CASE REPORT

Delayed progression of bull's eye maculopathy

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SUMMARY

Chloroquine-induced maculopathy may progress years after drug cessation and an apparent period of visual stability. Both doctor and patients should be fully aware of the risks of retinal toxicity, including delayed onset and progression. It is therefore crucial that regular monitoring continues in affected patients, long after the initial diagnosis of maculopathy.

BACKGROUND

Chloroquine was first used for malaria prophylaxis and treatment and later widely used for rheumatological conditions, such as rheumatoid arthritis and systemic lupus erythematosus. Long-term usage may be limited by retinopathy, which can progress to produce a characteristic 'bull's eye' pattern of concentric hypopigmentation of the macula and irreversible visual loss. This is now rare, as chloroquine has largely been replaced by hydroxychloroquine, an analogue which is less toxic to the retina. Both drugs bind to melanin in the retinal pigment epithelium (RPE), causing cytotoxic effects, particularly affecting the macula. We present a case of a chloroquine maculopathy which continues to progress, despite cessation of the medication and apparent previous stabilisation of the visual loss 12 years earlier.

CASE PRESENTATION

A 72-year-old woman presented with bilateral central visual loss. She had been started on 250 mg once daily of chloroquine in 1993 for seronegative rheumatoid arthritis, which was stopped in 1998 as she developed blurred vision and distortion, signally maculopathy and corneal keratopathy. Following this, the keratopathy regressed, and her vision remained stable for the next 12 years, with no evidence of progression of the maculopathy. She had a medical history of Crohn's disease, and no family history of eye problems.

In 2010, she presented to her optician complaining of a dark crescent shape from top to bottom of her left eye, which she noticed on eye movement. Her vision was 6/6N8 right eye and 6/6N6 left eye, with some Amsler distortion. By 2013, this had progressed to 6/9N8 right eye and 6/7.5N5 left eye, with an increasing Amsler distortion and a particular deterioration in her right eye. By late 2015, it was 6/60 (unable to read passages) right eye and 6/12-1N8 left eye.

Figure 1 shows the posterior pole retinal photographs with typical 'bull's eye' maculopathy. Fluorescein angiography, optical coherence tomography

(OCT) imaging and electroretinography were confirmative of the diagnosis. Despite the cessation of chloroquine, her maculopathy continued to progress.

OUTCOME AND FOLLOW-UP

Unfortunately, there is currently no treatment beyond cessation of chloroquine. The patient attends regular appointments, where any further progression may be monitored.

DISCUSSION

In the treatment of rheumatological conditions, chloroquine and hydroxychloroquine are used long term. It is therefore essential that all patients and doctors are aware of the risk of developing maculopathy, which is believed to be linked to both daily dose and duration of use.¹ Other risk factors include concomitant retinal disease, poor renal function and tamoxifen use.²

The Royal College of Ophthalmologists recommends hydroxychloroquine over chloroquine, with doses not exceeding 6.5 mg/kg of lean body weight. As clinically significant maculopathy is rare at such doses, and at the time of publishing there was no reliable test for detecting reversible maculopathy, they do not recommend a systematic screening programme. Patients are advised to consult an optometrist if any visual impairment is suspected, where they may be referred to ophthalmology.³ In this case report, the patient was taking the more toxic chloroquine at a dose of more than 3 mg/kg, before the dangers of such dosing were well documented. Current US guidelines recommend a maximum dose of 2.3 mg/kg for chloroquine, based on a recommended maximum for hydroxychloroquine of 5 mg/kg.² These US guidelines also recommend screening via automated visual fields and spectral domain OCT annually after 5 years of exposure to the drug, as these may detect early, toxic, potentially reversible changes.

Various case reports confirm that chloroquine retinopathy tends to remain stable after drug cessation, with some regression for early stage disease, and occasionally progression for severe disease.^{4,5} There are also some reports of a delayed onset retinopathy occurring years after discontinuing the drug in patients with no previous visual symptoms,^{6,7} which could also bear a similar pathophysiology.

The progression of retinopathy after cessation of the drug may be related to the severity of the damage at the time. In particular, it appears to be less in cases recognised before RPE damage, highlighting the benefits of early detection.⁸ The late

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Figure 1 Retinal photographs and fluorescein angiography showing 'bull's eye' maculopathy.

progression is unlikely to be due to remaining drug, which is cleared in a matter of months, but it may represent a decompensation of cells initially affected by the drug.²

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Learning points

- ▶ Chloroquine-induced visual loss may progress years after cessation of the drug and an apparent period of visual stability.
- ▶ It is therefore crucial that regular monitoring continues in affected patients, long after the initial diagnosis of maculopathy.
- ▶ The physician and the patient must weigh up the risks and benefits carefully before commencing this treatment.

Contributors NJ analysed the case and contributed to the research and writing of the manuscript. SJ is the consultant for this patient. She diagnosed and is looking after the patient.

Competing interests None declared.

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