Histological Resolution and Bacterial Clearance with Pulse ROM Therapy in Borderline Lepromatous Leprosy

TO THE EDITOR:

Single-dose rifampin, ofloxacin and minocycline (ROM) has been advocated and proved effective in single lesions of leprosy ([1, 3, 5]). The bactericidal activity of a single dose of ROM against *Mycobacterium leprae* was tested in mice and in lepromatous patients. The combination exhibited definite bactericidal activity and was well tolerated ([2]). Pulse ROM has been advocated in multibacillary (MB) leprosy patients who cannot be given the World Health Organization-recommended multidrug therapy (WHO/MDT) due to poor response or hypersensitivity, or for other reasons ([6, 7]). There are no reports on its use as a pulse regimen in MB leprosy as to its efficacy in clinical improvement, histological resolution of lesions, or fall of the bacterial index (BI).

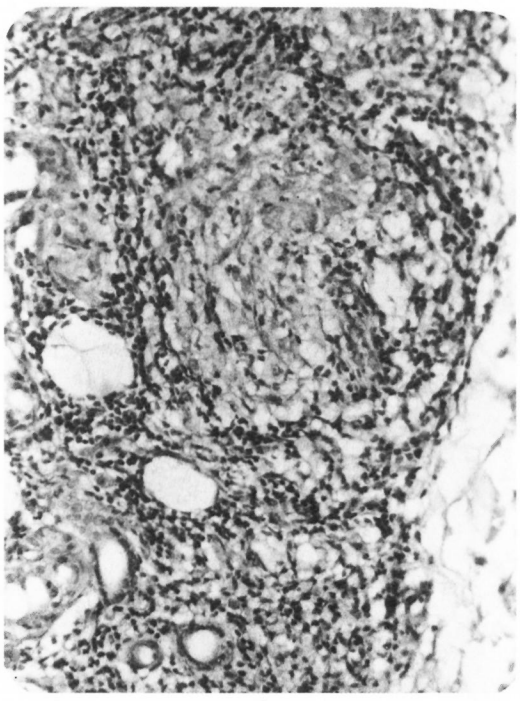
We report here a case of borderline lepromatous (BL) leprosy in a 16-year-old female patient who presented with multiple hypopigmented, hypoesthetic patches mainly on the limbs. Slit-skin smears revealed an average BI of 3+ (highest individual site BI 5+ in right knee). Initial skin histopathology revealed active BL leprosy with a granuloma fraction (GF) of 70% and a BI of granuloma of 5+. The patient refused MB WHO/MDT in view of the pigmentation due to clofazimine (she was to be married soon) and was started on monthly supervised treatment with ROM (rifampin 600 mg, ofloxacin 400 mg and minocycline 100 mg).

Over a period of 1½ years and 18 monthly doses of ROM, the patient showed significant clinical improvement with clearance of lesions from the face and limbs. Some of the lesions on the lower limbs showed mild hyperpigmentation. The patient developed mild type 1 reaction both 1 month and 10 months after the start of therapy for which she received a short course of prednisolone. There was no associated sensory or motor deficit in hands or feet.

Histology at 1 year revealed borderline lepromatous leprosy in reaction (The Figure) with features suggestive of histological upgrading toward borderline tuberculoid (BT) leprosy and resolution of the granuloma (GF 40% and BI 2+).

The average BI on slit-skin smears reduced from 3+ at start of therapy to 1+ at 1 year and 0.5+ at 18 months. The highest individual site BI of 5+ in the right knee dropped to 2+ at 1 year and was negative at 1½ years.

In view of her pregnancy, treatment was stopped after dose 22 and the patient was followed up regularly. Six months after stopping therapy the patient has shown no signs of reactivation or reaction. All lesions have disappeared completely. The average BI is 0.4+ with a BI of 1+ at two sites among 5 sites tested. Histologically, granulomas have resolved, with a GF of less than 10% and a BI of 1+, consisting of occasional frag-



THE FIGURE. BL leprosy in reaction: collections of macrophages and lymphocytes with aggregates of epithelioid cells (H&E ×200).

mented and granular bacilli. The pregnancy and subsequent delivery were uneventful both with regard to its effect on the course of the disease or reactions and with regard to the effect of the drug on the mother or child.

