

Case report

Pericentral hydroxychloroquine retinopathy in a Caucasian female

Nikhil Anand^a, Robert A. Prinzi^a, Cory Hoeflerlin^b, Jiong Yan^a, Nieraj Jain^{a,*}^a Department of Ophthalmology, Emory University, Atlanta, GA, USA^b Emory University School of Medicine, Atlanta, GA, USA

ARTICLE INFO

Keywords:

Hydroxychloroquine
Pericentral
Toxicity
Bull's eye maculopathy
Plaquenil
Multifocal electroretinogram

ABSTRACT

Purpose: To report a rare presentation of the pericentral pattern of hydroxychloroquine (HCQ) retinal toxicity in a Caucasian female.

Observations: The patient presented with 20 years of exposure to HCQ, at a daily dose of 5.2mg/kg of actual body weight, and manifested a pericentral-only phenotype of HCQ toxicity, as demonstrated with detailed structural and functional testing.

Conclusions and importance: Although rare, the pericentral pattern of HCQ toxicity may occur in Caucasian patients in the absence of paracentral changes.

1. Introduction

Hydroxychloroquine (HCQ) associated retinal toxicity classically presents as a “bull's-eye” retinopathy with parafoveal atrophy of the outer retina and retinal pigment epithelium.^{1–3} At an early stage, toxicity manifests in attenuation and thinning of outer retinal bands on SD OCT imaging,⁴ paracentral depressions on HVF 10–2 testing, and characteristic changes on multifocal ERG testing.⁵

A recently described “pericentral” form of HCQ retinopathy predominantly affects patients of Asian descent.⁵ This form of HCQ toxicity localizes to 8° or more from the foveal center, in contrast to the parafoveal pattern, which localizes to 2°–6° from the foveal center. This form may rarely affect Caucasian patients, although typically in combination with paracentral changes.⁶ We present detailed structural and functional findings in a Caucasian patient with a rare pericentral-only phenotype of HCQ toxicity.

1.1. Case report

A 70-year old Caucasian female presented with nyctalopia, photopsias, and one year of progressive field loss in both eyes. She had recently stopped driving at night due to her visual difficulties. The patient had a history of systemic lupus erythematosus and Sjogren's syndrome managed by her rheumatologist with HCQ 400 mg daily for approximately 20 years (5.2mg/kg actual body weight). Annual toxicity screening including Humphrey visual field (HVF) 10–2 testing had been unremarkable.

Her past medical history was also notable for osteoarthritis,

gastroesophageal reflux disease, and hypothyroidism. She had no renal or hepatic disease, and no prior exposure to tamoxifen. Medications on presentation included levothyroxine, dexlansoprazole, ramipril, atorvastatin, and coenzyme Q10.

The patient previously underwent extensive neurologic evaluation for her vision loss. An MRI of the brain and orbits was suggestive of bilateral optic nerve compression at the intracranial opening of the optic canals due to ectatic internal carotid arteries. On the basis of these findings, the patient underwent a craniotomy with left optic nerve decompression at her local healthcare facility. She did not note any subjective visual improvement following this intervention.

The patient was referred to our center for a second opinion regarding a possible right optic nerve decompression. On presentation, her best corrected visual acuity was 20/25 and 20/20 in the right and left eye, respectively, without a relative afferent pupillary defect. Anterior segment examination was notable for pseudophakia OU. Posterior segment examination was notable for a cup-to-disc ratio of 0.4 with pink optic nerves, no vitreous cell, mild retinal arteriolar attenuation, intact macula, and subtle granularity to the fundus pigmentation nasal and inferior to the optic disc.

Widefield fundus autofluorescence imaging demonstrated perimacular hyperautofluorescence and irregular speckled hypo-autofluorescence suggestive of retinal pigment epithelium loss that is most prominent nasal to the disc in both eyes (Fig. 1). No abnormalities were noted on HVF 10–2 white stimulus testing (Fig. 2) obtained from an outside facility. HVF 30–2 testing was notable for superior sensitivity loss in both eyes (Fig. 3). Spectral domain optical coherence tomography (SD-OCT) imaging demonstrated outer retinal atrophy in the

* Corresponding author. 1365B Clifton Road NE, Suite 2400, Atlanta, GA 30322, USA.
E-mail address: nieraj.jain@emory.edu (N. Jain).



Fig. 1. Widefield fundus autofluorescence imaging of the right eye showing perimacular hyperautofluorescence and speckled hypoautofluorescence suggestive of RPE loss nasal to the disc and to a lesser extent temporally.

perimacula with intact parafoveal structure (Fig. 4). A full field electroretinogram (ERG) demonstrated mild attenuation of cone-derived responses with mildly delayed timing, and normal rod-derived responses. A multifocal ERG demonstrated asymmetric responses with mild diffuse attenuation of responses OS > OD (Fig. 5).

