MELKERSSON-ROSENTHAL SYNDROME RESPONDING TO CLOFAZIMINE THERAPY

K Pavithran

Two patients had Melkersson-Rosenthal syndrome. One of them had all the 3 components of the syndrome—facial paralysis, plicated tongue and macrocheilia, while the other had only 2 components—macrocheilia and plicated tongue. Oral antihistamine therapy for 3 weeks was ineffective in both cases. But appreciable clinical response occurred after clofazimine therapy in both cases.

Key words : Melkersson-Rosenthal syndrome, Cheilitis granulomatosa, Clofazimine, Therapy.

Melkersson-Rosenthal syndrome (MRS) consists of a triad of recurrent facial paralysis, recurrent and eventually permanent labial swelling and plication of the tongue. Miescher's granulomatous cheilitis, in which there is only swelling of the lip, is now accepted as an oligo-symptomatic form of MRS.[1-3] The aetiology of this syndrome is not known. It is viewed as a peculiar nosologic entity that results from a circumscribed segmental neurologic or neuro-vascular disturbance.[1] Several familial cases have been reported suggesting a genetic component.[3,4] Rarely, it has been associated with lymphoma or leukemia.[5,6] There is no specific treatment for this condition. Various drugs tried include antihistamines, gamma globulin and corticosteroid which is administered orally or intralesionally. Long-standing cases with chronically enlarged tissue may require surgical excision. This communication describes use of clofazimine in two patients with MRS.

Case Reports

Case 1

A 20-year-old male developed recurrent swelling of the upper lip since 4 years and fissures on the tongue since 5 years. To begin with, the swelling used to subside completely without any treatment. But later on, there was persistence of some residual swelling, and finally it resulted in permanent enlargement of the lip. There was a diffuse, soft, non-tender, non-compressible and non-pitting swelling of the upper lip (Figs. 1 and 2). The skin on the swelling was not atrophic and all modalities of sensations were intact. There was no weakness or paralysis of the muscles of the face. There were many deep fissures on the dorsum of the tongue. All other systems were clinically normal. Routine laboratory tests on blood, urine and stools were normal. Earlobe smears and slit-skin smears from the lip lesion were negative for AFB. Blood VDRL test was negative. A course of oral pheniramine maleate given for 3 weeks was ineffective. He was then given clofazimine 100 mg daily for 6 weeks. There was about 70% reduction in size of the swelling of the lip. The dose of clofazimine was then reduced to

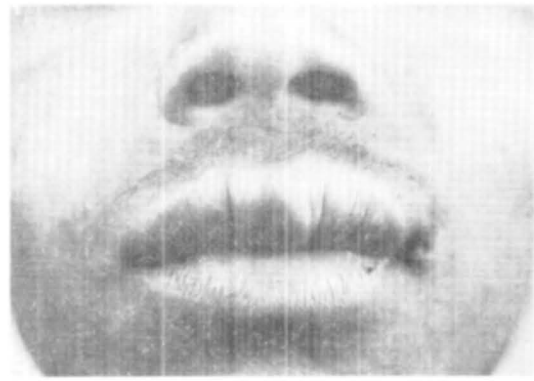

Fig. 1. Swelling of the upper lip in case 1.

From the Department of Dermato-Venereology, Medical College Hospital, Kottayam-686 008, India.

Fig. 2. Swelling of lip.

100 mg on alternate days for 2 months after which he was maintained on 100 mg twice weekly for a further period of 6 months. When seen at the end of 6 months the swelling had completely disappeared, though fissures of the tongue still persisted. Except for diffuse brownish-red pigmentation of the skin of the face, neck and arms, there were no significant side effects attributable to clofazimine therapy.

