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BULL'S EYE: IS THIS PHENOMENON GIVEN ENOUGH ATTENTION

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Abstract

Chloroquine maculopathy is not such a rare complication of long-term use of chloroquine preparations in the treatment of rheumatological diseases. Its early detection is of exceptional importance for timely discontinuation of the drug in order to prevent irreversible vision damage.

The aim of this Article is to present a case of a 62-year-old patient with bull's eye maculopathy as a result of long-term use of chloroquine due to systemic lupus erythematosus. The patient appeared with blurring and distortion of the pericentral vision.

She was ophthalmologically evaluated with fundoscopic examination, autofluorescence, perimetry, optical coherent tomography which together with her medical history established a diagnosis of chloroquine maculopathy.

Chloroquine therapy was discontinued and the patient is regularly monitored by a Rheumatologist and an Ophthalmologist, with no disease progression so far.

Keywords: Bull's eye, retinopathy, hydroxychloroquine

Introduction

Ocular complications of rheumatologic therapies may be related to direct drug-specific toxic effects, such as chloroquine retinopathy, indirect drug-specific side-effects, such as corticosteroid-induced ocular hypertension resulting in secondary glaucoma and drug non-specific complications relating to immunosuppression, such as opportunistic infections [1].

Chloroquine was first used as an antimalarial drug in World War II. Currently, together with its less toxic metabolite – hydrochloroquine, they are used to treat amoebiasis, rheumatoid arthritis, systemic lupus erythematosus and for malaria prophylaxis [2,3].

Possible, although infrequent, side effects from the use of these drugs can be: gastrointestinal complaints, cardiomyopathy, cardiac conduction defects, neuromyotoxicity, cytopenias, skin hyperpigmentation and ophthalmological disorders.

The retinopathy encountered with the prolonged use of chloroquine or related drugs is a much more serious adverse effect and can lead to irreversible damage to the retina and loss of vision. However, it is not possible to predict in which patients and in what proportion of patients an early retinopathy will progress to blindness [4].

Detection of retinopathy in the early stages is imperative as discontinuation of the drug at this stage may arrest the progress of the condition and also may allow resolution to normal pretreatment levels.

Case Report

A 62-year-old female with systemic lupus erythematosus was treated with Chloroquine 250mg per day for 23 years. The last few years, the patient has not had an ophthalmological check-up due to the COVID 19 pandemic.

In May 2023, the patient appeared with distorted and blurred pericentral vision, which she described as bow-shaped shadow and which lasted for several months.

Her central and peripheral vision were not affected. Because of these symptoms, the patient was sent for an ophthalmological examination to rule out chloroquine retinal toxicity.

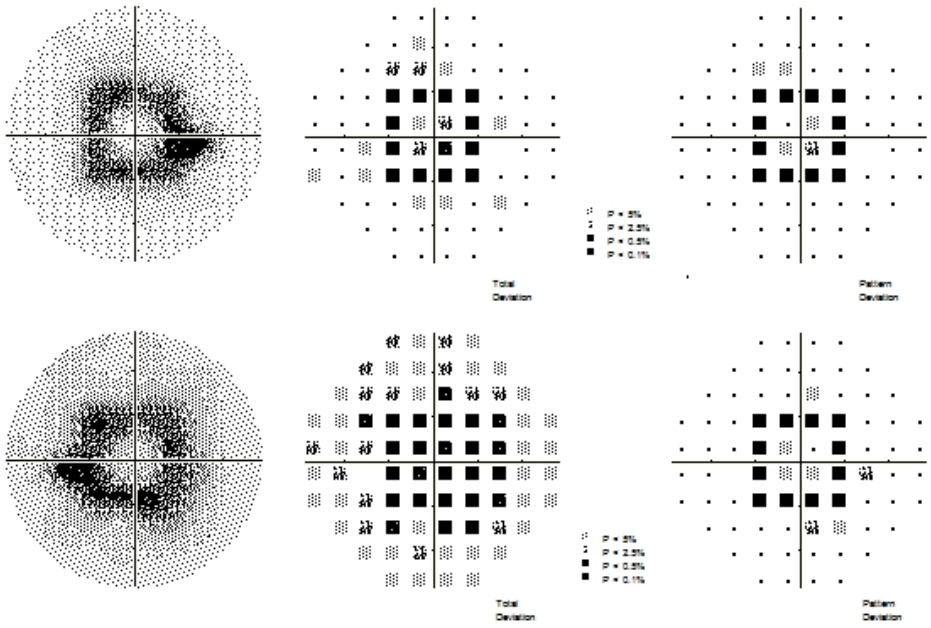

Figure 1. Perimetric findings of the right [top] and left eye [bottom]. Visible pericentral ring scotoma of 5-15°, bilaterally.

