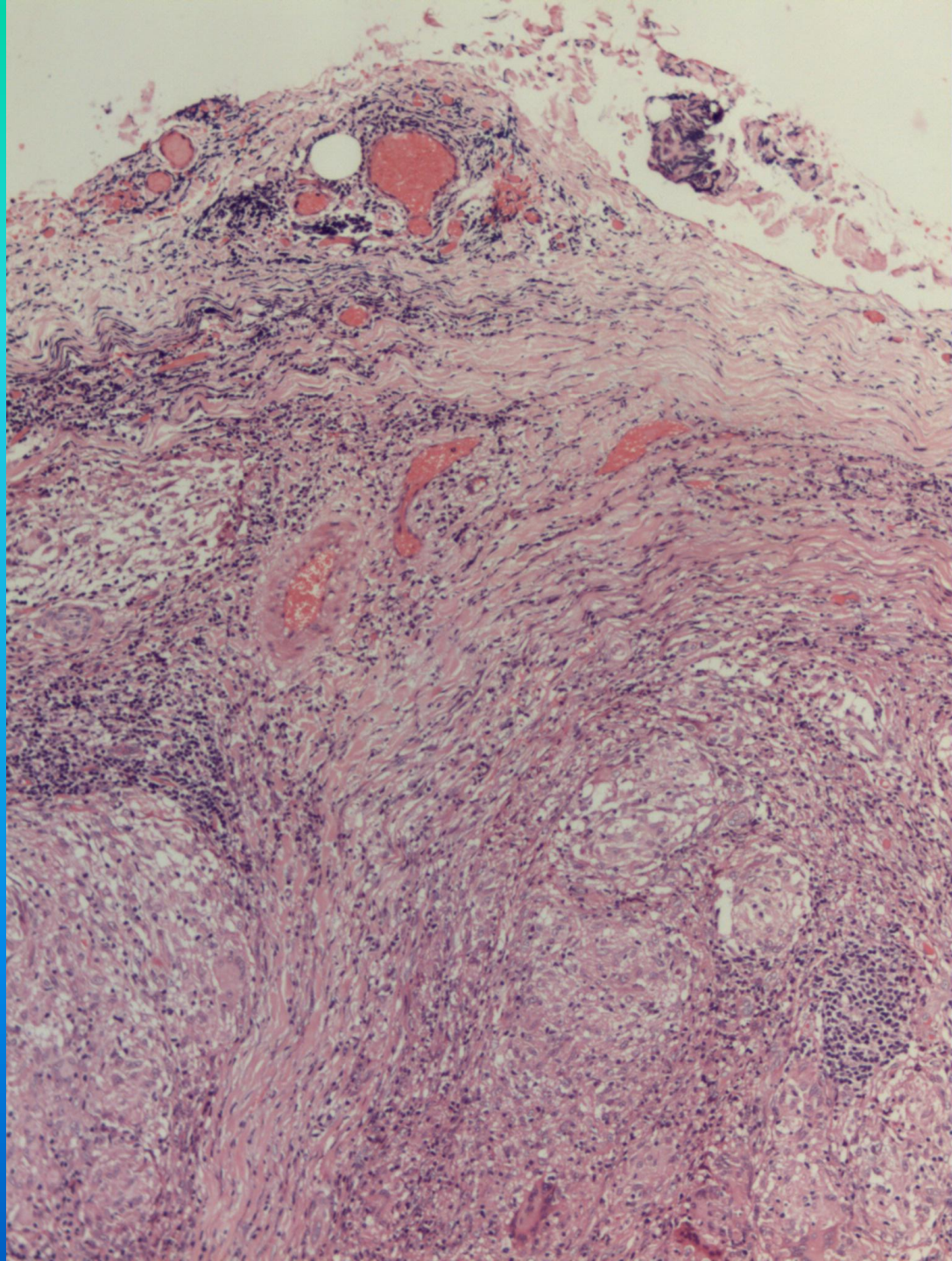


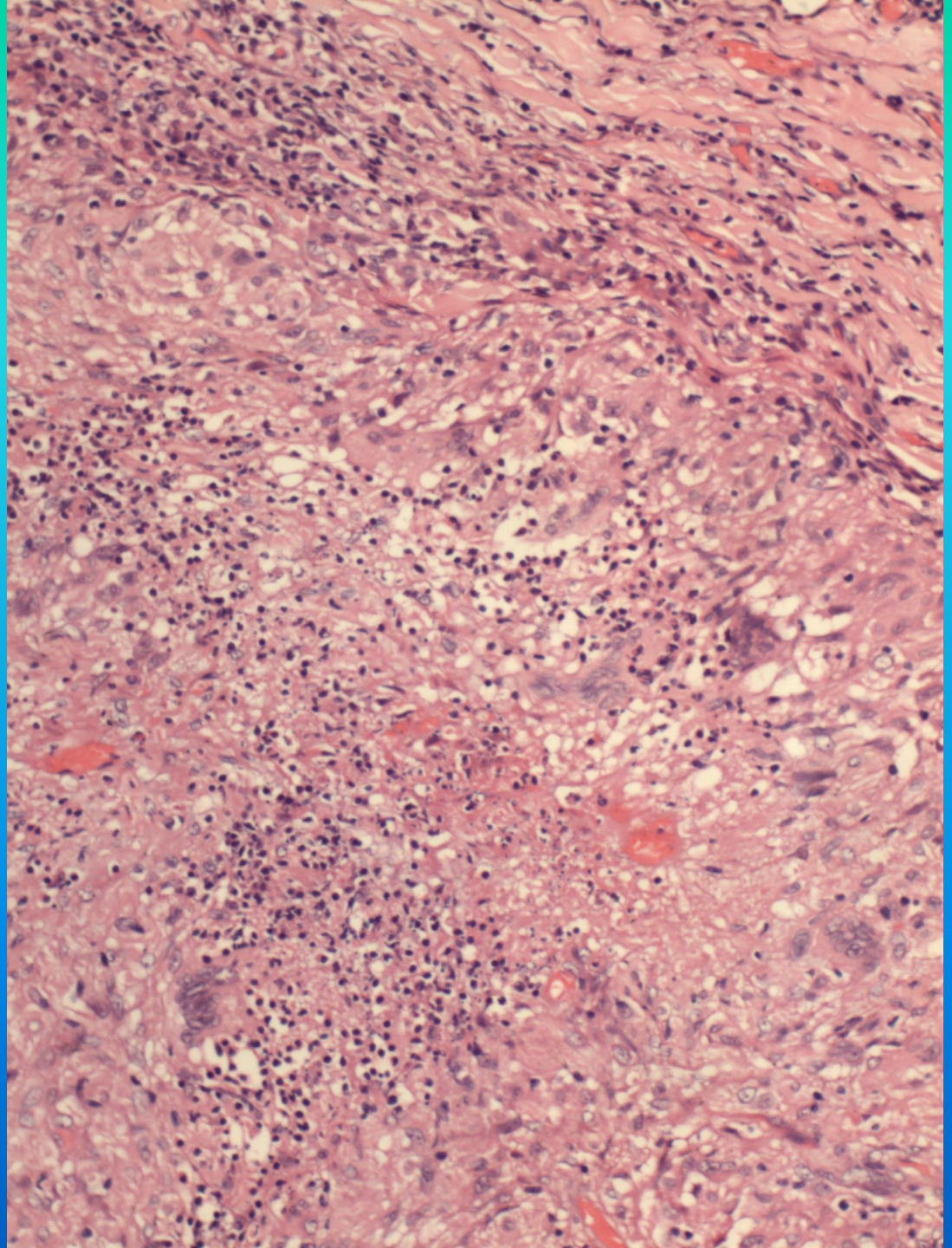
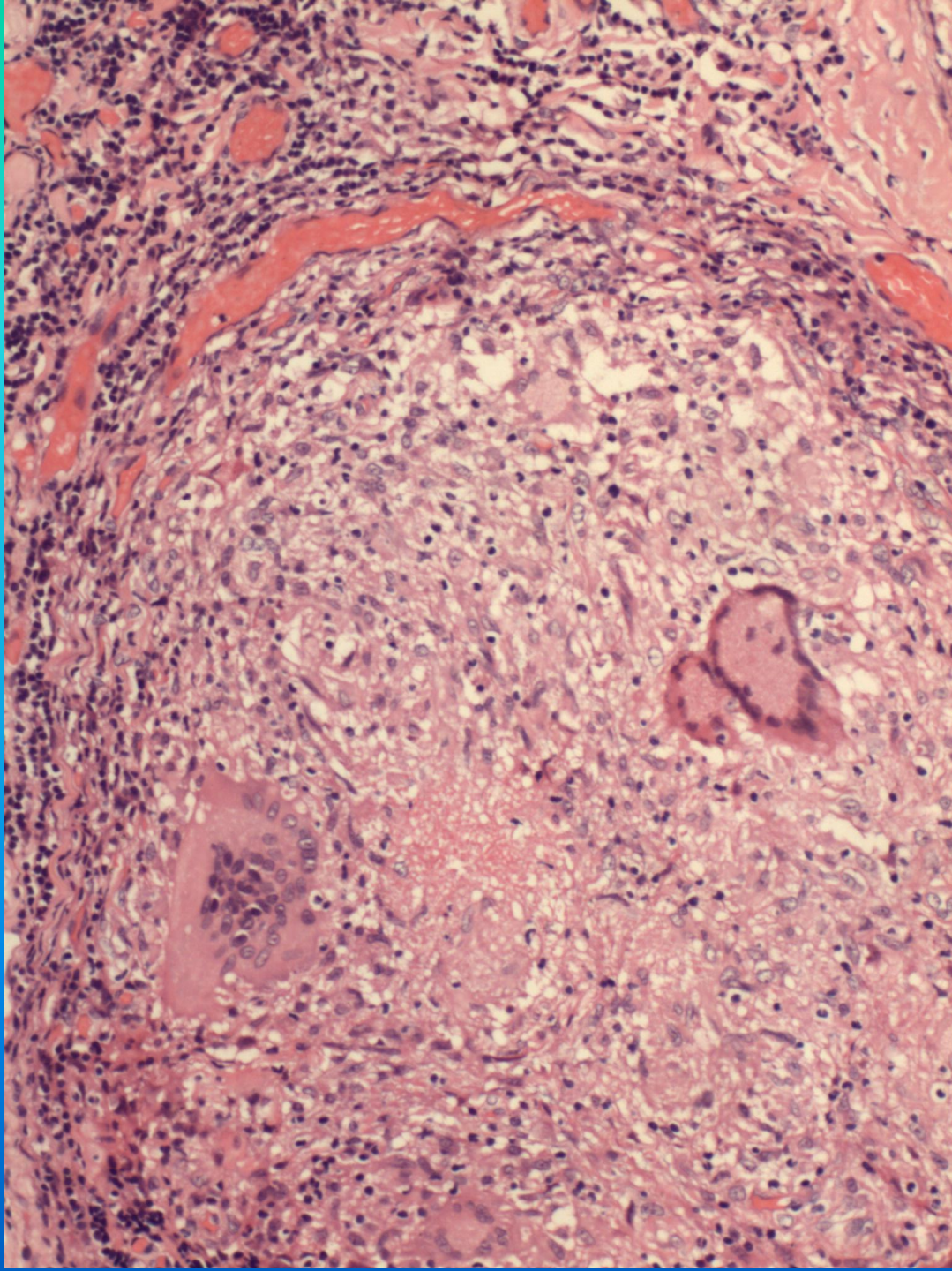
- **Granuloma (n-14) :**
 - Endoneurial : 14 (70%)
 - Perineurial : 3 (15%)
- **Foam cells (n-13) :**
 - Endoneurial : 13 (65%)
 - Perineurial : 4 (20%)
- **Granuloma only : 4 (20%)**
- **Foam cells only : 3 (15%)**
- **Both granuloma and foam cells : 10 (50%)**
- **None of them : 3 (15%)**