The number of patients who refuse clofazimine is not very large. Some patients, however, particularly young unmarried girls, refuse it because of the skin pigmentation and its social consequences. In such cases, the combination of rifampin, ofloxacin and minocycline as a convenient pulse regimen is effective in reducing the BI.

Regimens containing ofloxacin are found to increase the likelihood of reactions ([4]). Although reaction occurred twice in this patient, it was mild and was controlled with a course of low-dose prednisolone (20 mg tapered over 4 months) with no permanent residual nerve damage. Histology was that of an upgrading reaction, indicating an increase in cell-mediated immunity with the overall benefit of bacterial clearance and resolution of granuloma. However, further studies need to be carried out to closely monitor the frequency and severity of reactions and neuritis in patients on ROM.

In conclusion, this case highlights the operational ease of administration of a pulse ROM regimen in MB leprosy and its therapeutic efficacy in producing clinical improvement and bacterial killing, fall of BI and resolution of the granuloma.

—Sujai Suneetha, M.B.B.S., D.C.P, Ph. D.
Director

—Rajgopal Reddy, M.B.B.S.
Medical Officer
LEPRA India-Dhoolpet Leprosy Research Centre
and Blue Peter Research Centre
Hyderabad 501 301, India

Acknowledgment. The Dhoolpet clinic and BPRC are supported by the Mycobacterial Research Division of NIMR, (MRC), U.K.

REFERENCES

1. Ebenezer, G. J. and Job, C. K. Histological activity in paucibacillary leprosy patients after ROM therapy. Int. J. Lepr. **4** (1999) 409–413.
2. Ji, B., Sow, S., Perani, E., Lienhardt, C., Diderot, V. and Grosset, J. Bactericidal activity of a single-dose combination of ofloxacin plus minocycline, with or without rifampicin, against *Mycobacterium leprae* in mice and in lepromatous patients. Antimicrob. Agents Chemother. **42** (1998) 1115–1120.
3. Ramu, G. Single-dose rifampicin, ofloxacin and minocycline (ROM) therapy for single leprosy lesions. Lepr. Rev. **69** (1998) 78–82.
4. Rao, P. S., Ramachandran, A., Sekkar, B. and Ravi, S. Oflaxacin containing combined drug regimens in the treatment of lepromatous leprosy. (Abstract) Int. J. Lepr. **61** (1993) 8A.
5. Single Lesion Multicenter Trial Group. Efficacy of single dose multidrug therapy for the treatment of single lesion paucibacillary leprosy. Indian J. Lepr. **69** (1997) 121–129.
6. World Health Organization. Drugs used in leprosy. Geneva: World Health Organization, 1998. WHO/DMP/DSI/98.1
7. World Health Organization. MDT; questions and answers. Geneva: World Health Organization, 1997. WHO/DMP/DSI/97.8

Does Dapsone Resistance Really Matter in the MDT Era?

To the Editor:

In a Letter to the Editor ([4]), Dr. Paul W. Roche and his colleagues presented the results of drug susceptibility testing of 268 clinical isolates of *Mycobacterium leprae* by means of the mouse foot pad technique between 1987 and 1999 at Anandaban Leprosy Hospital, Kathmandu, Nepal. Their results are interesting. However, their opinion about the significance of high-level, primary resistance to dapsone (DDS) in the era of multidrug therapy (MDT) is open to argument.

Roche, *et al.*, proposed that "It will be important to monitor the trends in the level of resistance as well as the frequency of primary dapsone resistance . . ." ([4]), because "MDT efficacy could be severely compromised if high-level primary dapsone resis-