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<td>Author(s)</td>
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<tr>
<td>Citation</td>
<td>Hong Kong Medical Journal, 2005, v. 11 n. 1, p. 55-57</td>
</tr>
<tr>
<td>Issued Date</td>
<td>2005</td>
</tr>
<tr>
<td>URL</td>
<td><a href="http://hdl.handle.net/10722/137049">http://hdl.handle.net/10722/137049</a></td>
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CASE REPORT

Chloroquine-induced bull’s eye maculopathy

chloroquine

We report the case of a 51-year-old woman who presented with bilateral progressive deterioration in vision after taking chloroquine for severe rheumatoid arthritis for 10 years. She was found to have a bull’s eye pattern of depigmentation in the macula of both eyes. Despite cessation of chloroquine, her vision did not improve. The clinical presentation of chloroquine retinopathy is discussed, along with the importance of scheduled eye examination for individuals taking chloroquine or hydroxychloroquine.

Introduction

Chloroquine is prescribed as an antimalarial, as well as a treatment for inflammatory conditions including rheumatoid arthritis and systemic lupus erythematosus. It has been recognised that prolonged use of chloroquine may result in degeneration of the retinal pigment epithelium and the neurosensory retina, causing a ‘bull’s eye’ pattern of depigmentation of the macula, and subsequent central visual loss.1,2 We report a case of bull’s eye maculopathy developed as a result of chronic use of chloroquine.

Case report

A 51-year-old woman from Mainland China presented with a history of progressive deterioration in vision in both eyes for 6 months. Her medical history included severe rheumatoid arthritis, for which she had received chloroquine therapy for approximately 10 years. There was no record of the cumulative dosage given. On examination, her visual acuity was 20/100 in both eyes. Slit lamp examination was within normal limits in both eyes. Dilated fundus examination revealed a ring of depigmentation of the retinal pigment epithelium in the macula (Fig). The remainder of the fundus examination was normal. Fluorescein angiography (Fig) was then performed, which showed a bull’s eye pattern of granular hyperfluorescence, corresponding to window defects in both eyes. A diagnosis of chloroquine-induced bull’s eye maculopathy was made. Following discussion with the patient’s physician, chloroquine treatment was discontinued. Azathioprine was substituted as a treatment for her rheumatoid arthritis and she responded well. On follow-up examination 3 months later, the woman’s vision remained unchanged.
Chloroquine, and to a lesser extent its analogue, hydroxychloroquine, have been used for the treatment of malaria for many years. More recently, they have also been used in the treatment of systemic lupus erythematosus, rheumatoid arthritis, and other inflammatory and dermatologic conditions. Prolonged use of these agents may result in toxicity to the retina. The earliest sign of toxicity is paracentral visual field loss.\(^1\)\(^-\)\(^4\) This may occur in advance of any ophthalmoscopic findings. However, many patients may be asymptomatic in the early stages.\(^1\)\(^-\)\(^3\) As the condition worsens, alterations in the macula occur, characterised by atrophy of the retinal pigment epithelium in the form of a bull’s eye.\(^1\)\(^-\)\(^3\) A small, central island of the fovea may be spared initially. The ring of depigmentation may progressively enlarge and affect the foveola, at which time central vision may be affected. The bull’s eye pattern of depigmentation may be best appreciated on fluorescein angiography.

The exact mechanism of chloroquine toxicity is not fully understood. Reversal of visual field loss has been documented. However, most cases in which paracentral scotomas have developed or in which bull’s eye maculopathy has become evident have not shown any significant recovery of vision.\(^5\)

Most individuals who develop evidence of toxicity have received a cumulative chloroquine dose of 300 g, or a daily dose greater than 3 mg/kg,\(^3\)\(^,\)\(^4\) or a daily dose of hydroxychloroquine greater than 6.5 mg/kg.\(^6\) It must be highlighted that although irreversible damage to the retina may occur with these medications, the incidence is very low. During the early stages of use of these medications, toxicity is rare. Most patients who develop loss of vision have used the medication for more than 5 years. The incidence of toxicity increases with higher doses and longer duration of use.\(^7\)\(^-\)\(^10\)

Individuals who are taking chloroquine or hydroxychloroquine should undergo periodic and comprehensive eye examinations. The aim of the

**Fig.** The bull’s eye pattern of depigmentation associated with chloroquine maculopathy is evident on fundus photographs and highlighted by fluorescein angiography: photographs of the (a) right eye and (b) left eye; and angiograms of the (c) right eye and (d) left eye.
examination is to allow early identification and min- 
imisation of toxicity. It must be emphasised that there 
is no established criteria for diagnosing toxicity be- 
fore a stage where permanent visual loss develops.9 
The examination should include testing of best- 
corrected visual acuity, as well as slit lamp and di- 
lated fundus examinations. Baseline central visual field 
testing using the Amsler grid (Keeler, Windsor, United 
Kingdom) or the automated Humphrey visual field 
analyser (Humphrey, Dublin, United States) should 
also be performed. Optional testing, such as assess- 
ment of colour vision, fundus photography, fluorescein 
angiography, and multifocal electroretinography may 
be considered depending on the presentation.

The frequency of eye examinations is based on the 
relative risk of developing retinopathy. If a baseline 
ophthalmologic examination is normal in someone 
who has just started treatment with chloroquine or 
hydroxychloroquine, screening during the next 5 years 
can be done at the same frequency as that recom- 
mended by the American Academy of Ophthalmology 
for regular eye examinations (Table10).

Individuals at high risk of developing retinopathy 
include: those taking more than 3 mg/kg/d of 
chloroquine, or more than 6.5 mg/kg/d of 
hydroxychloroquine; those who have used the 
medication for more than 5 years; individuals with 
obese body habitus; those with liver or renal disease 
(because these drugs are dependent on both hepatic 
and renal clearance); those with pre-existing retinal 
disease; and those older than 60 years.9 These high- 
risk individuals should undergo annual and compre- 
hensive eye examinations. They should be asked to 
perform regular Amsler grid testing of their central 
visual field at home and to return promptly for a com- 
plete eye examination should there be any changes 
noted on the examination.

To date, there is no medical treatment for chloro- 
quine and hydroxychloroquine toxicity other than 
cessation of the medication. Prior to discontinuing the 
drug, consideration must be given to the management 
of the underlying systemic condition. Discussion 
with the rheumatologist or other physician managing 
treatment is important, because the cessation of the 
drug may lead to worsening of the systemic disease. 
Individuals with possible signs of toxicity may be 
followed closely (eg every 3 months). Those with 
definite toxicity may have to discontinue the medica-
tion immediately. It must be noted that vision loss may 
continue for several months after discontinuing the 
drug. Early detection is important because theoretically, 
some degree of visual recovery is possible at the very 
early stage of functional loss after cessation of the 
medication.

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