Clinico-Histological Correlation in Hansen’s Disease: Three-year Experience at a Newly Established Tertiary Care Center in Central India

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Abstract

Background: Hansen’s disease is a chronic infectious disease caused by Mycobacterium leprae. It is characterized by a wide range of clinical and histological manifestations. Ridley–Jopling criteria are widely used for classifying leprosy. The demonstration of acid-fast bacilli on slit-skin smear examination and in skin biopsy aids in its diagnosis. Aim: The aim of the present study was to perform clinico-histological correlation of skin lesions in all patients with a clinical suspicion of Hansen’s disease. Materials and Methods: The study included skin biopsies of all suspected cases of Hansen’s disease received over a period of 3 years. Hematoxylin and eosin and Fite-Faraco stained sections of all cases were examined. Corresponding slit-skin smears, if available, were also reviewed. Results: During the study, a total of 116 cases were clinically diagnosed as Hansen’s disease. Clinico-histological correlation was obtained in 62.9% of the cases (73/116). The most common histological subtype of Hansen’s disease was borderline tuberculoid (TT) (40/116). Seven cases were diagnosed as lepromatous leprosy, five as TT, four as histoid, one as indeterminate, and three cases diagnosed as erythema nodosum leprosum. Fite-Faraco stain was positive in 33/73 cases. Out of 116 cases, slit-skin smears were available for 43 cases and were positive in 23 cases. Conclusion: Correlation between clinical, bacteriological, and morphological features is required for accurate classification of Hansen’s disease. Clinical detection and morphological diagnosis of early lesions remain challenging, and the histological findings should always be interpreted in correlation with clinical findings.

Key Words: Clinico-histological, correlation, fite-faraco, hansen’s disease

Introduction

Hansen’s disease is a chronic granulomatous infectious disease caused by Mycobacterium leprae. It is a slowly progressive disease which mainly affects peripheral nerve and skin. It presents as different clinicopathological forms depending on immune status of the host. Many classifications for leprosy have been proposed based on clinical, bacteriological, immunological, and histological status, for example, Madrid classification, Ridley and Jopling classification, and Indian classification. In 1960s, Ridley and Jopling proposed a histological classification for leprosy as indeterminant (I) leprosy, tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), borderline lepromatous (BL), and lepromatous (LL) leprosy. However, in 1982, the World Health Organization classified leprosy as multibacillary (MB) and paucibacillary (PB) on the basis of bacillary index (BI). I, TT, and BT cases of leprosy were classified as PB, and BB, BL, and LL cases of leprosy were classified as MB.

Under this method of classification, a BI value 2 or more at any skin site indicated therapy for MB leprosy and a BI value <2 indicated therapy for PB leprosy. By 1988, a positive skin-smear result at any site has become sufficient to indicate treatment for MB leprosy.

The diagnosis of leprosy is based on different clinical parameters which involve detailed examination of skin lesions and peripheral nerves along with slit-skin smear examination, histopathological examination, and demonstration of acid-fast bacilli.
The present study was carried out to assess the concordance between clinical and histopathological diagnosis in cases of leprosy using Ridley–Jopling scale.

Materials and Methods
The present cross-sectional study was conducted in the Departments of Pathology and Dermatology at a tertiary health-care teaching institute in central India. Skin biopsies of all suspected cases of Hansen’s disease received over a period of 3 years (June 2013–July 2016) were included in the study. Hematoxylin and eosin and Fite-Faraco stained sections of all cases were reviewed. The cases were classified according to Ridley–Jopling classification into TT, BT, BB, I, BL, and LL. Clinico-histological correlation was done for all the cases. In addition, wherever available the corresponding slit-skin smear was also reviewed.

Results
During the study, a total of 116 cases were clinically diagnosed as Hansen’s disease. The common clinical presentations were macules, nodules, and plaques. Clinico-histological correlation was obtained in 62.9% of the cases (73/116). The most common histological subtype of Hansen’s disease was BT (40/116). Seven cases were diagnosed as LL, five as TT, four as histoid, one as indeterminate, and three cases diagnosed as erythema nodosum leprosum (ENL) [Table 1 and Figure 1].

The age of the study participants varied from 5 to 75 years with a mean age of 33.9 years. Out of 116 cases, 80 were male and 36 were female. The male-to-female ratio of BT, BL, and LL was 2.5:1, 4.5:1, and 1:1.3, respectively. All the cases affected with TT, indeterminate, and histoid leprosy were males.

The clinico-histological correlation in BT and BL was 44.8% and 47.3%, respectively. One case was clinically diagnosed as mid-borderline; however, on histopathology, it came out as BT. The correlation in clinically diagnosed cases of TT (1/116), histoid (3/116), and ENL (2/116) was 100% [Table 2].

Fite-Faraco stain was positive in 33/73 cases. Of the 43 cases which had slit-skin smear reports, 23 (53.4%) were positive [Table 3].

