Ophthaproblem

Wei Liu, MD, PHD **Sanjay Sharma,** MD, MSC, MBA, FRCSC

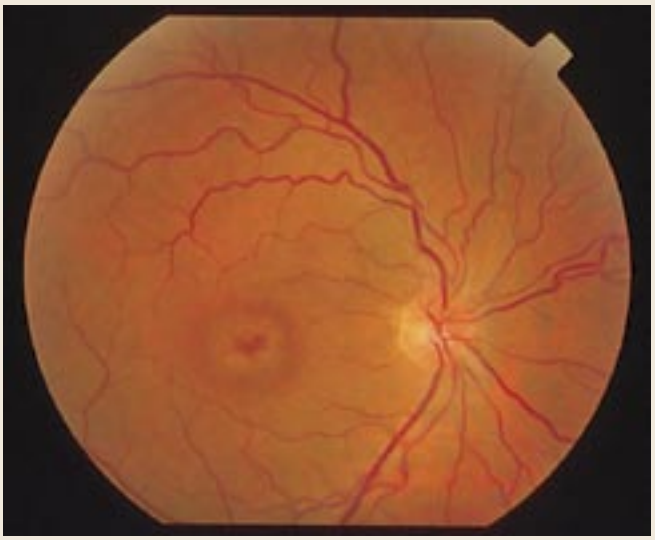

Photo credit: *Ophthalmic Photography, Hotel Dieu Hospital, Kingston, Ont*

Bull's-eye pattern of retinal pigment epithelium disturbance in the foveal region of the right eye

A 48-year-old man reported that his vision had been gradually decreasing in both eyes during the past few years. He had a history of rheumatoid arthritis for which he had been taking chloroquine daily for approximately 3 years (1992 to 1995). His visual acuities at presentation were 6/12 in his right eye and 6/6 in his left eye.

The fundus photograph is compatible with the patient having which of the following?

1. Age-related macular degeneration
2. Chloroquine or hydroxychloroquine retinopathy
3. Stargardt disease
4. Cone degeneration

Answer on page 679

Dr Liu *is a visiting scholar from China doing a research fellowship in the Department of Ophthalmology at Queen's University in Kingston, Ont.* **Dr Sharma** *is an Associate Professor in the Department of Ophthalmology and an Assistant Professor in the Department of Epidemiology at Queen's University.*

← FOR PRESCRIBING INFORMATION SEE PAGE 734

Answer to Ophthaproblem continued from page 671

2. Chloroquine or hydroxychloroquine retinopathy

Chloroquine was first used to prevent and treat malaria during World War I. Since then, it and its analogue, hydroxychloroquine, have been used to treat certain connective tissue diseases, such as rheumatoid arthritis and systemic lupus erythematosus. Chloroquine retinopathy, first reported in 1957,[1] is a rare condition characterized by a bull's-eye appearance of the macula. Patients with this condition often note a decrease in central vision that they usually relate to central or paracentral scotomas. Other symptoms reported include photophobia (sensitivity to light), nyctalopia (difficulty seeing in the dark), photopsias (flashing lights), and impaired colour vision.

The earliest fundus findings of chloroquine toxicity are parafoveal retinal pigment epithelium irregularities and loss of the foveal reflex. In the early stages, these changes can be indistinguishable from changes that occur with aging. As the disease progresses, the pigment epithelium continues to atrophy. In the final stages, a classic "bull's-eye" (granular hyperpigmentation of the parafoveal area surrounded by a concentric zone of hypopigmentation) usually appears (**Figure 1**). In some advanced cases, pallor of the optic disk, attenuated retinal arterioles, and mottling of the peripheral retinal pigment epithelium occur. In early cases of chloroquine toxicity, a patient's fundus can appear morphologically normal, but threshold visual field and Amsler chart testing can detect paracentral scotomas. Fluorescein angiography shows hyperfluorescence in a bull's-eye pattern and is helpful in demonstrating faint changes before the disease is detected biomicroscopically.

The mechanism of chloroquine toxicity is not fully known. Chloroquine clears very slowly from the body, however, and its deposition in the melanin-containing tissues of the eye might contribute to its retinal toxicity.[2,3]

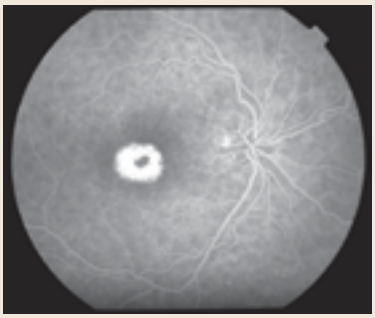

Figure 1. Window defects corresponding to the area of macular retinal pigment epithelium changes are shown in an early fluorescein angiogram in the right eye

The incidence of hydroxychloroquine retinopathy is low. A review of more than 1200 hydroxychloroquine prescriptions filled in a Kaiser Permanente Medical Care Program found only one case of definite retinopathy (0.08%) and a few cases of indeterminate but probable toxicity (0.4%).[4] The condition is closely related to daily dose of medication and duration of treatment.[5] Risk factors for developing retinopathy include doses of chloroquine higher than 3 mg/kg daily and doses of hydroxychloroquine higher than 6.5 mg/kg daily, doses of hydroxychloroquine higher than 400 mg/d,[5] and cumulative doses higher than 500 g.[6] Other factors that increase risk of chloroquine toxicity include using the medication for longer than 5 years, high serum fat level, having renal or liver disease, having concomitant retinal disease, and being older than 60 years. Loss of vision is usually irreversible, even after cessation of the drug.[2]

In 2000, the American Academy of Ophthalmology issued recommendations on screening for chloroquine and hydroxychloroquine toxicity.[5] They suggested that all patients beginning either chloroquine or hydroxychloroquine therapy should have a baseline examination within the first

Answer to Ophthaproblem

continued from page 679

year. This should include best-corrected visual acuity, dilated examination of the cornea and fundus, and baseline field testing with an Amsler chart or Humphrey 10-2 fields. Patients with risk factors should have annual examinations.

Management

This patient was referred on an urgent basis to an ophthalmologist. Examination of the fundus revealed a well-defined yellow circummacular ring approximately 1 disk diameter in size in the macular region of the right eye. Inside the ring was a small pink (normal appearance) fovea—a bull's-eye maculopathy. In the left eye, there was a subtle central maculopathy. Visual field testing demonstrated bilateral central field loss. Angiography demonstrated a "window defect" characteristic of this lesion (**Figure 1**). Despite cessation of the drug 9 years ago, the patient's visual acuity continues to deteriorate.

Recommendation

Ophthalmologists and other physicians should be aware that use of chloroquine or hydroxychloroquine can cause retinopathy with or without permanent visual impairment. To detect signs of toxicity at the earliest stages, patients should be carefully screened.

References

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