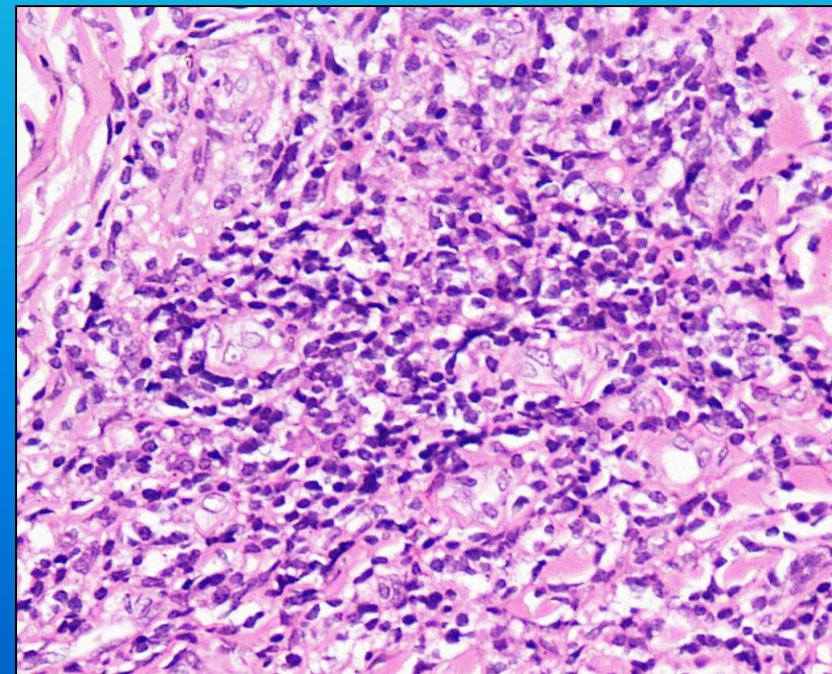
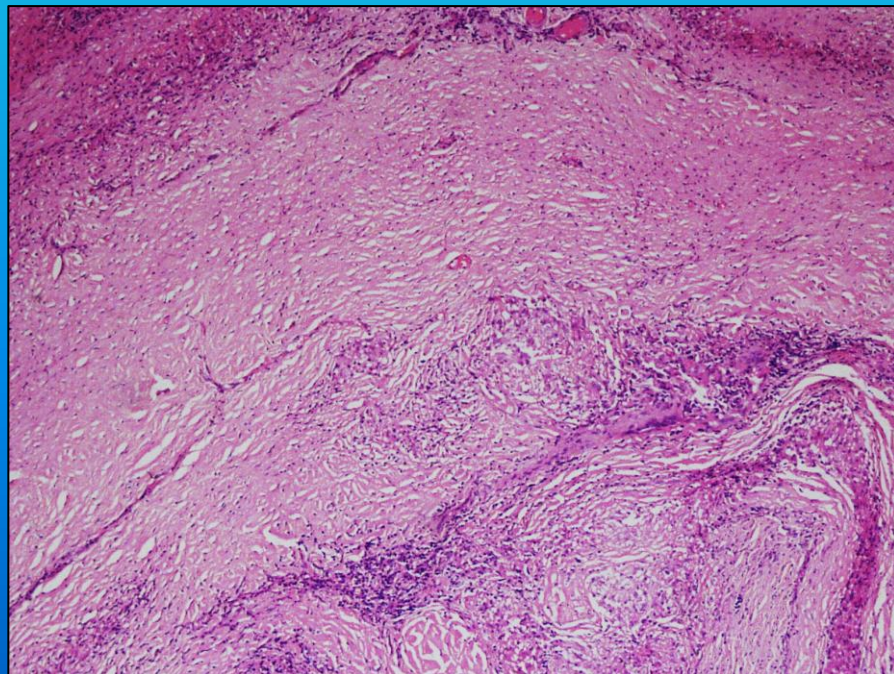
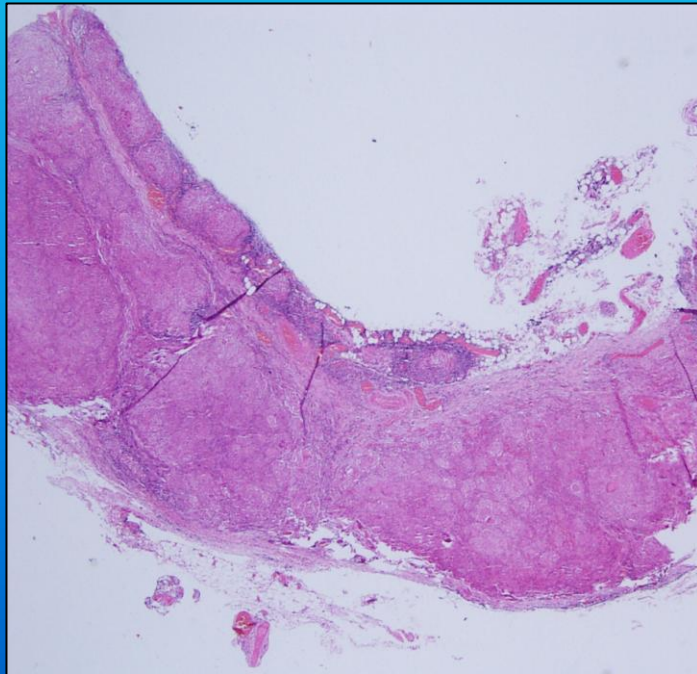
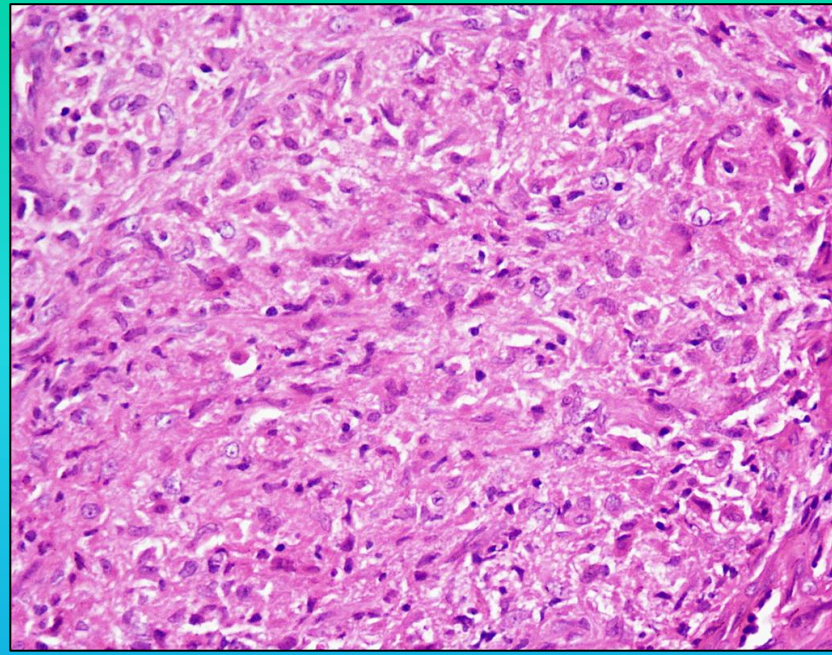
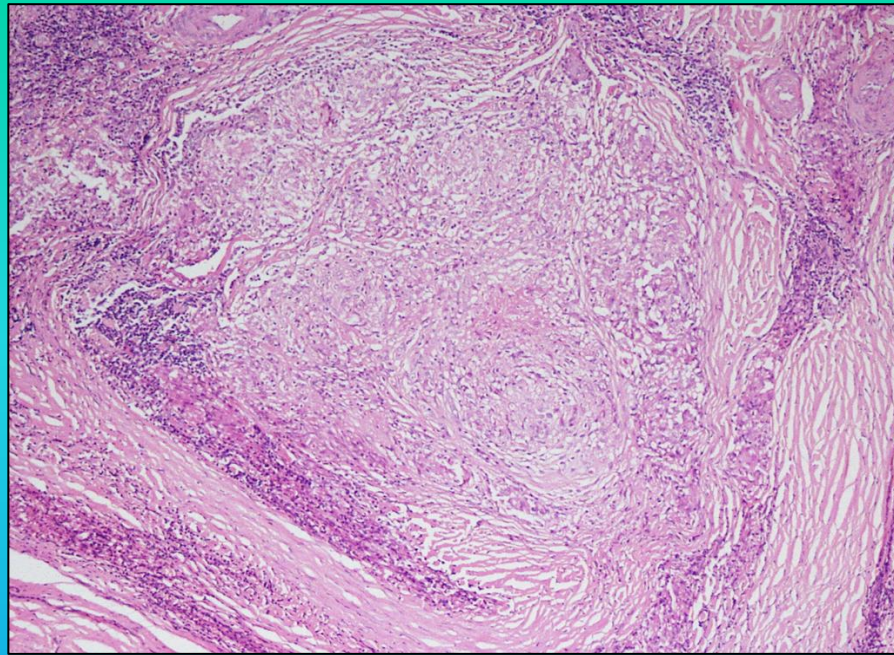
Histopathological Findings (n-20)





