

PRIMARY DAPSONE RESISTANCE IN MULTIBACILLARY LEPROSY AMONG NEPALESE CHILDREN

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INTRODUCTION

Chemotherapy of leprosy has in the past relied almost entirely on dapsone monotherapy. This has evolved a dangerous epidemiological situation in which resistant infection occurs in patients on therapy and they in turn spread the resistant bacilli to their contacts in the community. (1) In addition, inadequate basic health care delivery system has made the whole of leprosy control a failure. Several reports have appeared over the past decade on secondary dapsone resistance (2) and a few reports on primary dapsone resistance. (3, 4)

Clinical leprosy among children has usually been self healing indeterminate or tuberculoid types; smear positive leprosy has rarely been diagnosed in them before puberty. (5) Multibacillary leprosy probably requires long incubation periods. We have recorded multibacillary leprosy in children of Mongoloid races in mountain regions who invariably had one of the parents as index cases.

Between 1980 and 1983 and newly diagnosed patients (i.e., LL and BL) at our clinics had skin biopsies taken. In patients with a B1 > 2.5 the *M. leprae* obtained from the biopsies were inoculated into swiss albino and nude mice to detect *M. leprae* resistant to dapsone.

In this communication, we report —

1. Multibacillary leprosy in eleven Nepalese Child patients.
2. In all except one the index cases were relapsed multibacillary patients.
3. Nine patients were tested for dapsone sensitivity in the mouse foot pad test system.

MATERIALS AND METHODS

Patients

Patients attend a weekly skin clinic conducted by Anandaban Hospital staff at Shantha Bhawan Hospital in Patan. Children in the study presented to the clinic between 1980 and 1983. All patients were clinically examined and classified on the Ridley Jopling Scale. (6) All the particulars of the patients name, age, sex, history of past treatment, household contacts and other particulars were entered in the standard charts. A black and white photograph was taken for identification.

Bacteriological Assessment

Skin smears were routinely undertaken from six skin sites. This was repeated every three months. Other routine investigations were undertaken in our laboratories.

Skin Biopsy

A skin biopsy from an active lesion was taken from patients. A portion was placed in the container with FMA fixative (7) and other placed in a sterile container and despatched to the Mycobacterial Research Laboratories for mouse foot pad investigation for dapsone sensitivity.

Mouse Foot Pad test

All the swiss albino and nude mice for the study were bred locally. The mouse diet pellets were prepared locally in the laboratories and dapsone was incorporated into the diet in a concentration of 0.0001; 0.001; and 0.01 per 100 g diet. For each experiment 20 mice were used. Five of the mice that served as controls received normal diet while other groups of 5 mice were fed on a diet in which dapsone was incorporated. Nude mice diet was prepared by CLEA Japan and air freighted from Tokyo to Kathmandu.

Inoculum and Inoculation

A suspension of *Mycobacterium leprae* was prepared using aseptic techniques from the patients skin biopsy according to techniques published before. (8) Mice were inoculated in the plantar surface of the foot pad.

Harvests

The experimental and the control mice foot pads were harvested from six months.

RESULTS

Of eleven patients 7 are male and 4 female. The age range varied from 3 to 14 years. In all patients except one, there was a known household contact who had multi-bacillary leprosy and was currently under treatment.

After routine examination all the patients were administered MDT for varying periods up to 30 months. The patients showed no deterioration clinically. The bacteriological indices showed a remarkable fall in the skin smears following MDT.

M. leprae obtained from 9 patients were inoculated into mouse foot pads. In two, control mice did not show growth rendering the test a failure. 5 were resistant to a dapsone concentration of 0.01% (Table).

TABLE 1: CLINICAL DETAILS OF UNTREATED PATIENTS AND THE RESULTS OF THE MOUSE FOOT PAD TEST FOR THE DETECTION OF *M. LEPRAE* RESISTANT TO DDS

No	Name	Sex	Age	Contact	Type	MFP Result	Growth of <i>M. leprae</i> in mice fed (g% DDS in diet)			
							Nil	0.0001	0.001	0.01
1.	NL	F	4	Mother LL	LL	Resistant	+	+	+	+
2.	DT	M	3	Mother LL	BL	Resistant	+	+	+	+
3.	OP	F	10	Relative	BL	Failure	—	—	—	—
4.	AB	M	13	Mother LL	LL	Resistant	+	+	+	+
5.	SM	F	10	Father BL	LL	Failure	—	—	—	—
6.	KM	M	11	Father BL	BL	Resistant	+	+	+	+
7.	GBS	M	13	Relative BL	LL	Resistant	+	+	+	—
8.	AD	M	13	Father LL	LL	Not done	×	×	×	×
9.	BS	M	5	Mother LL	BL	Resistant	+	+	+	—
10.	DKP	M	10	Father BL	LL	Resistant	+	+	+	+
11.	SM	F	14	Father LL	LL	Not done	×	×	×	×

DISCUSSION

Chemotherapy of multibacillary leprosy is to cure the patient and to interrupt transmission of *M. leprae* in the community. In the community the detection of index cases is important and the examination of close contacts, especially children. All eleven patients except one in the study has close household contacts who were multibacillary leprosy patients. Clinical examination of them revealed that they were clinically relapsed patients.

Multibacillary leprosy in all the children in the study is remarkable. Three of them were below 5 years. It is possible that from early childhood the massive bacterial load may result in an immune paralysis to mount effective defences against leprosy infection. Tests to monitor the lack of cell mediated immunity and the estimation of anti-*M. leprae* antibodies by means of ELISA and FLA-abs tests will be valuable in them. (9)

Seven of the 9 tested showed evidence of primary dapsone resistant infection in the mouse foot pad system. Although this study has the limitation of a small number of patients, it supports the view that treated patients who have relapsed are an important source of drug resistant *M. leprae*. Monitoring drug resistance in untreated patients is of paramount importance if primary dapsone resistance is to be detected.

ACKNOWLEDGEMENTS

We thank the laboratory staff, medical record clerk

and para-medical workers of Anandaban Hospital for their assistance.

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