Clinico-histopathological correlation of leprosy in western region of Nepal-A pioneer pilot study

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Abstract

Background: Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* disease affecting mainly cutaneous and peripheral nervous system. This entity expresses with a wide array of clinical manifestations and may mimic variety of disparate diseases, therefore is difficult to diagnose clinically, so for the adequate treatment and better prognosis, the diagnosis must be made early and it should be accurate, therefore clinic-pathological correlation is extremely important. Hence, the present study was conducted to correlate different types of leprosy clinically and histopathologically.

Objectives: To analyze different histological types of leprosy, correlate histopathological diagnosis with clinical diagnosis and study the uniformity of clinical and histological findings in the diagnosis of leprosy.

Methodology: This study was conducted on 21 biopsy samples received in Department of Dermatology, Nepalgunj Medical College and Teaching Hospital, Nepalgunj over a period of one year from December 1, 2014 to December 31, 2015. All the clinically diagnosed new skin lesions (clinical classifications noted) were subjected for biopsy; tissue specimen were fixed in 10% formalin and sent for histopathological analysis. 5 micron sections were stained with haematoxylin and eosin for morphological assessment and with modified Fite-Farcao stain for identification of the lepra bacilli. Ridley and Jopling classification was applied for histopathological taxonomy. Data was analyzed using SPSS software version 15.0 and kappa test was applied to evaluate the concordance results.

Results: The present study comprised of 21 patients, 12 were males (57.1%) and 9 females (42.9%) with a male: female ratio of 1.33:1. Majority of the patients were between 31 to 40 years of age. Based on histopathology, 14 (66.7%) patients had Tuberculoid leprosy (TT); 5 patients had Borderline Lepromatous (BL) leprosy; 1 (4.8%) had Borderline Tuberculoid (BT) leprosy and Lepromatous Leprosy (LL) each. Out of the 21 patients included in the study, 16 (76.1%) presented a clinical suspicion of paucibacillary leprosy and 5 (23.8%) of multibacillary leprosy. Maximum clinico-histopathological correlation was seen in BL (100%), followed by TT (84.6%), LL (50%) and 0% in BT. Overall clinico-histopathological agreement was seen in 15 (71.4%) cases and disagreement in 6 (28.7%) cases.

Conclusion: Clinical and histopathological diagnosis of leprosy is imperative for proper treatment and prevention of complications.

Keywords: Leprosy, Histopathology, Mycobacterium leprae

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Introduction

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* and expresses with a wide array of clinico-pathological forms depending on the host immune status.[1] It is also known as Hansen's disease and is indeed one of the oldest documented infectious diseases known to mankind.[2] The history of leprosy dates back to 600 B.C. when the first case was documented in the *Sushruta Samhita*, an ancient Sanskrit text on Medicine and Surgery. Since ancient times, it is referred as "Kushtaroga", and the cardinal signs of the disease include skin lesions, skin anesthesia and enlarged peripheral nerves.[3] It affects chiefly the skin and peripheral nervous system, however, may also affect other systems of the body.[4]

Leprosy is one of the leading causes of physical disabilities associated with grave morbidity and also remains a disease of public health concern because of the social stigma attached.[5] In 2010, Nepal declared abolition of leprosy nationwide under the National Leprosy Elimination Programme of Nepal (2006/07). Though the goal of abolition was achieved in 2010, the disease is still prevalent.[6]

Due to its clinical diversity and resemblance to other diseases, leprosy is difficult to diagnose clinically. Classification is used to identify the different aspects of disease presentation as this affects prognosis, treatment and scientific understanding. According to World Health organization (WHO), leprosy can be broadly classified as paucibacillary (up to five skin lesions and/or only one affected nerve trunk) and multibacillary (over five skin lesions and/or more than one affected nerve trunk).[7] Ridley and Jopling classification is most accepted by pathologists and leprologists; based on the clinical, histopathological and immunological status of the host and promotes a better understanding of the

pathology, prognosis and the risk factors for complications.[8] It includes early in determinant leprosy (IL), polar tuberculoid leprosy (TT), borderline tuberculoid leprosy (BT), mid-borderline leprosy (BB), borderline lepromatous leprosy (BL), and polar lepromatous leprosy.[9]

Histopathology helps in prompt diagnosis and exact typing of the disease. Demonstration of acid fast bacilli in the histopathological sections is also considered as a key factor in diagnosis. Modified Fite's procedure has proved to be the most valuable in demonstrating leprae bacilli in tissues sections.[10] Due to varied clinical presentation and aptitude to mimic other diseases, leprosy is sometimes difficult to diagnose clinically, making histopathological examination a compelling tool for confirmation.[11]

Clinical classification gives information confined to only gross appearances of the lesions. A great variation has been observed in the interpretation of both the histopathological examination and pathological reports in view of clinical presentations of the disease.[12] Against this backdrop, the present study was conducted to correlate different types of leprosy clinically and histopathologically.

