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Streptomycin Ototoxicity: Bilateral Vestibular Hypofunction

Streptomisin Ototoksisitesi: Bilateral Vestibüler Hipofonksiyon

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ABSTRACT

Streptomycin is an aminoglycoside antibiotic which may cause permanent damage to the cochleovestibular system. Our case had treatment for cutaneous tuberculosis in March 2014. The treatment was started with rifampicin, and after an increase in the patient's liver enzyme levels, the drug was changed to streptomycin. Severe loss of balance and fullness in the ear were observed in the initial examination. Bilateral vestibular hypofunction was detected in audiological and vestibular tests. In this paper, we presented the patient's evaluation, follow-up and rehabilitation and outcomes as well as mechanism of vestibular toxicity in the light of literature.

Keywords
Streptomycin; bilateral vestibulotoxicity; vestibular rehabilitation

ÖZET

Streptomisin aminoglikozid grubu bir antibiyotik olup, ototoksisite nedeni ile kokleovestibüler sistemde kalıcı hasara neden olabilir. Sunulan vakada hastaya cilt tüberkülozu nedeni ile Mart 2014 de tedavi başlanmış. Tedavi rifampisin ile başlanmış ve tedavi sırasında karaciğer enzim yüksekliği nedeni ile streptomisin tedavisine geçilmiş. İlk muayenede ciddi denge kaybı ve kulaklarda dolgunluk saptandı. Odyolojik ve vestibüler değerlendirmede ise bilateral vestibüler hipofonksiyon saptandı. Makalede hastanın değerlendirilmesi, takip ve rehabilitasyon sonuçları ile beraber literatür bilgisi ışığında vestibüler toksisite oluşum mekanizmaları tartışılmıştır.

Anahtar Sözcükler
Streptomisin; bilateral vestibüler toksisite; vestibüler rehabilitasyon

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INTRODUCTION

Streptomycin is a bactericidal antibiotic, which shows its effect on microorganisms by inhibiting protein synthesis. There is a wide range of a bacterial profile in which it is effective. Streptomycin is specific, its transport facility and low cost increases the frequency of use of these kinds of antibiotics. However, its side effect profile limits its use.[1]

While bilateral vestibular hypofunction (BVH) may be idiopathic, it may also result from ototoxicity developing usually due to gentamicin or other aminoglycosides. There is limited information on the frequency of BVH cases, and it is reported at the rate of %0.05. Frequency of BVH cases related to ototoxicity has been reported as 17%.[2,3] In the treatment of patients with vestibular hypofunction, it is recommended to use vestibular rehabilitation to minimize the complaints of the patients, and allow them to regain their independent daily life activities in the shortest time possible.[4]

CASE REPORT

A 44-year-old female patient's treatment began in March 2014 with the diagnosis of cutaneous tuberculosis. The patient was first administered rifampicin, and due to the increase in liver enzyme levels, the antibiotic was changed to streptomycin. The patient was evaluated for a cochleovestibular pathology due to severe balance loss and aural fullness.

The patient did not have any history of dizziness. She was diagnosed with otosclerosis in another center where she admitted with the complaints of fullness in her right ear and hearing loss (The patient did not have her test results; this is only the patient's verbal explanation); however, she did not receive any treatment. Afterwards, the patient did not admit to another medical center, and did not receive any additional treatment. She did not have any other medical problems, and she was not on any regular drugs for any other disorder. The patient was smoking a pack of cigarettes a day for the past 20 years, and consumed alcohol. Any additional disorders were not present in her or her family's medical history.

The patient's otoscopic examination was normal. On the psychical examination done with the Frentzel glasses, extra ocular eye movements were normal; in addition, spontaneous and evoked gaze nistagmus were not observed. The patient had been using betahistine for about 10 days, and it was stopped 72 hours prior to vestibular tests. Pure tone audiometry, speech tests, impedancemetry and Auditory Brainstem Responses (ABR) analyses were carried out. Cervical vestibular evoked myogenic potentials (cVEMP), Romberg, Fukuda Step Test were also done. The results of the tests are presented in Table 1 and Figure 1. In order to evaluate rehabilitation efficiency, Dizziness Evaluation Form (DEF) was applied prior to and after the rehabilitation.

Table 1. Results of vestibular evaluation.