2. Discussion

The pericentral-only phenotype of HCQ toxicity typically manifests in Asian patients, and pericentral screening techniques are typically reserved for such patients. A recent study of 2657 patients with at least 5 years of HCQ exposure showed that the purely pericentral pattern was found in 2 of 111 Caucasian patients with toxicity compared to 16 of 29 Asian patients with toxicity.⁶ More commonly, Caucasian patients with pericentral toxicity will also have paracentral changes that are readily detected with conventional screening techniques.^{6,7}

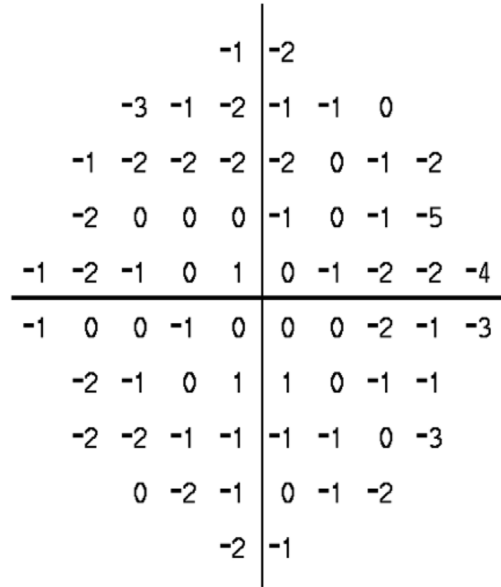
We are not aware of any predisposing factors that led to this unique presentation in our patient. She had an approximate cumulative HCQ dose of 2.92 kg, with a daily dose of 5.2mg/kg of actual body weight. Notably, the toxicity was not immediately apparent on conventional screening methods, such as HVF 10–2 testing. Unfortunately, the atypical presentation contributed to a late diagnosis, leading to disabling visual disturbances and ultimately an unnecessary neurosurgical procedure.

This unique presentation highlights the difficulties in detecting early pericentral HCQ toxicity, and the importance of extramacular screening techniques in Asian patients.⁴ In this case, the extent of toxicity, and particularly the typical inferior predilection of damage, was readily apparent with appropriate imaging and visual field testing protocols. Although we do not typically screen Caucasian patients for this rare form of toxicity, we do recommend HVF 30–2 testing, high resolution OCT scanning across the inferotemporal arcade, and widefield autofluorescence imaging (if available) in any patient with suggestive symptoms, regardless of ethnicity.

In sum, although rare, the pericentral pattern of HCQ toxicity may occur in Caucasian patients in the absence of paracentral changes. Extramacular screening techniques, where appropriate, allows for early detection of this form of toxicity. Awareness of this manifestation of toxicity may prevent unnecessary vision loss as well as unnecessary interventions.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the



Pattern Deviation

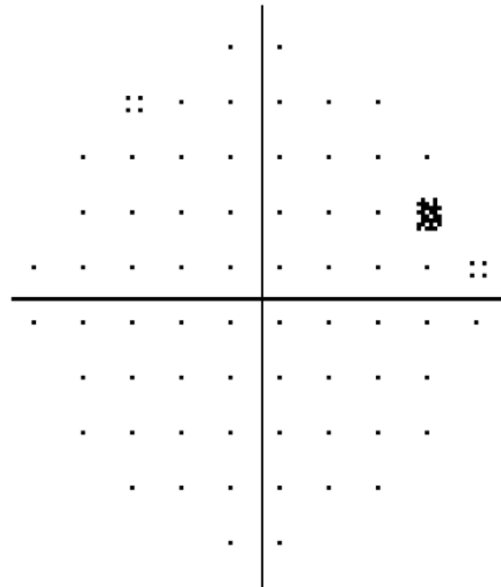


Fig. 2. Pattern deviation plot of SITA-Standard 10-2 Humphrey Visual Field white stimulus testing of the right eye showing normal sensitivities at the paracentral loci.

identification of the patient.

Acknowledgements and disclosures

Funding

No funding or grant support.