Aim and Objectives

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.

Materials and Method

This study was conducted on 21 biopsy samples received in Department of Dermatology and Venereology, Nepalgunj Medical College and Teaching Hospital, Nepalgunj over a period of one year from December 1, 2014 to December 31, 2015. Cases were selected regardless of their age, sex, socio-economic status and occupation. Approval by ethical committee and signed consent was obtained from all the patients enrolled in the study. All the clinically diagnosed new skin lesions (clinical classifications noted) were subjected for biopsy; tissue specimen were fixed in 10% formalin and sent for histopathological analysis. 5 micron sections were stained with haematoxylin and eosin for morphological assessment and with modified Fite-Farcao stain for identification of the lepra bacilli. Ridley and Jopling classification was applied for histopathological taxonomy.

Statistical analysis: Data was analyzed using SPSS software version 15.0 and kappa test was applied to evaluate the concordance results. The kappa values and their interpretations were as follows: <0, no agreement; 0–0.19, very weak agreement; 0.20–0.39, weak agreement; 0.40–0.59, moderate agreement; 0.60–0.79, substantial agreement; and 0.8–1.0, excellent agreement.[13] The significance level used for the analyses was 5% ($p < 0.05$).

Results

The present study comprised of 21 patients, 12 were males (57.1%) and 9 females (42.9%) with a male: female ratio of 1.33:1 **(Table 1)**.

Table 2 shows the distribution of patients according to age group and gender; majority of the patients (7 patients; 3 males and 4 females) were between 31 to 40 years of age; whereas least affected were between 61 to 70 years (1 patient).

Ridley and Jopling classification was used to classify leprosy on both clinical and histopathological diagnosis. Based on histopathology, 14 patients had Tuberculoid leprosy (TT) [10 males, 4 females]; 1 (female) had Borderline Tuberculoid leprosy (BT); 5 patients had Borderline Lepromatous leprosy (BL) [1 male, 4 females]; 1 (female) had Lepromatous leprosy (LL). None of the patients in our study had Borderline borderline (BB) and Intermediate leprosy (IL). Based on the histopathological type, TT was found to be maximum (66.7%), whereas BT and LL were found to be minimum in number (4.8%). All subtypes of leprosy were dominant in males than females **(Table 3)**.

Out of the 21 patients included in the study, 16 (76.1%) presented a clinical suspicion of paucibacillary leprosy and 5 (23.8%) of multibacillary leprosy. Out of 14 patients with TT; 9 had single lesion, 3 had 2 lesions and remaining 2 had 3 lesions. Patients with BT had 5 lesions; out of 5 patients with BL, 1 patient had 4 lesions, 1 patient had 7 lesions, 1 had 11 lesions and 2 had 13 lesions. Patient with LL had diffuse lesions. The overall distribution of the number of lesion in different types is described in **Table 4**.

Table 5 shows clinico-histopathological correlation of various types of leprosy. Maximum clinico-histopathological correlation was seen in BL (100%), followed by TT (84.6%), LL (50%) and 0% in BT. Overall clinico-histopathological agreement was seen in 15 (71.4%) cases and disagreement in 6 (28.7%) cases. The Kappa value was calculated as 0.475 and the strength of agreement was considered to be 'moderate' with p-value of 0.3.

