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Original Article

Correlation of Clinico-pathological Classification of Hansen's Disease in a South Indian City

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Hansen's Disease (HD) presents itself in different forms depending on the individual's immune status, and based on this Ridley-Jopling classified the disease into five sub-groups. The aim of this study was to evaluate the role of histopathology and bacteriological index (BI) in accurate staging of HD with clinical correlation. Fifty HD patients with clinical diagnosis confirmed by histopathology were included. Patients in reaction and on treatment were excluded. Case records and histopathological slides were viewed and BI was recorded. In 10/50 cases, a diagnosis of HD was made or suspected, but were not clinically classified. In these, histopathology proved useful in diagnosis and classification. Indeterminate HD was the most common histopathological diagnosis (6 cases). The remaining 40 patients, were clinically classified using the Ridley-Jopling classification, as Indeterminate Leprosy (IL) in 10/40 (25%), Tuberculoid Leprosy (TT) 5/40 (12.5%), Borderline Tuberculoid (BT) 16/40 (40%), Borderline Lepromatous (BL) 4/40 (10%) and Lepromatous Leprosy (LL) 5 (12.5%). HD was common in males with male to female ratio of 1.66:1 and affected the younger individuals (maximum in 21 to 30 years). On histopathology BT was the most common type (40%) followed by IL (27.5%), BL (12.5%), TT (10%) and LL (10%). No case of Mid-Borderline (BB) type was diagnosed clinically or histopathologically. Overall concordance between clinical and histopathological diagnosis was 65% (26/40 cases) and for each type was IL=80%, TT=20%, BT=75%, BL=50% and LL=60%. Where classification seemed difficult as in cases of BT and BL, BI played an important role. The overall concordance between clinical classification and histopathological diagnosis of HD is 65% in this study. The discordance that is observed is between BT and TT, the paucibacillary type and BL and LL the multibacillary type and hence the treatment is not affected. Overall, IL was a common diagnosis on histopathology in this study (11/40 cases and 6/10 cases). If clinically warranted, a repeat deeper punch of skin biopsy may be required for a proper categorization of the cases.

Key words : Hansen's disease, Clinical classification, Histopathological classification, Correlation, Ridley-Jopling

Introduction

Although the prevalent rates of Hansen's disease (HD) have shown a downward trend in India, about 50% of the world's burden of 800,000 cases of HD is from India (Government of India 2008).

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Accurate classification of the disease is very important for treatment and risk assessment for reactions. Besides, because of the social stigma attached to this disease, the diagnosis should be made with a degree of certainty. The widely accepted clinical classification by Ridley and Jopling (Ridley 1977) gives recognition to a combination of clinical appearance, histo-pathological features, microbiologic index and the immunologic status. The concordance between clinical and histopathological classification can be low as described by Sharma A et al, 2008 (53%) and high i.e. 90% as observed by Narayan P et al 2001. The aim of this study was to evaluate the role of histopathology and bacteriological index in accurate staging of HD with clinical correlation and identify the possible pitfalls.

Materials and Methods

The study was conducted between 1st March 2010 to 31st August 2010 in the departments of Pathology and Dermatology of our institute and affiliated hospitals. Cases of HD where a clinical diagnosis was proved by histopathology from 1st January 2009 to 31st august were included. Case records were studied for clinical diagnosis, and histopathology slides were viewed. Six to 8 serial sections were studied.

The patients were then categorized according to the Ridley-Jopling classification (Jopling and McDougall 2008). Nerve biopsies when present were included in the study.

Fite Faraco staining of sections was done (Ridley 1977) to determine the Bacteriological Index (BI) according to Ridley's Logarithmic Scale (Jopling and McDougall 2008). This is based on the number of bacilli seen in an average microscopic field using an oil-immersion objective. Three to 4 serial sections were stained.

Exclusion criteria included patients on prior treatment for HD and patients in reaction recognized clinically or histopathologically. The study was approved by the institutional ethics committee.

