Crystalline deposition in the cornea and conjunctiva secondary to long-term clofazimine therapy in a leprosy patient

Dear Editor,

The continuous introduction of new systemic medications and dosing changes in current drug regimens has resulted in ever-increasing reports of ocular toxicities.[1] We report an unusual side-effect of long term therapy with clofazimine, which caused numerous polychromatic crystalline deposits within the cornea and conjunctiva in a leprosy patient.

A 30-year-old woman, case of lepromatous leprosy with recurrent type II lepra reaction, on tablet clofazimine 100 mg/day was referred to us from dermatology clinic for brownish discoloration of conjunctiva. She was diagnosed as a case of lepromatous leprosy three years ago and started on multi drug therapy-multi bacillary (MDT-MB), which included clofazimine 50 mg/day and 300mg/ month as pulse dose. She was not on any other medication. After three months of treatment, she developed type II lepra reaction and was treated with clofazimine and corticosteroids. The dose of clofazimine was 300 mg/day for two months, which was tapered over the next three months. Over the next two years, she developed two more episodes of type II lepra reaction for which she had again received reactional doses of clofazimine. Estimated cumulative dose of clofazimine was 891.0 gm.

Her best corrected visual acuity was 20/50 in both eyes. On slit lamp examination, brownish-red discoloration of peripheral cornea and conjunctiva in inter-palpebral region was noted [Fig. 1]. There were multiple polychromatic crystalline deposits scattered diffusely over peripheral cornea and conjunctiva of both eyes [Figs. 2 and 3]. The lens had Grade 2 nuclear sclerosis in both eyes but no similar deposits. Fundoscopy was normal in both eyes. She also had reddish-brown discoloration of skin. Clofazimine therapy was stopped after two months as treatment of type II lepra reaction was completed. On follow-up after 6 months of discontinuing clofazimine, best corrected visual activity was 20/50 in both eyes and the conjunctival and corneal crystalline deposits had decreased along with conjunctival discoloration [Fig. 4]. The absence of any other known cause of crystalline corneal deposits confirmed long-term clofazimine therapy as a cause of crystalline deposition in the cornea and conjunctiva.

Corneal stromal deposition may develop from a number of medications such as clofazimine, gold, immunoglobulins, indomethacin, phenothiazines, retinoids, sparfloxacin, and silver. The deposits of drugs and drug metabolites within corneal stroma may be predominantly pigmented, crystalline,

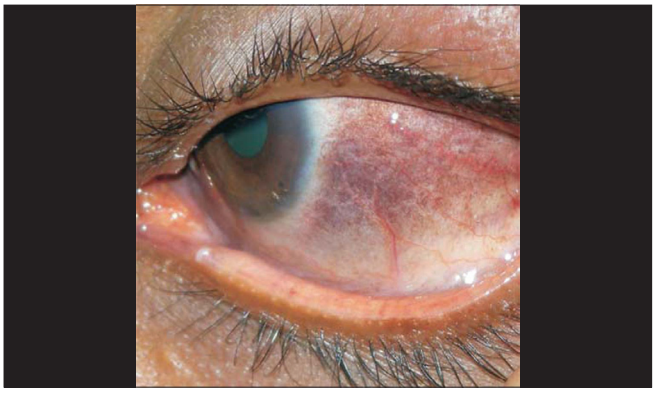

Figure 1: Brownish-red discoloration of peripheral cornea and conjunctiva

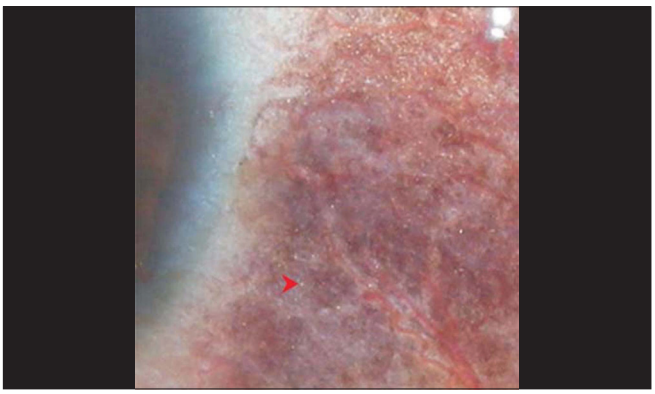

Figure 2: Polychromatic crystalline deposits over conjunctiva (➤) represents crystalline deposits

