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Letter to the Editor

Role of Nerve Biopsies in the Diagnosis of Leprosy in the Post Multidrug Therapy Era

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Sir,

Early diagnosis of leprosy is not always easy. Following world wide use of multidrug therapy (MDT), there has been a significant reduction in its prevalence and a relative increase in the reporting of early patients. Many leprosy workers feel that most of the patients can be diagnosed by clinical examination alone. However, the value of skin biopsies to identify the disease in its early stages is well recognized but under utilized. For the identification of pure neural leprosy (PNL), nerve biopsy is mandatory (Pannikkar et al 1983, Jacob and Mathai 1988) but it is hardly performed. In this brief communication, we have attempted to emphasize the importance of skin and nerve biopsies in diagnosis and management of leprosy and also to show over diagnosis of the disease if we depend only on clinical examination.

Schieffelin Institute of Health - Research and Leprosy Centre, Karigiri has a large dermatology outpatient clinic with nearly 200 to 300 patients per day of which about 1/5 are leprosy patients. During the year 2005, 35 patients suspected to have leprosy and 6 suspected to have leprosy with relapse of the disease who were willing to undergo skin and nerve biopsies were selected for this study. The nerves sampled are radial cutaneous nerves and superficial peroneal nerves. A length of 1 cm of the nerves were obtained for proper evaluation.

The skin and nerve biopsies immediately after removal were placed on small bits of filter paper, were properly oriented and dropped into 10% neutral formalin (Antia and Shetty 1997). After a minimum 24 hours of fixation, they were processed for paraffin sections. The skin and both cross and longitudinal sections of the nerve were stained using the following procedures: haematoxylin and eosin stain, modified Fite stain for *M. leprae*. In addition, the sections of the nerves were stained with Glee's stain for axons and solochrome stain for myelin. Of the 41 patients biopsied in 8, nerve tissue was not obtained. The remaining 33 patients were divided into 4 groups and further studied (Table 1).

Group I

In this group of 4 patients, clinically there were no skin lesions but only sensory loss. The skin biopsies from them showed minimal

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Table 1 : 33 patients clinically diagnosed as leprosy grouped according to the skin and nerve biopsy results

Groups	No. of patients with active leprosy	No. of patients with residual leprosy	No. of patients with other diseases	Total
Group I - No skin lesions - Marked sensory deficit	4	-	-	4
Group II - No skin lesions - Sensory and motor deficit	-	5	4	9
Group III - Skin lesions resembling leprosy - No nerve deficit	-	-	6	6
Group IV - Skin lesions resembling Leprosy - Sensory and motor deficit	12	2	-	14
Total	**16**	**7**	**10**	**33**

perivascular collection of lymphocytes and histiocytes but no significant lesion. Three nerve biopsies showed pathological features of borderline lepromatous leprosy and one, polar tuberculoid group. All 4 patients had pure neural leprosy both clinically and histopathologically.

Group II

In this group of 9 patients, clinically there were no skin changes but all had both sensory and motor impairment. The skin biopsies from these 9 patients had only sparse perivascular collection of mononuclear cells but no significant lesion. Nerve biopsies from 5 patients did not show any granulomas or acid fast organisms (AFB). But there was fibrosis of perineurium and also replacement of the nerve parenchyma by fibrous tissue. A few scattered nonspecific mononuclear cells were present. These features were consistent with healed and residual lesions of leprosy. The other 4 nerve biopsies, showed varying degrees of demyelination with no evidence of inflammation and therefore are not patients of leprosy. Further detailed studies were not done to specifically identify their disease. In this group of 9 patients clinically diagnosed as pure neural leprosy, histopathologic study showed 5 had healed lesions most probably following leprosy and the other 4 had demyelinating disease of undetermined origin. None of the 9 had active leprosy.

Group III

This group of 6 patients had no sensory or motor loss but only skin lesions suspicious of leprosy. Of the 6 patients, the skin biopsies of 2 showed chronic dermatitis and the other 4 showed mild chronic non specific inflammation. Of the nerve biopsies from 6 patients, 2 showed minimal perineurial thickening, the other 4 had the appearance of normal tissue. Although clinically leprosy was suspected histopathological examination showed no evidence of leprosy in any of them.

Group IV

Of the 14 patients from this group, 8 had skin lesions suspicious of leprosy accompanied by sensory or sensory and

motor loss and 6 were treated patients reporting with symptoms of relapse of the disease such as appearance of new patches and new onset of paralysis. Skin and nerve biopsies from 10 patients showed leprosy lesions belonging to the same classification (Indeterminate-1, Polar Tuberculoid-1, Borderline Tuberculoid-1, Borderline Lepromatous-5, and Lepromatous Leprosy-2). Two had leprosy lesions in both skin and nerves with different classifications (borderline lepromatous neuritis with indeterminate lesion of the skin-1 and borderline tuberculoid neuritis with no significant lesion in the skin -1). In 2, the skin biopsies showed no significant lesion but there was end stage neuritis with fibrosis and hyalinization of the nerves and fibrous thickening of the perineurium (Job 1989). In this group of 14 patients, 12 had active leprosy which included 6 with relapse and 2 had end stage neuritis.

This study is of 33 patients, who reported to the institution for the first time with symptoms and signs suspicious of leprosy and were diagnosed as leprosy which include 6 with suspected relapse of the disease. They were clinically diagnosed as leprosy and were placed on anti-leprosy therapy. Nowadays, there is a distinct possibility of healed patients treated elsewhere reporting to another clinic for the first time after varying periods of time to check on their disease status. Some of the healed patients may be those who are healed but prone to develop gradual onset of sensory and motor paralysis long years after adequate therapy (Job et al 1977). Five patients from group II and 2 patients from group IV belong to this category.

Skin and nerve biopsies from all the 9 patients with sensory and motor nerve deficit in group II and all the 6 patients with skin lesions suspicious of leprosy in group III and 2 patients with obvious sensory and motor deficit from group IV did not show any evidence of active leprosy. All these 17 patients clinically suspected as leprosy would have received unnecessary anti-leprosy treatment but for the skin/nerves biopsies.

Skin biopsies do help greatly to diagnose and classify leprosy especially in its early stages when there is no or only slight impairment of sensations. Nerve biopsies are mandatory to identify pure neural leprosy. They will also help to identify nerve diseases due to other causes. More importantly nerve biopsies will surely differentiate clinically non-identifiable healed leprosy lesions which will be more frequently encountered in the post MDT era. The failure to obtain nerve tissue in 8 of the 41 patients is unacceptable and it is recommended that nerve biopsies should be done only by experienced surgeons trained to do nerve biopsies (Heimanot et al 1984).

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