Table 1: Distribution of patients according to gender

Gender	No. (%age)
Males	12 (57.1)
Females	09 (42.9)
Male: Female ratio	1.33:1

Table 2: Distribution of patients according to age group and gender

Age group (in years)	Gender		Total	*p*-value
	Males	Females		
10-20	03	--	03	
21-30	05	--	05	
31-40	03	04	07	
41-50	--	03	03	0.6^{ns}

51-60	01	01	02	
61-70	--	01	01	
Sub total	12	09	21	
Mean±SD	2±2	1.5±2.7	1.75±1.8	

^{ns} – *non-significant*

Table 3: Distribution of histopathological diagnosis according to gender

Histopathological diagnosis	Gender		Total	*p*-value
	Male	Female		
TT	10	04	14	0.8^{ns}
BT	--	01	01	
BB	--	--	--	
BL	01	04	05	
LL	01	--	01	
IL	--	--	--	
Subtotal	12	09	21	
Mean±SD	3±4.7	2.3±2.1	2.6±3.4	

TT= Tuberculoid, BT= Borderline Tuberculoid, BB= Borderline Borderline, BL= Borderline Lepromatous, LL= Lepromatous, IL= Indeterminate Leprosy, ^{ns} – *non-significant*

Table 4: Distribution of histopathological diagnosis according to age group

Age (in years)	Histological diagnosis						
	TT	BT	BB	BL	LL	IL	Total
10-20	03	--	--	--	--	--	03
21-30	05	--	--	--	--	--	05
31-40	03	01	--	03	--	--	07
41-50	01	--	--	02	--	--	03
51-60	01	--	--	--	01	--	02
61-70	01	--	--	--	--	--	01
Subtotal	14	01	--	05	01	--	21

Table 5: Number of lesions in different types of leprosy

No. of lesions	Type of leprosy						
	TT	BT	BB	BL	LL	IL	Total
1	09	--	--	--	--	--	09
2	03	--	--	--	--	--	03
3	02	--	--	--	--	--	02
4	--	--	--	01	--	--	01
5	--	01	--	--	--	--	01
7	--	--	--	01	--	--	01
11	--	--	--	01	--	--	01
13	--	--	--	02	--	--	02
Diffuse	--	--	--	--	01	--	01
Subtotal	14	01	--	05	01	--	21

Table 6: Clinico-histopathological correlation of leprosy

Clinical types	Clinically diagnosed cases	Histological diagnosis						
		TT	BT	BB	BL	LL	IL	Agreement, n (%)
TT	13	11	01	--	01	--	--	11/13 (84.6)
BT	03	03	--	--	--	--	--	00/03 (00)
BB	--	--	--	--	--	--	--	--
BL	03	--	--	--	03	--	--	03/03 (100)
LL	02	--	--	--	01	01	--	01/02 (50)
IL	--	--	--	--	--	--	--	--
Subtotal	21	14	01	--	05	01	--	15/21 (71.4)

Kappa= 0.475. The strength of agreement is considered to be 'moderate'. P=0.3 (non-significant)

Discussion

There are many classifications of leprosy among which Ridley and Jopling classification is the most accepted classification. The classification was published in 1966 and is based on uses clinical, histological and immunological criteria.[8] In our study, this classification was used to for the correlation. Out of 21 cases, the diagnosis of 15 cases correlated clinically and histopathologically (71.4%).

In the present study, out of 21 patients, 12 were males (57.1%) and 9 females (42.9%) with a male: female ratio of 1.33:1. This is in concordance with the study conducted by Manandhar et al[14], where male predilection was seen in 75% cases.

Majority of the patients in our study were between 31 to 40 years of age (7 patients; 3 males and 4 females). In a study conducted by Tiwari M et al[15], majority of the patients were in the age group of 20-40 years. This tendency can be explained by reasons like illiteracy and poor knowledge, and strong tradition leading to under reporting of leprosy in females.[16]

Based on the histopathological type, TT was found to be maximum (66.7%), whereas BT and LL were found to be minimum in number (4.8%). These findings were contrary to the studies conducted by Shiwaswamy et al[17] and Mathur et al[18] where BT type was found to be the most common type. In 4 patients with TT (clinically and histopathologically), physical disability like clawing of hands and foot drop was noted that was not seen in any other type.

Veena et al[19] and Murthy et al[20] found majority of cases of paucibacillary type of leprosy, 77.0% and 85.7% respectively. In our study also, paucibacillary was majorly found (76.1%).

