Case Report

ANTIMALARIA AND BULL IN THE EYE

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ABSTRACT

Hydroxychloroquine (HCQ) and chloroquine (CQ) are antimalaria medications that have been widely accepted and used to treat systemic lupus erythematosus (SLE). It has been improving the outcome and increase life expectancy. However, long-term intake of HCQ/CQ or at high dose of these medications may cause irreversible ocular toxicity. In the eyes, it can manifest as maculopathy and keratopathy. The damage done will continue to progress even years after stopping the medication. Early detection and stopping the medication is recommended in order to limit the potential blinding complication especially in young SLE patient.

INTRODUCTION

Chloroquine (CQ) was initially developed as an anti-malaria medication. Later, it was found that it is beneficial in the treatment of rheumatological conditions such as rheumatoid arthritis and systemic lupus erythematosus (SLE) [1,2]. Among the side effect that is caused by this antimalarial drug is retinopathy. It is irreversible despite stopping the drug. We present a case of Bull's eye maculopathy in a young SLE patient that received CQ therapy.

CASE PRESENTATION

A 38-year-old Malay lady was diagnosed with SLE for the past 17 years. She was first diagnosed at the age of 15. She first presented with chronic multiple joints pain, facial rash, and alopecia. She was then started on CQ 250 mg daily together with oral prednisolone. The ocular screening was performed within the first month of starting CQ treatment. Her vision was 6/6 in both eyes. The ocular assessment was normal with no retinopathy and normal optic nerve function test.

She was on regular CQ and oral prednisolone treatment. Her compliance was good. She had yearly ocular review. After 7 years of therapy, both medications were discontinued in view of stable SLE. A year later, she was restarted on hydroxychloroquine (HCQ) 200 mg together with oral prednisolone 30 mg daily due to relapse of SLE with recurrence of joint pain and facial rash. Yearly fundus assessment was normal with 6/6 vision bilaterally.

Six years after HCQ therapy, both fundi showed parafoveal hypopigmented lesion at macular area (Figure 1). She was otherwise asymptomatic and her visual acuity remained 6/6 in both eyes. There was deficit of Ishihara pseudoisochromatic color plate test bilaterally which was worst on the right eye. Optical coherence tomography (OCT) showed normal central macular thickness bilaterally with bilateral parafoveal thinning evidenced by loss of the foveal contour giving the shape of flying saucer. Hypopigmented lesion surrounding the fovea correspond to the loss of outer segment of photoreceptor and retinal pigment epithelium (RPE)

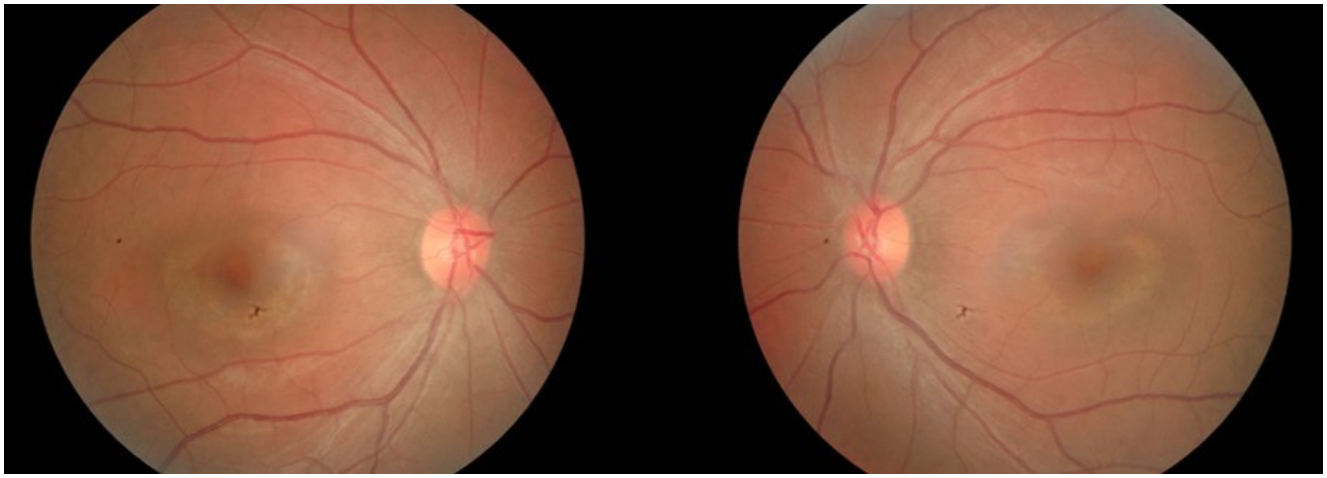

Figure 1: Bilateral parafoveal hypopigmented lesion surrounding the fovea at 6 years of hydroxychloroquine therapy (RE: right eye, LE: left eye).

