Single-Dose Treatment for Single Lesion Leprosy; Histopathological Observations

TO THE EDITOR:

The World Health Organization (WHO) in 1997 recommended single-dose rifampin-ofloxacin-minocycline (ROM-1) as the therapy for single lesion paucibacillary (PB) leprosy and, subsequently, the National Leprosy Elimination Program in India adopted this and implemented it all over the country. The single-dose therapy has also been tried for two to five lesions of leprosy with satisfactory results ([2, 4, 5, 7]).

This short course (single-dose) chemotherapy has been implemented for the treatment of leprosy. Apart from its clinical efficacy, this strategy has the additional advantages of saving manpower and resources, and increasing patient compliance. The clinical response to ROM-1 therapy has been found to be as effective as PB-MDT for single lesion PB leprosy ([6, 10]). The observations on feasibility of long-term follow up ([2]), clinical problems and management ([5]), and the field implication ([7]) suggest satisfactory results.

However, some of the problems encountered with ROM therapy in single lesion PB patients reported so far are: a) persistence of existing lesions; b) increase in the size of old lesion and c) appearance of new lesions. These problems are reported to be encountered in about 4% of patients. Of these, 1.3% of the cases responded to steroid therapy, but 1.5% showed no improvement. The delayed clearance of granuloma may be associated with such clinical problems. However, no histopathological study has been reported following ROM-1 therapy.

We report our histopathological observations on 26 patients with single patch leprosy treated with ROM therapy. All of the patients underwent pre-treatment as well as post-treatment skin biopsy at the end of 12–18 months. The hematoxylin and eosin (H&E) sections were studied for the following parameters: a) type of infiltrate (granulomatous/lymphocytic); b) granuloma index (GI), and c) presence of acid-fast bacilli (AFB). GI is the fraction of the dermis in a section occupied by the granuloma. The GI is observed under low power objective and expressed decimally, e.g., 1 indicates the whole of the dermis is occupied by the granuloma, 0.1 indicates that 1/10 is occupied by the granuloma ([3, 8]).

The histopathological changes were termed "active" when there was dermal infiltrate of epithelioid granuloma and the GI was more than 0.1 in the dermal tissue with nerve inflammation. It was termed "resolving" when the GI was less than 0.1 and "inactive" when granuloma was absent and/or the lymphocytic infiltrate was approximately <5%.

GI before and after ROM-1

	No. cases and %	
Granuloma Index	Pre-treatment	Post-treatment
0.4	4 (20%)	2 (10%)
0.3	5 (25%)	2 (10%)
0.2	5 (25%)	0
0.1	3 (15%)	1 (5%)
<0.1	3 (15%)	0
Total	20 (100%)	5 (25%)

The above table shows a reduction in GI following ROM therapy. Out of 26 patients, 20 patients had granulomatous infiltrate (Fig. 1) and 6 patients showed perivascular, periappendageal and perineural lymphocytic infiltrate suggestive of indeterminate leprosy prior to initiation of therapy. These 20 patients were studied further for resolution of granuloma using the GI scale. At the end of the study, only 5 patients had granulomatous infiltrate, with total clearance of granuloma in the remaining 15 patients, indicating marked improvement following therapy (Fig. 2). Of these 5 patients with granulomatous infiltrate, 2 had a GI of <0.1, suggestive of resolving granuloma whereas only 3 patients had active granuloma at the end of the study. A striking resolution of granuloma was observed in patients with a high GI.

Histopathologically, signs of reaction were observed in one patient in the form of edema and extravasation of red blood cells.

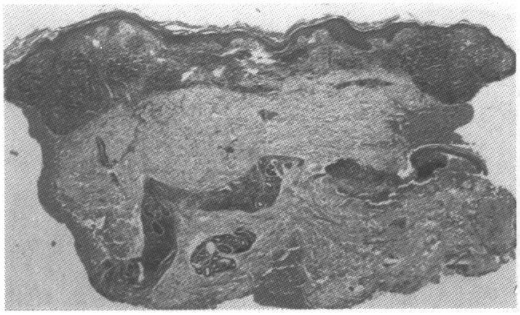

FIG. 1. Pretreatment photograph showing dense tuberculoid granulomatous infiltrate in close apposition to thin epidermis before therapy (GI 0.4).

