ILEP

TECHNICALBULLETIN
Advice from the Medico-Social Commission

Issue No. 9, May 1996

THE MANAGEMENT OF ERYTHEMA NODOSUM LEPROSUM

1 INTRODUCTION

Immunologically mediated episodes of acute or subacute inflammation known as a reaction, may occur in any type of leprosy except indeterminate. Unless reactions are promptly and adequately treated they can result in permanent deformity. Most reactions belong to one of two major types, erythema nodosum leprosum (ENL) or type 2 reaction or reversal reaction (type 1 reaction).

ENL occurs exclusively in patients with multibacillary leprosy, especially lepromatous (LL) and borderline lepromatous (BL) leprosy. In general, it appears to be less of a problem among patients treated with standard multidrug therapy (MDT) than among those treated with dapsone monotherapy, probably owing to the anti-inflammatory activity of clofazimine in the MDT regimen.

2 DESCRIPTION OF MILD AND SEVERE ENL

ENL is variable in severity, duration and organ involvement.

Mild ENL consists of crops of a few red nodules in the skin with low grade fever and malaise. It can be treated with analgesic / antipyretic drugs such as aspirin or acetaminophen. The justification in using antimalarial drugs such as chloroquine for the treatment of leprosy reactions has never been proved.

Severe ENL may include any or all of the following:

- Neuritis with painful or markedly tender nerves with or without loss of nerve function.
- Prolonged moderate or high fever along with severe general malaise.
- Pustular skin lesions which may progress to extensive ulceration.
- Tender and enlarged lymph nodes.
- Iridocyclitis, orchitis, periostitis or joint swelling.
- Albumin and red blood cells in the urine.

Wherever possible, such severe ENL cases should be immediately hospitalized for treatment.

3 TREATMENT OF SEVERE ENL WITH CORTICOSTEROIDS

The treatment of choice for severe ENL is prednisone, the cheapest and most widely available corticosteroid. The lowest possible dose sufficient to control the ENL should be used. The usual course of prednisone begins with 30 to 60mg daily, and the ENL is generally controlled within 24 to 72 hours. The dose can then gradually be reduced every week by about 10mg for each reduction until a dose of 20mg daily, and by 5mg thereafter. Before stopping completely, a maintenance dose of 5-10mg daily or every other day for several weeks may be useful for preventing the recurrence of ENL in patients with chronic reaction.

It is important to point out that there is no fixed schedule for reducing prednisone, this all depends upon the situation. If the ENL deteriorates or recurs, returning to a higher dose or a repeat course of prednisone treatment will be necessary. The reaction tends to be chronic in patients with high bacterial loads and therefore a number of patients require continuous and often high doses of prednisone treatment and may become steroid dependant. The potential risk of serious adverse effects caused by longer duration corticosteroid treatment must not be ignored, particularly under field conditions. The most common problems include peptic ulcer, diabetes, reactivation of tuberculosis, menstrual irregularities, depression and other emotional problems. If such cases can be maintained on an every other day schedule of prednisone, these adverse effects may be less common.

4 TREATMENT OF SEVERE ENL WITH CORTICOSTEROIDS AND CLOFAZIMINE

Clofazimine is also efficacious for the treatment of ENL. It is less potent than corticosteroids and often takes 4 to 6 weeks to develop its full effect, therefore it is only an additional drug and never started as the sole agent for the treatment of severe ENL.

However, clofazimine may be extremely useful for reducing or withdrawing corticosteroids in steroid-dependant cases. At the beginning, the prednisone therapy is supplemented with higher doses of clofazimine. The patients may be put on clofazimine 300mg daily (or 100mg thrice a day to reduce the gastrointestinal effects) for 3 to 4 months, this is then gradually reduced to 100mg clofazimine daily and maintained at such level for an additional 3 to 6 months. The maximum daily dosage of clofazimine is 300mg.

The ENL reaction is usually controlled within 2 to 4 months of treatment with clofazimine, and then the prednisone can gradually be reduced and eventually withdrawn. If ENL recurs after reduction of prednisone, it is overall less severe than in those cases under treatment with prednisone alone and it may be controlled by increasing the dose of clofazimine before trying to increase the dose of prednisone. For the treatment of ENL reaction, the total duration of clofazimine therapy can last 8 to 12 months or more.

The major problem of continuous higher doses of clofazimine therapy is the intolerance of the drug by some patients due to serious gastrointestinal side effects, such as crampy abdominal pain and diarrhoea, particularly with doses above 100mg daily. Thus, the dose of clofazimine needs to be reduced to tolerable levels as quickly as possible. Because most patients appreciate the efficacy of clofazimine in controlling ENL, its acceptance is better even when the skin pigmentation is quite obvious.

5 TREATMENT OF SEVERE ENL WITH THALIDOMIDE

Thalidomide is also very effective for controlling ENL. It has fewer adverse effects than corticosteroids but has the major serious disadvantage of teratogenicity. For patients with severe ENL who have not responded to the above approach, thalidomide may be considered. Thalidomide is started at 200mg twice daily or 100mg four times daily, and ENL is usually controlled within 72 hours. The dose can then gradually be tapered off, although chronic ENL cases may require a maintenance dose of 50-100mg daily for prolonged periods of time.

It must, however, be emphasized that because of its well-known teratogenicity, thalidomide should be given only to males and postmenopausal females. **Women of child-bearing age should never be given thalidomide. Thalidomide must be administered under the strictest possible supervision**. For drug safety reasons ILEP does not assist countries or programmes in the purchase of thalidomide. Responsibility for the use of thalidomide must rest entirely with the health authorities including the programme manager.

Remember

- In case of nerve involvement, in addition to the medicaments, immobilization of the affected limb will minimize damage to the nerve.
- During the whole period of the ENL reaction the multidrug therapy must be continued.

Further reading

Hastings RC (Ed.), *Leprosy,* Second edition, Churchill Livingstone, Edinburgh, 1994.

Chemotherapy of Leprosy, WHO Study Group, WHO Technical Report Series 847, WHO, Geneva, 1994.