Case Report

Chloroquine Induced Retinal Toxicity- A Case Report

Nazmun Nahar[1], Palash Barua[1], Kaniz Ahmed Shahnaz[2]

Abstract

Chloroquine (CQ) and hydroxychloroquine (HCQ) is used increasingly in the management of variety of autoimmune disorders with well-established role in dermatology, rheumatology, and oncology. Retinopathy in the form of maculopathy occurs due to long term use of CQ or HCQ in large dose, have been associated with irreversible visual loss. A middle aged diabetic patient had been complaining of profound dimness of vision following uncomplicated cataract surgery on both eyes. She had a very good vision (6/6) in both eyes which reduced to 6/60 and 5/60 in right and left eye respectively. Colour fundus photography (CFP), Visual field analysis (VFA), Optical coherence tomography (OCT) and Fundus fluorescein angiography (FFA) revealed the changes consistent with "bulls' eye maculopathy". Treatment was unsatisfactory with antioxidant and neuro vitamin.

Keywords: Chloroquine toxicity, maculopathy, bull's eye

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Introduction

Chloroquine (CQ) and hydroxychloroquine (HCQ) are very useful drugs in the treatment of various rheumatic diseases(1). Retinopathy is a severe form of retinal toxicity caused by long term use of chloroquine with an incidence of 1-16 %. Retinal photoreceptors and retinal pigment epithelium have been postulated as the primary sites of involvement in chloroquine retinopathy.

Retinal involvements also occur due to direct toxicity to retinal ganglion cells. Other melanin containing structures like choroid have also been affected. Significant damage can occur without sign on fundus examination, so ancillary testing is a key part of assessment. Hepatic or renal impairment might increase the risk of toxicity. Other then use as immunomodulating therapies, they also have anti-viral properties and empirically used for treatment of COVID-19. Duration of use was the most important predictor of toxicity, while age, daily dose and patient weight correlate significantly with toxicity. In a more recent study suggest that, the patient using hydroxychloroquine 6.5mg/kg/day for at least 5 years or more, the overall prevalence of retinopathy was 7.5% and it rises up to 20% after 20 years (2).

[1] Registrar, Department of Ophthalmology, Medical Collage for Women and Hospital Uttara, Dhaka-1230
[2] Associate Professor, Department of Ophthalmology, Medical Collage for Women and Hospital Uttara, Dhaka-1230
[3] Resident surgeon, Department of Ophthalmology, Medical Collage for Women and Hospital Uttara, Dhaka-1230

Address of correspondence:
Dr. Nazmun Nahar
MBBS; D. Ophth
Registrar
Department of Ophthalmology,
Medical Collage for Women and Hospital Uttara,
Dhaka-1230
Contact number:01819240678
Email: drnnahar20@gmail.com

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Case report

Following an uneventful cataract surgery on both eyes, a patient was complaining of profound dimness of vision on both eyes. Her best corrected visual acuity was 6/6 on both eyes 7 months before. She was diabetic and had been suffering from rheumatoid arthritis for last 10 years and taking tab chloroquine and methotrexate.

On examination her best corrected visual acuity was 6/60 in right eye and 5/60 in left eye. Color vision was reduced specially red. Fundoscopic examination revealed 'bulls eye' maculopathy. Intraoccular pressure was 12 mm Hg in both eyes

respectively. She was adviced for color fundus photography (CFP), fundus fluorescence angiography (FFA), optical coherence tomography (OCT) macula and visual field analysis (VFA).

The CFP revealed "Bulls eye's" maculopathy characterized by a foveolar island of pigment surrounded by a depigmented zone of RPE atrophy which is itself encircled by a hyperpigmented ring.