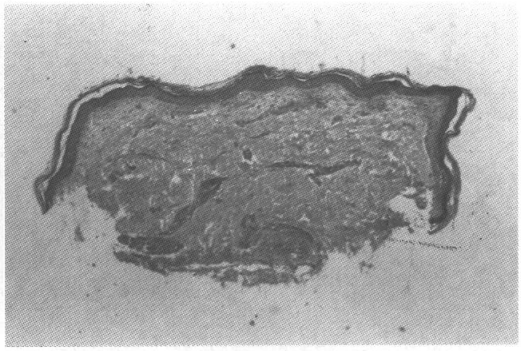

FIG. 2. Post-treatment photograph of the same patient showing complete resolution of granuloma 15 months after therapy (GI 0).

One patient with an indeterminate picture before therapy, showed granulomatous reaction (GI of 0.1) at the end of therapy. The remaining 5 patients with indeterminate histology had reached the inactive stage. One patient who developed a new lesion showed a reduction in GI in an old lesion (0.3 to 0.1) but the biopsy from the new patch showed a GI of 0.3. None of the patients showed the presence of AFB before or after therapy.

Although such studies are few, there are some reports of granuloma resolution following WHO/MDT. A histopathological study ([7]) of 30 patients treated with PB-MDT for 6 months showed active granuloma in 4 patients at the end of 18–23 months. This provides a comparison with our current study with ROM-1 in which 5 patients showed histopathological activity at the end of 18 months.

In yet another investigation ([1]) in which clinical and histopathological activity were studied in 37 PB leprosy patients after 6 months of MDT, 8 patients showed histologically active persistent granuloma with significant reduction in GI at the end of 6 months. On follow up these patients showed continued regression of granuloma without further treatment ([9]). The histological improvement in 81% of the cases after 18 months following ROM-1 can be considered as satisfactory and is comparable to PB-MDT.

The results of these studies show that although histopathological improvement with reduction in granuloma size may take a longer time, eventually they all regress irrespective of which therapy (PB-MDT or ROM-1) is used. It was also observed that patients with a high GI show a faster resolution of granuloma, indicating the immunological basis of the granuloma formation and the resolution taking place perhaps once the bacterial antigen is eliminated.

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Childhood Leprosy in Chandigarh; Clinico-Histopathological Correlation

TO THE EDITOR:

Clinical features of leprosy in children may sometimes be confusing. Sensory testing is difficult in them and slit-skin smears (SSS) are usually negative ([10]). Histopathology may be unrewarding in early tuberculoid and indeterminate leprosy, and there may be a marked disparity between the clinical and histopathological features ([7]). It has been suggested that the clinical spectrum of leprosy is incomplete in the 0–14 year age group since most of the cases are indeterminate (I), tuberculoid (TT), borderline tuberculoid (BT), or mid-borderline (BB) and very few are borderline lepromatous (BL) or lepromatous (LL) ([9]). This study was carried out to define the histological spectrum of leprosy in children and to correlate it with the clinical spectrum.

From January 1990 to July 1999, we diagnosed 1360 new cases of leprosy. Of these, 61 (4.5%) were children in the age group 0–14 years. There were 40 males and 21 females with a M : F ratio of 1.9:1. Diagnosis in each case was established on the basis of a thorough clinical examination, histopathology and determination of bacteriologic status by SSS from appropriate sites. A clinical diagnosis of I was made in 4 (6.6%) children, BT in 48 (78.7%), BL in 5 (8.2%), LL in 3 (4.9%) and pure neuritic in 1 (1.6%) child (The Table). Clinically there was no child with TT or BB disease.

A skin biopsy was taken from the most representative lesion and stained with routine hematoxylin and eosin (H&E) and Fite-Faraco stains. Histopathological findings were assessed according to the criteria laid down by Ridley ([3]). A clinico-histopathological correlation could be established in only 37 (60.6%) cases (The Table). Positive correlation was found in 2 (50%) cases with I, 28 (58.3%) with BT, 5 (100%) with BL and 2 (66.6%) with LL leprosy. Thus, a positive clinico-histopathological correlation was better noted in the more infiltrated lesions of BT and BL disease in comparison with the less infiltrated lesions of indeterminate leprosy. Three (6.3%) cases clinically diagnosed as BT leprosy were TT on histopathology and 1 (2.1%) case was I. One (33.3%) case of LL was BL and 1 (33.3%) was histoid leprosy on histopathology. Nonspecific features were seen in 19 (31.1%) cases—2 (50%) with I, 16 (33.3%) with BT and 1 (100%) case of pure neuritic leprosy in which a skin biopsy was taken from the area of sensory loss. Since the formation of a granuloma is indicative of good immunity ([4]), nonspecific features in as high as 19 cases reflect the poor immune