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Clofazimine (Lamprene or B663) in lepra reactions

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Summary In view of some confusion in the literature as to the value of clofazimine in the treatment of patients with Type 1 reactions, due to cell-mediated immune mechanisms, 10 patients with this type of reaction were treated with this drug. The results were unsatisfactory; clofazimine had to be either stopped or withdrawn in favour of treatment and control of the reactions with prednisolone. Two of these cases are described in detail.

The anti-inflammatory effect of clofazimine, first suggested by Browne,[1–2] has proved to be effective in controlling erythema nosodum leprosum (ENL).[3–5] It is, however, important to distinguish the lepra reactions and to specify accurately where in the spectrum TT–LL the reactions occur.[6] Turk[7] describes two lepra reactions depending on the presence or absence of cell-mediated immune processes, i.e. the lepra reactions depending on the immunity present and those occurring in pure lepromatous patients (LL) where cell-mediated processes are depressed.

The two lepra reactions have also been described by Jopling[8] as lepra reactions Type 1, indicating that the reaction occurs in patients with immunity however slight, and lepra reaction Type 2 which occurs in the pure lepromatous patients (LL) where there is no cell-mediated immunity present. Type 2 reaction is known as erythema nodosum leprosum (ENL).

Using Jopling's terminology to stress the difference of the two lepra reactions indicating the presence or absence of cell-mediated immune processes, it is therefore clear that lepra reactions Type 1 are different clinically, immunologically and histologically from the lepra reactions Type 2. The therapeutic management of the two lepra reactions is also different. For example: most clinicians would stop dapsone therapy at the onset of a Type 1 reaction, but there is doubt regarding the need to do so in Type 2 reaction.[9] Also, though

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corticosteroids have an important place in the management of both types of reaction, Thalidomide is effective only in Type 2 reaction. There is a large literature on the good effect of clofazimine in Type 2 reactions and since early 1966 the author has found the drug consistently effective, but little is known of its effect in Type 1 reaction.

It is therefore important to find out if clofazimine was equally effective in lepra reactions Type 1, but after treating 10 patients with this type of reaction the use of clofazimine had to be abandoned as it was observed that clofazimine aggravated the reactional state of the patients and had either to be discontinued and prednisolone given or reduced and prednisolone added. Two of these case histories from patients seen and treated in Zambia will now be given in detail with photographs.

Case I

On 12 August 1969 an adult female African patient was admitted for treatment from another leprosarium after being classified a lepromatous case. From the scanty notes we learned that on admission two smears were recorded: left ear negative and right ear positive. Prior to admission she was treated with CIBA 1906, 1.5 g daily, without any improvement. On 24 February 1970 she had a 'reaction'. Treatment with CIBA 1906 continued but the patient's condition worsened. On 23 March 1970 CIBA 1906 was discontinued and after a course of chloroquin she was given clofazimine, 500 mg daily. As the patient's reaction worsened she was transferred to Liteta Leprosarium (Zambia) on 28 May 1970. On examination the patient showed raised hyperpigmented facial skin lesions with definite edges (Figure 1). Her nose was swollen, hyperpigmented due to clofazimine treatment, dry and crusty. She had numerous raised lesions, varying in size with good edges, distributed all over her trunk and limbs. The areas between these lesions were healthy skin. Out of 7 smears, 6 were negative and the left ear was 2+, fragmented bacilli only.

The patient was reclassified BT in lepra reaction. A biopsy from a lesion on the right upper arm was reported as BB leprosy and a second opinion from Dr D J Harman, Leprosy Study Centre, London confirmed this classification. No leprosy drugs were prescribed but a course of prednisolone started at a dosage of 3 x 10 mg daily and gradually reduced. On 15 August 1970 the skin lesions were quiescent and flat and treatment with low-dosage dapsone commenced. The patient responded without complications and was discharged on 28 April 1971 on dapsone, 100 mg three times weekly (Figure 2).

