CASE REPORT

Two microbiological relapses in a patient with lepromatous leprosy

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Summary  A lepromatous patient treated with dapsone in the pre-MDT era to the point of smear negativity (>6 years), relapsed 5 years after stopping treatment. He was then put on WHO-MDT for multibacillary (MB) leprosy, and was treated again; he had negative slit skin smears (3 years). He again presented with a relapse of leprosy 17 years after stopping treatment, and this time he presented with borderline leprosy in reaction.

Introduction

WHO-MDT for leprosy has been found to be very robust with most field studies having shown low relapse rates in both PB and MB patients. However, patients with relapse of leprosy in multi-bacillary leprosy (BL/LL) patients, especially those with high bacillary index, are not uncommon and are being reported in patients who have had long-term follow-up.1–4 Compared with those given 12 or 24 months of WHO-MDT, fewer relapses have also been observed in MB (BL/LL) patients when they have been treated with WHO-MDT for MB leprosy to the point of smear negativity.2,4 Relapses have presented as fresh lesions of varied clinical types, reactions and or just microbiological worsening.2

Most of the relapsed patients responded well to re-treatment with the same drugs, indicating multiplication of drug sensitive persister bacilli. We report here a patient who relapsed twice, once after dapsone therapy and then years after having been cured with WHO-MDT for MB leprosy.

The Case Report

A 56 year old male cultivator of average build was first diagnosed with lepromatous leprosy (L, Indian Classification) in 1973. His slit skin smear was positive with a mean BI of 3+.
He was treated with dapsone 100 mg daily for 6½ years. He had improved clinically and his skin smears had become negative. Dapsone was stopped and he was kept under regular follow-up, with placebo (B. Complex) 1 tablet daily.

In April 1985, 5 years after stopping treatment with dapsone, he presented with fresh infiltration over the face and other parts of his body of about 3 to 4 months’ duration. He had no significantly thickened nerve or any anaesthesia. His repeat skin smears showed a mean BI of 2+. A diagnosis of relapse was made and patient was put on WHO-MDT for MB leprosy. His infiltration regressed in 6 to 7 months, and he was treated for 3 years till his skin smears became negative. After stopping treatment, he came for regular check-ups at 6 and 12 month intervals.

At every visit, he was thoroughly examined and slit skin smears were repeated. Seventeen years after finishing WHO-MDT for MB leprosy, in April 2005, he came with an eruption of new erythematous lesions of various sizes over the face, body and extremities (Figure 1) of about 2 to 3 months duration with a history of gradual progression. He also complained of a tingling sensation in his hands and feet.

On examination, he had skin lesions in the form of erythematous, some annular and gyrate, plaques of varying sizes over his face, body and extremities (Figure 1).

The lesions were smooth, oedematous with mild sensory loss. He had no significant nerve thickening or deformity. He was diagnosed with borderline leprosy (BB) in reaction. His investigations (complete haemogram, blood sugar, liver and renal function tests) were all within normal limits. His skin smears was repeated and mean BI of 3+ was observed. A skin biopsy was taken from the left upper back lesion, for histopathology and mice inoculation. His skin biopsy showed an atrophic epidermis with a clear sub dermal zone, extensive granuloma with branching; predominant cells were macrophages with moderate numbers of lymphocytes and partially disorganised and destroyed focal area of the reticulum. No edema was seen. The vasculature was normal and dermal nerves fibres were infiltrated and partially destroyed – suggestive of BL leprosy (Figure 2).

![Figure 1. Right cubital fossa showing erythematous plaques.](image-url)
Fite-Faraco staining of biopsy sections showed 2+ A.F.B. The procedure involved in the mice inoculation was as follows: The biopsy specimen was minced with scissors, homogenised and suspended in Hanks balanced salt solution. After allowing the suspension to stand for 3 minutes the supernatant fluid was collected and a bacterial count was carried out and adjusted so that 0.03 ml of suspension contained 5000 bacilli. A batch of five randomly bred BALB/C mice was inoculated into each hind foot pad with a 0.03 ml suspension. The inoculated mice were housed at 25°C in an air-conditioned room. Half of the mice were scheduled to be harvested at 6 months and the remaining at 8 months after inoculation.

The patient was again put on standard WHO-MDT (monthly dose – rifampicin 600 mg, clofazimine 300 mg, dapsone 100 mg and daily dose – clofazimine 50 mg, dapsone 100 mg) for MB leprosy. Because of the possibility of resistance to one or more of the MDT components, in addition he was given daily supervised doses of ROM (rifampicin 600 mg on an empty stomach, ofloxacin 400 mg, minocycline 100 mg) for 4 weeks in the ward and prednisolone 20 mg daily for 8 weeks with gradual reduction thereafter. The patient responded well to this course of treatment. With 1 year’s regular MDT, all his skin lesions have completely regressed. He has had no episode of reaction or neuritis and his BI has decreased by one log-unit in the last year.

Discussion

In this lepromatous patient, the first relapse occurred 5 years after the stoppage of dapsone therapy and this could well have been due to either the multiplication of dapsone sensitive persisters or dapsone resistant organisms. With WHO-MDT for MB leprosy, in all likelihood possible dapsone resistant organisms, if any, would have been killed.

The second relapse occurred in this patient 17 years after stopping treatment with WHO-MDT for MB leprosy. The possible explanation for this second relapse could be the long survival of drug sensitive persister M. leprae following MDT, which might have multiplied slowly over the years after the stoppage of treatment as happens in secondary or reactivation tuberculosis. However the possibility of multi-drug resistance (MDR) in the

Figure 2. H & E stained tissue section showing foamy granuloma with interspersed lymphocytes (×40).
causative organism *M. leprae*, though small, cannot be excluded. With this in mind, after taking a biopsy for mice inoculation, the patient was given other, differently acting bactericidal drugs (Ofloxacin/minocycline) in addition to standard multi drug therapy. Unfortunately, the mice inoculated with *M. leprae* of the patient did not survive long enough for the answer. The possibility of presently active disease being due to re-infection cannot be ignored. But non-availability of the earlier *M. leprae* strains, and the death of all inoculated mice have left us with only theoretical possibilities. Had the earlier strains been available, a comparison of the molecular strains present in *M. leprae* from skin scrapes or biopsy material could have been done. However micro-satellite mapping of *M. leprae* has not yet been established for differentiating leprosy relapse from re-infection, because the micro-satellites change rapidly as was shown in DNA isolated from a group of leprosy patients, and also in different tissues from the same patient. The appearance of borderline disease in the form of varied annular and gyrate lesions may be due to some local regaining of specific cell mediated immunity (C.M.I) where even BT relapses have been reported in LL patients long after cure. This case report re-emphasises that lepromatous patients must be kept under clinical and bacteriological surveillance for as long as possible after completion of recommended regimens.

References