Clofazimine-induced premaculopathy in a vitiliginous patient

Nirupama Kasturi, Renuka Srinivasan
Department of Ophthalmology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

ABSTRACT
A 26-year-old male vitiliginous patient presented with decreased visual acuity because of a central scotoma in the left eye with no significant retinal changes on fundus examination. In this case report, a diagnosis of possible drug-induced premaculopathy was made, and the drugs were withdrawn. On the follow-up, after 3 months, the visual acuity in the left eye gradually improved. Early suspicion of drug-induced maculopathy and withdrawal of the drug may prevent the progression of maculopathy.

Key words: Central scotoma, clofazimine drug toxicity, maculopathy

INTRODUCTION
Clofazimine is a drug used to treat leprosy and mycobacterium avium infections. It is well tolerated when the dose does not exceed 100mg/day. Clofazimine is known to cause conjunctival and corneal pigmentation but drug induced retinopathy is rare. It is to be used with caution in immunocompromised individuals and patients taking other drugs due to its toxic effects on the eye.

CASE REPORT
A 26-year-old nonimmunocompromised male presented with a history of blurring of vision in the left eye for 8 months. He was diagnosed with vitiligo and under oral therapy with clofazimine 100 mg/week and methoxsalen 10 mg/day along with some herbal products for 1 year. Ocular examination revealed a drop in the best-corrected Snellen visual acuity by 5 lines in the left eye with prolonged photostress recovery time indicating a maculopathy. Visual examination was normal in the right eye. Fundus examination in the left eye was within normal limits [Figure 1a and b]. Fluorescein angiography did not reveal any abnormalities in the retina [Figure 1c and d]. Color vision discrimination was low in both eyes. Visual field analysis of the macula was normal in the right eye and showed a central scotoma in the left eye [Figure 2]. A diagnosis of possible drug-induced premaculopathy was made using the WHO causality assessment and scoring of 3 using the Naranjo’s scale. The patient was referred to his treating dermatologist for withdrawal of the drugs. Other causes of central scotoma such as multiple sclerosis, optic nerve glioma, toxic, nutritional, and hereditary optic neuropathies were ruled out with detailed history and investigations. On follow-up after 3 months with

Access this article online
Quick Response Code:
Website: www.jpharmacol.com
DOI: 10.4103/0976-500X.189685

Address for correspondence:
Nirupama Kasturi, Department of Ophthalmology, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry - 605 006, India.
E-mail: kasturiniru@gmail.com

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Kasturi N, Srinivasan R. Clofazimine-induced premaculopathy in a vitiliginous patient. J Pharmacol Pharmacother 2016;7:149-51.
discontinuation of clofazimine, methoxsalen, and the herbal products, the visual acuity in the left eye improved. Photostress recovery time decreased with improvement in the color vision discrimination scores. Visual field analysis was normal in the right eye and showed reduction in the size and density of the central scotoma in the left eye [Figure 3].

**DISCUSSION**

Clofazimine is an iminophenazine drug with antimycobacterial and anti-inflammatory activities and it is used for the treatment of lepromatous leprosy, dapsone-resistant leprosy, and *Mycobacterium avium* complex infections in patients with acquired immunodeficiency syndrome (AIDS).[1]

It causes an increase in both the number of strata of pigment-bearing cells and the density of the pigment in stratum germinativum of the skin. Later, melanocytes rupture, with the release of their melanin content into the papillary layer of the dermis.[2] This property of clofazimine to stimulate melanogenesis prompted the use of this drug in patients with established vitiligo, pyoderma gangrenosum, and discoid lupus in an attempt to restore pigment to the affected skin.

After several months of treatment, clofazimine crystals may accumulate in the ocular tissues and cause side effects such as cornea verticillata, brownish discoloration of the conjunctiva and tears, crystals in the iris and sclera, and toxic retinopathy.[3] Clofazimine-induced retinopathy have been reported in two patients with AIDS following a higher dose of 200 mg/day.[4,5] Unlike the two previously mentioned cases, in
the present case study, the patient received a lower dose, was not immunocompromised, and had a unilateral presentation. Methoxsalen is a psoralen drug used to treat psoriasis, eczema, vitiligo, and some cutaneous lymphomas in conjunction with exposing the skin to ultraviolet A light from lamps or sunlight. Photosensitization in ducklings has shown vacuolization of retinal ganglion cells, pigmentary retinopathy, and congestion of choroidal vessels.\(^6\) It is plausible that in our patient, methoxsalen being a photosensitizing drug may interact with clofazimine, making the macula more sensitive to light-induced damage as the drug is reported to be very safe in the usual doses in nonimmunocompromised adults.\(^7\) The appearance of central scotoma before visible changes in the fundus suggests that the initial site of damage is in the outer segment of the photoreceptors, which is then followed by degeneration of the retinal pigment epithelium (RPE) and choriocapillaris. Fundus autofluorescence imaging and multifocal electroretinogram although not available in our setup have been used to detect early retinal changes in drug-induced retinopathy.\(^8\)

**CONCLUSION**

Accumulation of clofazimine in RPE in the outer retina with phototoxic damage and reduction of photoreceptors leads to maculopathy. Ophthalmologists should be aware of this entity in spite of its unilateral presentation. Early suspicion and withdrawal of the drug may result in reversibility of the retinal side effects and prevents the progression of maculopathy.

**Financial support and sponsorship**
Nil.

**Conflicts of interest**
There are no conflicts of interest.

**REFERENCES**

1. W oolons A, Black MM. Clofazimine. In: Wakelin SH, Howard IM, editors. Handbook of Systemic Drug Treatment in Dermatology. 1st ed. USA: Manson Publishing Ltd.; 2004. p. 101-4.
2. Bor S. Clofazimine (lamprene) in the treatment of vitiligo. S Afr Med J 1973;47:1451-4.
3. Agarwal A. Clofazimine retinopathy. Toxic diseases affecting the pigment epithelium and retina. In: Gass’ Atlas of Macular Diseases. 5th ed., Vol. 1, Ch. 9. US: Elsevier Health Sciences; 2011. p. 764.
4. Cunningham CA, Friedberg DN, Carr RE. Clofazimine-induced generalized retinal degeneration. Retina 1990;10:131-4.
5. Craythorn JM, Swartz M, Creel DJ. Clofazimine-induced bull’s-eye retinopathy. Retina 1986;6:50-2.
6. Barishak YR, Beemer AM, Egved MN, Shlosberg A, Eilat A. Histology of the iris in geese and ducks photosensitized by ingestion of Ammi majus seeds. Acta Ophthalmol (Copenh) 1975;53:585-90.
7. Kumar B, Kaur S, Kaur I, Gangowar DN. More about clofazimine – 3 years experience and review of literature. Indian J Lepr 1987;59:63-74.
8. Kellner U, Renner AB, Tillack H. Fundus autofluorescence and mfERG for early detection of retinal alterations in patients using chloroquine/hydroxychloroquine. Invest Ophthalmol Vis Sci 2006;47:3531-8.