The data was analysed as follows: The descriptive statistics were computed for the range, mean and standard deviation for quantitative variables and category frequency counts and percentages for qualitative variable. To evaluate the correlation between clinical and histopathological classification Pearson's correlation was done. All statistical tests were carried out using Statistical Package for the Social Sciences version 10 (SPSS vs. 10). $P<0.05$ was considered to be statistically significant.

Results

A total of 50 cases were included in this study of which in 10 cases a diagnosis of HD was made (6 cases) or suspected (4 cases) but not classified to any particular type. The age group was 19 to 66 years (mean 40.8 years) and; six were males and 4 females. In all these 10 cases (20% of the total number of cases) a histopathological assessment of the lesion helped confirming the diagnosis of HD and in the grouping of the cases (6 were IL, 3 BT and 1 was TT).

In the 40 patients included for analysis, there was a male predominance seen, with 25/40 (62.5%) males and 15/40 (37.5%) females (ratio 1.66:1). The age range of the study patients was 13 to 60 years with a mean ($\pm$SD) of 36.85 ($\pm$13.78) years. The maximum number of cases were seen in the age group 21 to 30 years.

Greater than 5 lesions in a patient, was more likely to occur in lepromatous spectrum of cases, while fewer lesions were more likely to occur in the tuberculoid spectrum and this was found to be statistically significant (p=0.001), (Table 1).

Macules were more likely to occur in the tuberculoid type, while plaques and nodules were

Table 1 : Correlation between number of skin lesions and histopathological classification

Histopathological classification		Number of skin lesions in each patient		
Group	**Total**	**=1**	**2-5**	**>5**
HD*	10	6	4	-
IL	11	7	4	-
TT	4	2	-	2
BT	16	7	7	2
BB	0	-	-	-
BL	5	-	-	5
LL	4	-	-	4
Total	40	16	11	13

*Cases that were diagnosed as only HD and not included in analysis.

Table 2 : Correlation between type of skin lesion and histopathological classification of HD

Histopathological classification		Number of skin lesions in each patient		
Group	**Total**	**Macules**	**Plaques**	**Nodules**
HD*	10	10		
IL	11	11	-	-
TT	4	2	2	-
BT	16	11	5	-
BB	0	-	-	-
BL	5	4	-	1
LL	4	-	-	3
Total	40	28	8	4

*Cases that were diagnosed as only HD and not included in analysis.

Table 3 : Correlation between the number of peripheral nerve involvement and histopathological classification

Histopathological classification		Peripheral nerve involvement		
Group	**Total**	**No nerves involved**	**Single nerve involved**	**>1 nerve involved**
HD*	10	2	4	4
IL	11	9	-	2
TT	4	2	-	2
BT	16	3	2	11
BB	0	-	-	-
BL	5	-	-	5
LL	4	-	-	4
Total	40	14	2	24

*Cases that were diagnosed as only HD and not included in analysis

Table 4 : Comparing clinical and histopathological classification

Clinical Classification (CC)		Histopathological Classification (HPC)						Concordance CC versus HPC	Concordance HPC versus CC
Group	Total	IL	TT	BT	BB	BL	LL		
HD*	10	6	1	3	-	-	-		
IL	10	8	1	1	-	-	-	80%	72.7%
TT	5	1	1	3	-	-	-	20%	25%
BT	16	2	1	12	-	1	-	75%	75%
BB	0	-	-	-	-	-	-	-	-
BL	4	-	1	-	-	2	1	50%	40%
LL	5	-	-	-	-	2	3	60%	75%
Total	40	11	4	16	0	5	4		

*Cases that were diagnosed as only HD and not included in analysis

Table 5 : Clinical versus histopathological diagnosis - Comparison with other studies

Type of leprosy	Jerath & Desai, 1982[13]	Bhatia AS et al, 1993[12]	Kar PK et al, 1994[14]	Moorthy BN et al, 2001[7]	Sharma A et al, 2008[3]	Bijjaragi S et al, 2012[8]	Present study, 2014
IL	88.8	35	81.2	20	100	66.7	80
TT	74.5	50	87.5	46.15	47.37	75	20
BT	64.7	77	60.9	66.66	53.01	57.3	75
BB	53.8	25	54.5	50	37.35	16.7	-
BL	28.5	43	53.8	70	58.82	40	50
LL	61.5	91	71.4	80	75.86	76.9	60

more likely to be seen in lepromatous spectrum and this was found to be statistically significant (p=0.003), (Table 2).

