CASE REPORT: RETINOPATHY AFTER MALARIA PROPHYLAXIS WITH CHLOROQUINE

SILVIA BERTAGNOLIO, EVELINA TACCONELLI, GAETANO CAMILLI, AND MARIO TUMBARELLO
Department of Infectious Diseases, Catholic University, Rome, Italy

Abstract. Chloroquine retinopathy (CR) is a major complication of long-term malaria prophylaxis (LTMP) causing permanent visual dysfunction and occasionally blindness. After an extensive review of the published accounts of CR, we concluded that the risk of retinopathy in subjects receiving LTMP is limited to a cumulative dose that does not exceed 140 g. We present a case of CR that occurred after 8 years of malaria prophylaxis with chloroquine at a cumulative dose of 125 g. Because a threshold dose of chloroquine for retinal toxicity has not been established, careful, ongoing screening is required, especially as the cumulative dose increases.

INTRODUCTION

Chloroquine retinopathy (CR) is a severe complication of chloroquine treatment that can be observed during therapy for rheumatic diseases, with an incidence that varies from $<1$ to 16%.1 In addition, chloroquine given for long-term malaria prophylaxis (LTMP) can cause the same visual impairment. Chloroquine toxicity affects the retinal pigment epithelium,2,3 occasionally progressing to bull’s-eye maculopathy. Several reports have been published describing this disease, either as premacular or true retinopathy,4,5 since Hobbs and others6 first made an observation regarding CR in 1959. Premacularopathy consists in subtle changes in the thelium, 2,3 occasionally progressing to bull’s-eye maculopathy. Several reports have been published describing this disease, either as premacular or true retinopathy,4,5 since Hobbs and others6 first made an observation regarding CR in 1959. Premacularopathy consists in subtle changes in the visual field that are usually completely reversible once the drug is discontinued. True maculopathy, on the other hand, leads to an irreversible loss of central vision.

CASE REPORT

A 55-year-old woman, an Italian missionary nurse, was admitted to our ward in January 1998 with persistent high fever, headache, blurred distance vision, difficulty in reading, blind spots, and photophobia. A physical examination revealed only moderate hepatosplenomegaly. Total white blood cell count was 7,500/mm$^3$, hemoglobin was 9.6 g/dL, and platelet count was 98,000/mm$^3$. Hepatic and renal function tests were within normal ranges. The patient reported 8 years of use of chloroquine (150 mg base twice a week) as malaria prophylaxis since she had been living in Kenya; the cumulative dose was 125 g. The clinical features and the history suggested a diagnosis of malaria that was confirmed by a positive thick blood smear for Plasmodium falciparum. The malaria was successfully treated with mefloquine (1,250 mg by mouth), and the fever and headache disappeared, although ocular symptoms persisted.

Bilateral fundus examination showed macular hyperpigmentation and depigmentation around the macula, producing a bull’s-eye appearance, which was confirmed by angiofluorography. Examination of the patient’s visual field showed a pericentral scotoma to a red target. The patient’s visual acuity was impaired, although her color vision was normal. The diagnosis of CR was supported by the absence (excluding age) of known risk factors for retinal disease (i.e., diabetes, hypertension, and neoplastic diseases). The patient had not taken any drugs that could have caused retinal lesions, other than chloroquine. Moreover, her family history was negative for macular dystrophy or retinal degeneration. The patient was discharged from the hospital after being advised to stop chloroquine prophylaxis and to return for an ophthalmological follow-up. Two years after the acute episode of malaria, an ophthalmological examination revealed the persistence of maculopathy.

DISCUSSION

Several cases of retinopathy in people who take LTMP with chloroquine have been reported. Considering the increasing number of international travelers and migrant workers in the last few years, many of whom use chloroquine as LTMP, we feel that it is advisable to consider the risk of this side effect because of its potential severe prognosis. More precisely, it is important to establish when LTMP should be discontinued and to determine the safe daily and cumulative dosage that can be tolerated without incurring the risk of developing retinopathy. Despite the fact that CR has already been extensively described in the literature, the dosing regimen and the total dose of chloroquine associated with the risk of retinopathy are still controversial.9,10 Chloroquine retinopathy was initially described in patients receiving an overdose of this drug.9,10

Further cases of maculopathy were reported in subjects who used chloroquine prophylaxis at 100 mg daily for $>10$ years, with cumulative doses ranging 300–1,300 g.11-14 It has been suggested that a cumulative dose of $>700$ g might be toxic, corresponding to a prophylaxis of 100 mg per day for 20 years.13,15 Balo and others16 recommended that 185 g should be the threshold dose to avoid retinopathy. In any case, subjects should be systematically screened before this cumulative dose is reached because a single case of toxicity has been reported with a cumulative dose of only 140 g.17

A study by Lange and others18 explored the correlation between total body burden of chloroquine and the development of retinopathy among 53 missionaries who had taken a median cumulative dose of $\geq 300$ g. This study failed to demonstrate any association between a weekly chloroquine dosing regimen and retinopathy. Our report is to our knowledge the first description of a case of CR occurring after only 8 years of malaria prophylaxis at a correct dosing regimen, with a cumulative dose of 125 g. Recently, CR has also been described in a patient with rheumatoid arthritis after 1 year of treatment with a 250 mg daily dose of chloroquine, with a cumulative dose of 110 g.19 Taken together, these 2 observations seem to indicate that CR is more related
to the achievement of a cumulative dose rather than to the dosing regimen of chloroquine—that is, weekly versus twice weekly versus daily. In fact, it is possible that taking the drug weekly may not prevent but only delay the onset of retinopathy. In addition, individual variation in susceptibility to the toxic effect of chloroquine should also be considered.

In conclusion, we suggest early ophthalmological examinations and follow-up examinations every 6 months for subjects undergoing LTMP because a precise threshold dose for retinal toxicity cannot be defined. Prompt cessation of chloroquine may result in the stabilization of maculopathy at a clinically benign stage.

Authors’ addresses: Silvia Bertagnolio, Evelina Tacconelli, Gaetano Camilli, and Mario Tumbarello, Istituto Clinica Malattie Infettive, Università Cattolica S. Cuore, Largo Gemelli 8, 00168, Roma, Italy.

Reprint requests: Mario Tumbarello, Istituto Clinica Malattie Infettive, Università Cattolica S. Cuore, Largo Gemelli 8, 00168, Roma, Italy, Telephone: +39-06-30155373, Fax: +39-06-3084519 (e-mail: tumbarello@rm.unicatt.it).

REFERENCES