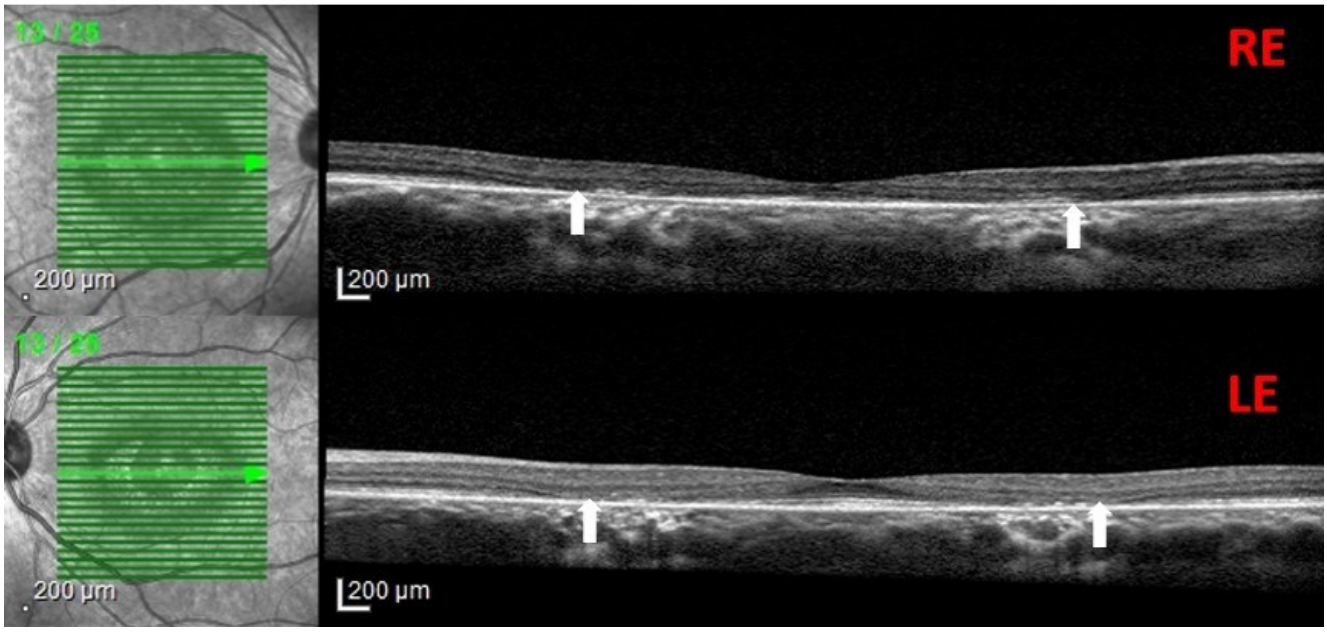

Figure 2: Optical coherence tomography of macula at 6 years of hydroxychloroquine therapy showing parafoveal thinning on both eyes (RE: right eye, LE: left eye) evidenced by loss of the foveal contour giving the shape of flying saucer. Hypopigmented lesion surrounding the fovea corresponds to the loss of the outer segment of photoreceptor and retinal pigment epithelium (arrow).

(Figure 2). In view of bilateral maculopathy HCG therapy was stopped. However, the oral prednisolone was continued with tapering dose and azathioprine (AZA) 50 mg daily was added.

Her vision continued to deteriorate over time despite stopping the HCQ medication. Review at 5 year after stopping HCQ therapy, her best corrected visual acuity (BCVA) was 6/60 and 6/7.5 in the right and left eye respectively. Fundus examination showed complete RPE depigmentation ring on the right macula and incomplete hypopigmented (RPE depigmentation) ring in the left macula (Figure 3). Central macular thickness by OCT was 173 µm in the right eye and while the left macular thickness was 215 µm. The parafoveal thinning was more pronounced in the right eye (Figure 4). Visual field was performed in this patient; however, the finding was not reliable.