Case 2

A 45-year-old female developed persistent swelling of the upper lip since 4 years, fissures of the tongue since 3 years and recurrent episodes of weakness of the right side of the face since 5 years. To start with, the swelling of the lip used to subside completely within a day or two without any treatment. But later on, there were recurrent episodes at irregular intervals and each episode lasted longer, and finally resulted in permanent enlargement of the upper lip. Examination revealed a diffuse, firm, non-tender swelling of the upper lip. All modalities of cutaneous sensations were intact over the swelling. There was lower motor neuron type of facial palsy on the right side. Many deep,irregular fissures were seen on the dorsum of the tongue. There was no thickening of the peripheral nerves. All other systems were clinically normal. All the laboratory tests as done for case 1 were either negative or within normal limits. Histopathological study of the biopsy specimen taken from the lip lesion revealed perivascular lympho-histiocytic infiltration in the dermis. Acid-fast staining of the sections did not show any bacillus. Since oral antihistamine therapy was found to be ineffective, she was treated with clofazimine 100 mg twice daily for 1 month. There was significant reduction in the size of the swelling of the lip and it became less firm in consistency. The dose of clofazimine was reduced to 100 mg daily and after 3 months, it was further reduced to 100 mg twice weekly. There was 80% reduction in the size of the swelling and most muscles of the face on the right side regained power, though only partially. The fissures of the tongue were still persisting.

Comments

Incomplete manifestation of MRS is not uncommon. Among 7 cases reported recently by Lindelof et al,[7] only 3 had full blown picture of the syndrome. The cases reported by Yuzuk et al and by Pavithran also had only macrocheilia and fissured tongue.[8,9] Clinical, bacteriological and histopathological features readily distinguish this syndrome from leprosy.

In addition to its mycobacteriostatic effect, clofazimine has a profound anti-inflammatory action also, which is made use of in controlling lepra reactions. Its antiinflammatory and immunosuppressive effects may be due to its stimulatory effect on the synthesis of PGE_2 by human polymorphonuclear leucocytes, monocytes and macrophages in response to pro-inflammatory stimuli.[10] It also stabilizes lysosomal enzymes and stimulates phagocytosis.[10-12] Clofazimine is well tolerated and virtually non-toxic, except for reversible dose-related pink to brownish black discoloration of

the skin. It has occasionally been used for the treatment of discoid lupus erythematosus, pustular psoriasis, pyoderma gangrenosum and facial granuloma. Two recent reports on the beneficial effect of clofazimine in cheilitis granulomatosa and MRS,[11,13] made us try this drug in our patients and the response was good. Except for pigmentation of the skin there were no serious side effects.

References

1. Hornstein OP : Melkersson-Rosenthal syndrome : a neuro-muco-cutaneous disease of complex origin, Curr Prob Dermatol, 1973; 5 : 117-156.
2. Wadlington WB, Riley H and Lowbeer L : The Melkersson-Rosenthal syndrome, Paediat, 1984; 73 : 502-506.
3. Graft-Radford SB : Melkersson-Rosenthal syndrome, South Afr Med J, 1981; 60 : 71-74.
4. Carr RD : Is Melkersson-Rosenthal syndrome hereditary, Arch Dermatol, 1966; 93: 426-427.
5. Mulvihill JJ, Eckman WW, Fraumani JF Jr et al : Melkersson-Rosenthal syndrome, Hodgkin's disease and corneal keratopathy, Arch Int Med, 1973; 132 : 116-117.
6. Connelly TJ, Kauh YC, Luscombe HA et al : Leukemic macrocheilitis associated with hairy-cell leukemia and the Melkersson-Rosenthal syndrome, J Amer Acad Dermatol, 1986; 14 : 353-358.
7. Lindelof B, Eklund A and Liden S : Kveim test reactivity in Melkersson-Rosenthal syndrome (cheilitis granulomatosa), Acta Dermato-Venereol, 1985; 65 : 443-445.
8. Yuzuk S, Trau H, Levy A et al : Melkersson syndrome, Internat J Dermatol, 1985; 24 : 456-457.
9. Pavithran K : Melkersson-Rosenthal syndrome masquerading as tuberculoid leprosy, Ind J Leprosy, 1987; 59 : 26-29.
10. Anderson R : Clofazimine potentiates the synthesis of prostaglandin E_2 in vitro, Leprosy Rev, 1985; 56 : 82-84.
11. Neuhoffer J and Fritsch P : Cheilitis granulomatosa : therapy with clofazimine, Hautarzt, 1984; 35 : 459-463.
12. Sarracent J and Finlay CM : The action of clofazimine on the level of lysosomal enzymes of cultured macrophages, Clin Exp Immunol, 1982; 48 : 261-267.
13. Podmore P and Burrows D : Clofazimine—an effective treatment for Melkersson- Rosenthal syndrome or Mieschers' cheilitis, Clin Exp Dermatol, 1986; 11 : 173-178.