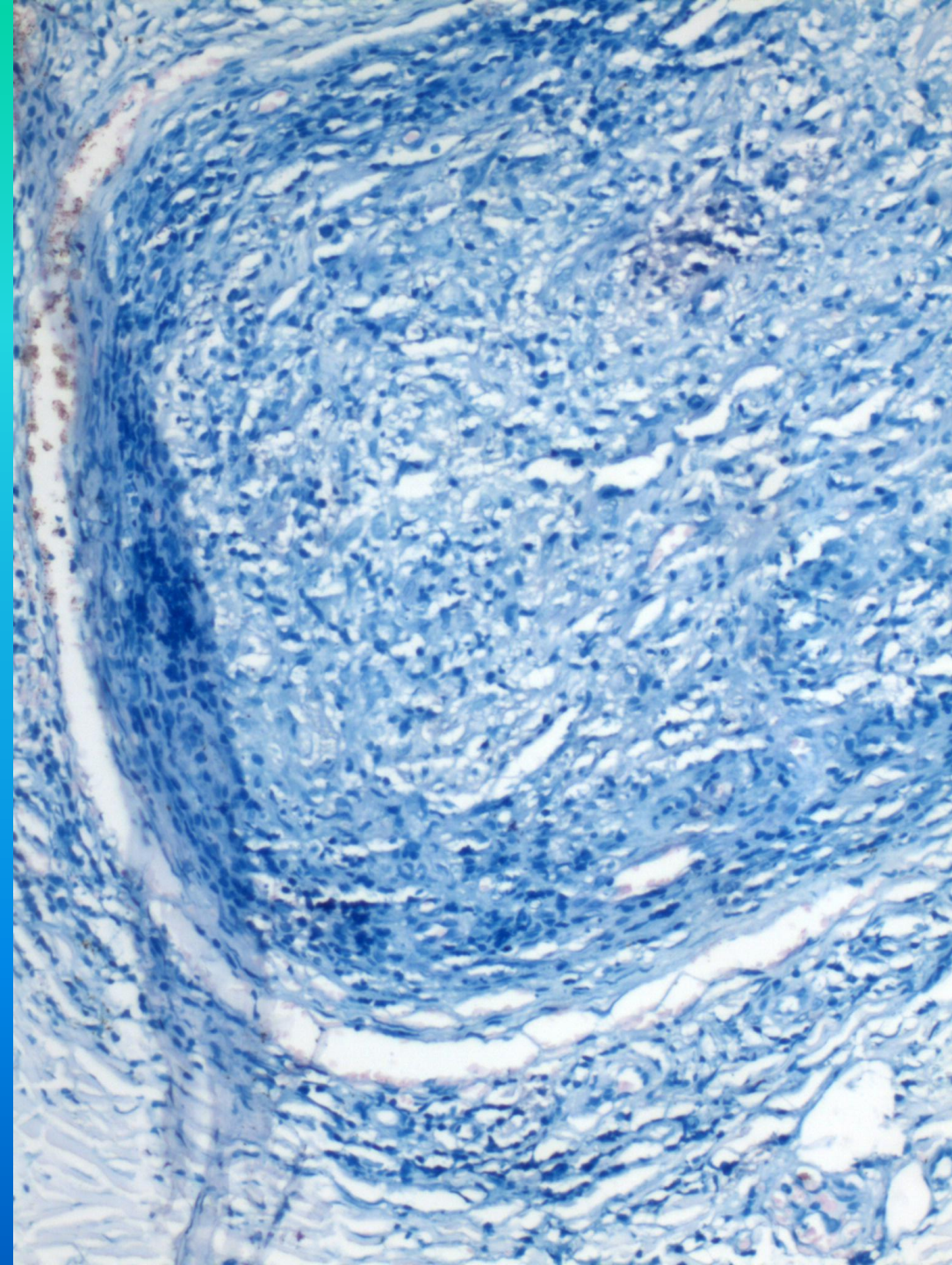
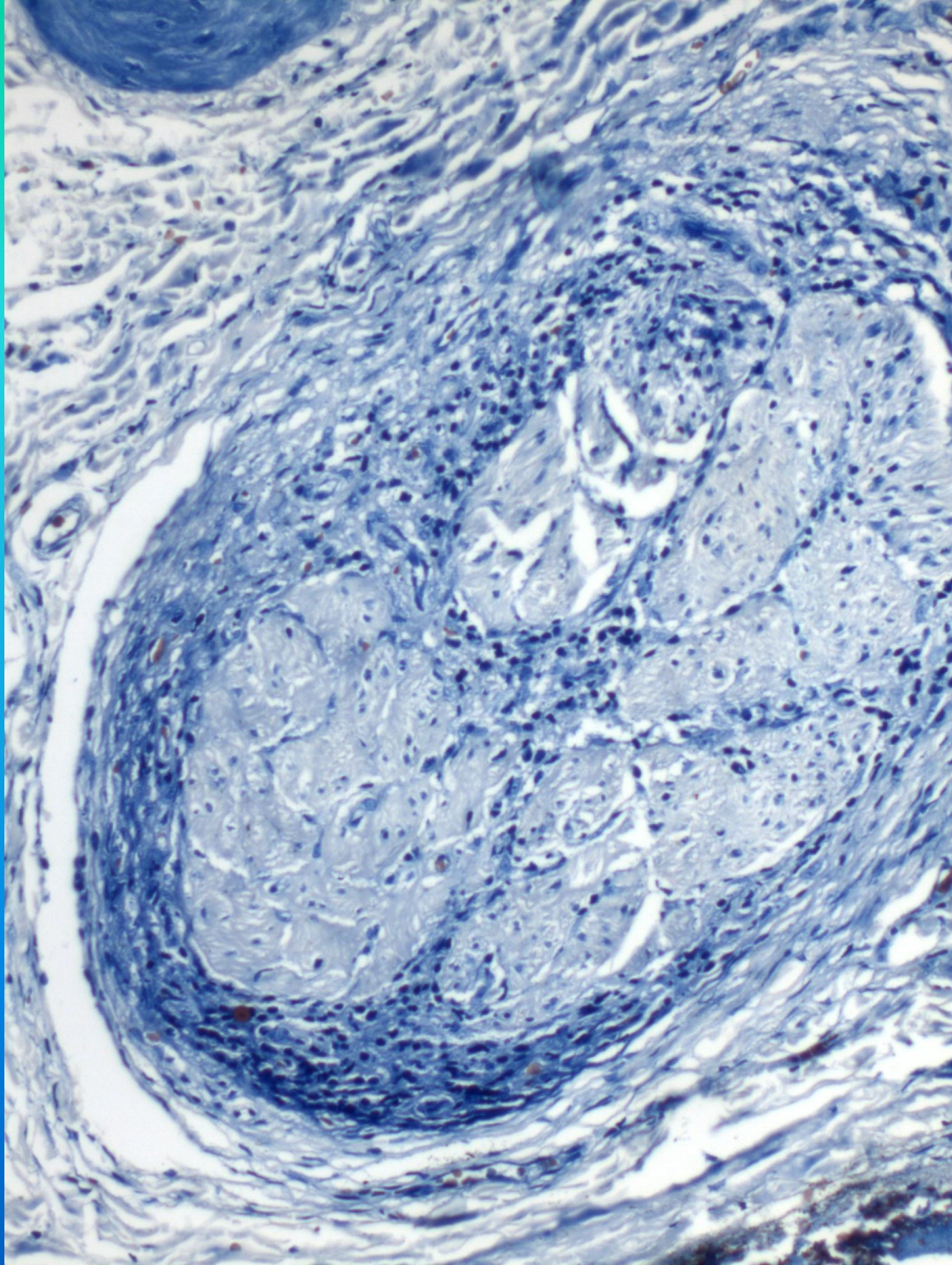


