CASE REPORT

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Streptomycin Induced Ototoxicity in Patient with Brucellosis

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ABSTRACT Streptomycin is aminoglycoside antibiotic that typically used in tuberculosis, Meniere's diseases, and other advanced gram-negative bacterial infections. All aminoglycosides have the potential to induce irreversible/reversible ototoxicity and nephrotoxicity. In this report, we present a case of 51-year-old male patient applied to the hospital complaining with weakness, fever, arthralgia and, concomitant prostatitis. The patient diagnosed with Brucellosis and doxycycline+streptomycine was prescribed. On the 5th day of the treatment, he developed vertigo, dizziness, bilaterally ear fullness and in following days hearing loss. Audiogram was revealed that the patient has a bilateral sensorineural hearing loss. Due to suspicion of streptomycin induced vestibulocochlear toxicity, drug treatment was stopped immediately and methylprednisolone treatment (40 mg/day, iv) was administered for ten days to rehabilitate hearing loss. Although there are several case reports for aminoglycoside ototoxicity particularly in cystic fibrosis patients, we depict the first case of aminoglycoside ototoxicity in Brucella patient.

Keywords: Ototoxicity; aminoglycoside; streptomycin; hearing loss

Aminoglycosides are widely-used antibiotics which can inhibit protein synthesis of bacteria, thus act as a bactericidal agent unlike most of the other protein synthesis inhibitors, which are bacteriostatic.[1] However serious toxicity limits their utility and dosage. All aminoglycosides have the potential to induce irreversible/reversible ototoxicity and nephrotoxicity. Aminoglycoside treatment may exhibit permanent and bilateral high-frequency hearing loss and temporary vestibular hypofunction.[2] These adverse effects render their proper administration difficult.

The generation of reactive oxygen species (ROS) which leads to oxidative damage mediates aminoglycoside ototoxicity.[1] Once sensory hair cells are damaged, regeneration does not occur, subsequently degeneration of nerve cells leads to irreversible hearing loss. Degeneration of outer hair cells and auditory neurons in the cochlea correlates with the severity of hearing loss, which typically occurs at high frequencies outside of the audiometric range.[1,3] Patient susceptibility to aminoglycoside otoxicity depends on varied factors, such as route of administration, dosage, genetic predisposition, and medical conditions.[2]

Streptomycin is aminoglycoside antibiotic that typically uses in tuberculosis, Meniere's diseases, and other advanced bacterial infections usually

in combination with other antimicrobials, because it is pharmacologically less active than other members of the aminoglycosides.[1] Streptomycin causes damage to a cochlear and vestibular portion of the inner ear. Loss of vestibular sensitivity causes difficulty walking and oscillopsia. Hearing loss, generally occurs after a short latent period (7-10 days) at 1g/day or higher doses and slowly worsens. If treatment is continued, permanent and complete deafness may ocur.[4] Vestibular function is much more sensitive to aminoglycosides than hearing function and must vestibulotoxicity cases without hearing loss go undiagnosed.[5]

It is known that aminoglycoside ototoxicity is related to genetic susceptibility. Different individuals from the same family have hearing loss after aminoglycoside administration indicates that aminoglycoside ototoxicity has a genetic background. A mutation in the mitochondrial 12S ribosomal RNA gene at position 1555 (A→G) was identified as the predisposition factor for aminoglycoside-induced hearing loss and also non-syndromic deafness in three Chinese families in 1993.[6] A1555G mutation in mitochondrial 12S rRNA gene increases the binding rate of these antibiotics and thus, leads the alteration of mitochondrial protein synthesis by reducing translation rate that is required for normal cellular function.[7] In another study, thymidine deletion at position 961 and a number of inserted cytosines in the mitochondrial rRNA gene was also found as a predisposition factor to aminoglycoside ototoxicity.[8]

CASE REPORT

A 51-year-old man applied to the hospital complaining with weakness, fever, arthralgia and, concomitant prostatitis. The patient who is suspected with systemic infection was diagnosed with Brucellosis according to the results of Brucella agglutination (Wright) test (1/640) and guided to the Department of Infectious Diseases. The patient was started with combined therapy and intramuscular administered doxycycline+streptomycine (200 mg/day, 1000 mg/day, respectively). On the 5th day of the treatment, he developed vertigo, dizziness, bilaterally ear fullness and in following days hearing loss. Due to suspicion of streptomycin induced vestibulocochlear toxicity, drug treatment was stopped immediately. Audiogram was performed after patient complaints (Figure 1). Magnetic resonance (MR) imagination and cerebrospinal fluid (CSF) examination were recommended by neurologist for the suspicion of neurobrucellosis. MR results are shown in the Figure 2. However the patient refused consent of lumbar puncture, therefore CSF examination could not be performed. After neurologic consultation, it has been decided that severe sensorineural hearing loss is not caused by neurobrucellosis.[9,10]

