

# Hydroxychloroquine ototoxicity in a predisposed systemic lupus patient: a case report

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## ABSTRACT

This paper presents a case report of a 25-year old woman with systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) that were diagnosed 16 years earlier; a familial sensorineural hearing loss has been reported. Her deafness began to get worse after six months of hydroxychloroquine treatment.

## KEYWORDS

Hydroxychloroquine, ototoxicity, antimalarials

## INTRODUCTION

Since the 1950s, antimalarial drugs have been used to treat skin and joint symptoms of SLE and other rheumatic diseases. These drugs are usually well tolerated and have demonstrated a reduction in the number of disease exacerbations. Gastrointestinal side effects such as vomiting, diarrhoea or anorexia, skin rashes, retinopathy, myopathy and, less frequently, ototoxicity, have been reported as being associated with the use of these drugs. Some concomitant conditions, such as hereditary sensorineural hearing loss, could facilitate the appearance of ototoxicity because of hydroxychloroquine use and have to be considered in order to prescribe the right screening and diagnostic tests.

## CASE REPORT

A 25-year old Caucasian SLE patient was reviewed in the department of internal medicine because she suffered an acute hearing loss. SLE had been diagnosed 14 years before, after the patient developed arthritis, skin rashes, photosensitivity and fever. Positive antinuclear antibodies

(1/1,280), positive anti-dsDNA antibodies (>200 IU/L) and positive IgG anticardiolipin antibodies (>40 IU on two occasions, 12 weeks apart) were obtained and SLE was confirmed. At that point, the patient was treated initially with anti-inflammatory drugs and prednisone 30 mg once a day. Prednisone was reduced to a maintenance dose of 10 mg daily after the initial clinical symptoms improved. In 1991, the patient was diagnosed with antiphospholipid syndrome after she suffered a transient ischaemic attack and was treated with aspirin 100 mg once a day. At the beginning of 1992 the patient developed hypertension and renal impairment, with abnormalities in the urine. A renal biopsy was performed and a diffuse proliferative nephritis (SLE type IV nephritis) was diagnosed. Treatment with a short course of high-dose prednisone (1 mg/kg body weight) and cyclophosphamide was started in April 1992. Cyclophosphamide was maintained until 1998 and was suspended after renal function was stabilised. The prednisone dose was progressively decreased down to 10 mg daily and then stopped in June 2000. In January 2002 a transient hearing loss was observed and the patient was diagnosed with familial autosomal recessive sensorineural hearing loss. The patient was reviewed after a year by her otorhinolaryngologist and her hearing was stable until 2006. In June 2005 the patient started hydroxychloroquine as maintenance therapy for her SLE. In January 2006 her hearing worsened. An audiogram performed at that time showed a 25% diminution in her hearing. Ototoxicity because of hydroxychloroquine was suspected and the drug was stopped, with stabilisation of the hearing loss after withdrawal. The patient is still being followed up in our hospital and her hearing has been stable since January 2006.

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Received: 26 January 2007; revised manuscript received: 28 May 2008; accepted 29 May 2008

## DISCUSSION

The drugs that induce ototoxicity have been a well-recognised cause of cochlear hearing loss. Ototoxicity

because of classic antimalarial drugs such as quinine has been well established for many years. It manifests as both auditory and vestibular dysfunction, and it is typically mild to moderate, bilateral and symmetric; hearing is usually restored after cessation of the drug [1]. However, ototoxicity is a rare but well-established side effect of hydroxychloroquine. Only five other cases have been reported; one in a child with idiopathic pulmonary haemosiderosis [2] and four in adults [3-5]. Three of these four cases were reported in SLE patients [3, 4] and one case was reported in a patient suffering rheumatoid arthritis [5]. In most of the cases, the hearing loss was irreversible [2-4].

To the best of our knowledge, we now report the sixth case of hydroxychloroquine-related ototoxicity. Our case differs from the other reported ones because of the presence of a concomitant cause of sensorineural hearing loss. Our patient suffered an autosomal recessive isolated sensorineural bilateral hearing loss that developed in early adult life; the hearing loss was stable until hydroxychloroquine was started and now remains stable after that drug was stopped. The temporal relation established between hearing loss and treatment with hydroxychloroquine led us to hypothesise that this patient suffered ototoxicity because of hydroxychloroquine rather than a worsening of her underlying condition.

There is another cause of hearing loss that has to be kept in mind in this case. SLE and APS are infrequently related to a condition, often accompanied by vertigo and tinnitus, called autoimmune sensorineural hearing loss (ASNHL) [6, 7]. Some immune pathogenic mechanisms have been proposed to explain this condition including humoral-type antibody attack on inner ear antigens [8] and immune-complex disease in microvessels of the inner ear [9]. Thrombotic mechanisms related to antiphospholipid antibodies have also been proposed [10]. ASNHL is strongly associated with SLE activity [11]. Low levels of complement components C4 and C3 in patients with antiphospholipid antibodies or high levels of anti-dsDNA have been strongly associated with development of this

condition. The illness progresses to deafness if treatment with corticosteroids or immunosuppressant drugs is not used. Our patient's SLE was inactive during the period of hearing loss and worsening stopped after hydroxychloroquine was withdrawn. So it seems most improbable that the hearing loss was associated with ASNHL. Hearing loss because of APS-related microthrombotic events seems rare but cannot be completely excluded, particularly if we keep in mind that the patient was not anticoagulated.

It is possible that more than one factor could have contributed to the hearing loss observed in this patient. Probably the underlying hereditary sensorineural hearing loss, suffered by this patient, predisposed to the hydroxychloroquine ototoxicity; in other patients it could have gone unnoticed.

While the use of quinine is not recommended in patients with hereditary sensorineural hearing loss, to our knowledge, there is no evidence that the use of hydroxychloroquine in patients with SLE or APS and hereditary sensorineural hearing loss should be avoided. It is important to remember that hydroxychloroquine not only seems to be most effective for the amelioration of skin, joint, and constitutional symptoms, and for prevention of clinical relapse [12-14], but it also improves survival of SLE patients [15]. So the use of hydroxychloroquine may be recommended to SLE patients without a formal contraindication.

Just as ophthalmological tests must be performed periodically in patients treated with hydroxychloroquine, so should audiometric evaluation also be performed in patients at risk of developing ototoxicity because of hydroxychloroquine. Pure tone testing has been shown to be the best way of documenting ototoxicity from hearing loss. Transient evoked acoustic emissions has been proposed recently as a better way of monitoring hearing loss produced by ototoxicity and can be suggested as an alternative to monitor hearing loss in these patients [16, 17].

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