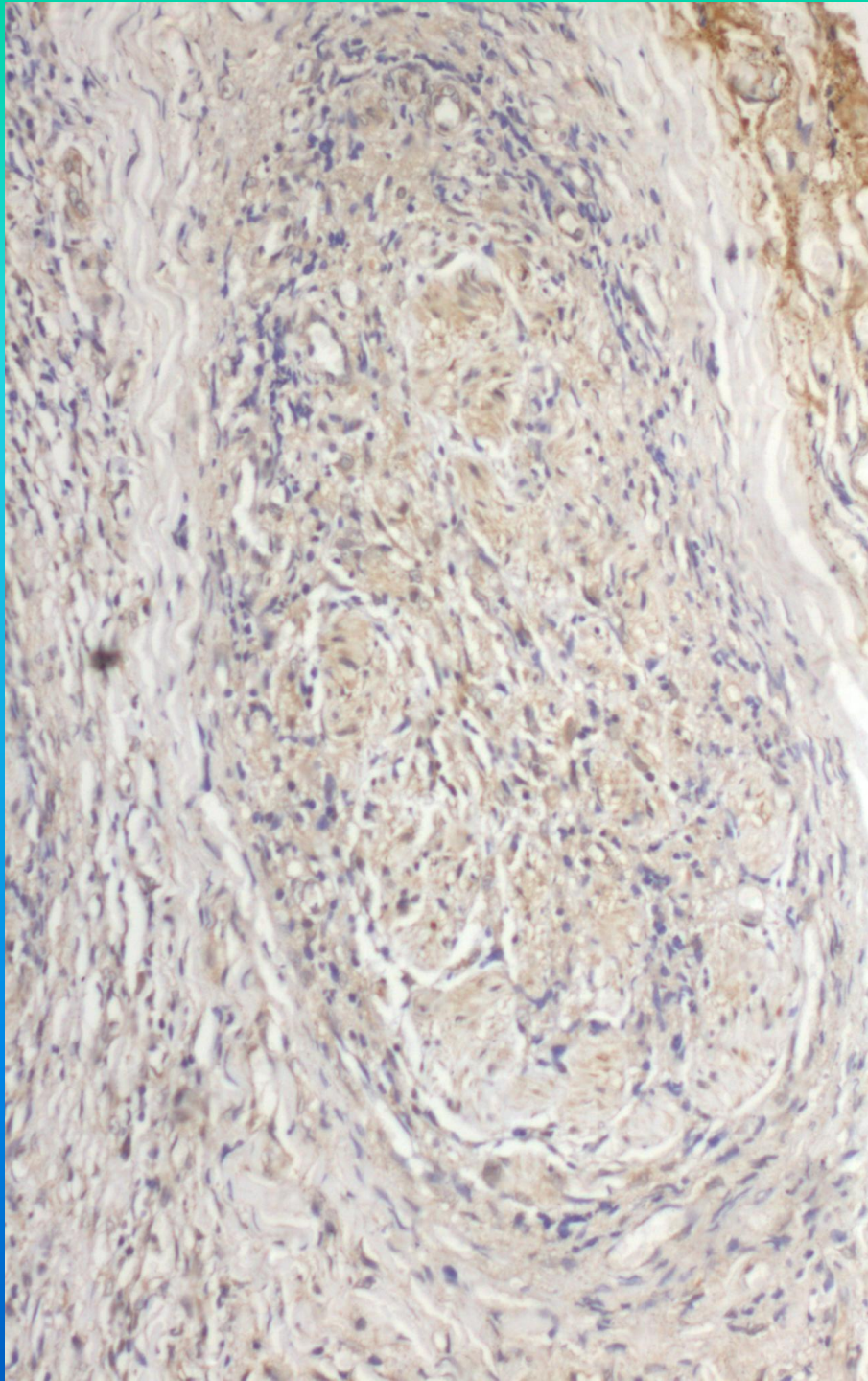




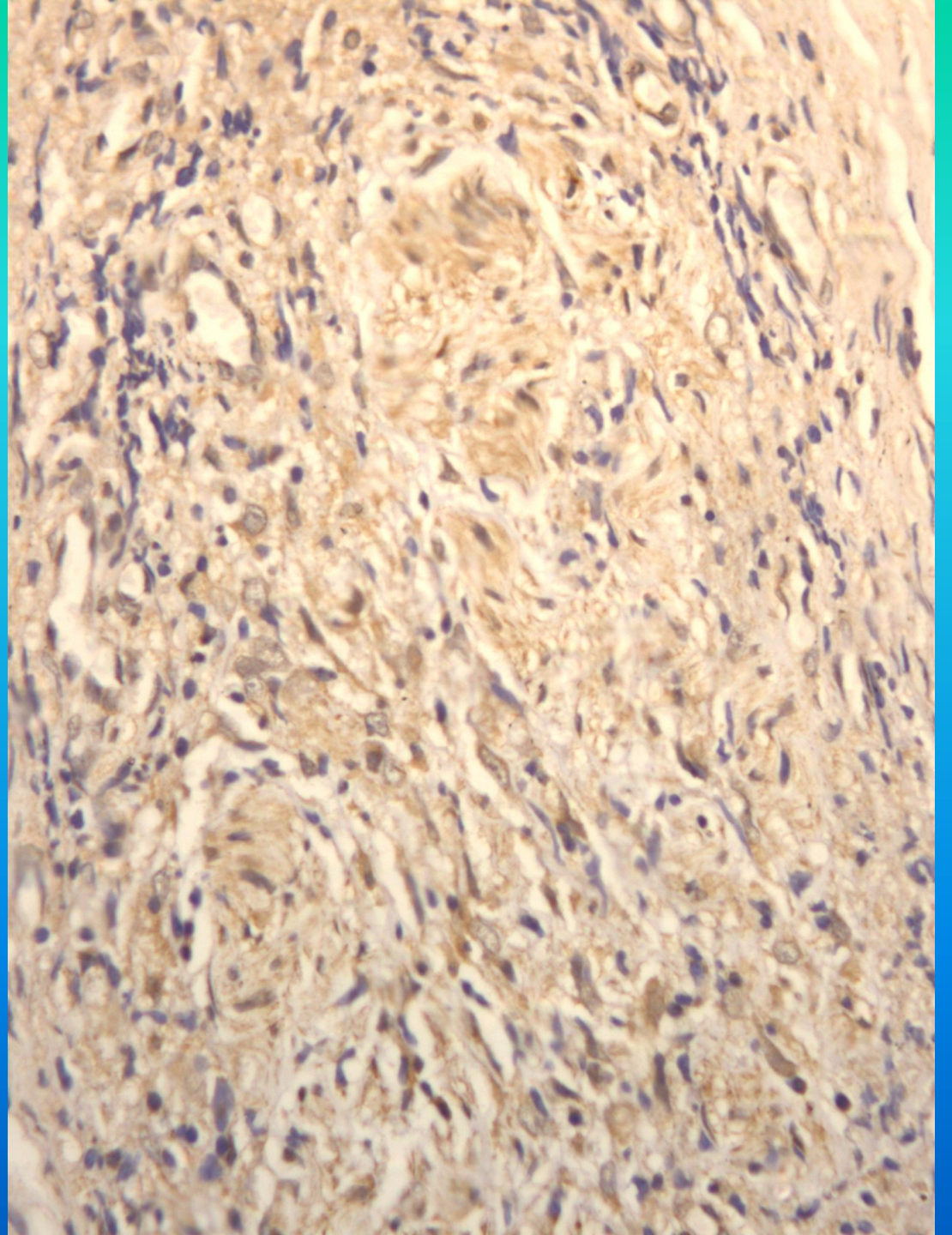
- **Lepra stain** for acid fast bacilli was **positive in 11 cases(55%)** and negative in 9 cases(45%).
- **One case showed normal histology with lepra bacilli positivity**
