The Journal of Laryngology and Otology
May 1984. Vol. **98.** pp. 523–525

Chloramphenicol ototoxicity

A Case Report

by

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Abstract

A case of bilateral profound sensori-neural hearing loss following systemic administration of chloramphenicol is reported because of its rarity. The hearing loss was gradually progressive, involving one ear; and with a repeat course of the drug, the other ear too was involved. An idiosyncratic or allergic response to previous exposure to the drug may be the cause of the toxicity. One should be careful in prescribing the drug repeatedly; when this is done, the patient must be carefully observed for possible toxic effects.

Chloramphenicol is one of the antibiotics which is liberally being used in clinical practice. The toxic effect of the drug on bone marrow is always stressed, but very little is documented about the harmful effects of the drug on the inner ear. A patient who developed progressive bilateral profound sensorineural hearing loss after administration of Chloramphenicol is reported.

Case Report

A.V., a 20-year-old girl, attended the E.N.T. OPD Main Hospital, Bhilai Steel Plant, Bhilai, on 11 July 1980 with complaints of tinnitus and diminished hearing in the left ear of seven days' duration. The tinnitus was continuous and its intensity was gradually progressive. She had no complaint of giddiness and there was no symptom suggestive of ear disease in the past. There was no history of deafness in the family. She had been treated for typhoid fever two months earlier in the Department of Medicine. Chloramphenicol was administered in a dose of 500 mg. six hourly for a period of seventeen days. Initially it was given intra-muscularly, for nine days, and then continued by the oral route. She recovered completely without developing any complications of typhoid fever.

Examination of ears, nose and throat did not reveal any abnormality. There was no spontaneous nystagmus. A pure tone audiogram revealed normal hearing in the right ear and sensorineural hearing loss in the left ear involving the higher frequencies (Fig. 1). The differential caloric test revealed a left canal paresis. The skiagram of the internal auditory meatus was normal. She was put on vasodilator therapy, with heavy doses of multivitamins, and advised regular follow-up.

She developed a fever on 22 September 1980 and another course of Chloramphenicol was given in the same dosage as previously, for a period of seven days. She reported to us on 9 December 1980 with complaints of tinnitus and diminished hearing in both ears. The audiogram revealed a high frequency sensorineural hearing loss in the right ear and profound sensorineural hearing loss in the left ear (Fig. 2).

The hearing continued to deteriorate in both the ears and finally she developed bilateral profound sensorineural hearing loss (Fig. 3). The caloric test revealed an absence of response in both the ears.

Discussion

The clinical protocol of this patient is highly suggestive of ototoxicity due to chloramphenicol. The hearing loss following an ototoxic drug is usually insidious in onset and gradually

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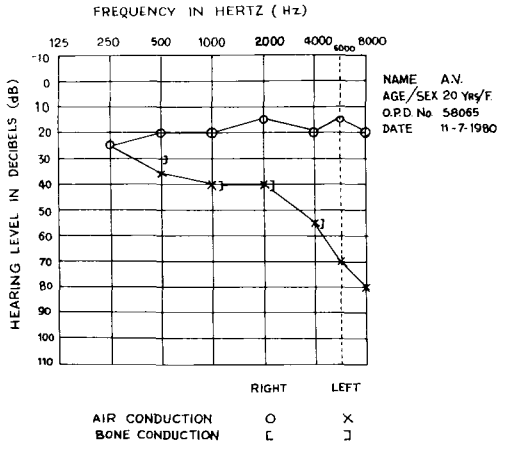


FIG. 1
Audiogram showing normal hearing in the right ear and high frequency sensori-neural hearing loss in the left ear.

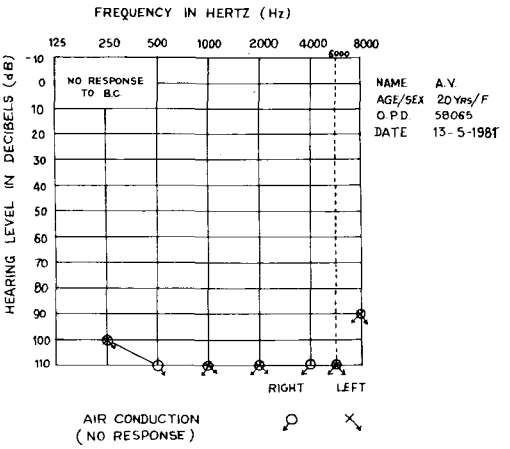


FIG. 3
Audiogram showing bilateral profound sensori-neural hearing loss.