Maximum clinico-histopathological correlation was seen in BL (100%), followed by TT (84.6%), LL (50%) and 0% in BT. Overall clinico-histopathological agreement was seen in 15 (71.4%) cases and disagreement in 6 (28.7%) cases. These results were in concordance with the studies conducted by Thapa et al[12] and Tiwari et al[15] wherein a strong correlation was found amongst the BL type. Negative correlation can be explained on the basis that the diagnosis is usually made according to clinical examination, awaiting histopathological confirmation. Variation in other studies may be due to different criteria used to select the cases: biopsy site, lesion characteristics, immune status of the patient, etc.

Limitations of the study

In our study, disagreement was seen in 6 out of 21 cases. This may be as the parameters used for the histopathological classification are accurate; whereas, the clinical classification is based only to the gross appearances of the lesions. The sample size was limited, therefore, higher level of study designs with multidisciplinary approach and a large sample size is recommended to further corroborate the study.

Conclusion

Due to its clinical diversity and resemblance to other diseases, leprosy is difficult to diagnose clinically. Thus, studies have shown the significance of histopathological correlation among patients with leprosy, in order to improve the prognosis and treatment.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

References

1. Panday AN, Tailor HJ. Clinico-histopathological correlation in leprosy. Ind J Dermatol Venerol Leprol 2008;74:174-6.
2. Jacob JT, Franco-Paredes C. The stigmatization of leprosy in India and its impact on future approaches to elimination and control. PLoS Negl Trop Dis 2008;2: e113.
3. Lowe J. Comments on the history of leprosy. Lepr Rev 1947;18:54-63.
4. Robertson Jo. Leprosy and the elusive M. leprae: colonial and imperial medical exchanges in the nineteenth century. Hist. Cienc. Saude-Manguinhos 2003;10(1):13-40.
5. Kumar A, Negi SR, Vaishnav K. A study of clinico-histopathological correlation of leprosy in a tertiary care hospital in western district of Rajasthan. J Res Med Den Sci 2014;2(3):43-8.
6. Patro BK, Madhanraj K, Singh A. Is leprosy 'Elimination' a conceptual illusion? Indian J Dermatol Venereol Leprol 2011;77:549-51.
7. World Health Organization. Guide to eliminate leprosy as a public health problem, 1st ed., Geneva: World Health Organization; 1995.
8. Lockwood DNJ, Sarno E, Cairnsmith W. Classifying leprosy patients—searching for perfect solution? Lepr Rev. 2007;78:317-20.
9. Parkash O. Classification of leprosy into multibacillary and paucibacillary groups: An analysis. FEMS Immunol Med Microbiol 2009;55:1-5.
10. Job, C.K., Chacko, C.I.G, A modification of Fite's stain for demonstration of M. leprae in tissues sections, Int J Lepr 1986;58:17-9.
11. Nayak SV, Shivarudrappa AS, Nagarajapa AH, Ahmed SM. Role of modified rapid AFB method in histopathological sections of Hansen disease, Ind J Dermatol Venerol Leprol 2003;69:173-4.
12. Thapa DP, Jha AK. Clinico-histopathological correlation in leprosy: A tertiary care hospital based study. Our Dermatol Online 2013;4(3):294-6.
13. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;67:119–25.
14. Manandhar U, Adhikari RC, Sayami G. Clinico-histopathological correlation of skin biopsies in leprosy. Journal of Pathology of Nepal 2013;3:452-8.
15. Tiwari M, Ranabhat S, Maharjan S. Clinico-histopathological correlation of leprosy: A retrospective study of skin biopsy specimens in Chitwan Medical College. Inter J Medical Sci Res Prac 2015;2(1):8-11.

16. Varkevisser CM, Lever P, Alubo O, Burathoki K, Idawani C, Moreira TM et al. Gender and leprosy: Case studies in Indonesia, Nigeria, Nepal and Brazil. Lepr Rev 2009;80:65-76.
17. Shivaswamy KN; Shyamprasad AL; Sumathy TK; Ranganathan C, Agarwal V. Clinico-histopathological correlation in leprosy. Dermatology Online Journal 2012;18(9):2.
18. Mathur MC, Ghimire RBK, Shrestha P, Kedia SK. Clinico-histopathological correlation in leprosy. Kathmandu Univ Med J 2011;36(4):248-51.
19. Veena S. Histo-morphological study of leprosy (unpublished Doctoral dissertation) Rajiv Gandhi University of Health Sciences, 2008.
20. Murthy N. Histopathological study of leprosy (unpublished Doctoral dissertation) Rajiv Gandhi University of Health Sciences, 2000.