- There was no significant histological difference between lepra bacilli positive and negative cases.
- **Myelin and Axonal loss:**
 - Absent in only 1 case (5%)
 - Moderate in 4 cases (20%)
 - Severe in 15 cases (75%)

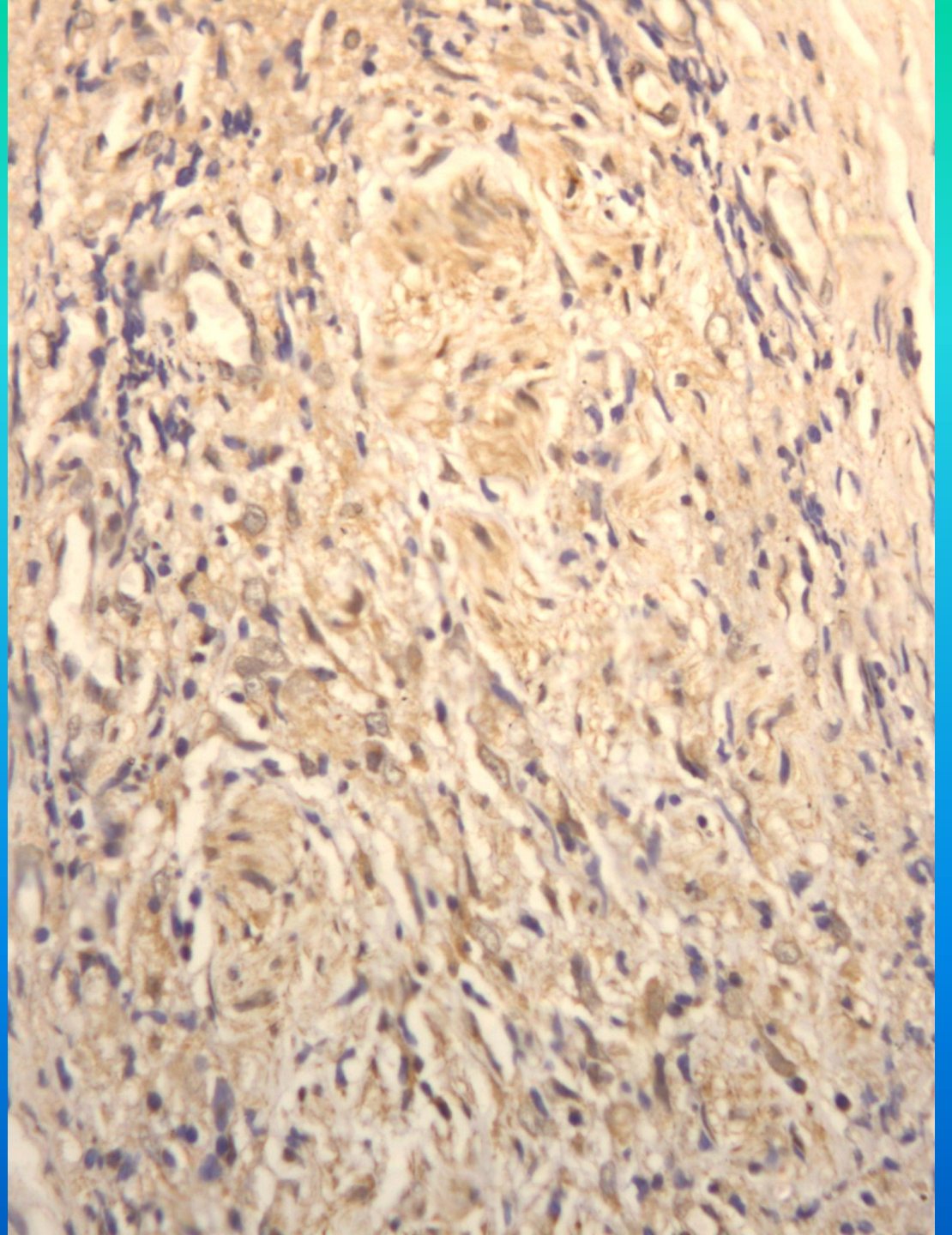
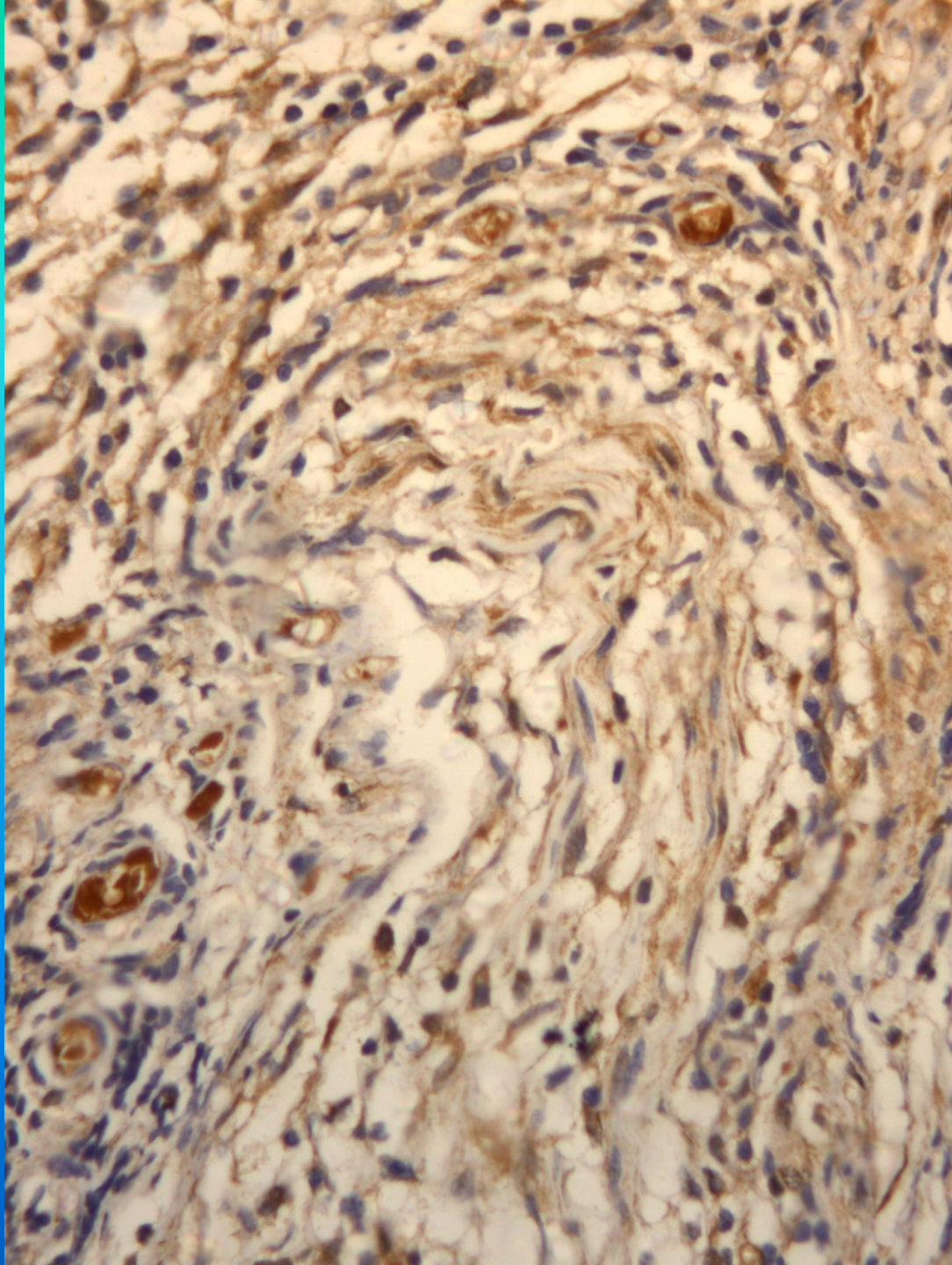
LFB:
Myelin
stain

