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Limitations of Clinico-histopathological Correlation of Skin Biopsies in Leprosy

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ABSTRACT

Background: Skin biopsies play an important role in diagnosing and classifying different types of leprosy. The aim of this study was to analyse different histologic types of leprosy, to correlate histopathological diagnosis with clinical diagnosis, to study the uniformity of clinical and histological findings in the diagnosis of leprosy and to evaluate difficulties faced during clinicopathological correlation according to Ridley- Jopling classification due to inadequacy of data provided.

Methods: This is a retrospective study of all skin biopsies reported from Department of Pathology of Tribhuvan University Teaching Hospital from 14 April 2007 to 13 April 2009, for which leprosy was the diagnosis or was strongly suspected on histopathology. Results: Out of 40 cases included, 33 were males and seven were females. Tuberculoid leprosy was the most common type comprising 23 /40 cases (57.5%). In 18/ 40 cases (45%), clinical diagnosis was leprosy. Only in three, leprosy was classified according to Ridley-Jopling criteria clinically. Thus clinicopathological correlation according to Ridley-Jopling criteria could not be done. Histopathological reporting lacked uniformity too. In 13/40 reports (32.5%), exact location of granuloma, presence or absence of Grenz zone and enroachment of epidermis by granuloma was not mentioned. None mentioned the number and distribution of lymphocytes or relative proportion of epithelioid cells and foamy histiocytes.

Results: Out of 40 cases included, 33 were males and seven were females. Tuberculoid leprosy was the most common type comprising 23 /40 cases (57.5%). In 18/ 40 cases (45%), clinical diagnosis was leprosy. Only in three, leprosy was classified according to Ridley-Jopling criteria clinically. Thus clinicopathological correlation according to Ridley-Jopling criteria could not be done. Histopathological reporting lacked uniformity too. In 13/40 reports (32.5%), exact location of granuloma, presence or absence of Grenz zone and enroachment of epidermis by granuloma was not mentioned. None mentioned the number and distribution of lymphocytes or relative proportion of epithelioid cells and foamy histiocytes..

Conclusions: Histopathological diagnosis of leprosy did not correlated with clinical diagnosis significantly. Uniformity was not seen in the clinical or histopathological informations provided making it difficult to conduct retrospective clinico pathological correlation.

Key words: granuloma, histopathology, leprosy, Ridley-Jopling classification, tuberculoid

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INTRODUCTION

Nepal is a known leprosy endemic country.[1] Along with clinical judgment and skin smear examination, skin biopsies help to diagnose different types of leprosy and also separate it from other granulomatous lesions.[2] Classification of the disease is used to identify the different aspects of disease presentation as this affects prognosis, treatment and scientific understanding. Though the World Health organization (WHO) classification which divides leprosy into multibacillary and paucibacillary group remains useful for allocating patients to treatment groups, in context of research it is better to use the Ridley-Jopling classification, which promotes a better understanding of the disease pathology, prognosis and the risk factors for complications.[3]

The aim of this study was to analyze different histological types of leprosy, correlate histopathological diagnosis with clinical diagnosis, study the uniformity of clinical and histological findings in the diagnosis of leprosy and to evaluate difficulties faced during

clinicopathological correlation according to Ridley-Jopling classification due to inadequacy of data provided.

METHODS

A retrospective observational study was done at Department of Pathology of Tribhuvan University Teaching Hospital (TUTH) from 14 April 2007 to 13 April 2009. Ethical approval was taken from the hospital and the patient party. Cases where histopathological diagnosis of leprosy was made or considered differential diagnosis irrespective of age and sex of the patient or nature of the lesion were selected for study. Those cases where leprosy was suspected clinically but histopathology did not agree with the diagnosis were not included. The Ridley- Jopling classification was used histologically to make diagnosis of leprosy. Cases of indeterminate leprosy were also included. The requisition forms accompanying the biopsy specimen as well the copy of issued histopathology reports that are preserved in the department routinely were used to obtain data pertaining to age, sex, clinical information and histopathological findings. Also the microscopic description of the slides given in the reports were studied to obtain the information regarding a) morphology of granulomas and proportion and distribution of lymphocytes, epithelioid cells, foamy histiocytes and giant cells, b) distribution of granuloma in dermis and encroachment on the epidermis, c) infiltration of nerves ,blood vessels and adnexa d) presence or absence of Grenz zone e)results of Fite's stain and f) epidermal changes . We did not review the Hematoxylin and eosin stained or Fite stained sections. Data were analyzed with the help of Microsoft excel.

RESULTS

Total of 40 skin biopsies were histopathologically reported as leprosy during the two years study period, of which 33 were from males and 7 were from females. Age of these patients ranged from 15 years to 85 years. Most of the patients (17/40) were in 21-30 years age group. Tuberculoid leprosy was the commonest diagnosis, site of lesion with histopathological diagnosis and their correlation with clinical features have been presente (Table 1, 2).