Her current medication includes AZA 50 mg daily and oral prednisolone 10 mg daily. She is currently well with BCVA stable at 6/45 and 6/7.5 in right and left eye. Her natural lens is clear and intra-ocular pressure (IOP) is within normal range despite prolong usage of oral corticosteroid. She remains on yearly ocular assessment to closely monitor the progression of HCQ maculopathy.

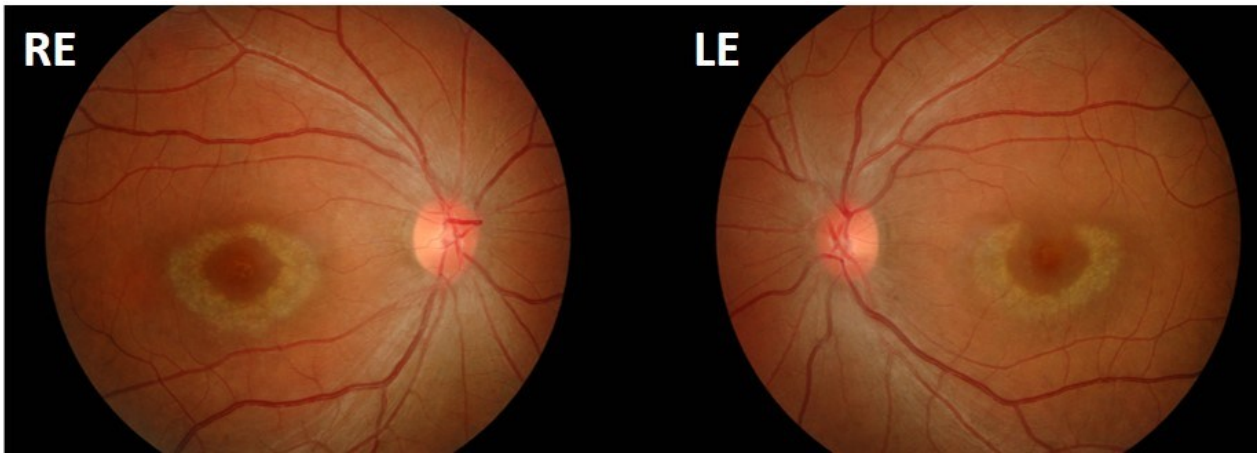

Figure 3: Funduscopic finding 5 years after discontinuation of hydroxychloroquine therapy showing worsening parafoveal hypopigmented (retinal pigment epithelium depigmentation) ring on both eyes (RE: right eye, LE: left eye).