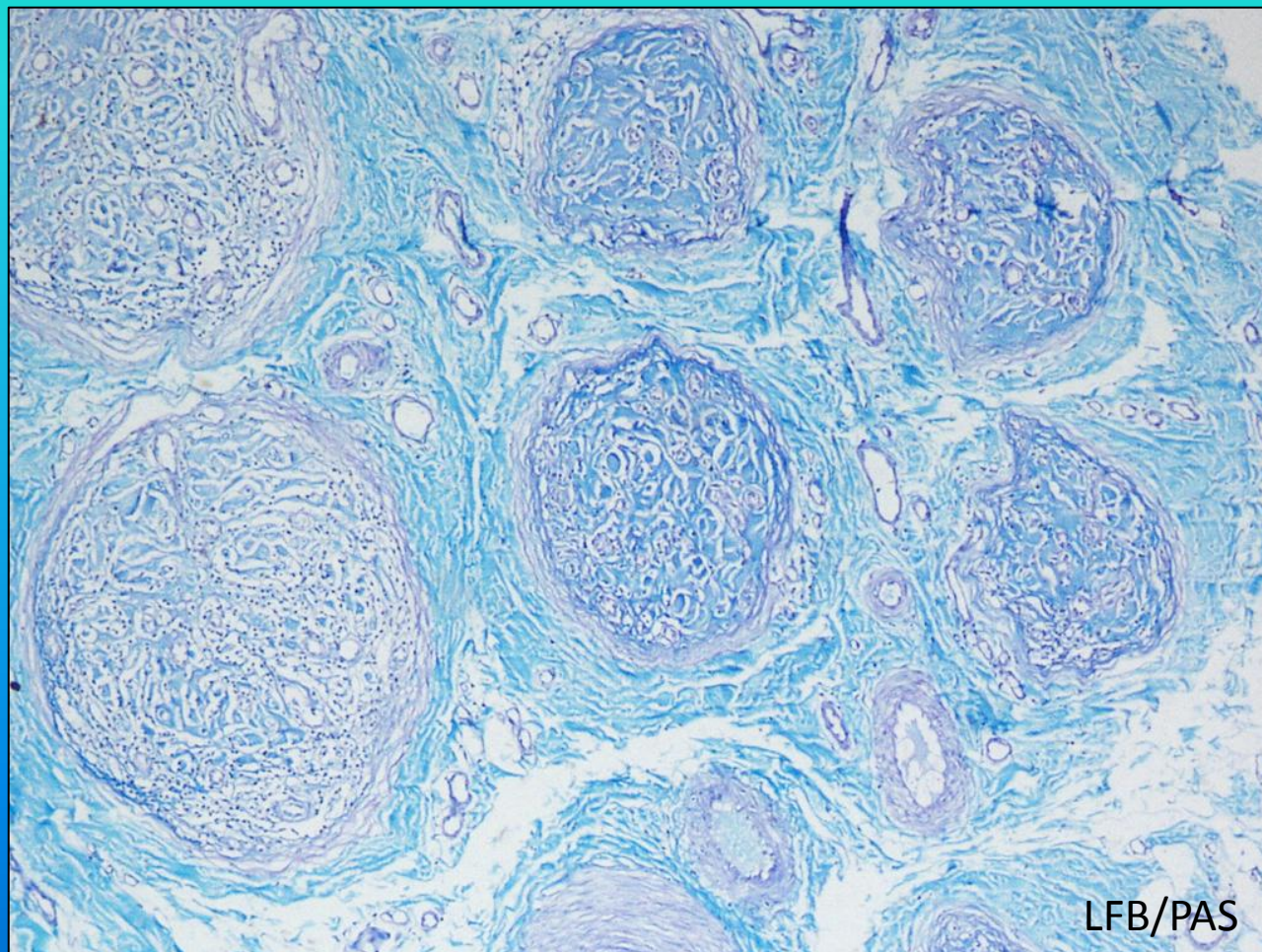




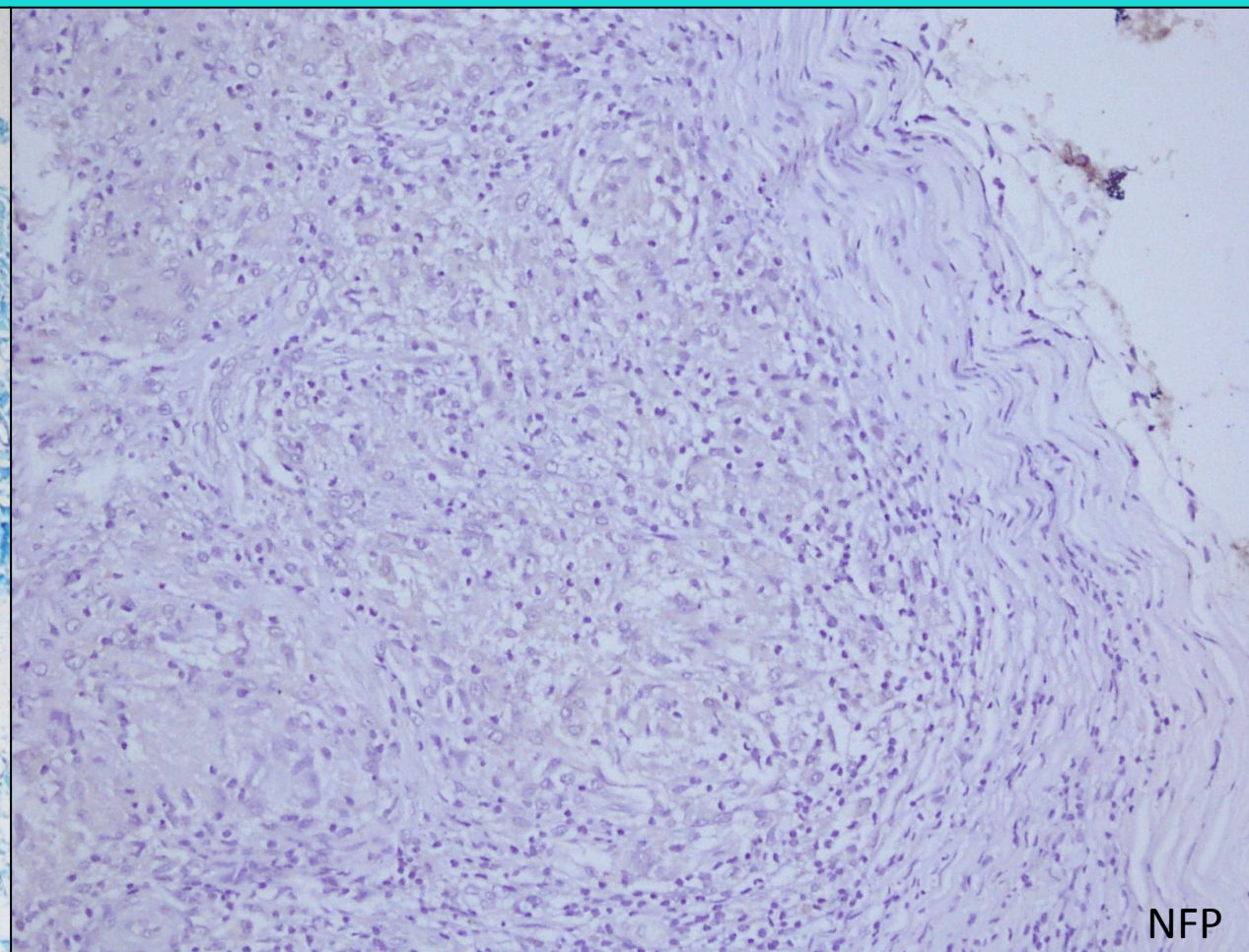
IHC:
NFP







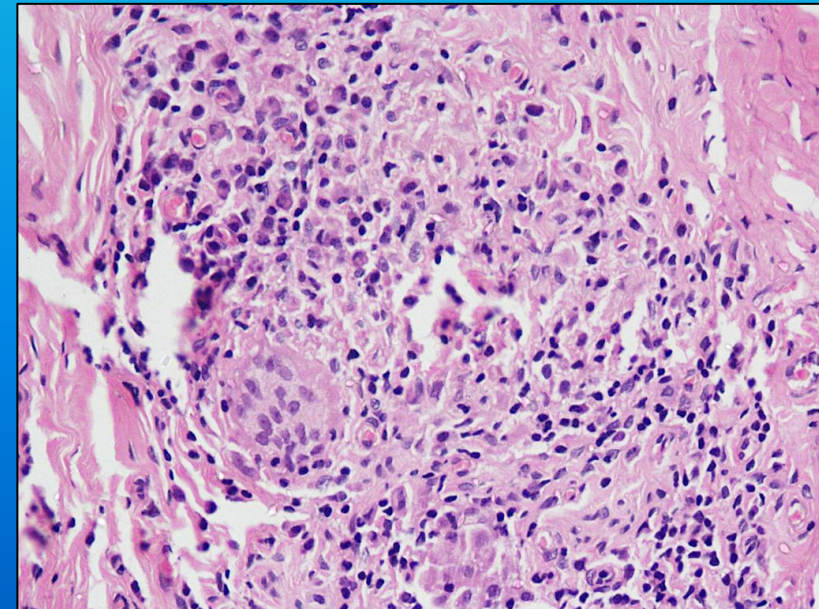
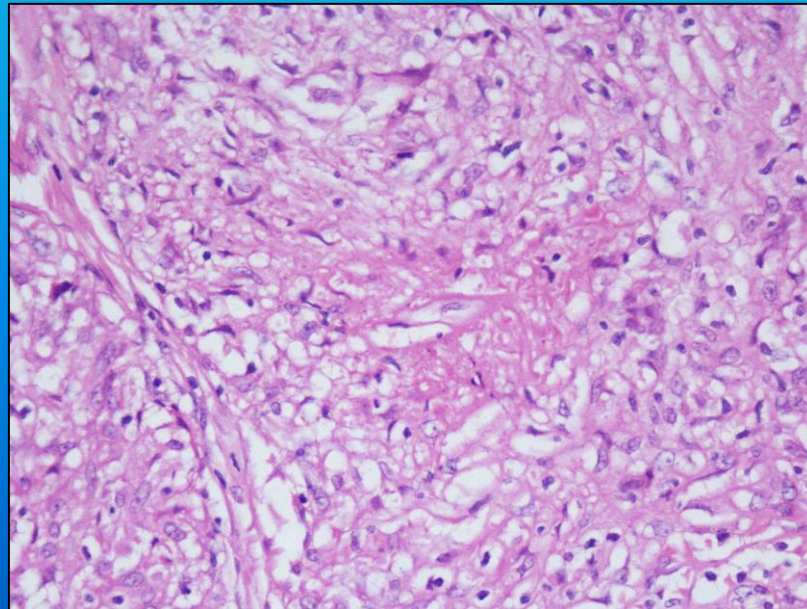
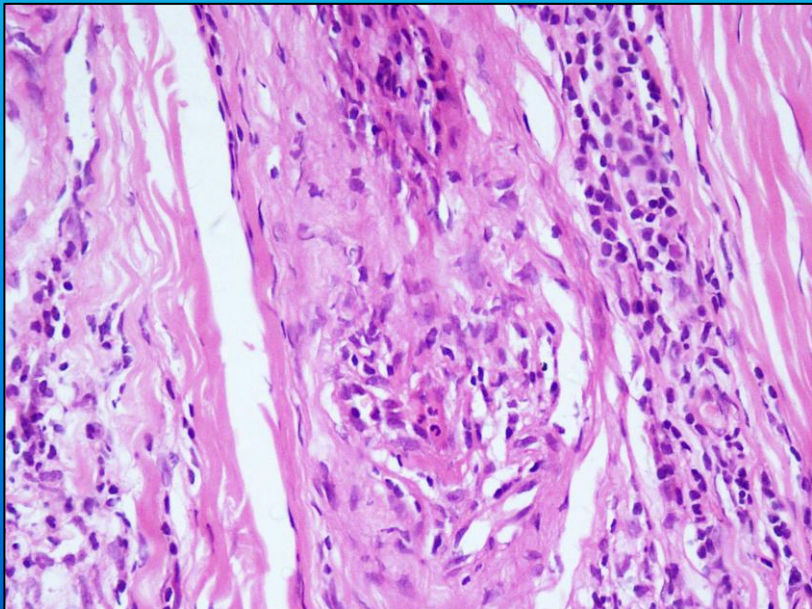
LFB/PAS



NFP

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%)



Histological Parameters	AFB positive cases (11)	AFB negative cases (9)
Perineural thickening	10(90.9%)	9(100%)
Endoneural thickening	4(36.3%)	4(44.4%)
Perineural inflammation	10(90.9%)	9(100%)
Endoneural inflammation	10(90.9%)	9(100%)
Perineural granuloma	2(18.1%)	1(11.1%)
Endoneural granuloma	9(81.8%)	7(77.7%)
Perineural foam cells	2(18.1%)	2(22.2%)
Endoneural Foam cells	8(72.7%)	6(66.6%)
Perivascular inflammation	10(90.9%)	9(100%)
Vasculitis	1(9%)	1(11.1%)
Necrosis	0	1(11.1%)
Myelin loss	10(90.9%)	9(100%)
Axonal loss	10(90.9%)	9(100%)