In 38 cases, straight forward histopathological diagnosis of leprosy was made and in two cases, leprosy was strongly considered as differential diagnosis of granulomatous lesion. These two cases showed few epithelioid cells around adnexal structures. However other histological findings needed to categorize them in one of the subtypes were not seen. Out of 40 cases, in 18 cases (45%) clinical diagnosis of leprosy was mentioned in the requisition form and only in 3 of 18 cases the clinical diagnosis was according to Ridley Jopling scale.

When histopathology report was studied it was found that though the terminology used for the final diagnosis was according to Ridley Jopling scale, the reports lacked uniformity in microscopic description. It was found that 13 (32.5%) reports did not mention the exact location of granuloma, presence or absence of Grenz zone and whether the granuloma was enroaching the epidermis or not. Two reports did not mention whether the granuloma were infiltrating around the nerves, blood vessels or adnexa. In only eight cases, the result of Fite stain was included. None of the reports mentioned the number and distribution of lymphocytes or the relative proportion of epithelioid cells and foamy histiocytes. The epidermal changes were not described in 19(47.5%) cases. Where mentioned, epidermal atrophy was the most common finding in leprosy (Table 3).

Table 1. Site of lesion.

Site of lesion	Number (Percentage)
Not mentioned	23 (57.5)
Head and neck	8 (20)
Upper limb	5 (12.5)
Lower limb	2 (5)
Trunk	2 (5)
Total	40 (100)

Table 2. Correlation between histopathological diagnosis and clinical information.

Clinical information	Histopathological diagnosis					
	BL*	BT**	Granulomatuos inflammation	TT***	Indeterminate leprosy	Total
Hansens' disease	1	6	1	6	1	15
Erythematous plaque		2	1	9		12
Hypoanasthetic patch				4		4
Hypopigmented patch		1		2		3
BT		2		1		3
Not mentioned	1			1		2
Hyperpigmented patch		1				1
Total	2	12	2	23	1	40

*BT: Borderline tuberculoid, **BL: Borderline Lepromatous, ***TT:Tuberculoid

Table 3. Epidermal changes in various types of leprosy.

Epidermal changes	Histopathological diagnosis					
	BL	BT	Granulomatous inflammation	TT	Indeterminate leprosy	Total
Not mentioned	1	8		10		19
Atrophic	1	4	2	3	1	11
Unremarkable				6		6
Acanthosis				3		3
Epidermis not Seen				1		1
Total	2	12	2	23	1	40

DISCUSSION

There are many classifications of leprosy among which Ridley- Jopling classification is recommended to use unless there is a good reason not to use it.[3]

The Ridley-Jopling classification published in 1966 uses clinical, histological and immunological criteria to classify leprosy patients and is widely accepted by pathologists and leprologists.[4] They suggested five member groups, Tuberculoid (TT), Borderline tuberculoid (BT), Borderline (BB), Borderline Lepromatous (BL) and Lepromatous (LL). Histopathologically well formed epithelioid cell granulomas with a rim of lymphocytes distributed through out the dermis, particularly along adnexal structures and neurovascular bundles and enroaching the basal layer of the epidermis are TT. Cases with granulomas having fewer number of lymphocytes and more giant cells and not encroaching upon the epidermis are BT. Cases having granuloma rich in foamy histiocytes and few epithelioid cells are BL and cases with diffuse sheets of foamy histiocytes with Grenz zone are classified as LL.[5] In BB, the macrophages are uniformly activated to epithelioid cells but are not focalized into distinct granulomas and lymphocytes are scanty. There are no giant cells and dermal edema is prominent between inflammatory cells.[6] Infiltration of sub epidermal zone is seen invariably in TT, is inconstant in BT and clear in BB, BL and LL.[7] In indeterminate leprosy, there is mild lymphocytic infiltration around neurovascular bundles, sweat glands and erector pili muscle. No formed epithelioid cell granulomas are observed.[6]

Tuberculoid leprosy was the most common diagnosis in this study followed by borderline tuberculoid leprosy. Other studies have found BT leprosy to be the commonest. In a study of Moorthy BN et al, out of 372 cases , only 26 (6.98%) were TT and 269 (72.31%) were BT.[8] In a study of Bal A et al, out of 303 leprosy cases, 206 was BT and only 27 was TT.[5] The cases included in our study were reported by six different pathologists. When the microscopic description and diagnosis were reviewed it was found that many cases which best fitted the diagnosis of BT were actually reported as TT. In most the description was incomplete and did not mention the proportion of lymphocytes, giant cells and epithelioid cells and also did not describe whether the granulomas were encroaching the epidermis or not. These are the findings which differentiate TT and BT. Thus the high frequency of TT in this study may be due to not strictly adhering to the morphologic criteria given by Ridley and

Jopling for reporting leprosy histologically.