Multiple peripheral nerve thickening was more likely to occur towards the lepromatous pole, while one or no nerve involvement was more likely to occur towards the tuberculoid pole and this was found to be statistically significant. (p=0.002), (Table 3).

Using the Ridley-Jopling classification, the clinicopathological allocation of 40 patients is shown in Table 4. Both clinically and histopathologically BT type of HD was the most common followed by IL cases. None of the cases were classified as BB type of HD both on clinical and histopathological evaluation. The best concordance was seen in the IL (80%) followed by BT (75%) and LL (60%). When histopathology was compared with clinical diagnosis best concordance was seen in LL and BT (75% in both) followed by IL (72.7%). The lowest concordance was seen in TT in both directions.

The BI was zero in all cases of IL and TT. It ranged from 0-1+ in BT and 2-4+ in BL and 4-6+ in LL.

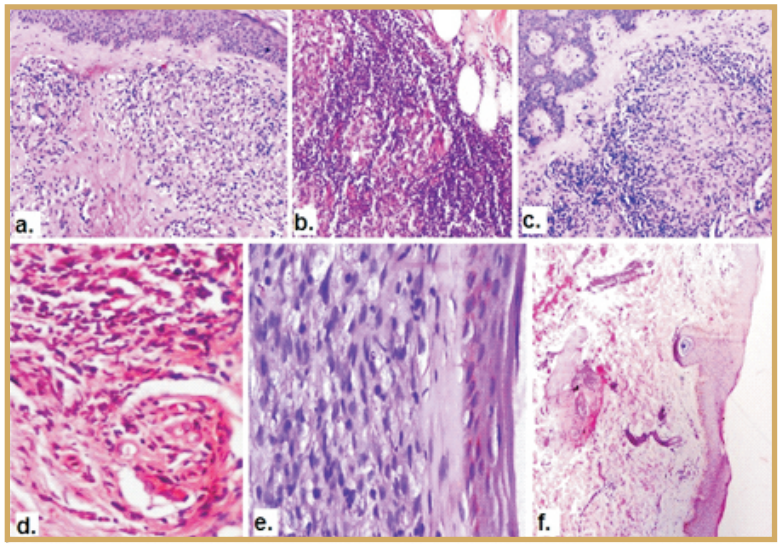

Fig 1 : a. Poorly defined epithelioid cell granuloma, multinucleated giant cell, intermingling lymphocytes and a Grenz zone in BT (H&E×10) b. Small epithelioid cell granulomas with intense lymphocytic reaction in the deeper dermis in BT (H&E×10) c. Well defined granuloma with lymphocytic cuffing and absent giant cells in TT (H&E×10) d. Perineurial onion-skin proliferation of fibroblasts in BL (H&E×40) e. Grenz zone and foamy macrophages in LL (H&E×40) f. Chronic inflammation in neurovascular bundles and in relation to arrector pili muscle in IL (H&E × 10).

All IL were AFB negative and the diagnosis was therefore presumptive. It is noteworthy that in one case of distinctive BL the BI was 2+. Among the separate ten cases one IL showed AFB 1+.

Discussion

Hansen's disease has a diverse and heterogenous cutaneous manifestation and it is the nerve involvement which allows a clinical diagnosis. However, clinical classification into the spectrum of Ridley Jopling (RJ) is difficult. Yet another classification that was brought out by WHO in 1982 for the treatment purpose, has changed over a period of time from bacillary count on slit-skin smear(paucibacillary and multibacillary) to number of skin lesions (>6). With this classification there is always a risk of under and overdiagnosis, but it complements the RJ classification (Lockwood et al 2007). Histo-pathology reflects the immune status more readily (as tuberculoid and lepromatous spectrum) and plays an important role in the classification along with BI. It identifies the changing immunologic spectrum of the disease. Classification determines the treatment schedule. The indeterminate category was added later to the RJ classification as very early lesions that cannot be classified along the immuno-pathologic spectrum. The clinical diagnosis of IL is imperfect and can overlap with the tuberculoid spectrum and other dermatological conditions also come in the differential diagnosis. In any study that correlates clinical diagnosis of HD with histopathology will show variable concordance due to interobserver variations among clinicians

