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A STUDY ON THE ROLE OF IMMUNOHISTOCHEMICAL MARKER S -100 IN HISTOLOGICAL CLASSIFICATION OF LEPROSY.

Pathology

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ABSTRACT

Background: Leprosy is a chronic disease caused by Mycobacterium leprae and affects predominantly the peripheral nervous system, skin, mucosa of upper respiratory tract and eyes. The difficulty in recognizing small nerve twigs or their fragments on routine Hematoxylin and Eosin sections has led to the use of immunohistochemical marker S-100 as an aid to demonstrate the nerve changes in the entire spectrum of Leprosy. There are four patterns of nerve damage demonstrable on S-100 immunostaining namely, Infiltrated, fragmented, absent, and intact. These patterns had sensitivity, specificity, positive and negative predictive value of 100% in diagnosing Tuberculoid and Borderline Tuberculoid leprosy. **Aims and Objectives:** To analyse the utility of S-100 in demonstration of nerve changes across the histopathological spectrum of leprosy by Immunohistochemistry. **Material And Methods:** The present study is a cross-sectional study done over a period of two years at a tertiary care hospital. The Histologic typing of leprosy followed by S-100 immunostaining for nerve changes is done which shows membranous and cytoplasmic positivity and the pattern of nerve destruction is observed. Four different patterns of nerve destruction were observed in S-100 immunostaining. **Results:** In the present study, the majority of cases of Borderline Tuberculoid (BT) and Borderline (BB) showed fragmented pattern of nerve damage whereas Lepromatous Leprosy (LL) showed absent pattern. The difference in the staining pattern of nerve fragments by S100 provides a clue about the spectrum of leprosy.

KEYWORDS

Leprosy, S100 immunohistochemistry, nerve damage

INTRODUCTION:

Leprosy is a neurotropic disease caused by Mycobacterium leprae and affects predominantly the peripheral nervous system,skin, mucosa of upper respiratory tract and eyes.[1] According to the widely accepted Ridley-Jopling classification , the disease is divided into two poles and an intermediate state, including polar tuberculoid leprosy (TT) , borderline tuberculoid leprosy (BT), mid-borderline leprosy (BB), borderline lepromatous leprosy (BL),and lepromatous leprosy (LL).[1]The first sign of leprosy is usually the appearance of light patches on the skin accompanied by a reduction or loss of sensation over the patches.

The World Health Organization (WHO), working through the country office in India, supports the National Leprosy Eradication Programme (NLEP). The prevalence rate of leprosy in India is 0.4 per 10000 population in the country. Leprosy is endemic in several states and union territories of India, with the annual case detection rate of 4.56 per 10,000 population.[2]Nerve damage and sensory impairment are central to the pathogenesis of leprosy.

The difficulty in recognizing small nerve twigs or their fragments on routine Haematoxylin and Eosin sections has led to the use of S-100 stain as an aid to the histological differentiation of Leprosy. Nerve damage and sensory impairment are central to the pathogenesis of leprosy. There are four patterns of nerve damage demonstrable on S-100 immunostaining namely infiltrated, fragmented, absent and intact. These patterns had sensitivity, specificity, positive and negative predictive value of 100% in diagnosing Tuberculoid and Borderline Tuberculoid leprosy[3,4,5].

Aim And Objectives:

1. To analyze the clinicopathologic features of Leprosy.
2. To demonstrate the various patterns of nerve damage in the entire spectrum of leprosy using S-100 immunohistochemical staining.

MATERIALS AND METHODS:

The present study is a cross-sectional study done over a period of two years from January 2020 to December 2022 in the Department of Pathology, Osmania Medical College, Hyderabad. A total of 50 cases were studied. Age, sex distribution, clinical presentation and histologic typing of spectrum of leprosy on Hematoxylin and Eosin sections of biopsies were done under light microscopy following Ridley Jopling classification. Immunohistochemistry with S-100 was done on all cases following Diagnosis protocol- Primary antibody S-100 protein, antigen retrieval with Montage Opus, detection methods by Avidin-biotin complex method, chromogen substrate used was 3,3'-Diaminobenzidine and counterstain with Meyer's Hematoxylin. S-100 expression done based on positivity of cells with cytoplasmic immune staining. The negative control was done on a case of other granulomatous lesions. All the collected data was analyzed by using software SPSS 21.0 for statistics and results represented by percentages, graphs, figures and tabular forms.