The best-corrected visual acuity [BCVA] bilaterally was 1.0 according to the Snellen optotype. Tonometric values and biomicroscopic findings of the anterior segment of the eyes were normal.

During examination of Amsler's grid, the patient gave information about pericentral scotoma in the shape of a "doughnut" with distortion of the vertical and horizontal lines during central fixation.

Humphrey perimetry [30-2] showed relative pericentral scotoma, bilaterally, extending from 5-15° in the visual field. The rest of the perimetry findings were without pathological changes.

During the fundoscopic examination in the macular region, an oval yellow-orange atrophic zone well delimited by the surrounding retinal tissue was observed, both bilaterally and symmetrically.

On FAF [fundus autoflurescence], bilaterally, the lesion had preserved foveolar autofluorescence, around which a hypoautofluorescent ring with granular features spread surrounded by a rim of hyperautofluorescence.

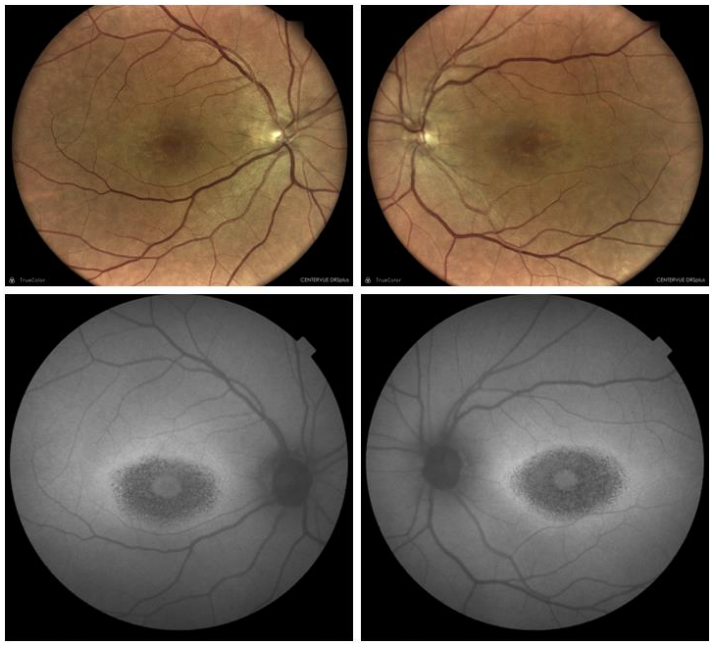

Figure 2. Native fundus photograph and fundus autofluorescence of the right and left eye of the patient, respectively. An oval well-circumscribed lesion in the macula.

OCT [optical coherent tomography] of macula, an atrophic macular zone was observed, with disturbed architecture of the outer layers of the neurosensory retina and discontinuity with atrophy of the retinal pigment epithelium (RPE).

The average thickness of the retina in the macula was 225-230um, and the central thickness was 70-75um. According to the performed examinations and medical history, the patient was diagnosed with chloroquine-induced maculopathy [type of Bull's eye maculopathy]. In consultation with a rheumatologist, the chloroquine therapy was discontinued. No worsening of the maculopathy was observed during the further follow-up of the patient.

