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CASE REPORT

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Hydroxychloroquine ototoxicity in a patient with rheumatoid arthritis

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Abstract We report a case of reversible sensineural hearing loss due to hydroxychloroquine (HQ) treatment. The patient was a 34-year-old woman with 1 year of rheumatoid arthritis (RA). She developed reversible hearing loss after 5 months of HQ treatment. Sensineural deafness has previously been reported with chloroquine treatment, but this is the first report of ototoxicity associated with HQ in RA.

Key words Hydroxychloroquine · Ototoxicity

Introduction

Rheumatoid arthritis (RA) is a chronic multisystemic disease characterized by inflammation of the synovial membrane of the diarthrosis, which may be followed by cartilage destruction, bone erosion, and weakening and destruction of ligaments, tendons, and joint capsules [1]. The antimalarials chloroquine (CQ) and hydroxychloroquine (HQ) have been widely used in the treatment of RA and other connective tissue diseases [2]. Side effects such as skin eruption, bleaching of the hair, retinopathy, and blurred vision are not unusual in CQ treatment, whereas HQ is generally regarded as a safer member of the family [3]. Regarding the toxicity of antimalarials, ototoxicity has received less attention. However, both CQ and HQ are chemically related to quinine and have therefore also been suspected of being ototoxicdrugs. It has been reported that large doses of CQ may lead to both reversible and permanent deafness [2]. Here we present a case of RA in which ototoxicity developed after 5 months of HQ therapy.

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Case report

In 1999, a 34-year-old woman presented with a 1-year history of swollen right and left wrist and proximal interphalangeal joints. During this time, nonsteroidal anti-inflammatory drug therapy (NSAID) was partially controlling her symptoms, but as the last exacerbation of her symptoms did not respond to NSAID therapy alone, she was hospitalized. Her physical examination revealed swollen wrists, MCP and PIP of both upper extremities, and swollen ankle joints. Laboratory investigations showed an erythrocyte sedimentation rate of 43 mm/h, white cell count of 7730/mm^3 with normal differential counts. The level of C-reactive protein (CRP, was 14 mg/dl, rheumatoid factor (RF) was 51.7 IU/ml; and ANA and anti dsDNA were negative). All the other routine laboratory examinations were within the normal range. X ray films of the hand and chest did not reveal any abnormality. A diagnosis of RA was made and a combination therapy of sulfasalazine 2 g/day and HQ 400 mg/day was begun. Over the following 3 months, the swelling in her hands and ankles responded to that therapy, with complete remission of the clinical and laboratory parameters. In November 1999, at the sixth month of the combination therapy, she became aware of reduced hearing and tinnitus. At this time, she had no morning stiffness and all the laboratory examinations were within the normal range. Otolaryngological consultation revealed a normal otoscopic and neurologic condition. The results of a timpanometric examination were also within the normal range. The pure tone audiogram showed sensorineural hearing loss bilaterally. The hearing loss on the right side was in the range of 10–35 dB and on the left side in the range of 10–25 dB. As the clinical and laboratory examination of the patient revealed complete remission of the disease, a diagnosis of ototoxicity due to HQ was made and the treatment with HQ was discontinued. Her tinnitus vanished 2 weeks after the withdrawal of HQ. Two months later, the symptoms of hearing loss had improved and the second pure tone audiogram was normal.

Discussion

A small number of clinical studies has shown dysfunction of conductive or sensorineural hearing, usually

clinically mild, in patients with RA. Conductive hearing loss could be related to involvement of the synovial joints between the middle ear ossicles, while sensorineural loss may be due to neuritis or vasculitis [4]. It has been suggested that pathological stiffening of the middle ear and associated hearing loss occur mainly in RA patients with severe polyarthritis of long duration [5]. While some authors suggest that hearing loss may be related to disease activity, others claim that there has been a greater incidence of sensorineural hearing loss in patients with rheumatoid nodules [4, 5]. As our patients have neither active severe polyarthritis of long duration nor rheumatoid nodules, this sensorineural hearing loss might not be related to disease activity. Partial remission of the symptoms 2 weeks after the cessation of the HQ treatment and nearly complete improvement after 2 months leads us to believe that this hearing loss occurred as a result of HQ ototoxicity.

Although it is regarded as a relatively safe drug, there have been two previous cases of irreversible deafness due to HQ treatment [2]. CQ is known to accumulate and to be fixed selectively in melanocytes with high levels of the drug in the stria vascularis, retinal pigment, skin, hair follicules, and endocrine glands. However, the relationship between the ototoxicity and melanin metabolism is still unknown [3, 6]. Ototoxicity is associated with the destruction of the cochlear sensory hair cells to varying degrees, a decrease in neuronal population, alteration of the supporting structures and atrophy and vacuolization of the stria vascularis, which may result from ischemia [3, 6, 7]. Although it is believed that CQ ototoxicity is irreversible, there are some reports describing partial recovery after prompt institution of corticosteroids [2, 3, 7]. In previous studies, we did not observe any other medication besides corticosteroid therapy, which may had been responsible for the recovery of the patient. Our patient was receiving 150 mg/day indomethacin at the beginning of the first symptoms of ototoxicity and this anti-inflammatory therapy might have caused the complete recovery of this patient. Sensorineuronal deafness has previously been reported in connection with HQ treatment in two systemic lupus erythematosus patients, but, to the best of our knowledge, this is the first report of ototoxicity associated with HQ treatment in RA patients. Although it may be considered a very rare event, the possibility of drug-induced ototoxicity should always be kept in mind when a patient receiving HQ complains of decreased hearing and tinnitus, and such symptoms should lead to the prompt discontinuation of the drug.

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