Inclusion Criteria:

Patient of all ages who undergo biopsy for clinically suspicious leprosy cases including both males and females. Adequate skin biopsy including epidermis dermis, and subcutis.

Exclusion Criteria: Individuals who are diagnosed with other granulomatous diseases and inadequate biopsy.

RESULTS:

A total of 50 cases of leprosy were included in the present study. Clinicopathological findings and immunohistochemical results are described below.

Out of 50 cases studied, male predominance was observed constituting 54% of cases and females constituted 46% of cases with a male to female ratio of 1.2:1.

Table 1: Demographic Details

Total no of cases	**50**
Males	27 (54%)
Females	23 (46%)
Male: Female ratio	1.2:1
Age range	18-24 years
Mean age in males	33.11years
Mean age in females	33.65 years

The age range observed in the present study was between 18 to 74 years, which signifies that the patients are diagnosed with leprosy at any age. The distribution of age according to gender shows mean of 33.1 years and median of 24 years in males whereas in females the mean age of diagnosis is 33.65 years and median of 23 years. It signifies that the mean age of diagnosing the case of leprosy in both genders is almost similar.

Table 2: Distribution of cases based on site of lesion

Site of lesion	**Number of cases**	**Percentage**
Face	11	22
Upper limb	28	56
Lower limb	30	60

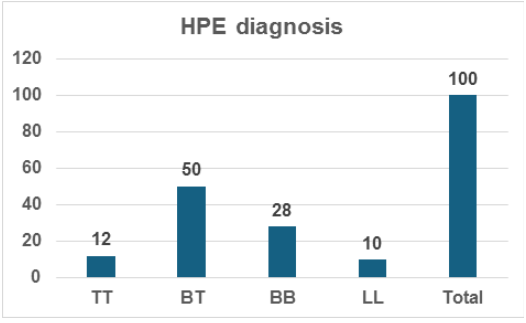
Trunk	9	18

Majority of the cases presented with lesions on lower limb, followed by upper limb, face and trunk in descending order with 60%, 56%, 22% and 18% respectively.

Table 3: Distribution of cases based on clinical presentation

Clinical presentation	Number of cases	Percentage
Decrease sensation	44	88
Decrease in hot/ cold sensation	41	82
Dry/ erythematous patch	31	62
Hypo pigmented patch	27	54
Ulceration	15	30
Foot ware slippage	10	20

Most of the cases presented with clinical features like decreased sensation (88%) and decreased in hot /cold sensation (82%) followed by dry/erythematous patch, hypopigmented patch, ulceration and foot ware slippage.



Bar Graph 1-Histopathologic Spectrum of Leprosy

The present study on histologic evaluation of skin biopsies showed predominantly borderline tuberculoid cases (50%) followed by mid-borderline (28%), tuberculoid (12%) and lepromatous leprosy (10%) cases