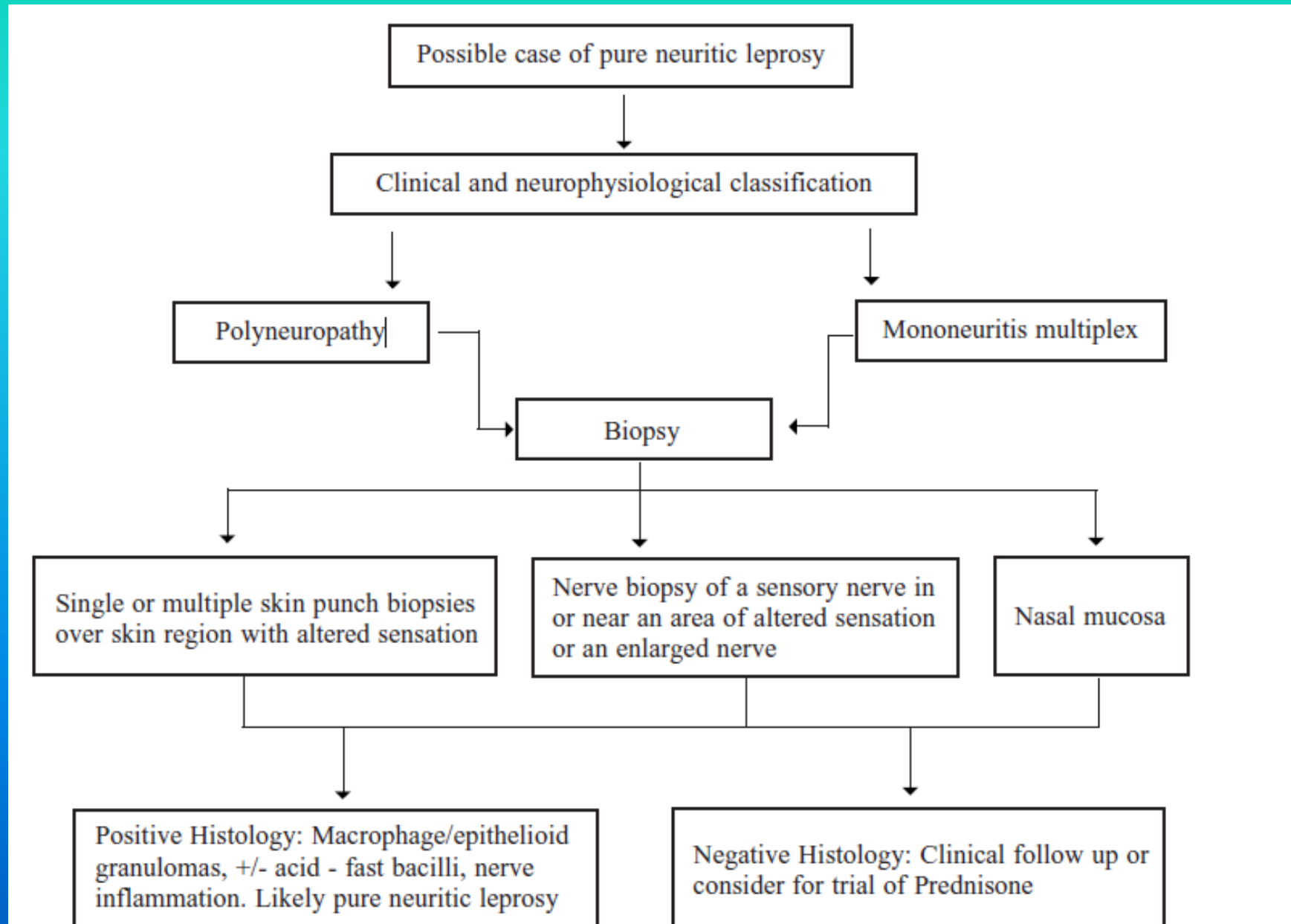
CONCLUSION

- 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

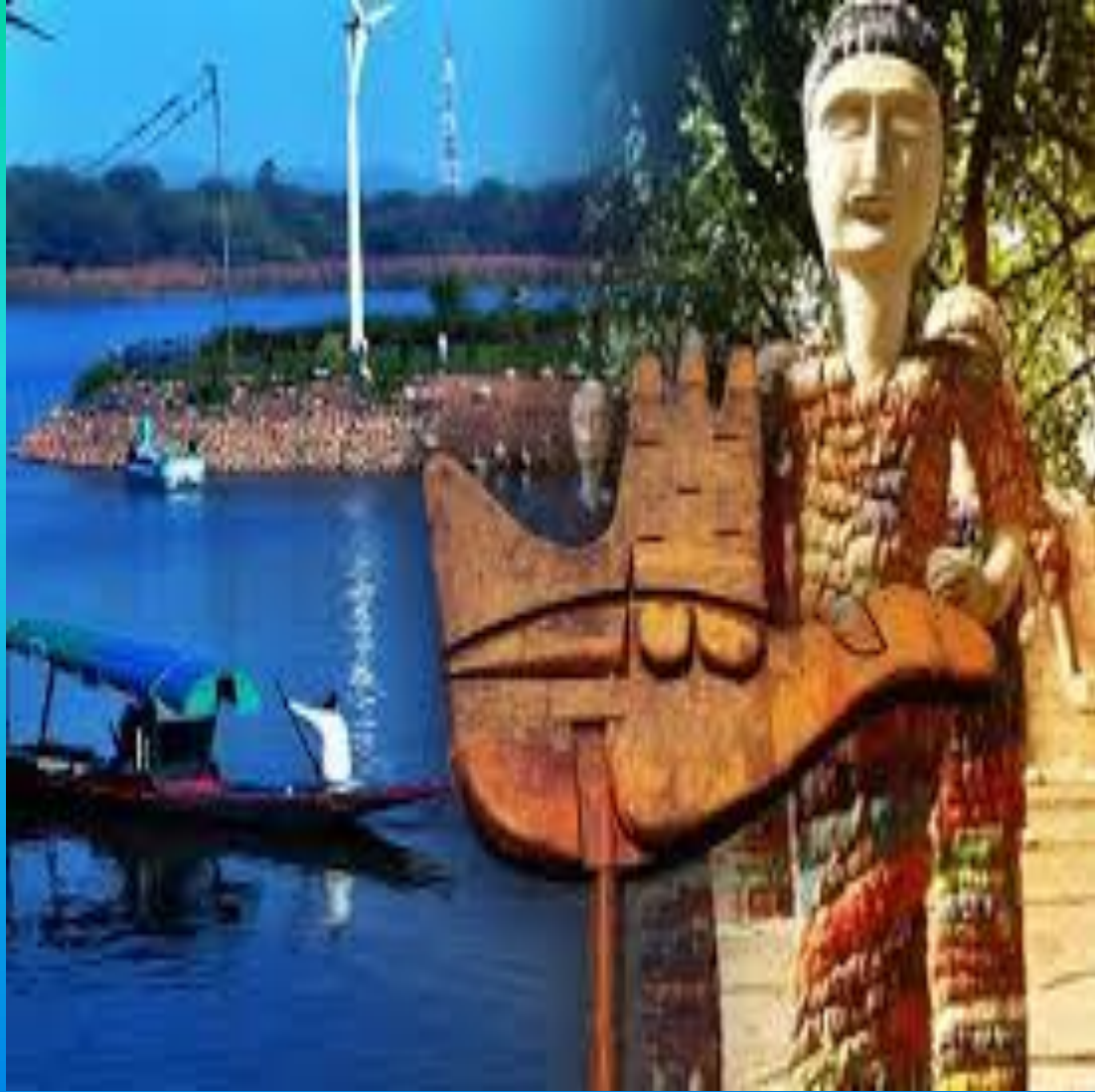
- Necrosis and vasculitis can be rarely found in PNL
- Even if morphologically biopsy is normal, lepra stain should be performed in all suspected cases of PNL
- Anti-PGL1 antibodies in patient's sera can be helpful in early diagnosis
- PCR may be done in cases with negative Lepra stain

Summary: Flowchart for the investigation of pure neuritic leprosy



Einar WILDER-SMITH

*Neurol J
Southeast Asia
December 2002*



THANK YOU