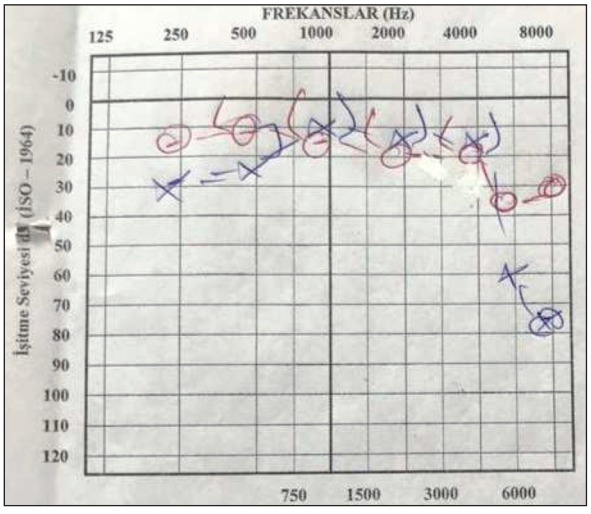

FIGURE 1: Pure tone audiometry shows slight to mild bilateral high-frequency hearing loss.

The patient continued to receive doxycycline+rifampicin (200 mg/day, 600 mg/day, respectively) treatment. It has complied with the recommendations of the otolaryngologist and methylprednisolone treatment (40 mg/day, i.v) was administrated for ten days to rehabilitate hearing loss and the patient was monitored. The patient's hearing loss was not completely reversed, and dizziness were observed periodically. Written informed consent was obtained from the patient for this study after explanation of the confidentiality.

DISCUSSION

Although there are several case reports for aminoglycoside ototoxicity particularly in cystic fibrosis

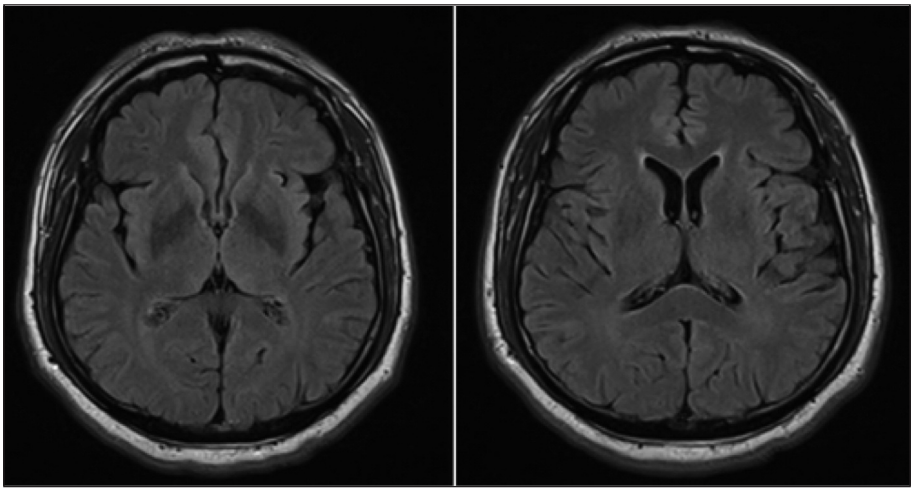

FIGURE 2: Normal magnetic resonance findings of the patient.

patients, this report is preliminary in patient with brucellosis.[11,12]

Recently; new strategies have been suggested to prevent the molecular and cellular damage caused by aminoglycoside-induced ROS. In some animal experiments, aminoglycosides in combination with dexamethasone, salicylates, antioxidants (alpha-lipoic acid, glutathione) has been shown to reduce ROS levels and therefore, the risk of aminoglycoside ototoxicity.[13] Streptomycin can be replaced by gentamicin for most cases because gentamicin primarily causes renal toxicity which is reversible, whereas streptomycin has ototoxicity which is irreversible.[1] Transtympanic/intratympanic route may manifest less severe ototoxicity than systemic route for Meniere's disease.[14] Patients treated with ototoxic aminoglycosides should be avoided to expose to high volume sound during and after treatment, as the ear is sensitive for noise injury and therefore the situation might be worsen.[15]

Before the treatment, the genetic screening for A1555G mutation of patients under risk of aminoglycoside ototoxicity will reduce potential adverse effects. This will ensure that physicians can protect against aminoglycoside ototoxicity where possible, or at least the patients can be informed about the potential risk of deafness. In addition serum concentrations should be monitored during the treatment, because the advers effest is dose-dependent. Alternative therapies might be considered especially for the older people with preexisting hearing problems, if available.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Dolunay Merve Fakıoğlu;* ***Control/Supervision:*** *Beril Altun;* ***Data Collection and/or Processing:*** *Beril Altun, Dolunay Merve Fakıoğlu, Aslınur Albayrak;* ***Analysis and/or Interpretation:*** *Beril Altun, Dolunay Merve Fakıoğlu;* ***Literature Review:*** *Beril Altun, Dolunay Merve Fakıoğlu;* ***Writing the Article:*** *Beril Altun, Dolunay Merve Fakıoğlu, Aslınur Albayrak;* ***Critical Review:*** *Beril Altun.*

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