REACTIONS IN LEPROSY-II
(Management)

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Summary

Limited information available on the pathogenetic mechanisms involved in reactional states of leprosy makes the task of management difficult. In the recent past a number of new drugs have been introduced. Various known etiopathogenetic factors and the present status of management of reactions in leprosy is briefly reviewed herein.

Little is known about various factors responsible for precipitating reactions in leprosy. Though reactions are known to occur spontaneously without any apparent cause, a number of causative agents have, from time to time, been incriminated. It is commonly believed that incidence of reactions in leprosy has increased since the introduction of sulfones. This is especially true of Erythema Nodosum Leprosum[1] (ENL). A large percentage of cases of ENL occur after 6 to 12 months of start of sulfone therapy. Other drugs reported to have precipitated reactions in leprosy include potassium iodide, sulfonamides, thiourea compounds, alcohol and hetrazan[2]. The evidence is scanty that concomitant infections precipitate reactions in leprosy. Smallpox and TAB vaccinations have been reported to precipitate ENL and at times surgical operations and stress from pregnancy or parturition have been incriminated[2,3].

Management of Reactions

With limited knowledge of the etiopathogenetic mechanisms involved in reactions, one is frequently confronted with the difficult task of managing the reactional states in leprosy. The management of reactions in leprosy depends largely on the type of reaction, its severity and any associated complications. There are no fixed criteria for assessing the severity of reaction. It can, at most, be graded into mild and severe types, depending upon the intensity of signs and symptoms. The severity of ENL may be graded according to the number of lesions, degree of fever and arthritis, presence of associated complications viz., renal involvement, hepatosplenomegaly, tender lymphadenopathy and rise in erythrocyte sedimentation rate. To an extent, the degree of impairment of fibrinolytic activity appears to be directly related to the severity of the reaction.

The first and foremost question that arises is whether to stop the specific therapy during the reaction or not. It had been customary to either reduce the dose of dapsone or stop the drug altogether at the slightest sign of a reaction. Today, the opinion regarding this practice is divided. Some workers still follow this routine, while others continue to give dapsone during the reactional phase. In 1959, it was decided at the leprosy research unit at

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Sungei-Buloh, to continue dapsone in full dosage in ENL and a report published in 1968 by Waters[4] revealed that maintenance of dapsone treatment throughout the reaction had not altered the course of ENL. Since then continuation of dapsone therapy during the reactional phases is being followed at a number of centers. A more conservative approach is made at other centers where dapsone dose is reduced or the drug is stopped altogether especially in moderate to severe type of reactions such as those with accompanying complications of acute neuritis, iridocyclitis or epididymoorchitis.

Mild reactions are best managed by reducing the dose of dapsone, administering salicylates, reassuring the patient, providing sedation and allaying the anxiety of the patient. Salicylates can be given in the form of soluble aspirin up to a total daily dose of 2-4 grammes orally after meals. Most reactions of mild nature are controlled with this treatment. In case of failure to control the reaction, antimonials or antimalarials may be used[2,3,5]. Of the various antimonials, trivalent compound-Fantorin (Glaxo) is commonly employed in doses of 2ml (12.8 mg) intramuscularly daily or on alternate days for 7-10 injections. Alternatively, chloroquin sulfate or diphosphate is given in a dose of 200 mg tablet (equivalent 150 mg of the base) 2-3 times a day till the fever subsides and the lesions fade. Reactions of even moderate severity usually get controlled within 2-4 weeks of therapy with antimonials or chloroquin. The various side-effects of antimonials include gastrointestinal upset, loss of appetite, metallic taste in the mouth, tremors of fingers and occasionally, exfoliative dermatitis. In patients with recurrent reactions, one must be careful not to use chloroquin for long term therapy because of the risk of irreversible retinal damage, which may appear long after the therapy is discontinued. The drug should not be given unless an initial and a regular eye examination every 3-6 months is performed by an ophthalmologist. Other untoward effects of chloroquin include neuromyopathy, gastrointestinal distress, band keratopathy and bleaching of hair. The other anti-inflammatory drugs viz., oxyphenbutazone, phenbutazone, indomethacin and flufenamic acid may be avoided because of their toxic nature.