Financial disclosures

The following authors have no financial disclosures: NA, NJ, RP, CH, JY.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

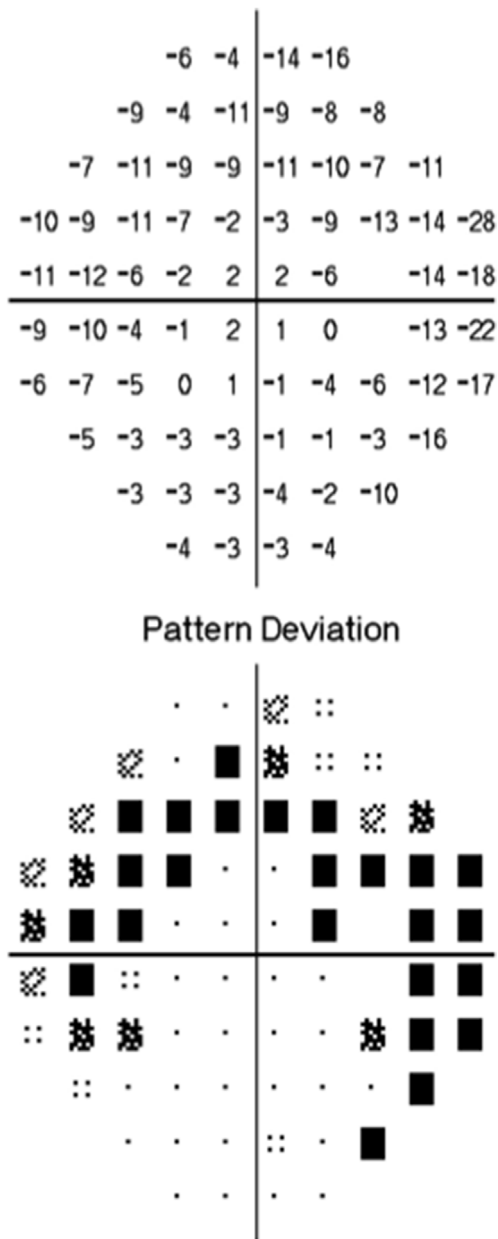


Fig. 3. Pattern deviation plot of SITA-Standard 30-2 Humphrey Visual Field testing of the right eye showing an incomplete ring scotoma most prominent superiorly.

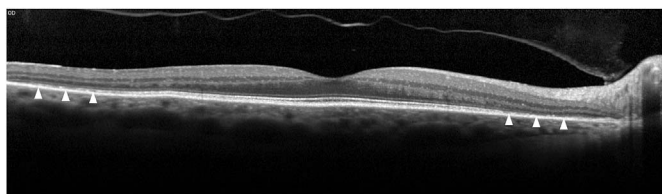


Fig. 4. Spectral domain optical coherence tomography B scan through the fovea of the right eye demonstrating intact retinal structure through the central macula with outer retinal atrophy in the perimacula (arrowheads).

Acknowledgements

None.

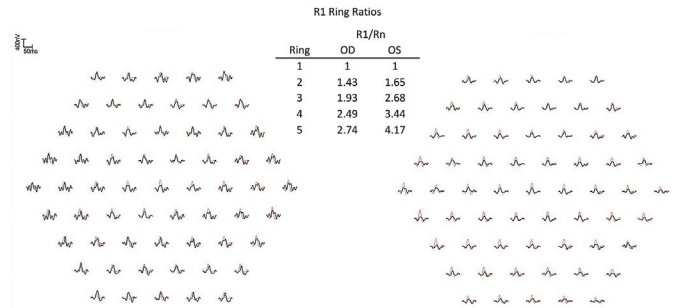


Fig. 5. Multifocal electroretinogram trace array demonstrates mild diffuse attenuation and delay of responses OS > OD that is most evident in the inferior pericentral hexagons OS (black = patient trace array; red = normative trace array). R1 ring ratio analysis of P1 responses (P1 nV/deg²) highlights the pericentral nature of the dysfunction, particularly in the left eye. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

References

- Marmor MF, Kellner U, Lai T, et al. Revised recommendations on screening for chloroquine and hydroxychloroquine retinopathy. *Ophthalmology*. 2011;118(2):415–422.
- Marmor M. Efficient and effective screening for hydroxychloroquine toxicity. *Am J Ophthalmol*. 2013;155(3):413–414.
- de Sistiernes L, Hu J, Rubin DL, et al. Localization of damage in progressive hydroxychloroquine retinopathy on and off the drug: inner versus outer retina, parafovea versus peripheral fovea. *Invest Ophthalmol Vis Sci*. 2015;56(5):3415–3426.
- Marmor MF, Kellner U, Lai T, et al. Recommendations on screening for chloroquine and hydroxychloroquine retinopathy (2016 revision). *Ophthalmology*. 2016;123(6):1386–1394.
- Lee DH, Melles RB, Joe SG, et al. Pericentral hydroxychloroquine retinopathy in Korean patients. *Ophthalmology*. 2015;122(6):1252–1256.
- Melles RB, Marmor MF. Pericentral retinopathy and racial differences in hydroxychloroquine toxicity. *Ophthalmology*. 2015;122(1):110–116.
- Tripp JM, Maibach HI. Hydroxychloroquine-induced retinopathy: a dermatologic perspective. *Am J Clin Dermatol*. 2006;7(3):171–175.