Indian J Lepr 2017, 89 : 9-14

http://www.ijl.org.in

Original Article

Clinico-histopathological Correlation of Leprosy in Western Region of Nepal - A Pilot Study

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Received : 29.04.2016 Accepted : 15.12.2016

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*, affecting mainly cutaneous and peripheral nervous system. Clinically leprosy presents with a wide array of clinical manifestations and may mimic variety of disparate diseases, therefore, occasionally it may be difficult to diagnose and accurately classify the disease clinically. With more active detection and wide use of multi-drug treatment (MDT), spectrum of disease may be changing which can be better understood by histopathology which can better characterize the immunological spectrum. Hence, the present pilot study was conducted to correlate different types of clinical forms of leprosy with histopathology in Western Nepal. This study was conducted on 21 biopsy samples from Department of Dermatology, Nepalgunj Medical College and Teaching Hospital, Nepalgunj over a period of one year from December 1, 2014 to December 31, 2015. Biopsies were taken from skin lesions of all ?? the clinically diagnosed leprosy cases during this period. Ridley and Jopling classification was applied for histopathological taxonomy. 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 (7/21) 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. Maximum clinico-histopathological correlation was seen in BL 3/3 (100%), followed by 11/13 in TT (84.6%), 1/2 in LL (50%) and 0% in BT (all three diagnosed as TT by histopathology). Overall clinico-histopathological agreement was seen in 15 (71.4%) cases and disagreement in 6 (28.7%) cases. This limited data shows the need of further population based studies, need for development of better markers, may be better expertise and may be second opinion for improving the clinicopathological correlation in leprosy.

Keywords : Leprosy, Histopathology, clinical, correlation, Nepal

Introduction

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* and expresses in the form of wide array of clinico-pathological forms depending on the host immune status (Pandey and Tailor 2008). It is also known as Hansen's disease and is indeed one of the oldest documented infectious diseases known to

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mankind (Jacob and Franco-Paredes 2008). 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 (Lowe 1947). It affects chiefly the skin and peripheral nervous system, however, may also affect other systems of the body (Robertson 2003).

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 (Kumar et al 2014). In 2010, Nepal declared elimination of leprosy nationwide under the National Leprosy Elimination Programme of Nepal. Though the goal of elimination as a public health problem was achieved in 2010, the disease is still prevalent (Patro et al 2010).

Due to its clinical diversity and resemblance to other diseases, sometimes leprosy may be difficult to diagnose and classify 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) (WHO 1995). By and large this clinical diagnosis has been successful in diagnosing most of cases, however, it is not perfect and problems of sensitivity and specificity as well as matching with histological diagnosis have been reported in a small section of cases. Ridley and Jopling classification is most accepted by pathologists and leprologists; based on the clinical, histopathological and immunological status of the host and helps in gaining a better understanding of the pathology, prognosis and the risk factors associated with complications (Lockwood et al 2007). 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 (Parkash 2009). It is generally accepted that histopathology helps in arriving at an accurate 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 lepra bacilli in tissues sections (Job and Chacko 1986). 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 (Nayak et al 2003). 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 (Thapa and Jha 2013). With number of cases becoming small in Nepal, it is important to know the relative merits and as well benefits of having using clinical and histopathological approaches together or sequentially. The present pilot study has been conducted to correlate different types of leprosy clinically and histopathologically.

Materials and Methods

This study was conducted on 21 biopsy samples from the 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 new clinically diagnosed leprosy cases reporting to this hospital were included. Biopsies were taken from active lesions, tissue specimens were fixed in 10% formalin and processed for histopathological analysis. 5 micron sections were stained with haematoxylin and eosin for morphological assessment and with modified Fite-Farcao stain for acid fast 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 (Landis and Kock 1977). 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). 11/12 of male patients were below 40 years, whereas 4/9 females were below 40 years.

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

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*

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 tobe minimum in number (4.8%).

Out of the 21 patients included in the study, 16 (76.1%) were classified as paucibacillary leprosy and 5 (23.8%) of multibacillary leprosy by WHO criteria. 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 3.

Table 4 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. One case clinically diagnosed as TT, turning out to be BL histopathologically was a significant observation. Overall clinico-histopathological agreement was seen in 15 (71.4%) cases and disagreement in 6 (28.7%) cases. The

Table 3 : 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 4 : Clinico-histopathological correlation of leprosya

Clinical types	Clinically diagnosed cases	Histological diagnosis						Agreement, n (%)
		TT	BT	BB	BL	LL	IL	
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)

Kappa value was calculated as 0.475 and the strength of agreement was considered to be 'moderate' with p-value of 0.3.

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 clinical, histological and immunological criteria (Lockwood et al 2007). 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 (2013), where male preponderance was higher, 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). 11/12 (90%) of male and 4/9 (45%) females were below 40 years. In a study conducted by Tiwari et al (2015), majority of the patients were in the age group of 20-40 years. Though one need to study significant numbers before coming to any conclusion, such trends can be explained by possible reasons like illiteracy and poor knowledge, and strong tradition leading to reporting of leprosy in females (Varkevisser et al 2009) and may be partly due to late reporting.

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 Shivaswamy et al (2012) and Mathur et al (2011) 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, which was not seen in any other type. It will, therefore, be important to carry out studies in larger numbers and preferably directly in the community.

In the present study, maximum clinico-histopathological correlation was seen in BL (100%), followed by TT (84.6%), LL (50%) and 0% in BT. Among 13 cases diagnosed clinically as TT, 11 were confirmed as TT, one BT and one BL. Similarly, out of two LL clinical cases, one was diagnosed as LL and BL histopathologically. Overlap between TT/BT, BL/LL is well known and does not affect the line of management. However, 1/21 (5% approx.) identified as TT clinically but turning out to be BL would have resulted in under treatment, such cases will be benefitted by histopathology or smears for AFB (Sapkota et al 2009).

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 (2012) and Tiwari et al (2015) 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 based on gross appearance of lesions, 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 patients etc. The sample size of our study was limited, therefore, higher level of study designs with multidisciplinary approach and a large sample size is recommended to confirm the trends in leprosy patient population in western Nepal.

To conclude the limited data from our study shows the need of further population based studies in Nepal. As this problem has been faced for the last 50 years, there is clear need for better markers, may be better expertise and may be second opinion for improving the clinicopathological correlation in leprosy.

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How to cite this article : Pokhrel K, Parajuli S, Shah M and Subedi S (2017). Clinico-histopathological Correlation of Leprosy in Western Region of Nepal - A Pilot Study. *Indian J Lepr.* **89** : 9-14.