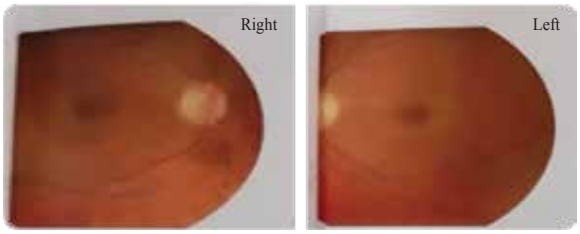

Fig 1: CFP both eye showing foveal island of pigment with surrounding depigmented zone "Bulls Eye" maculopathy.

FFA revealed foveal area of hypofluorescence surrounded by an area of hyperfluorescence.

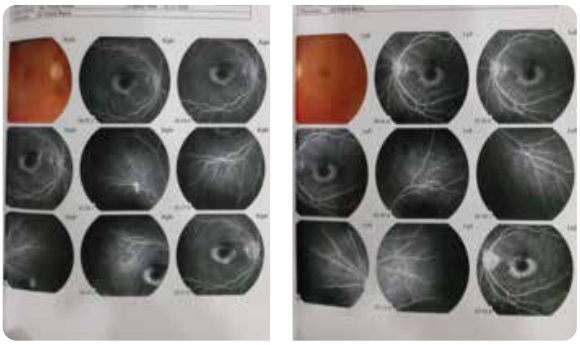

Fig 2: FFA both eyes showing the area of hypofluorescence

Peri foveal visual defect was found in VFA correlated well with clinical findings.

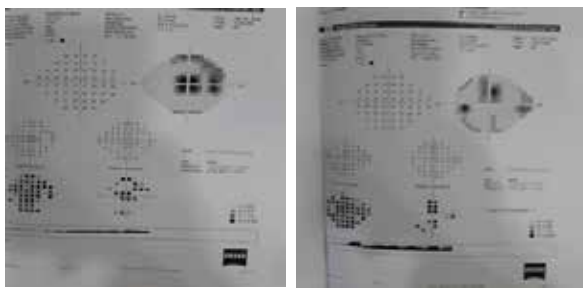

Fig 3: VFA showing perifoveal visual field defect

OCT macula revealed retinal pigment epithelium (RPE) defect consisting with chloroquine toxicity. She was prescribed anti oxidant, neuro vitamin and refer to a retina specialist. Same treatment was continued with regular follow up.

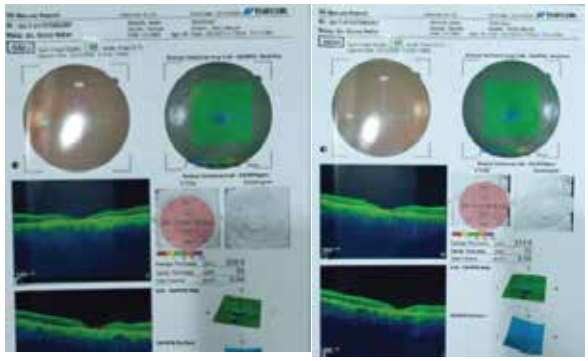

Fig 4: OCT macula of both eyes showing focal RPE defect

Discussion

Anti-Malerial drugs such as CQ and HCQ are melanotropic. They are concentrated in melanin containing structure of the eye, such as RPE(retinal pigment epithelium) and Choroid. Retinal changes are irreversible. and toxicity develops in a small proportion of patients for which are sometimes used in the treatment of auto immune disorder like rheumatoid arthritis. The expanding indications for HCQ adjunctive use with biologic drugs and other disease modifying therapies,it,s role in the maintanance of disease remission and favourable systemic safety profile during long term use,predict a large and growing patient cohort on long term HCQ therapy in developed nations. It is crucial therefore that ophthalmologist are aware of indications for HCQ, identify risk factors for disease, request appropriate test and know how to interpret them. Decreased and blurred vision with glare, flashes, distorted vision, reduced color vision are common clinical findings noticed by the patient. Though retinal toxicity is very rare and depends upon dose and duration of the drug,age is also a major dominating factor for implicating the complications[3]. American Academy of Ophthalmology(AAO) revised the guideline in 2016 suggested in 2002 from 6.5 mg/kg ideal body weight (IBW) to 5 mg/kg/real body weight (RBW). Majority reports suggest that hydroxy chloroquine toxicity have occurred in individuals taking more