and pathologists (Lockwood et al 2007). It is finally required that an accurate diagnosis is made with clinicopathological correlation so that the patient receives appropriate treatment and undesirable complications prevented. The most common type of HD diagnosed clinically as well as histopathologically was BT followed by IL (Table 4). A similar predominance in BT cases was also observed in other studies with fewer cases of IL (Moorthy et al 2001, Bijjargi et al 2012 and Thakkar and Patel 2014).

The overall concordance in the classification clinically and by histopathology was seen in 65% of the patients. A similar percentage of concordance is described in the studies by Bhatia AS, et al 1993 (69%) and Moorthy et al 2001 (62.63%). The highest concordance was seen in IL (80%) in the present study. In Indeterminate type of HD the concordance rate has ranged from 20% in the study by Moorthy et al (2001) to 100% in the study by Sharma et al (2008) as shown in the Table 5. A concordance of 88.8% (Jerath and Desai 1982) and 81.2% (Kar et al 1994) is recorded in other studies. The lesions in all our cases were macular, single to few, with none to definite impairment of sensation and some cases had palpable thickened nerves (Tables 2-4). A diagnosis of indeterminate HD on histopathology with BI enables the treatment of the patient depending on the number of lesions thus integrating the WHO classification.

On comparison with other studies (Table 5) in the determinate spectrum the correlation was least in TT subtype (20%). The best concordance was seen in BT (75%) similar to the study by Bhatia et al (1993) as compared to the superior correlation that was seen at the polar end of the spectrum in some other studies (Kar et al 1994, Nadkarni and Rege 1999 and Bijjargi et al 2012). The discordance was mainly between BT and TT. With the presence of epithelioid cell granulomas there is a tendency to categorise it as TT. The diagnosis of TT requires that the granulomas are mature, compact with cuffing by lymphocytes and larger nerves are involved with nerve destruction. Erosion into the epidermis with absence of Grenz zone when present is a useful feature. In BT it is lymphepithelioid granulomas with immature epithelioid cells. If the TT and BT are combined as paucibacillary type the treatment is not affected as described in some studies (Bhatia et al 1993, and Singh et al 2000) However, a proper recognition of borderline cases allows risk assessment for reaction (Lockwood et al 2007).

The concordance in lepromatous end of the spectrum was less (BL 50% and LL 60%) in the present study. A better concordance is recorded in LL type in other studies (Table 5). The paucity of lymphocytes and presence of globi are important features in LL. It is important to distinguish between LL and BL as the risk of developing erythema nodosum leprosum (ENL) is higher in LL as compared to BL. Type 1 reactions are prevalent in borderline cases with risk of disabilities (Lockwood et al 2007).

The bacteriological index (BI) is a definitive indicator to the bacterial load and consequentially the cell mediated immune (CMI) response. We found that BI played an important role in differentiating BT cases from BL cases, because occasionally in these cases there is a strong lymphocytic reaction that may obscure findings, such as the nature of granulomas or onion-skin perineurium a feature of BL is absent in the biopsy. A case of BL with distinctive features on histopathology showed a BI of 2+. The BI can range from 2+ to 4+ in BL cases and 4+ in TT, thus correlation with histopathology is critical. The diagnosis cannot be solely based on BI (Lockwood et al 2007).

It is known that nerves may contain more number of bacilli as skin lesions do and discrepancy of bacillary index between the two is high (50%) (Lucas and Ridley 1989). One case in the present study nerve biopsy reflected the unstable immune status of the patient with the skin biopsy showing BT (BI 0) and nerve biopsy BB with BI of 2. Hence, findings on nerve biopsy provide a more accurate picture of the immunological status and these should be weighted over findings on skin histopathology (Reddy et al 2005).