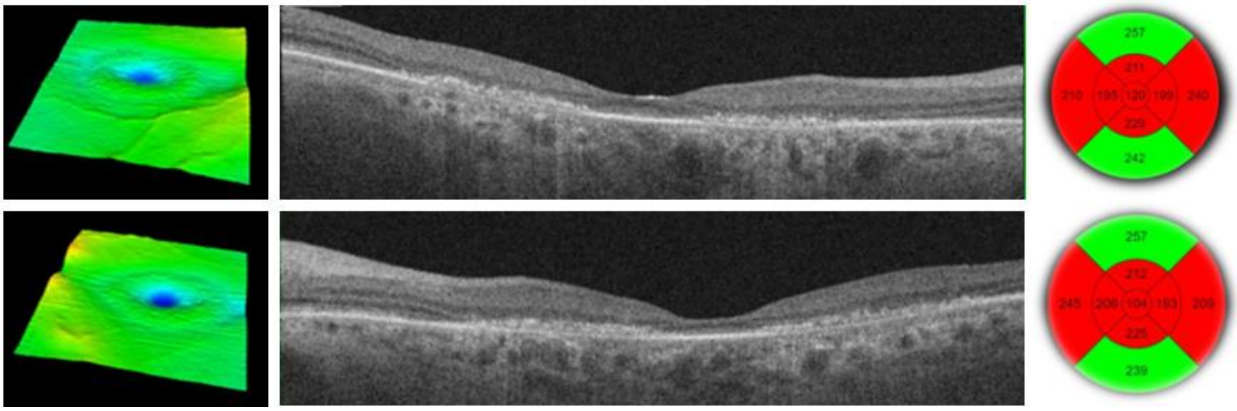

Figure 3. Topograph and OCT-tomogram of the macula, right [top] and left eye [bottom]. Atrophic macula, disturbed architectonics of outer layers of neurosensory retina and rearrangement of retinal pigment epithelium. Altered foveolar depression.

Discussion

Chloroquine was first used as an antimalarial agent. It subsequently played an important therapeutic role in various rheumatologic diseases including: systemic lupus erythematosus [SLE], rheumatoid arthritis [RA] and other inflammatory and dermatologic conditions. Retinal toxicity from chloroquine has been recognized for decades [5].

Bull's eye maculopathy is the most serious of the ocular adverse effects as the associated visual changes can be severe and there is little chance of visual recovery. In addition, visual loss associated with bull's eye maculopathy can progress even after the treatment is discontinued due to the long half-life of the drug [6,7].

Other ophthalmic manifestations as a result of toxicity from this drug can be: corneal deposits in the form of vortex keratopathy, subcapsular posterior cataract, ciliary body dysfunction with impaired accommodation, redistribution of retinal pigment epithelium in the macula, peripheral bone spicule formation, vascular attenuation and optic disc pallor [8].

The precise mechanism of retinal toxicity remains unclear. However, chloroquine has the ability to bind to melanin in the RPE and thus act toxically on photoreceptor cells outside the foveolar region. Upon binding to melanin, chloroquine inhibits the lysosomal activity of RPE, which results in reduced phagocytic activity of RPE, accumulation of undegraded disks from photoreceptor cells and a toxic effect on them with subsequent destruction. The RPE also suffers irreversible damage and atrophy [9]. These changes continue to progress despite cessation of medication [5].

Patients with retinopathy usually manifest central visual loss, visual field defect, color vision deficiency, photoaversion, night blindness and entoptic phenomenon [10]. 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 [11,12].

In differential diagnosis, the condition should be distinguished from dry form of senile macular degeneration, hereditary maculopathies (such as Stargard's disease), cone dystrophies and cone and rod dystrophies. The risk factors for the occurrence of chloroquine maculopathy are as follows: length of exposure to the drug, dose of the drug, preexisting retinal disease, renal failure and concomitant use of tamoxifen [13].

Chloroquine is associated with a higher prevalence of toxic retinopathy when compared to hydroxychloroquine. Guidance on safe dosing suggests a dose of less than 2.3 milligrams per kilogram per day for chloroquine and the recommended maximum for hydroxychloroquine is 5 mg/kg [14,15].

In this particular case the patient was treated with chloroquine for a very long period of time without any ophthalmologic examinations. The risk of toxicity is low for the first five years of therapy, but increases to 20-50% after 20 years [14,15]. Therefore, monitoring should begin five years from the start of chloroquine and hydroxychloroquine therapy. Annual ophthalmological controls should include: Amsler grid, color vision, perimetry, fundus examination, OCT and autofluorescence in order to detect the initial reversible changes of retinal structures.

Conclusion

Chloroquine is used in the treatment of several rheumatological diseases. However, its long-term use can cause retinal damage and irreversible vision loss.

Rheumatologists should be aware of potential ophthalmic complications and suggest that patients treated with this drug undergo regular ophthalmic monitoring. Detection of changes at an early stage and timely discontinuation of the drug can prevent irreversible vision damage.

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