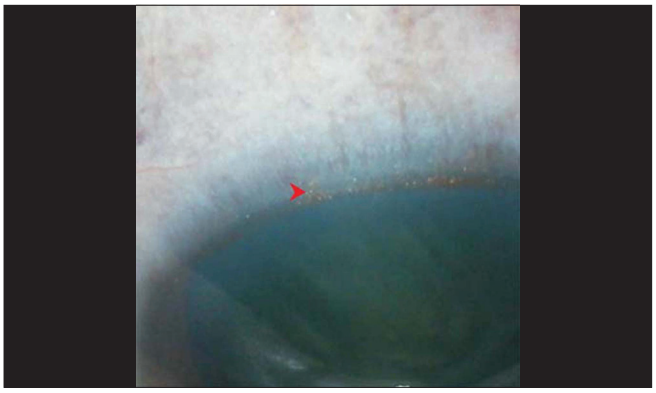

Figure 3: Polychromatic crystalline deposits over cornea. (➤) represents crystalline deposits

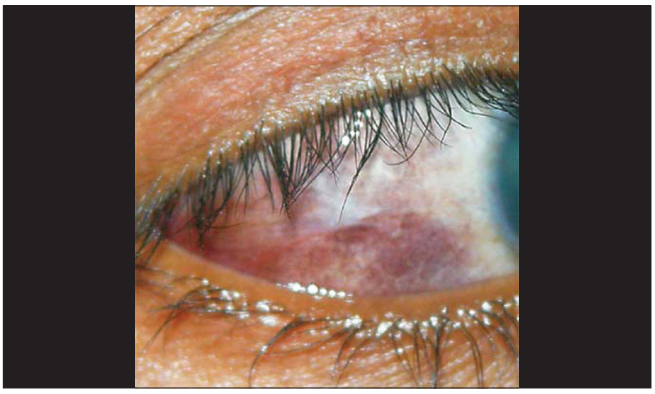

Figure 4: Follow-up at 6 months

or refractile.[1] Crystalline deposits in cornea are reported following exogenous immunoglobulin therapy and the crystals appear in mid periphery in annular fashion.[2] Gokhale observed multiple refractile crystalline deposits in the corneal stroma following prolonged topical sparfloxacin therapy.[3]

Corneal and conjunctival changes have been reported previously in association with clofazimine therapy. Kaur *et al*., observed conjunctival pigmentation in 46% and corneal pigmentation in 53% patients treated with clofazimine for 6–24 months.[4] Our patient had polychromatic crystalline deposits along with brownish-red discoloration in bulbar conjunctiva and peripheral cornea, which did not affect the vision. Careful literature search revealed that only one such case is reported by Font *et al*.,[5] having estimated cumulative dose of clofazimine of 219 gm as compared to 891 gm in our patient In the case reported by Font *et al*., ultrastructural study of conjunctival biopsy demonstrated that many of fibroblasts and macrophages contained rectangular or rhomboidal empty spaces corresponding to crystals, which ranged from 1.5 to 7 μm in length.[5]

In greater than 1% of patients on clofazimine therapy diminished vision and ocular dryness, burning, itching, and irritation have been reported, which were absent in our case. Craythorn *et al*.,[6] reported macular pigmentary abnormalities but in our patient macula was normal.

Further studies of clofazimine-treated patients are necessary in order to determine the frequency and spectrum of corneal and conjunctival abnormalities associated with the drug. It is suggested that patients being treated with clofazimine should undergo periodic ophthalmic examination. Clofazimine-induced crystalline keratopathy should be included in the differential diagnosis of crystalline deposits of cornea and conjunctiva.

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