

## **Borderline–tuberculoid relapse in lepromatous leprosy**

B. K. GIRDHAR, A. GIRDHAR, S. L. CHAUHAN,  
G. N. MALAVIYA, S. HUSAIN & A. MUKHERJEE\*  
*Central JALMA Institute for Leprosy, Tajganj, AGRA; and*  
*\*Institute of Pathology (ICMR), New Delhi*

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*Summary* We report details of 2 patients who had been treated for a long time by dapsone monotherapy and who had remained smear negative for over 10 years, but were found to have relapsed with borderline–tuberculoid (BT) leprosy.

### **Introduction**

Relapses in lepromatous leprosy (LL) following treatment are not uncommon. Long after smear negativity has been achieved with DDS monotherapy, patients are known to relapse.<sup>1–6</sup> Almost all of these relapses have been of lepromatous or borderline lepromatous type with skin smear positivity and continued lepromin negativity.

However, in the past, a few patients on relapse or reactivation presented with a tuberculoid picture, and this was usually because of late reversal reaction secondary to continued treatment.<sup>7</sup> In retrospect, it is now considered that these patients were more probably of BL rather than of lepromatous type.

In contrast to the above, reports of Jonquieres<sup>8</sup> and Waters & Ridley<sup>9,10</sup> concern the appearance of BT relapses in long-treated LL patients. A similar observation of BT relapse in 2 old lepromatous patients, treated for long periods with dapsone monotherapy and who had remained skin smear negative for a number of years, was made by us and is reported.

### **PATIENT 1**

This Indian female was diagnosed as a case of leprosy 28 years ago. To begin with she had impaired sensation on the right lower limb. She had no patch or any other problem 5 years later, following her first child's birth, she had painful eruptions, appearing rapidly over the buttocks and face. This was associated with fever, joint pains and severe pain in the limbs. She was diagnosed as a case of leprosy and put on DDS together with antireaction drugs. She improved in the ensuing 3–4 weeks. Subsequently, she was continued on 25 mg DDS doses, which she took irregularly. During her next ENL

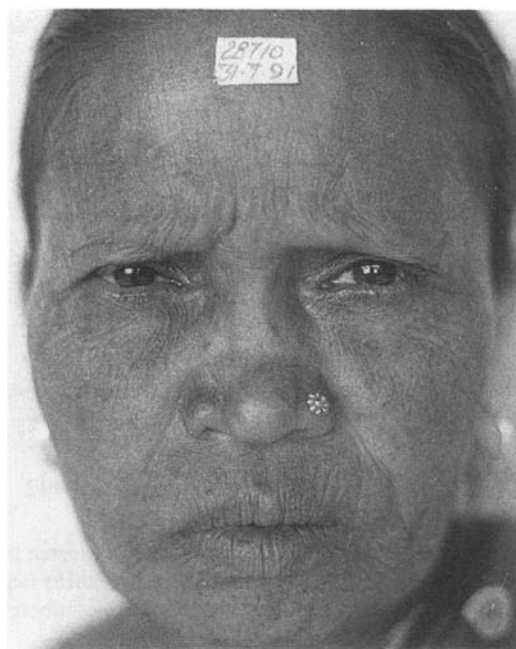


Figure 1.

episode, which was 3 years later, she had severe pain, down the left elbow initially and later in the right hand. This resulted in clawing of the hands. She was treated with steroids but without improvement. She was continued on increasing doses of DDS, which she took irregularly for the next 18 years (regularity around 70%). All her symptoms subsided except the deformities.

She was seen in this hospital for the first time in 1987. She had shrivelling all over the face, ears and other parts of the body and no obvious infiltration/induration or active skin lesions on any part of her body (Figure 1). Her nerves were mildly thick, soft but not tender. She was considered as a clinically regressed patient of lepromatous leprosy, with residual signs including supraorbital and ciliary madarosis, a depressed tip of the nose, looked old for her age, and had a bilateral partially fixed ulnar claw. Her skin smears, repeated on 3 occasions, from 4 different sites each time, were uniformly negative. Because she had taken prolonged DDS treatment and was available for regular follow-up, she was not put on any further anti-leprosy treatment. Since that time she had been regularly examined once every 3 months and her skin smears were taken every year. These had indicated no problems. In February 1991, she had herpes zoster of the right lower back (T11) with neuralgia. Since she presented very early and had neuralgia, she was given a short course of steroids. After 3 weeks, she noticed 3 asymptomatic, raised, mildly oedematous, red, moderate sized lesions, one each on the left flank, right side abdomen and left shoulder. The left shoulder lesion was arcuate (Figure 2) whereas the other two were oval, 10 cm and 4–5 cm in diameter, respectively. The surface was dry and scaly with slightly sloping edges and impaired sensations. There was no local nerve thickening. She