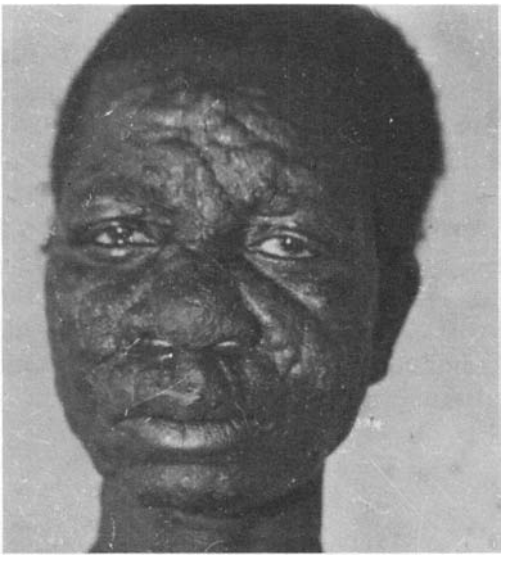

Figure 1. Case I. Condition on admission to Liteta Leprosarium. Worsening of reaction after taking clofazimine.

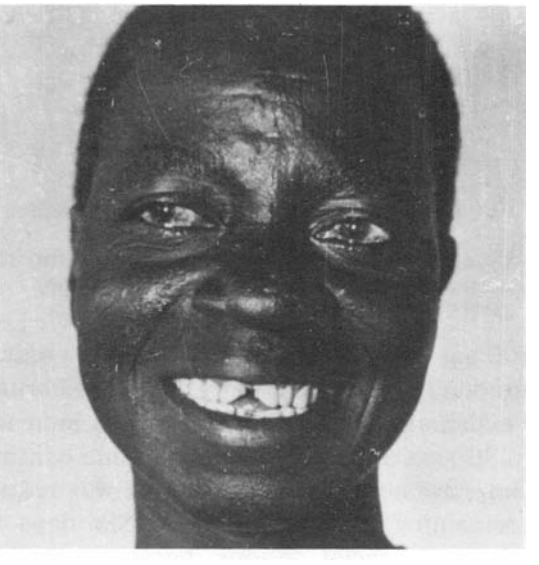

Figure 2. Case I. After discontinuation of clofazimine treatment and replacement by prednisolone and dapsone. Marked improvement prior to discharge from hospital.

Case II

An adult female African patient, aged 35, was admitted to Liteta Leprosarium on 12 September 1968 and examined by an experienced Medical Assistant (at the time the author was away). She was classified as a BB leprosy in reaction. Smears on admission were: left and right ears negative. Right cheek 5+. After a course of Chloroquin and Stibophen she was given prednisolone, 5 mg t.d.s. increasing to 10 mg t.d.s. as from 25 November 1968.

The patient was seen and examined by the author on 4 January 1969. Raised, erythematous, infiltrated skin lesions covered forehead, nose, cheeks and upper lip (Figure 3). In addition she had a few raised, small lesions on the right and left breasts and one large raised lesion on the right shoulder, of which the edges were irregular and sloping.

Figure 3. Case II. Raised, erythematous infiltrated lesion on forehead, nose, cheeks and upper lip at time of treatment with clofazimine with prednisolone.

Clofazimine, 100 mg daily, was prescribed and prednisolone reduced to 20 mg daily and gradually to 7.5 mg daily. On 10 February 1969 the facial lesions were more oedematous and clofazimine was increased to 200 mg daily and a week later to 300 mg daily, while prednisolone continued at 2.5 mg t.d.s.

After a slight improvement the prednisolone was reduced to 2.5 mg daily with clofazimine remaining at 300 mg daily. Six days later the condition of the patient worsened, facial lesions became more erythematous and oedematous and after another 2 weeks it was considered necessary to discontinue clofazimine completely (Figure 4). Prednisolone, 20 mg daily, finally