In BT and TT, epithelioid granulomas and Langhans' as well as foreign body giant cells are seen. In such cases, Fite stain is not of much help because of sparse bacilli.[9] In a study by Bal A et al, out of 206 BT only six were positive for Lepra bacilli where as none of the 27 TT were positive.[5] In this study, for only eight cases report of Fite stain was mentioned. These were four BT, two TT and two BL. None of the BT or TT was positive for Lepra bacilli.

Only two cases of borderline lepromatous leprosy were seen in this study. Both of these cases showed foamy cells in the dermis separated from epidermis by a Grenz zone and few epithelioid cells and lymphocytes in the dermis. Giant cells were absent. Fite stain showed Lepra bacilli in both these cases.

In two cases, definite diagnosis was not made and impression was just given as granulomatous inflammation with possibility of leprosy. These patients had non necrotizing epithelioid cell granulomas involving the periadnexal structures and erector pilli muscle. However, perineural inflammation was not seen and epidermis was atrophic. These patients had presented with erythematous plaque in head and neck region.

When the data pertaining to clinical features and provisional diagnosis were analysed, it was found that most cases were suspected of Hansen's disease .There are many studies describing clinico- histopathological correlation of leprosy.[7,8,10,11] But in these studies the Ridley-Jopling classification was strictly followed clinically as well as histopathologically. Proper clinico-pathological correlation according to Ridley- Jopling scale could not be done in this study because only in three requisition forms clinical diagnosis was given according to this classification. Most requisition forms just mentioned the provisional diagnosis of "Hansen's disease", some mentioned few signs and symptoms. Among the clinical features mentioned, erythematous plaque was the most common presentation. In more than half of the cases, even the site of lesion and biopsy sites were not mentioned. In those provided, head and neck was the commonest site involved. Other studies have found variable correlation ranging from 19% to 98.2% between clinical and histopathological classification. The correlation is better at lepromatous pole (LL and BL) than the tuberculoid pole (TT and BT) and is least in indeterminate leprosy.[8]

Various factors influence histopathological diagnosis of leprosy. This includes size of specimen, site of biopsy, age of lesion, nature and depth of biopsy, quality of sections, and immunological status of patient and treatment history.[10] Also there is some degree of overlap between different types of leprosy clinically as well as histopathologically and there is always a chance of interobserver variation as well.[12]

Since the study was retrospective with a limited sample size it has its own limitation. Higher level of study designs with multicentric approach is recommended to further validate the finding of the study.

CONCLUSIONS

Histopathological diagnosis of leprosy did not correlated with clinical diagnosis significantly. Uniformity was not seen in the clinical or histopathological informations provided making it difficult to conduct retrospective clinico-pathological correlation.

Hence it is recommended that in evaluating leprosy patients a standard classification system should be adopted by pathologists as well as leprologists particularly in academic institutions like TUTH where performing researches are defined as job responsibility. A proper clinical history and diagnosis according to the clinical aspect of Ridley-Jopling classification should always be mentioned in the requisition form and the same should be strictly followed by reporting pathologists.

REFERENCES

1. Jain MC. Leprosy scenario in Nepal. J Nepal Med Assoc. 2008;47:260-63.
2. Lucus SB, Ridley DS.The use of histopathology in leprosy diagnosis and research. Lepr Rev.1989;60:257-62.
3. Lockwood DNJ, Sarno E, Cairnsmith W. Classifying leprosy patients—searching for perfect solution? Lepr Rev. 2007;78:317-20.
4. Ridley DS, Jopling WH. Classification of leprosy according to immunity: A five group system.Int J Lepr. 1966;34:255-73.
5. Bal A, Mohan H, Dhami GP. Infectious granulomatous dermatitis: A clinico pathological study. Indian J Dermatol. 2006;51:217-20.
6. Elder DE, Elenitsas R, Johnson Jr. BL, Murphy GF, editors. Lever's histopathology of skin. 9th ed. Delhi: Lippincott Williams & Wilkins; 2005. p.569-76.
7. Pandya AN,Tailor HJ. Clinicohistopathological correlation of leprosy. Indian J Dermatol Venereol Leprol. 2008;74:174-6.
8. Moorthy BN, Kumar P, Chatura KR, Chandrasekhar HR, Basavaraja PK. Histopathological correlation of skin biopsies in leprosy. Indian J Dermatol Venereol Leprol. 2001;67:299-301.
9. Cree IA, Smith WB, Beck JS. A quantitative relationship between systemic and histologic parameters of immunity in individual leprosy patients. Int J Lepr other mycobact Dis. 1990;58:347-52.
10. Bhatia AS, Katoch K, Narayanan RB, Ramu G, Mukherjee A, Lavania RK. Clinical and histopathological correlation in the classification of leprosy. Int J Lepr. 1993;61:433-38.
11. Sharma A, Sharma RK, Goswsami KC, Bardwaj S. JK science. 2008;10:120-23.
12. Chacko CJG. Role of histopathology in the early diagnosis of leprosy. Indian J Lepr. 1993;65:23-27.