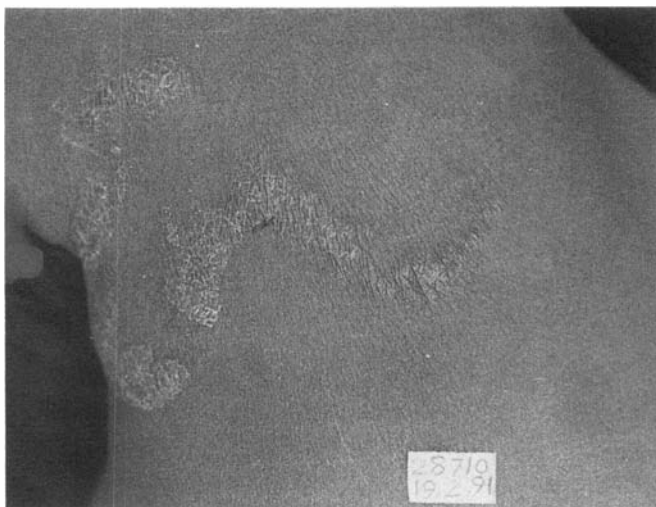


Figure 2.

was diagnosed as BT relapse (in treated LL). Her skin smears, from both ear lobes and 2 lesions, were found negative on 3 occasions. Her lepromin response, to Dharmendra antigen, was also negative. The biopsy from back lesions showed a typical BT picture with some oedema suggesting reaction. No AFB were seen in tissue sections. Biopsy suspension was also negative for AFB and therefore mouse foot pad inoculation, to confirm viability and drug sensitivity, was not attempted.

#### PATIENT 2

A Nepali man had an ulcer on the back of his left foot about 35 years ago, and shortly afterwards he developed a patch on his right buttock; 2–3 years later the patient had stuffiness of the nose and on blowing it had frequent blood stained nasal discharge. For this, he was prescribed some treatment, which he took for 9–10 months, and the symptoms disappeared.

About 6–7 years later, the patient had facial swelling and the blood stained nasal discharge reappeared. With this he was diagnosed to have leprosy. His skin smears were 3+ from each of the 4 sites (Dharmendra grading). He was put on DDS which he continued to take regularly. In 1969, when he first came to this hospital, he had in addition to the widespread infiltration, loss of eyebrows, depressed nose, nasal ulcers, symmetrical nerve thickening and impairment of superficial sensations over distal parts of his limbs. He had ENL eruptions, together with bilateral chronic uveitis (with firm posterior synechiae) and bone pains. He was treated accordingly and his DDS dose was gradually increased to 100 mg a day, which he continued to take regularly. His skin smears became negative in 1977. He continued on DDS for another 10 years i.e., till 1986, without any reactivation (Figure 3). He did, however, become blind.

He had no problems until 1991 (5 years without drugs). During this time he had been clinically examined at least once every 3 months and his skin smears were examined

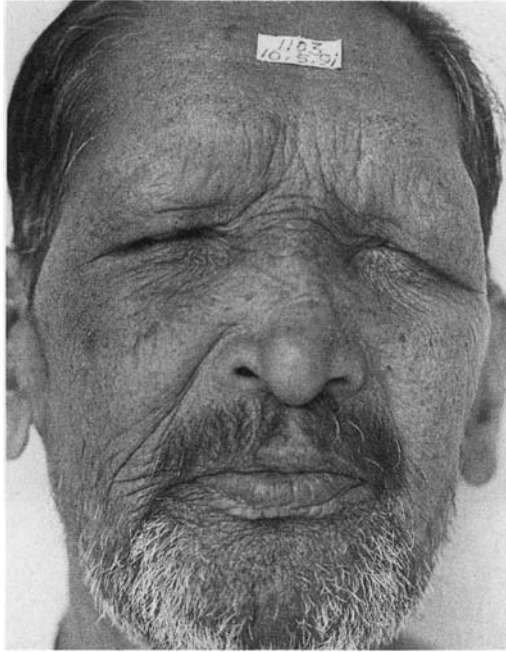


Figure 3.

yearly. In May 1991 he noticed 2 raised, red, asymptomatic lesions of approximately 10 and 4.5 cm diameter on the right pectoral region and mid back. Both the lesions had indistinct borders, dry surface and showed some sensory impairment (Figure 4). He was diagnosed as BT relapse on lepromatous background. His skin smears from both ears and both fresh lesions were found negative. A lepromin test, using Dharmendra antigen, showed negative early response. Biopsy of the chest lesion showed active BT with epithelioid cells, giant cells and a thick cuff of lymphocytes together with damage to nerve fibres. Biopsy showed no bacilli even in nerves. Biopsy suspension was also negative for AFB.