Discussion
Leprosy is a slowly progressive, chronic infectious disease which can express itself in different clinicopathological forms depending on immune status of the host.[7] It primarily affects the skin and the peripheral nerves.[8] It can be progressive and can cause permanent damage to the skin, nerves, limbs, and eyes.[2] In the present

| Table 1: Distribution of cases |
|--------------------------------|
| **Total cases** | **Case division** | **Histopathological diagnosis** | **Number of cases** | **Percentage** |
| 116              | 73 cases correlated (62.9%) | TT | 5 | 6.8 |
|                 |                        | BT | 40 | 54.8 |
|                 |                        | BB | 0 | 0 |
|                 |                        | BL | 13 | 17.8 |
|                 |                        | LL | 7 | 9.6 |
|                 |                        | IL | 1 | 1.4 |
|                 |                        | ENL | 3 | 4.1 |
|                 |                        | Histoid | 4 | 5.5 |
|                 | 43 cases discordant | Nonspecific | 36 |  |
|                 |                        | Granulomatous lesion | 2 |  |
|                 |                        | Epidermal atrophy | 1 |  |
|                 |                        | Polymorphous light eruption | 2 |  |
|                 |                        | Retiform hemangioendothelioma | 1 |  |
|                 |                        | Pityriasis rosea | 1 |  |

ENL: Erythema nodosum leprosum, TT: Tuberculoid, BT: Borderline tuberculoid, BB: Mid-borderline

Figure 1: Photomicrograph showing (a) lepromatous leprosy, (b) borderline lepromatous leprosy, (c) tuberculoid leprosy, and (d) borderline tuberculoid leprosy (H and E, ×200)
The results of slit-skin smear (SSS) were compared with histological diagnosis of the biopsied lesion. This might be attributed to the studies conducted by Moorthy et al.,[11] Bhatia et al.,[12] and Kar et al.[13]

In our study, the most common histological subtype was BT followed by BL. BT has been reported to be the most common histological type of leprosy in other studies as well.[8,10,16] The excellent clinico-histological correlation was observed for the polar spectra of leprosy. Since borderline lesions are clinically and immunologically unstable, clinico-histological correlation was not found to be as impressive for cases clinically diagnosed as BT or BL.

As expected Fite-Faraco stain was positive in 100% cases of LL type or MB type of leprosy. Slit-skin smear test helps in establishing an early diagnosis of Hansen's disease. However, this test has high specificity but low sensitivity and as many as 70% of leprosy cases are smear negative.[17] The results of slit-skin smear correlated with that of Fite-Faraco-stained sections in LL spectrum of leprosy. For lesions toward TT pole of leprosy, we found higher positivity rate on Fite-Faraco-stained histological sections as compared to SSS. This was probably because of the fact that increased step sections of the paraffin-embedded block increased the chances of detection of bacilli in PB cases. Bacillary index in granuloma was also found to be higher than that of slit-skin smear by Ridley who opined that slit-skin smear reflected density at a particular foci while sections also took into account the size of the lesion along with density.[18] In the present study, 43 cases of clinically diagnosed leprosy were discordant. In most of these cases (36/43), the findings on histopathological examination were nonspecific. However, confirmed diagnosis was established in 7/43 cases comprising of granulomatous lesion (2/43), polymorphous light eruption (2/43), retiform hemangioendothelioma (1/43), pityriasis rosea (1/43), and epidermal atrophy (1/43).

The cellular characteristics in leprosy lesions are related to the immunological modulation of the patient. Hence, different grades of modulation affect the host defensive response and result in different types of clinicopathological pictures.[14] Selection of the site for biopsy plays an important role in histopathological diagnosis since clinically dissimilar lesions biopsied from the same patient can show different types of histopathology.[15]

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Despite specific histopathological findings in different forms, there occurs an overlap of features between different types. Immunologically mid-borderline leprosy is the least stable and variety of clinical lesions may be found in the same patient. Hence, it is necessary to relate the histological features with the clinical
characteristics presented by the particular morphological lesion subjected to biopsy.[6]

Cases of indeterminate leprosy are also difficult to diagnose due to the nonspecific histology of the lesions. It also depends on factors such as nature and depth of biopsy, the acid-fast-stained sections examined, and the interobserver variation in both clinical and histopathological examinations. In the present study, one case was diagnosed as indeterminate leprosy both clinically and histopathologically with the aid of Fite-Faraco stain. In some early cases, clinical signs and symptoms may precede the presently known characteristic histological changes and vice versa. Hence, if biopsy is taken at an early stage, there are chances of discordance between the clinical and histopathological observation.

Clinico-histological correlation in leprosy is also required for monitoring the response to treatment and for assessing relapse or reactivation of the disease. Although there has been a substantial decrease in the number of leprosy patients after the implementation of MDT for leprosy, we are yet to achieve the goal of leprosy eradication.[6] It is known that inactive bacilli may persist in nerves of borderline or indeterminate cases for years even after complete treatment.[19] Only when all proven cases of Hansen’s disease undergo regular follow-up after treatment and are diligently screened for bacillary load before labeling them as disease free, we shall be able to realize our dream of making our country free from the scourge of leprosy.

Conclusion
Correlation between clinical, bacteriological, and morphological features is required for accurate classification of Hansen’s disease. Clinical detection and morphological diagnosis of early lesions remain challenging, and the histological findings should always be interpreted in correlation with clinical findings. Since the impact of finding one new case of leprosy is huge, such diligence is warranted both by the dermatologist as well as by the pathologist.

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Conflicts of interest
There are no conflicts of interest.

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