INTRODUCTION

Chloroquine and its derivative hydroxychloroquine were initially used in the treatment and prophylaxis of malaria. Later their use spread as very effective drugs for controlling connective tissue diseases, specially in rheumatoid arthritis and systemic erythematosus lupus (SEL). They can produce a dose-dependent iatrogenic disease that affects the retina, described for the first time by Hoobs in 1959.

CASE REPORTS

Case 1

A 50 year-old woman with SEL in treatment with a daily tablet of 0.25 grams of chloroquine dihydrate, equivalent to 150 mg of chloroquine base, for over 10 years (total dose of chloroquine: 700 g approximately). In previous annual checkups alterations were not appraised until the last visit, in which the patient exhibited: better corrected visual acuity.
(VA) of 10/10 in the right eye (RE) and of 10/10 in the left eye (LE), normal biomicroscopy and tonometry. An automated conventional perimetry was made (AP) which showed an important reduction of the central threshold values (fig. 1) in both eyes (BE). The Ishihara color test was normal. The eye fundus exhibited non-specific pigmentary changes at the macular level (fig. 2). Treatment with chloroquine was suspended and ophthalmological revisions were made, which did not reveal changes in VA or in the field of vision.

Case 2

A 40 year-old woman in treatment with a daily tablet of 0.25 grams of chloroquine diphosphate due to SEL, continued for almost 9 years (total dose of chloroquine: approximately 293 g). She had been assessed in another center without exhibiting any alteration. She referred difficulty to focus and differentiate colors 2 months earlier. The VAera of 1 in BE, biomicroscopy and tonometry gave normal results.

Fig. 1: Perimetry (Humphrey 30-2 complete threshold) of the first case report, showing the defect at the central level.

Fig. 2: Eye fundus of case report 1. It exhibited non-specific pigmentary changes.
The AP revealed a reduction of the central and paracentral threshold values in BE (fig. 3). In the Ishihara (15 sheets) the patient exhibited 6 failures in the RE and 5 failures in the LE. The eye fundus exhibited the characteristic image of ox eye hyperpigmentation (fig. 4). Treatment with chloroquine was withdrawn but the condition worsened. Two months later the VA was of 7/10 for RE and 8/10 for LE. A frequency duplication perimetry was made that gave threshold values of 0 dB at the central level (fig. 5). After 6 months the VA went down to 4/10 in BE. The AP strategy 10-2 was repeated (fig 6) which showed in greater detail the defect of the central visual field. The evoked visual potentials and electroretinogram were normal; nevertheless, an electrooculogram revealed reduced values. The funduscopic aspect was similar. In the following assessments no changes were observed.

Fig. 3: Perimetry (Standard Humphrey SITA 30-2) of the second case report, showing the defect at the central level which extends towards the temporal area in the left eye.

Fig. 4: Eye fundus of case report 2, exhibiting the typical image of ox eye maculopathy.
DISCUSSION

The mechanisms which produce toxic retinopathy are not well known, although it seems that oxidative stress caused at the level of the retina by antimalaria medications would play an important role (1). It has also been observed that the mutations of the ABCR gene (also known as ABCA4), related

Fig. 5: Perimetry of frequency duplication (C-20 strategy complete threshold) of the second case report, showing 0 dB threshold values at the central level.
to Stargardt disease and with age-related macular degeneration are predisposing factors for the development of toxic retinopathy (2).

The execution of screening tests for chloroquine retinopathy has been the subject of widespread controversy. Latest studies (3,4) agree in that it is not necessary to make screening tests when the treatment dosages are low (3 mg/kg/day for chloroquine and 6.5 mg/kg/day for hydroxychloroquine). In these cases, it would suffice to carry out the recommended ophthalmological assessments recommended for any person, the frequency of which depends on the age. Screening would be indicated only in high risk cases, determined by the type of drug, dosage, duration of treatment over 5 years, weight, age, kidney function and the presence or absence of concomitant retinal diseases (3). A complete ophthalmological assessment and a central field of vision exploration in the first visit as well as in the following ones (3). As optional tests the colors test has been suggested, in addition to the Amsler grid, eye fundus photographs and electrophysiological tests.

Electrophysiological tests have a relative validity. A multifocal electroretinogram seems more adequate to evaluate the retinal toxicity by chloroquine. It can exhibit a loss of the central and paracentral responses whereas the total field electroretinogram can remain normal (3,5). Fluorescein angiography does not help the diagnosis of the retinopathy very much but it can be useful to discard other concomitant pathologies.

No treatment has demonstrated to be effective once the toxic effect takes place, and for this reason the only approach is to suspend the administration of the drug.

The retinopathy can advance even after suspending the treatment. A completely normal eye fundus does not exclude the disease. Cases continue to appear even though the toxicity is well known and ophthalmological follow-ups are being performed.

REFERENCES