### Discussion

Even with the absence of earlier skin biopsies, from the details of the patients and their appearance (Figures 1 and 3), it is evident that both of them were lepromatous as they have the evidence of generalized shrivelling/atrophy (more marked on the face with the hanging of the ear lobes), ciliary and supra orbital madarosis, depressed nasal tip and history of frequent ENL with bone pains in the past, etc. The male patient also had bilateral uveitis and uniform skin smear positivity. A long duration of 8 years for bacillary clearance further supports such a contention. However, they do not seem to have had polar lepromatous disease, as the female patient had bilateral ulnar median palsy and the male patient had passed through a phase of possibly indeterminate leprosy, since he at one



Figure 4.

time had a hypopigmented macule on the right buttock. The patients had remained clinically inactive and bacteriologically negative *for at least* 5 and 15 years, respectively. The relapse in the first case was preceded by the appearance of herpes zoster associated with neuralgia (for which short course steroids were given) but in the male patient no precipitating factor was available, which could have caused or was indicative of immune suppression.

Most of the earlier reported relapses among long-treated patients have been of the lepromatous type.<sup>5,6</sup> Their frequency has been about 1 per 100 patient years of observation in conditions where drug intake was ensured.<sup>6</sup> The relapses have more often been secondary to the emergence of dapsone resistance.<sup>11,12</sup> Even the bacilli obtained from relapsed long-treated patients, reported by Waters & Ridley,<sup>10</sup> who had histologically BT relapse, were found to be fully resistant of dapsone in 3 patients with a suspicion of resistance in the rest. Thus, there is a strong possibility that the relapses in our patients were also on account of dapsone resistance, as the patients had received only DDS in the past and that, too, in comparatively smaller doses and not very regularly. However, dapsone resistance could not be proved or shown in our patients as even the biopsy homogenates from both the patients did not contain any countable bacilli, possibly because the relapses were detected very early. This was in line with the observation of not finding any bacilli, on repeated skin smear examinations and in the biopsies of both the regressed and the active lesion sites in these relapsed patients.

As indicated above, although relapses in DDS treated and long-smear negative patients are not uncommon, relapses with a clinical picture akin to tuberculoid pole have

not occurred frequently. Following a mention of such an occurrence in the literature,<sup>13,14</sup> Jonquieres *et al.*<sup>18</sup> and Waters & Ridley<sup>9,10</sup> have given details of such patients observed by them. In contrast to the above-reported patients, only 1 of the 2 patients observed by us had evidence of a reaction, both clinically and histologically. Further, the lesions in this patient were fairly rapid in evolution. It is possible that the symptoms of reaction in the patient were less pronounced on account of the viral infection (which could also be a manifestation of temporary immune-suppression) or secondary to steroid administration. No such precipitating factor(s) was observed in the male patient.

Another unusual finding has been the negative early (Fernandez) reaction to Dharmendra antigen, despite the relapses being of a BT type clinically, bacteriologically and histologically. The negative lepromin response could possibly be because of a rather shorter duration of treatment and a shorter length of time since smear negativity. Lepromin tests using both Dharmendra and Mitsuda antigens were repeated after 1 year follow-up. Although an 8 mm early reaction was noticed with Dharmendra antigen, the Mitsuda response was negative. This indicates that an adequate time had not yet passed for the clearance of some of mycobacterial products (antigens) which have been shown to produce generalized immunosuppression through stimulation of suppressor T cells.<sup>15-17</sup> It will, therefore, be worth while repeating the lepromin test periodically hereafter in these patients.

In view of the reports of relapses in long-smear negative patients treated with dapsone monotherapy years ago, it has been felt desirable and has also been recommended by some national agencies that a short course of combined chemotherapy similar to multibacillary patients should be given to cured smear +ve patients treated earlier with dapsone monotherapy. However, the duration of chemotherapy required to be given to these patients is not clear and needs to be researched.

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### **Rechute borderline-tuberculoïde dans la lèpre lépromateuse**

B. K. GIRDHAR, A. GIRDHAR, S. L. CHAUHAN, G. N. MALAVIYA,  
S. HUSAIN ET A. MUKHERJEE

*Résumé* Chez deux patients sous monothérapie à long term à la dapsone, dont les frottis étaient restés négatifs pendant plus de 10 ans, on a observé une rechute de lèpre borderline-tuberculoïde (BT). Les détails de ces patients sont rapportés.

### **Recaída tuberculoide-dudosa en casos de lepra lepromatosa**

B. K. GIRDHAR, A. GIRDHAR, S. L. CHAUHAN, G. N. MALAVIYA,  
S. HUSAIN Y A. MUKHERJEE

*Resumen* Se encontró que dos pacientes sometidos a la monoterapia de dapsona a largo plazo, que habían permanecido fróntis negativos por más de diez años, tuvieron recaída de lepra tuberculoide-dudosa (BT). Se presentan detalles sobre los pacientes.