than 6.5 mg/kg/day for more than 5 years[2]. Another recommendation was published by Royal College of Ophthalmology for monitoring in users of HCQ and CQ in United Kingdom in 2018 in order to reduce the risk of irreversible sight loss from toxic retinopathy.This recomendation have been replaced by recently published clinical guideline consistent with the guideline proposed by AAO[3,4].

Multifocul electro retinography (MFERG), fundus auto fluorescence, micro perimetry, 10-2 format standard automatic perimetry and spectral domain optical coherence tomography (OCT) lead to earlier detection of chloroquin induced retinopathy [5,6,7].

In our patient she was getting tab chloroquine and methotrexate for the treatment of rheumatoid arthritis for many years and she under went cataract surgery on both eyes six months apart on 2019 and 2020. Following surgery post operative conditions where uneventful. Refraction done and best corrected visual aquity was 6/6 , B/E on march 2020. But on December 2020 patient was come back with gross deterioration of vision. All the anterior segment structures were normal. Fundoscopic examination revealed area of hypo pigmentation surrounded by area of normal retina. FFA, OCT and visual field was done which are consistant with bulls eye maculopathy. Oral anti-oxidant and neuro vitamin had prescribed with further follow up.

Conclusion

An anti-malarial drug chloroquine and hydroxy chloroquine are used to treat the auto immune disease particularly in patient with rheumatoid arthritis and systemic lupus erythematosus (SLE), unless contraindicated because of multiple beneficial effects. Using pre 2016 dosing guideline from the American Academy of Ophthalmology (AAO), these benefits have been obtained with minimal side effects, the most significant of which is hydroxy chloroquine retinopathy. AAO revised the guideline in 2016 suggested in 2002 from 6.5 mg/kg ideal body weight (IBW) to 5 mg/kg/real body weight (RBW). Majority reports suggest that hydroxy chloroquine toxicity have occurred in individuals taking more than 6.5 mg/kg/day for more than 5 years.

References

1. Araiza-Casillas R, Cardenas F, Morales Y, Cardiel MH. Factors associated with chloroquine-induced retinopathy in rheumatic diseases. Lupus. 2004 Feb;13(2):119-24.
2. Melles RB, Marmor MF. The risk of toxic retinopathy in patients on long-term hydroxychloroquine therapy. JAMA ophthalmology. 2014 Dec 1;132(12):1453-60.
3. Michaelides, M., Stover, N.B., Francis, P.J. and Weleber, R.G., 2011. Retinal toxicity associated with hydroxychloroquine and chloroquine: risk factors, screening, and progression despite cessation of therapy. Archives of ophthalmology, 129(1), pp.30-39.
4. Fava A, Petri M. Systemic lupus erythematosus: diagnosis and clinical management. Journal of autoimmunity. 2019 Jan 1;96:1-3.
5. Mititelu M, Wong BJ, Brenner M, Bryar PJ, Jampol LM, Fawzi AA. Progression of hydroxychloroquine toxic effects after drug therapy cessation: new evidence from multimodal imaging. JAMA ophthalmology. 2013 Sep 1;131(9):1187-97.
6. Browning DJ. Impact of the revised American Academy of Ophthalmology guidelines regarding hydroxychloroquine screening on actual practice. American journal of ophthalmology. 2013 Mar 1;155(3):418-28.
7. Morita S, Takahashi T, Yoshida Y, Yokota N. Population pharmacokinetics of hydroxychloroquine in Japanese patients with cutaneous or systemic lupus erythematosus. Therapeutic Drug Monitoring. 2016 Apr 1;38(2):259-67.