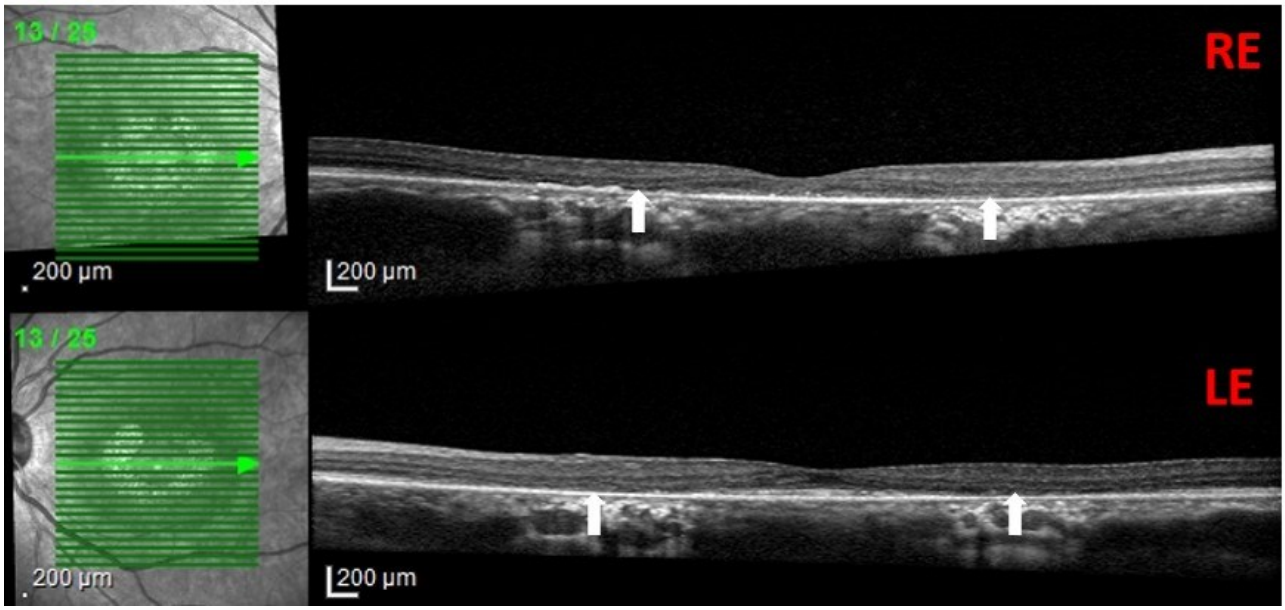

Figure 4: Optical coherence tomography of macula after 5 years discontinuation of hydroxychloroquine therapy showing worsening of parafoveal thinning (arrow) in both eyes (RE: right eye, LE: left eye), more pronounced temporally in the right eye.

DISCUSSIONS

Systemic Lupus Erythematous is a chronic systemic autoimmune disease affecting multiple organs thus the variable presentation, course and prognosis. It is characterized by remissions and flares [3]. It affects ocular structure from anterior to posterior segment, either partly or the whole ocular system. Damages to the ocular system could be due to the effect of the disease or due to the treatment of the SLE [4,5].

Drug induced maculopathy in SLE is usually cause by treatment with antimalarial drugs; CQ or HCQ. Patient that received more than 6.5 mg/kg/day of HCQ and 3 mg/kg/day of CQ have high risk of maculopathy based on ideal weight [6]. In recent publication it is recommended to screen patient receiving more than 5 mg/kg/day and 2.3 mg/kg/day of real body weight [5].

Mechanism of CQ and HCQ toxicity is not well understood. It is thought that the accumulation in retina by binding to the melanin in RPE which cause the prolong effect locally [5]. Beside the dose and duration of the drugs, other risk factors that contribute to the toxicity are underlying macular diseases, concurrent renal disease which is common in SLE patients, and concurrent treatment with tamoxifen [5].

Currently the only management of CQ and HCQ retinopathy is cessation of the drugs. Stopping of the

drugs does not prevent or halt the progression of retinopathy [5]. Hence, there is the needs to screen and monitor for the drugs induced retinopathy. The decision to stop medication in a patient needs to be discussed with the physician who is managing the patient, and another drugs should be considered [5].

The recommendation by The Royal College of Ophthalmologists is to screen the patients receiving CQ or HCQ 5 years after the baseline at the time of starting the medication. Patient who have severe risk factors such as renal impairment (eGFR less than 60ml/min/1.73m²), Tamoxifen use, high doses of CQ (> 2.3 mg/kg) or HCQ (> 5.0 mg/kg) need to be assessed yearly [7].

Automated visual fields and spectral-domain OCT (SD-OCT) are recommended for primary screening. Spectral-domain OCT is an objective screening to look for any changes in the retinal layer. Early finding in OCT includes thinning of photoreceptor layer, ellipsoid layer, outer nuclear layer and RPE. Most commonly seen are changes in the parafoveal area, however in Asian eyes changes are most commonly seen in more peripheral retina [8].

Automated visual field test is helpful when used together with other investigation in early detection of CQ retinopathy [5,8,9]. It shows changes in the macula with 10-2 testing. But for Asian patient wider test (24-2 or 30-2) are recommended as maculopathy tends to affect the more peripheral extramacular area.

Other additional screening tests are multifocal electroretinogram (mfERG) that can provide objective confirmation of visual field loss. Fundus autofluorescence may reveal early parafoveal or extramacular photoreceptor damage, demonstrated as area of increase autofluorescence. Later, in advanced stage it will show hypo-autofluorescence which indicate RPE death [8,9].

CONCLUSION

In conclusion screening of retinopathy in SLE patients receiving CQ or HCQ is important as the damage are irreversible [8,9]. Even with cessation of medication, the CQ or HCQ maculopathy can still progress. Early and timely detection is crucial in order to stop the medication as soon as possible. Maculopathy causes deterioration of visual acuity, leading to decrease in quality of life.

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