

Letters to the Editors

Tinnitus due to clarithromycin

Dear Sirs,

I report a 50-year-old man who developed tinnitus following treatment with clarithromycin for a peptic ulcer. There are innumerable causes of tinnitus, however, present evidence suggests that the most probable cause of the patient's reversible tinnitus might be related to clarithromycin.

Clarithromycin is one of the most commonly used macrolide antibiotics. Like other macrolides, clarithromycin is a relatively non-toxic drug. Occasionally, clarithromycin causes nausea, diarrhoea, abdominal pain, metallic taste, and headache.¹ It also has an ototoxic potential as the other macrolide antibiotics, erythromycin and azithromycin.² Reversible and mild hearing loss has been noted among the adverse reactions experienced by patients, who received high doses of clarithromycin for the treatment of *Mycobacterium avium* lung infections.^{3–5} An experimental study on clarithromycin ototoxicity revealed that clarithromycin has a reversible ototoxic effect on the inner ear. A single dose of 75 mg/kg clarithromycin given intravenously has been shown to reduce reversibly the transient evoked otoacoustic emissions (TEOAEs) in guinea pigs.⁶

Hearing loss due to clarithromycin has been reported.⁷ However, tinnitus due to clarithromycin has not been reported up to now.

The patient was a 50-year-old man, who experienced tinnitus in his right ear at the ninth day of the treatment of his peptic ulcer. He was examined by an otolaryngologist (the author) on the same day as his complaint. He was advised to receive per oral clarithromycin 500 mg (Deklarit, Deva) twice daily, amoxicillin 1 g (Largopen, Bilim) and lansoprazol 30 mg (Degastrol, Deva) once daily by a gastroenterologist. Clarithromycin was suspected to be the cause of tinnitus, as the other two drugs do not have such an ototoxic effect.⁸ The patient also indicated a kind of dizziness, 'momentary feeling of emptiness' accompanied with tinnitus. He did not indicate hearing loss. However, pure tone audiometry revealed bilateral sensorineural hearing loss at 4 KHz (60 dB at right, 40 dB at left). The patient said that he had had hearing loss for several years, which could have been the result of noise exposure due to his previous hunting experience. Pure tone average (PTA) at 500-1000-2000 Hz was 17 dB and 10 dB, speech reception threshold (SRT) 26 dB and 20 dB, and speech discrimination score (SDS) 56 per cent and 84 per cent at right and left ear, respectively. A-type tympanograms were recorded. The contralateral stapes reflex threshold (CLSRT) at 1000 Hz was 105 dB at right and 100 dB at left ear. CLSRT at 4000 Hz was 110 dB at left, but no

response was recorded at the right ear. The auditory brainstem response (ABR) audiometry supported cochlear type hearing loss at both sides (latency of the I. wave was prolonged – 2.3 msec – at both sides). TEOAEs were bilaterally negative (wave reproducibility (repro) was below 50 per cent at both sides). Individual band repro at 1, 2, 3, and 4 KHz was also below 50 per cent. Otolaryngologic and vestibular examinations were normal. Clarithromycin was stopped but the patient continued to receive the other drugs. Tinnitus recovered after two days and he did not complain of any other symptom. Previous audiological tests were repeated after six months. Pure tone audiometry revealed again the same sensorineural hearing loss at 4 KHz at both sides. However, PTA, SRT and SDS became better in the right ear. These values were almost the same in the left ear as the previous measurements. The tympanogram was normal. CLSRT at 1000 Hz was 110 dB at right and 100 dB at left ear. CLSRT at 4000 Hz was 105 dB at left and again, no response was recorded at the right ear. ABRs were almost the same. TEOAEs were again bilaterally negative. However, individual band repro at 1 KHz was better, 67 per cent and signal noise ratio at 1 KHz was 3 dB. Individual band repro at other frequencies were below 50 per cent.