In the present study, in the 10 cases where a diagnosis of HD was either made or suspected, but was not classified clinically, histopathological examination of the skin proved useful hence indicating the importance of histopathology in the confirming the diagnosis and classifying HD. It can also be noted that most of the cases belonged to the indeterminate category (6/10) and tuberculoid spectrum (4/10) on histopathology. Clinically the patients had single (7 cases) to fewer (3 cases) macular lesions. In 8/10 cases nerve thickening (one nerve and more) was present. IL is more often diagnosed histopathologically than clinically in some studies (Nadkarni and Rege, 1999, Moorthy et al 2001 and Bijjargi et al 2012). Nadkarni and Rege (1999) in their study have concluded that histopathological diagnosis coincided more often with clinical diagnosis than vice versa in whole spectrum except IL.

Conclusion

Both clinical and histopathological diagnosis of HD can be very challenging. BT is the most common type of HD followed by IL. The concordance was best seen in IL and BT and poor in TT. BB type is rarely diagnosed clinically as well as histopathologically. With high index of suspicion, IL tends to be frequently diagnosed clinically in endemic areas. It indicates active transmission of the disease. A histopathological diagnosis of IL needs to be correlated with the clinical findings and may need a repeat deeper punch biopsy if clinically indicated.

References

1. Bhatia AS, Katoch K, Rangarajan B et al (1993). Clinical and histopathological correlation in the classification of leprosy. *Int J Lepr Other Mycobact Dis.* **61**: 433-438.
2. Bijjargi S, Kulkarni V, Suresh KK et al (2012). Correlation of clinical and histopathological classification of leprosy in post elimination era. *Indian J Lepr.* **84**: 271-275.
3. Government of India (2008). National Leprosy Eradication Programme. Department of Deputy Director General Leprosy, DGHS, New Delhi. A report.
4. Jerath VP and Desai SR (1982). Diversities in clinical and histopathological classification of leprosy. *Lepr India*. **54**: 130-134.
5. Jopling WH and McDougall AC (eds) (2008). Handbook of Leprosy, 5th edition, Noida: CBS publishers.
6. Kar PK, Arora PN, Ramasastry CV et al (1994). A clinico-pathological study of Macular Lesions in Leprosy. *Indian J Lepr.* **66**: 435-442.
7. Lockwood DN, Sarno E and Smith WC (2007). Classifying leprosy patients – searching for the perfect solution? Editorial. *Lep Rev.* **78**: 317-320.
8. Lucas SB and Ridley DS (1989). Use of histo-pathology in leprosy diagnosis and research. *Lepr Rev.* **60**: 257-262.
9. Mitra K, Biswas S and Saha BD (2001). Correlation between Clinical and Histopathological Criteria for the Classification of Leprosy. *Indian J Dermatol.* **46**: 135-137.
10. Moorthy BN, Kumar P, Chatura KR et al (2001). Histopathological correlation of skin biopsies in leprosy. *Indian J Dermatol Venereol Leprol*. **67**: 299-301.
11. Nadkarni NS and Rege VL (1999). Significance of histopathological classification in leprosy. *Indian J Lepr.* **71**: 325-332.

12. Narayan P, Ramu G, Desikan KV et al (2001). Correlation of clinical, histological and immunological features across the leprosy spectrum. *Indian J Lepr.* **73**: 329-342.

13. Reddy RR, Singh G, Sachidanand S et al (2005). A comparative evaluation of skin and nerve histopathology in single skin lesion leprosy. *Indian J Dermatol Venereol Leprol.* **71**: 401-405.

14. Ridley DS (1977). Skin Biopsy in Leprosy Histological interpretation and clinical application, 3rd edition. Switzerland: Documenta Geigy.

15. Sharma A, Sharma RK, Goswami KC et al (2008). Clinico-Histopathological Correlation in Leprosy. *JK Science*. **10**: 120-123.

16. Singh PA, Agarwal R, Misra V et al (2000). Clinico-histopathological concordance in leprosy. *Tropical Doctor*. **30**: 228-231.

17. Thakkar S and Patel SV (2014). Clinical Profile of Leprosy Patients – A Prospective Study. *Indian J Dermatol.* **59**: 158-162.

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