Corticosteroids are employed when the above mentioned measures fail. An initial dose of 20-30 mg daily of prednisolone or a corresponding dose of any of its analogues is used. Once the fever subsides and the lesions start fading the dose is tapered off gradually and the patient is usually maintained on a small dose of 5-10 mg for 1-2 weeks after complete amelioration of reaction. In practice, however, it appears that many patients show rebound reactions on withdrawal of steroids and indeed, it sometimes becomes difficult taking such patients off the drug. Unfortunately, this leads to a state of psychic dependence on the drug and various untoward effects of long term corticosteroid therpy. Sometimes, ACTH is used parenterally in doses of 20-40 units daily to avoid adrenal suppression and various side-effects of corticosteroids. The action of ACTH however is slower and less reliable in controlling reactions in leprosy[2]. This is believed to be due to adrenal cortex being either already invaded by lepra bacilli in lepromatous leprosy patients or affected by an amyloid change thereby responding poorly to ACTH stimulation In patients on long term corticosteroid therapy, once a state of dependence has developed sometimes they may be weaned off corticoids by administering corticosteroids in powder form gradually in decreasing doses along with progressively increasing doses of chloroquin the latter being used as a decoy because of the

bitter taste of both drugs[5]. The dose of corticosteroid is finally tapered off but that of chloroquin is kept on for a few weeks till finally this is also withdrawn.

Of the various newer drugs; two viz. clofazimine (Lamprene) and thalidomide deserve mention, the latter being of great use especially in ENL[6]. Clofazimine was brought into use following the observation of Brown and Hogerzeil[7] that the incidence of ENL was lower in patients treated with clofazimine. A few years later its antibacterial, anti-inflammatory immunosuppressive properties were confirmed by the Working Party[8]. The drug is available in 100 mg soft gelatin capsules containing the micronized ingredient in suspension form in an oil/wax base. The starting dose is 1 capsule twice daily. This is gradually increased to 3-4 capsules a day. If the reaction breaks through it is important that the dose is increased rather than decreased. Clofazimine is also useful in reducing the dose of corticosteroids in patients who are being maintained on larger doses of corticosteroids. The various side effects of the drug include initial gastrointestinal irritation, ichthyosiform lesions and reddish discoloration of the skin and the mucous membranes that turn into dark charred tint in course of time. Frequently, the discoloration is localized specifically to the skin lesions.

Thalidomide is used in doses of 400 mg daily (available as 100 mg tablets) and restores body temperaturs to normal within 48 hours and usually brings about a complete remission of the reaction in a week's time[9],[10]. However, in patients who had been earlier treated with corticosteroids it takes longer to bring the reaction under control. Thalidomide is also useful in controlling complications arising during reactional phases of leprosy. Following remission the daily dose of the drug is reduced to 50 mg. At the same time dapsone is resumed in smaller doses. The untoward effects of thalidomide in addition to its well known teratogenicity include constipation, dryness of mucous membranes, drowsiness, dizziness, erythema of the face and chest, edema of distal extremities, psychiatric disturbances, skin rashes and irreversible peripheral neuropathy.

Various newer drugs used in the treatment of patients with reactions in leprosy include thiamphenicol[11], capyna compound[12] and griseofulvin[13]. All these have been shown to be effective in controlling reactions but further evalution is desired for their routine usage.

