Clinico-Pathological Correlation Across the Leprosy Spectrum: Relevance in Current Context

TO THE EDITOR:

The study of correlation between the morphologic features of different groups of leprosy and their histopathology has been a subject of intriguing dialogue. Bhatia, *et al.* [2] need to be complimented for refocusing attention on it. However, its academic significance has diminished over the years. Perhaps a meticulous and detailed study incorporating the latest, newer techniques for attempted early diagnosis would have provided a better insight into this fascinating undertaking.

It is a retrospective analysis and undoubtedly provides a considerably larger sample size as compared to some of the earlier prospective studies [10–12]. However, the lack of well-defined clinical and histopathological criteria, essential for maintaining the uniformity of observations, is its major lacunae. Their absence invariably results in interobserver variation, and seriously compromises the specificity and/or sensitivity of the ultimate outcome.

The histopathologists deserve special mention for their consorted endeavor resulted in a high clinico-histologic correlation. However, a low concordance in indeterminate leprosy once again compels one to reserve the complimentation, and cast doubt on its role in early diagnosis. Indeterminate leprosy is undoubtedly a prelude to determinate groups [13]. A hypopigmented macule, its cardinal morphology, may test the acumen of even an expert leprologist [8]. Evidently the task of a leprosy health worker engaged in active surveying is a difficult and demanding one. The present endeavor, therefore, reiterates the limitations of histopathology. The diagnosis of early leprosy continues to haunt the leprologists.

It would have been fitting had the definite clinical criteria utilized for the purpose of making diagnosis been recounted and shared among all individuals engaged in it. The scope could have been broadened further by utilizing the latest techniques to assist the diagnosis. The latest stains and histochemical techniques, including combined staining with periodic acid-ethanol and gelatin and methenamine silver, may demonstrate a bacterial cell wall and myelin in the same sections. The endoneural nerve involvement may be confirmed using antibodies to S-100 proteins [3, 5]. Immunocytochemical staining for neuropeptides may reveal neural damage. In addition, numerous diagnostic procedures, including the lymphocyte transformation test (LTT), migration inhibition factor (MIF), fluorescent leprosy antibody absorption test (FLA-ABS) [1], detection of specific antigens of *Mycobacterium leprae* using monoclonal antibodies, estimation of antibodies to the synthetic analog of phenolic glycolipid-I (PGL-I) of *M. leprae* [6, 7], DNA probes for *M. leprae,* polymerase chain reaction [4], and *in situ* characterization of lymphocytic subpopulation and cytokines and their receptors [9], may facilitate early diagnosis. However, these laboratory procedures await validation before they should be considered for field application.

—Virendra N. Sehgal, M.D., F.N.A.Sc., F.A.M.S., F.R.A.S.(Lon)

Department of Dermatology & Venereology
University College of Medical Sciences and Guru Tegh Bahadur Hospital
Delhi 110 095, India

—S. Jain, M.D.

Ex-Senior Resident
Lady Hardinge Medical College
New Delhi 110 001, India

REFERENCES

1. ABE, M., MINAGAWA, F., YOSHINO, Y., OZAWA, T., SAIKAWA, K. and SAITO, T. Fluorescent antibody absorption (FLA-ABS) test for detecting subclinical infection with *Mycobacterium leprae.* Int. J. Lepr. **48** (1980) 109–119.
2. BHATIA, A. S., KATOCH, K., NARAYANAN, R. B., RAMU, G., MUKHERJEE, A. and LAVANIA, R. Clinical and histopathological correlation in the classification of leprosy. Int. J. Lepr. **61** (1993) 433–438.
3. FLEURY, R. N. and BACCHI, C. E. S-100 protein and immunoperoxidase technique as an aid in the histopathological diagnosis of leprosy. Int. J. Lepr. **55** (1987) 338–344.

4. HARTSKEERL, R. A., DEWIT, M. Y. L. and KLATSER, P. R. Polymerase chain reaction for the detection of *Mycobacterium leprae*. J. Gen. Microbiol. **135** (1989) 2357–2364.
5. KARANTH, S. S., SPRINGALL, D. K., LUCAS, S., LEVY, D., ASHBY, P., LEVENE, M. M. and POLAK, J. M. Changes in nerves and neuropeptides in skin from 100 leprosy patients investigated by immunocytochemistry. J. Pathol. **157** (1989) 15–26.
6. PRAKASH, K., AGGARWAL, R. and SEHGAL, V. N. Significance of antibodies to phenolic glycolipid-I (PGL-I) in leprosy diagnosis. J. Dermatol. (Tokyo) **19** (1993) 953–958.
7. PRAKASH, K., SEHGAL, V. N. and AGGARWAL, R. Evaluation of phenolic glycolipid-I (PGL-I) antibody as a multidrug (MDT) monitor. J. Dermatol. (Tokyo) **20** (1993) 16–20.
8. SEHGAL, V. N. *Clinical Leprosy*. New Delhi: Japee Bros., 1993, pp. 27–41.
9. SEHGAL, V. N., GUPTA, R. P., KARMAKAR, S., LOGANI, K. B. and JAIN, S. *In situ* characterization of lymphocytic immunophenotypy and interleukin-2 (IL-2R) in cutaneous tuberculosis and leprosy; a comparative evaluation. Clin. Exp. Dermatol. **19** (1994) 312–316.
10. SEHGAL, V. N. and JOGINDER. Leprosy in children: correlation of clinical, histopathological, bacteriological and immunological parameters. Lepr. Rev. **60** (1989) 202–205.
11. SEHGAL, V. N., KORANNE, R. V. and SEHGAL, S. Correlation of morphological, bacteriological, histopathological and immunological feature of leprosy; a double blind study. J. Dermatol. (Tokyo) **12** (1985) 243–250.
12. SEHGAL, V. N., REGE, V. L. and REY, M. Correlation between clinical and histopathologic classification in leprosy. Int. J. Lepr. **40** (1977) 278–280.
13. SEHGAL, V. N. and SRIVASTAVA, G. Indeterminate leprosy: a passing phase in the evolution of leprosy. Lepr. Rev. **58** (1987) 291–299.

Bhatia and Katoch Respond

TO THE EDITOR:

Drs. Sehgal and Jain have highlighted some issues about our publication. By and large, their comments support our interpretations and conclusions. As detailed in the Materials and Methods section of our paper, the criteria for clinical, histopathological and reactional status were well defined (references nos. 4, 5, 8 of our paper). These criteria have some limitations regarding the differentiation of some leprosy types, such as TT/BT, borderline types, and indeterminate cases. There are always some limitations of any retrospective analysis and, as also highlighted in our Discussion (page 437), these might have affected the results to some extent. However, even after allowing some margin for these factors, there appears to be a need for the reassessment of the weight given to different signs and/or histopathological parameters for classifying leprosy cases (especially TT, BB, I). Further, as highlighted in our paper and in the comments of Drs. Sehgal and Jain, such studies are not likely to be of much therapeutic relevance. We entirely agree about the need to carry out prospective studies using fluorescence, immunological, biochemical and molecular/gene amplification techniques to gain a better understanding of these problematic areas. We have emphasized these aspects in our Discussion (page 437).

Drs. Sehgal and Jain have very nicely focused on the research needs as well as some possible methods to study these aspects further. We entirely agree with their logic and thank them for their valuable suggestions.

—A. S. Bhatia, M.Stat.
Assistant Director

—Kiran Katoch, M.D.
Assistant Director
Central JALMA Institute for Leprosy
Taj Ganj
Agra 282002, India