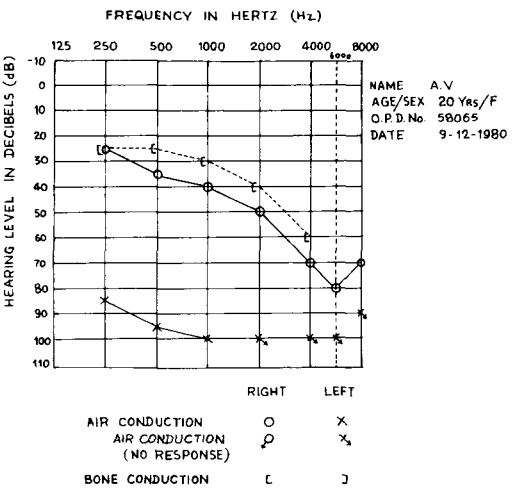


FIG. 2
Audiogram showing high frequency sensori-neural hearing loss in the right ear and profound sensori-neural hearing loss in the left ear.

progressive. However, a few drugs, such as chloroquine, can result in sudden severe sensorineural hearing loss (Dwivedi and Mehra, 1978). The hearing loss is usually preceded by tinnitus, and the appearance of tinnitus is so constant that it should be considered as an important sign in warning the otologist of impending deafness.

Chloramphenicol is readily absorbed from the gastrointestinal tract and is well distributed throughout the body. In adequate concentrations it crosses the blood-brain barrier. The ototoxic effect of the drug is well known when it is used topically in the ear. Extensive animal experiments have demonstrated this harmful effect on the inner ear. D'Angelo *et al.* (1967) reported that, when applied topically, chloramphenicol is toxic to the cochlea, and they advocated extra care in the topical use of chloramphenicol. Histopathologically also it has been confirmed that, when topically applied, chloramphenicol is harmful to the hair cells, supporting cells and stria vascularis of the basal turn of the cochlea (Proud *et al.* 1968). There is a paucity of literature on the ototoxic effect of chloramphenicol when administered systemically, and to the best of our knowledge only two reports have appeared so far in the literature: Gargye and Dutta (1959) reported a case of nerve deafness following heavy doses of chloramphenicol in a child. In their case the deafness was sudden in onset and did not recover; Svenungsson *et al.* (1976) described 8 cases of unilateral hearing loss following chloramphenicol therapy. Five of them were found to have severely impaired hearing and three had slight sensorineural hearing loss. In our own case, the onset was gradual and the hearing loss persisted, as evidenced by regular follow-up for ten months.

The exact pathogenesis of ototoxicity is not known. Retention of the drug in the body, due

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either to excessive administration (over-dosage/prolonged treatment) or to inadequate excretion of the drug (hepato-renal insufficiency) may lead to a cumulative effect, thus causing damage to a particular organ. In our own patient 2 grams of chloramphenicol were given daily for a period of seventeen days. The drug was then repeated, in the same dosage for a week, after a gap of almost four months. This does not fall into the category of over-dosage or prolonged treatment, as a daily dose of 4 grams of chloramphenicol for a period of up to 4 weeks has been recommended in cases of typhoid fever (Goodman and Gilman, 1975); nor did the patient exhibit any signs of hepato-renal damage during her illness. Therefore it is unlikely that the deafness was due to a cumulative effect of the drug in this patient.

An immunological basis has been postulated for the more serious toxic effect of chloramphenicol on bone marrow. This is an idio-syncratic response, in which the previous exposure to the drug is an important factor. It has also been suggested that a course of chloramphenicol should never be repeated (Bull *et al.* 1978). Joy *et al.* (1960) also postulated an allergic or idio-syncratic mechanism in attempting to explain the toxic effect of chloramphenicol on the optic nerve following intermittent exposure to the drug. In our opinion, the same hypothesis probably holds good in explaining the ototoxicity in the present case. It is possible that the administration of chloramphenicol for a second time served to enhance the toxic effect observed following the initial dose.

The caloric test showed no reponse in either ear and the patient did not exhibit any clinical signs of involvement of the vestibular system, such as spontaneous nystagmus or vertigo.

Acknowledgement

We are sincerely thankful to the Director of Medical and Health Services, Bhilai Steel Plant Main Hospital, Bhilai, for allowing us to use the hospital records for publication.

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