Management of Complications of Reactions in leprosy

Most important complications occuring during reactional episodes in leprosy which require immediate attention are acute painful neuritis, acute iridocyclitis, acute epididymoorchitis and the reaction hand[14]. It is better to stop dapsone at the earliest possible. Acute painful neuritis is managed by intraneural injection of a corticosteroid preparation which can be repeated daily if required[3]. One ml of 2% lignocaine, 1500 units of hyalase and 1 ml of hydrocortisone (25mg/ml) or equivalent amount of any analogue of hydrocortisone is drawn into a syringe and slowly injected into the swollen nerve using a size 14 needle after infiltrating the skin with a local anaesthetic. In case of threatened muscle paresis oral corticosteroids in doses of 20-40 mg daily should be started immediately. The weakened muscles are splinted in resting position and splints removed twice daily for passive exercises. In case of acute iridocyclitis 1% cortisone eyedrops are instilled 2-3 times a day and 2% cortisone eye ointment is applied at bed time. 1% homatropine eye drops are also instilled twice daily to keep

the pupil dilated so as to prevent the formation of synechiae. If secondary glaucoma has set in, diamox in dose of 150 mg two or three times a day is started to reduce the ocular tension. Oral corticosteroids may be employed depending upon the severity of eye involvement. In neglected patients presenting with synechia formation complete iridectomy is advocated[15]. This helps in delaying the onset of complicated cataract and reduces the frequency of subsequent iridocyclitis. Once the eye reaction has subsided, dapsone may be started in a small dose not exceeding a daily dose of 5mg[3]. Acute epididymoorchitis prompts treatment with oral corticosteroids; dapsone is stopped and scrotum supported by a suspensory bandage.

The inevitable question of whether reactions in leprosy have a beneficial or a deleterious effect on the patient remains of vital importance. As of today, while one could possibly predict that the reversal reactions are going to benefit the patient, most of other known patterns of reactions appear to have a deleterious effect. Better delineation of underlying immunological mechanisms in the future may help us foresee the type of reaction patient is going to manifest so that a timely action may be taken to prevent the downgrading reactions.

REFERENCES

1. Petis JHS and Waters MFR : The etiology of erythema nodosum leprosum, Internat J Lepr, 35 : 1, 1967.
2. Ramu G : Management of reactions in leprosy J Ind Med Assoc, 61 : 403, 1973.
3. Jopling WH : Leprosy reactions and Management of leprosy reactions in Handbook of Leprosy. William Heinmann Medical Books Ltd. London, 1971, pp 42, 59.
4. Waters MFR : The management of ENL with particular references to continued dapsone therapy Internal J Lepr, 36 : 638, 1968.
5. Ramu G and Ramanujam K : Factors influencing prognosis in recurrent lepra reaction. Leprosy in India 42 : 176, 1970.
6. Seshkin J and Sagher F : Trials with thalidomide derivative in leprosy reaction. Leprosy Rev 39 : 203, 1968.
7. Brown SG and Hogerzeil LM : Apparent resistance of M Leprae to B 663. Leprosy Rev 33 . 185, 1962.
8. Report of the Working Party on G-30 320 or B 663. Leprosy Rev 40 : 21, 1969.
9. Languillon J : The effect of thalidomide on leprosy reactions. Internat J. Leprosy reactions. Internat J. Leprosy 39 : 590, 1971.
10. Terencie de Las Aguas J : Thalidomide in the treatment of Lepra reaction. Internat J. Leprosy 39 : 593, 1971.
11. Belda W : The role of thiamphenicol in the treatment of Hansenic reaction. Internat J. Leprosy 36 : 703, 1968.
12. Ojha D. and Upadhyaya YN : Capyna compound in the treatment of reactions in leprosy. Internat J. Leprosy, 36 : 704, 1968.
13. Ramirez MM: Severe lepra reaction treated with griseofulvin. Internat J Leprosy. Internat J Leprosy 36 : 707, 1968.
14. Ramanujam K, Dharmendra and Ramu G : Treatment of lepra reaction with some of its special investigations. Leprosy in India 26 : 19, 1964.
15. Choyce DF : Diagnosis and management of ocular leprosy. British J Ophth 53, 217, 1969.