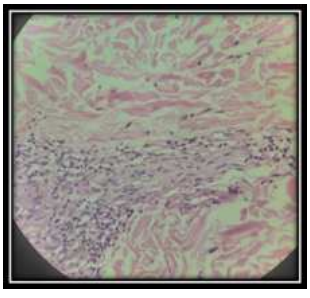


Figure1-Borderline tuberculoid H&E stain

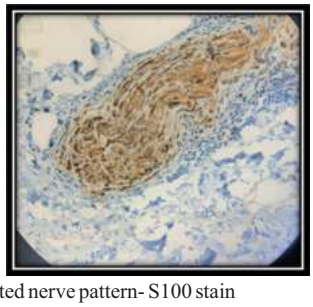


Figure 2 Infiltrated nerve pattern- S100 stain

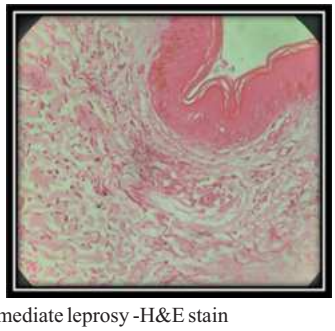


Figure 3-Intermediate leprosy -H&E stain

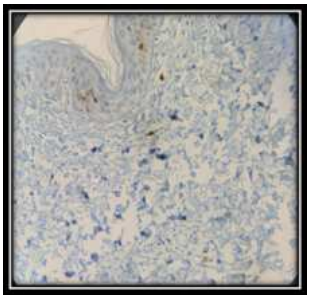


Figure 4-Intermediate leprosy-fragmented nerve pattern S100 stain

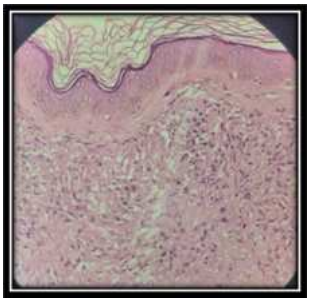


Figure 5-Lepromatous leprosy-H&E stain

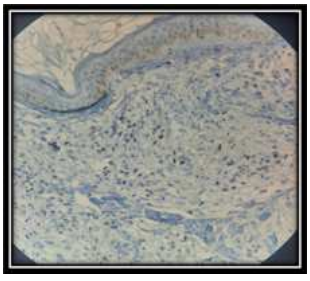


Figure 6-Absent nerve pattern -S100 stain

Bar Graph 2: Nerve pattern in histopathological spectrum of leprosy

In tuberculoid leprosy (TT) majority is infiltrated pattern (50%), in borderline tuberculoid (BT) majority pattern is fragmented (52%), mid-borderline (BB) fragmented pattern (43%) and in lepromatous it is absent nerve pattern (80%) demonstrated by S100 immunostaining.

DISCUSSION

Leprosy is a neurotropic disease and the evidence of nerve involvement by granulomatous infiltrate has been considered as an important feature of leprosy. The difficulty in recognising small nerve twigs on Hematoxylin and Eosin(H&E) stain has led to the use of S100 immunostain as an aid to histological classification of leprosy. The present study demonstrates change in nerve pattern in various forms of leprosy based on Ridley and Jopling classification by using S100 immunostaining. The diagnosis of Tuberculoid leprosy along with intermediate and borderline leprosy is difficult on routine H and E. S-100 immunostaining is superior to H and E in identifying the destruction of dermal nerves in leprosy. With the WHO goal of reducing the prevalence of leprosy, S-100 immunostaining could be effective aid in diagnosis and study of cutaneous nerve patterns involvement especially in Tuberculoid forms of leprosy.

Immunostaining for S100 protein showed different patterns of nerve involvement with tuberculoid leprosy infiltrated pattern of nerve involvement accounts for 50%, fragmented pattern of nerve

involvement accounts for 33% and absent nerve accounts for 16.7% of cases.

In Borderline tuberculoid it is observed that fragmented pattern of nerve involvement is the most common pattern which accounts for 52%, absent nerve 36% and infiltrated pattern of nerve involvement 12% of total cases. In Borderline borderline it is observed that fragmented pattern of nerve involvement is the most common 42.9% followed by absent nerve which accounts for 35.7% and infiltrated pattern of nerve involvement which accounts for 21.45%.In lepromatous leprosy form majority of cases showed absent nerve which accounts for 80% and fragmented pattern of 20%.In the present study majority of cases showed fragmented pattern of nerve damage, followed by absent and infiltrated which accounts for 44%;38% and 18% respectively.

CONCLUSION:

S100 is an immunohistochemical marker for Schwann cells in peripheral nerves which allows easy identification of even small nerve twigs and fragments of nerves and can be used to demonstrate nerve damage in various forms of leprosy. It is superior to routine Hematoxylin and Eosin staining in identifying nerves, infiltrated with or without fragmentation of nerve. In most cases of BT and BB, S100 staining showed fragmented pattern of nerve damage whereas LL showed absent pattern. The difference in the staining pattern of nerve fragments by S100 provides a clue about the spectrum of leprosy. We therefore emphasize performing S100 immunostaining as a valuable adjunct to Hematoxylin and Eosin stain in all clinically suspicious cases of leprosy in all biopsies for early diagnosis, management, prevents complications and morbidity.

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