Tests	Results
cVEMP	No response was detected in the right side; P1,N1 wave latency was normal in the left side
Fukuda Step test	Normal while eyes were open Difficulty in performance, and positive tendency to walk forward while eyes were closed
Romberg	Negative while eyes were open and positive while eyes were closed

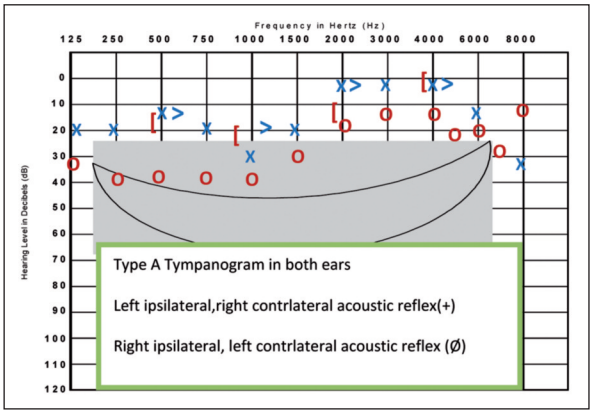

Figure 1. Result of hearing tests.

Although hearing was within the normal limits in the left ear, conductive hearing loss particularly in the low frequencies was observed in the right ear. The thresholds for understanding speech were in harmony with pure tone thresholds bilaterally, and rates of distinguishing speech were determined as 100%. On ABR, although 1st and 5th wave latencies were within the normal limits, an elongation of 3rd wave latency was observed particularly in the left ear. Narrowing of 3rd-5th interpeak latencies was observed in both ears. The patient

had trouble on walking independently, used a neck protector, and could walk with the help of two people. According to the DEF scoring, severe balance loss was determined.

A vestibular rehabilitation program was arranged for the patient diagnosed with BVH . She stopped using neck collar. In order to decrease her anxiety level and risk of falling, she and her family were informed about the disease, and suggestions were given. The rehabilitation steps were targeted to increase the following:

1. VOR function,
2. Postural stability,
3. Mobilization and endurance.

The patient came alone to a follow up visit on 45th day of the rehabilitation program. The Romberg test was negative with open and closed eyes, and eyes closed performance of the Fukuda step test was improved. DEF scores indicated a mild balance loss. The results of the hearing tests were similar to the ones prior to rehabilitation, and it was considered that the hearing loss in her right ear was due to otosclerosis. It was also considered that the reason for absence of cVEMP findings in the right ear might be related to otosclerosis.

The patient has been followed up for two years. The patient provided her informed consent for this publication.

DISCUSSION

Aminoglycosides are frequently preferred in certain aerobic Gram (-) bacterial infections such as *Mycobacterium tuberculosis*, *Haemophilus influenza* type B and *Pseudomonas aeruginosa,* which are resistant to multiple antibiotics, and when the risk of morbidity and mortality can be high. In addition, they are also used in combination with other antibiotics in endocarditis treatment.[5] Although new antibiotics have been started to be used in recent years, aminoglycosides have still being used for some diseases. The side effects of aminoglycosides limits their widespread use. Nephrotoxicity, ototoxicity and neuromuscular blockage are their well known side effects.

Systemic or local use of aminoglycosides can cause vestibulotoxicity besides cochleotoxicity, balance disorders, and visual dysfunction. For ototoxicity, which may develop due to use of aminoglycosides, vestibular side effects that may develop without hearing loss can go unnoticed even if the doctors are informed about the issue. Vestibular symptoms are frequently observed in the initial stage of systemic aminoglycoside treatment. However, although these side effects have a great negative effect on the patients' quality of life, they are rarely noticed.[6-8]

If the balance functions are bilaterally affected in vestibulotoxicity, this may cause vestibulopathy. Among the basic findings of vestibulopathic imbalance, oscillopsia and visual problems can be listed. Vestibular functions are more noticeable in the dark or in areas where the ground is not stable.[9]

Balance disorders may be observed in 3-5% of patients who receive streptomycin treatment.[10] Vestibulotoxicity that develops due to aminoglycosides is usually temporary, and usually develops when the functions of type 1 hair cells are affected.[11] This temporary effect seems potentially to be depending on the regeneration potential of hairy cells located in the vestibulum.[12] Permanent damage can be observed on the cochleovestibular system depending on ototoxicity, and this may cause long-term balance disorder problems.

In the vestibular system, cellular pathologies related to streptomycin can be observed in the dark cells before the hair cells. These cells play a role in the ion regulation of the vestibule. Vestibular endolymphatic homeostasis degeneration that develops in accordance with these cells getting affected causes the loss of vestibular hair cells.[13]

Electronystagmography, rotation test, head impulse test, vestibular-evoked myogenic potentials are used to evaluate vestibular functions. Aminoglycosides do not cover a specific area in the vestibular system, and findings that belong to all areas in the vestibular system can be observed for this reason. Therefore, those diagnosis methods can give information unique to each patient, in different levels.