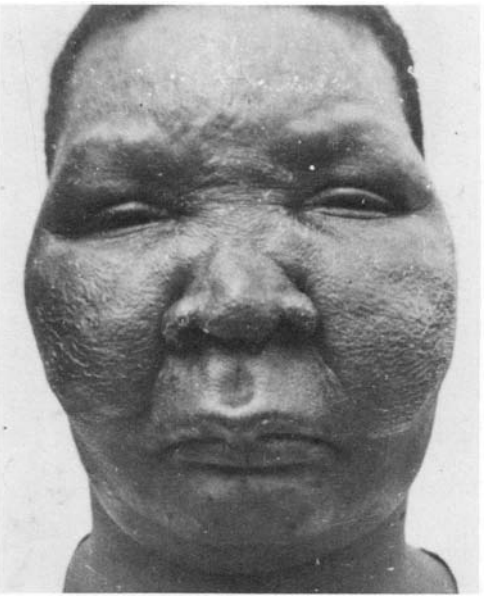

Figure 4. Case II. Worsening of reaction (see text).

controlled the reaction. Eight weeks later while the patient was still on 17.5 mg prednisolone daily, clofazimine at 100 mg *weekly* was resumed with no reaction occurring. After a further 7 weeks clofazimine was stopped and the patient given low-dosage dapsone. Prednisolone was discontinued after 2 more weeks and the reactional state was quiescent. The patient continued to improve without reacting to a gradual increase of dapsone and was finally discharged on 30 July 1971 to an out-patients' clinic (Figure 5).

Her facial lesions were inactive, the skin smooth and the hyperpigmentation caused by clofazimine was fading. Skin smears were negative.

Summary

It is important not to use the terminology 'lepra reaction' without specifying in which part of the TT–LL spectrum the reaction occurs. Jopling's terminology of reactions (Type I and Type 2) is greatly to be recommended. Clofazimine appears not to be effective in lepra reaction 1.

Acknowledgement

I wish to thank Dr D J Harman of the Leprosy Study Centre, London for his report on the biopsy on Case I.

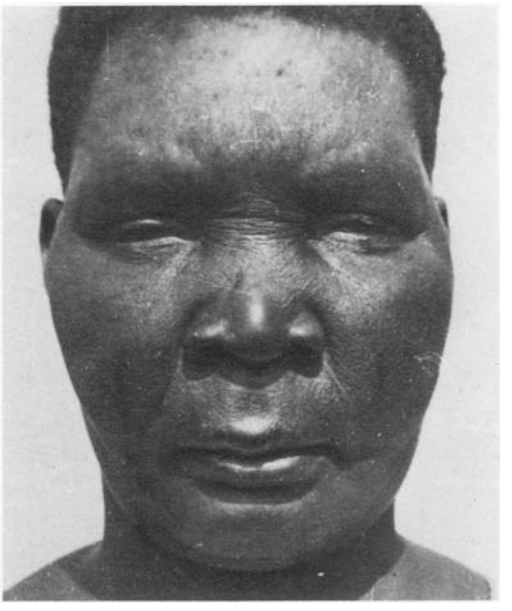

Figure 5. Case II. Marked improvement after discontinuation of clofazimine and maintenance on prednisolone (see text). Patient on dapsone only prior to discharge.

References

1 Browne SG. B663 – possible anti-inflammatory action in lepromatous leprosy. *Lepr Rev*, 1965, **36**, 9.

2 Browne SG. B663 (Geigy) – further observations on its suspected anti-inflammatory action. *Lepr Rev*, 1966, **37**, 41.

3 Imkamp FMJH. A treatment of cortico-steroid-dependent lepromatous patients in persistent erythema nodosum leprosum. A clinical evaluation of G30320 (B663). *Lepr Rev*, 1968, **39**, 119.

4 Jopling WH. *Management of Lepra Reactions* (9th Int. Leprosy Congress, London, 1968).

5 Morgan J. Management of steroid dependency with Clofazimine (Lamprene or B663, Geigy). *Lepr Rev*, 1970, **41**, 229.

6 Ridley DS, Jopling WH. Classification of leprosy according to immunity. A five-group system. *Int J Lepr*, 1966, **34**, 255.

7 Turk JL. Cell-mediated immunological processes in leprosy. *Lepr Rev*, 1970, **41**, 207.

8 Jopling WH. *Handbook of Leprosy*, 1971, London: Heinemann.

9 Pearson JMH *et al.* The effect of stopping Dapsone treatment for two months and then restarting it in full dosage in patients with moderately severe erythema nodosum leprosum.