Not only the patient's tinnitus recovered, but also the hearing loss in his right ear improved after clarithromycin treatment was stopped. The patient could not notice this slight hearing loss although it was at speech frequencies. This kind of hearing loss at speech frequencies and its reversible nature is typical for macrolide ototoxicity.^{2,9} However, rarely, irreversible hearing loss and hearing loss at high frequencies due to macrolides (erythromycin and azithromycin) have been reported, even during short-term and low-dose treatment protocols.^{10,11} A case of persistent tinnitus after intravenous erythromycin treatment has also been reported.¹² Such a possibility should also be taken into consideration if ototoxic symptoms (e.g. tinnitus, hearing loss) develop during clarithromycin therapy.

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Cem Uzun, M.D.

Department of Oto-Rhino-Laryngology, Head and Neck Surgery,
Trakya University,
Faculty of Medicine,
Edirne, Turkey.

Cholesterol granuloma of the frontal sinus

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Dear Sirs,

We read with interest the case report by Shykhon *et al.* on Cholesterol granuloma of the frontal sinus.¹ Cholesterol granuloma is indeed far less commonly found in the paranasal sinuses than the temporal bone, with the frontal sinus being less frequently affected than the maxillary sinus. Our own unpublished series of five frontal sinus cholesterol granulomas over a ten-year period in a specialist Rhinology unit reflects the rarity of this condition. As the paper indicates, most of the literature on the subject concerns the petrous temporal bone, or, in the para-nasal sinuses, the maxillary sinus. It is of significance, however, that while the authors state “few cases have been reported” in the frontal sinus, they fail to cite any of the publications reporting this condition in the medical literature, including a previous article in the *Journal of Laryngology and Otolology*.²

The lesion, which may follow a history of trauma, originates within the diploe of the frontal bone from where it expands extra-periosteally around the orbit. It is not surprising therefore that affected patients usually present to an Ophthalmologist. Our Medline search on cholesterol granuloma of the frontal sinus from 1974 to 2002 identified that the largest published series was from Moorfields Eye Hospital, who described 27 cases of orbito-frontal cholesterol

granuloma seen between 1967 and 1988.³ All but one of the patients presented with expansion of the lesion into the extra-periosteal space in the region of the lacrimal fossa. Six of the 29 patients had a history of trauma to the area and the authors suggested that haemorrhage into the diploe of the frontal bone was the most likely cause. All patients were cured by extra-periosteal drainage. The radiological findings of 31 patients from the same unit from 1974 to 1991 were published in 1992.⁴ All patients had been investigated by plain X-ray, 21 underwent CT imaging and one patient an MRI study. The typical CT findings of ragged bony destruction with a soft tissue mass no more dense than brain extending extra-periosteally into the orbit are discussed, together with the findings of high signal intensity on both the T1 and T2 images of the MRI scan. Very similar radiological findings were described in a report of 11 patients from Holland.⁵

Our Midline literature search on ‘cholesterol granuloma’ from 1966 to the present day identified 421 reports in total, 30 of which detailed the clinical, pathological or radiological features of between one and 31 patients with disease in the orbito-frontal region. The condition is clearly not as rarely reported as Shykhon *et al.* suggest and we feel that their paper would have benefited from a more comprehensive assessment of the current literature than was evidently performed.

Natalie Brookes

Specialist Registrar

Valerie Lund

Professor of Rhinology

Institute of Laryngology and Otology

Royal National Throat, Nose & Ear Hospital,
London

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Analytical and clinical evaluation of CYFRA 21-1 by electrochemiluminescent immunoassay in head and neck squamous cell carcinoma. *JLO* 2003;**117**:190–4

Dear Sirs,

While we took note of the investigation performed by Deng *et al.*¹ with great interest, we would like to state the following comments:

The clinical importance of the Cyfra 21-1 serum concentration as tumour marker in patients with squamous cell carcinomas of the head and neck has been described previously.^{2–4} In a recent publication⁴ the Cyfra 21-1 serum concentration is evaluated by means of an ELISA test kit. Deng