The evaluation of damage that occurs in the cochlea-vestibular system gives an idea about the results of treatment method applied to the patients.[2,14] A bedside evaluation along with performing objective tests and applying surveys on balance loss provide more valuable information flow to the clinicians and gives a different point of view particularly in vestibular disorders.[2]

In BVH patients, balance loss that occurs with VOR and VSR functions affects daily life activities negatively, and causes anxiety. Vestibular rehabilitation forms the first stage of treatment to improve indepen-

dent mobilization and to minimize the risk of falling. It is considered that it is possible to have success with the BVH patients with accurate informing, and exercise programs.[2,4,15]

In the absence of vestibular inputs, the main aim in rehabilitation is to stabilize gaze. Specific exercises including adaptation, substitution, balance and gait helps to decrease subjective complaints, improve visual activity and postural stability.

BVH diagnosis is based on history, physical examination, vestibular tests and perceived handicap as measured by questionnaires (e.g. the Dizziness Handicap Inventory). Although the diagnosis of BVH may be challenging, once diagnosed, vestibular rehabilitation process must be started which is tailored for disease severity. Medical treatment, and in severe cases, vestibular implants may be helpful in BVH treatment.[16]

REFERENCES

1. Walsh P. Physician's Desk Reference. In: Walsh P, ed. Physician's Desk Reference. 54th ed. Montvale, NJ: Medical Economics Company, Inc.; 2000.
2. Rinne T, Bronstein AM, Rudge P, Gresty MA, Luxon LM. Bilateral loss of vestibular function: clinical findings in 53 patients. J Neurol 1998;245(6-7):314-21.
3. Ward BK, Agrawal Y, Hoffman HJ, Carey JP, Della Santina CC. Prevalence and Impact of Bilateral Vestibular Hypofunction Results From the 2008 US National Health Interview Survey, JAMA Otolaryngol Head Neck Surg 2013;139(8):803-10.
4. Deveze A, Bernard-Demanze L, Xavier F, Lavieille JP, Elziere M. Vestibular compensation and vestibular rehabilitation. Current concepts and new trends. Neurophysiol Clin 2014;44(1):49-57.
5. Durante-Mangoni E, Grammatikos A, Utili R, Falagas ME. Do we still need the aminoglycosides? Int J Antimicrob Agents 2009; 33(3):201–5.
6. Selimoglu E. Aminoglycoside-induced ototoxicity. Curr Pharm Des 2007;13(1):119–26.
7. Bhattacharyya TK, Kumar A. Vestibular cytotoxicity in gentamicin-treated frogs: a preliminary report. Am J Otolaryngol 2005; 26(2):91–5.
8. Cheng PW, Lue JH, Lin CT, Day AS, Young YH. Assessment of gentamicin-induced vestibulotoxicity by click and galvanic vestibular-evoked myogenic potentials: a guinea pig investigation. Neurotoxicology 2010;31(1):121–5.
9. Hain TC, Cherchi M, Yacovino DA. Bilateral vestibular loss. Semin Neurol 2013; 33(3):195–203.
10. Cawthorne T, Ranger D. Toxic effect of streptomycin upon balance and hearing. Br Med J 1957; 1(5033):1444–6.
11. Minor LB. Gentamicin-induced bilateral vestibular hypofunction. JAMA 1998;279:541-44.
12. Berggren D, Liu W, Frenz D, van de Water T. Spontaneous hair-cell renewal following gentamicin exposure in postnatal rat utricular explants. Hear Res 2003;180 (1-2):114-25.
13. Park JC, Cohen GM. Vestibular ototoxicity in the chick: effects of streptomycin on equilibrium and on ampullary dark cells. Am J Otolaryngol 1982;3(2):117–27.
14. Huh YE, Kim JS. Bedside evaluation of dizzy patients. J Clin Neurol 2013;9(4):203-13.
15. Sedo-Cabezon L, Boadas-Vaello P, Soler-Martin C, Llorens J. Vestibuler damage in chronic ototoxicity: A mini-review. Neurotoxicology 2014:43:21-7.
16. Fridman GY, Della Santina CC. Progress toward development of a multichannel vestibular prosthesis for treatment of bilateral vestibular deficiency. Anat Rec (Hoboken) 2012;295(11):2010-29.