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Case Report

Downbeat Nystagmus and Bilateral Sudden Hearing Loss by Suicidal Aspirin Intoxication

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Ototoxic side effects such as sensorineural hearing loss and tinnitus can be caused by acute salicylate intoxication. Bilateral symmetric sensorineural hearing loss involving all tested frequencies is a typical pattern of hearing loss in acute salicylate intoxication, which usually resolves within 2 or 3 days without any specific treatment for ototoxicity. Herein, we report a case of suicidal aspirin intoxication resulting in sudden bilateral hearing loss and vertigo. The patient exhibited spontaneous downbeat nystagmus, and the mechanism underlying this characteristic nystagmus is discussed.

KEYWORDS: Nystagmus, ototoxicity, sudden sensorineural hearing loss, vertigo

INTRODUCTION

Aspirin is widely used and easily available as over-the-counter medications, and thus, aspirin intoxication is one of the most frequently reported drug intoxications. The clinical manifestations of acute aspirin intoxication may differ depending on the serum salicylate level, including hyperpnea, nausea, vomiting, hearing loss, tinnitus, or dizziness in mild intoxication and coma, seizures, cardiac failure, coagulopathy, or renal failure in severe intoxication.[1] Since the first case report on the ototoxic effect of long-term aspirin intake,[2] temporary hearing loss and tinnitus are now well-known side effects of high-dose aspirin consumption,[3] although the underlying mechanism has not been fully established. Spontaneous downbeat nystagmus may be indicative of a central nervous system disorder, and lesions in the vestibulocerebellum or lower brainstem are considered to be responsible.[4,5] Drug intoxications such as lithium and anticonvulsant have also been reported as causes of downbeat nystagmus.[5] However, spontaneous downbeat nystagmus by acute aspirin intoxication has not been reported. Herein, we report a case of spontaneous downbeat nystagmus and bilateral sudden hearing loss due to acute aspirin intoxication.

CASE PRESENTATION

A 27-year-old man presented himself to our emergency department with his mother. The patient reported that he had attempted suicide by taking 100 tablets of aspirin (100 mg × 100 tablets = 10000 mg) 6 hours earlier, and vomited 2 times after intake due to nausea and gastrointestinal discomfort. His mental status was alert, and he complained of hearing loss with tinnitus on both sides and dizziness. Otoendoscopic examination showed normal tympanic membrane on both sides, and neurological examination including cerebellar function test revealed no abnormality. Pure tone audiometry (PTA) revealed both sensorineural hearing loss, demonstrating a mean threshold of 45 dB (average at 0.5 kHz, 1 kHz, 2 kHz, and 3 kHz) with a speech discrimination score of 76% on the right side, and a mean threshold of 41 dB with a speech discrimination score of 80% on the left side (Figure 1). Bedsides, head impulse test (HIT) showed no catch-up saccades, and skew deviation was not observed. Video Frenzel Goggles examination showed spontaneous downbeat nystagmus, of which the intensity was increased in bowing or leaning position (Supplementary Video 1). Positioning maneuvers including a supine head-roll and Dix-Hallpike maneuvers did not change the direction of nystagmus. Transient nystagmus was observed with slow phases occurring against the direction of the former gaze when the patient returned the eyes to the neutral position from the lateral eccentric gaze (Supplementary Video 1). The patient was admitted to the department of nephrology, and activated charcoal and intravenous fluids were administered to facilitate the removal of the remaining aspirin in his body. The administration of intravenous sodium bicarbonate was performed for alkalinization. He reported

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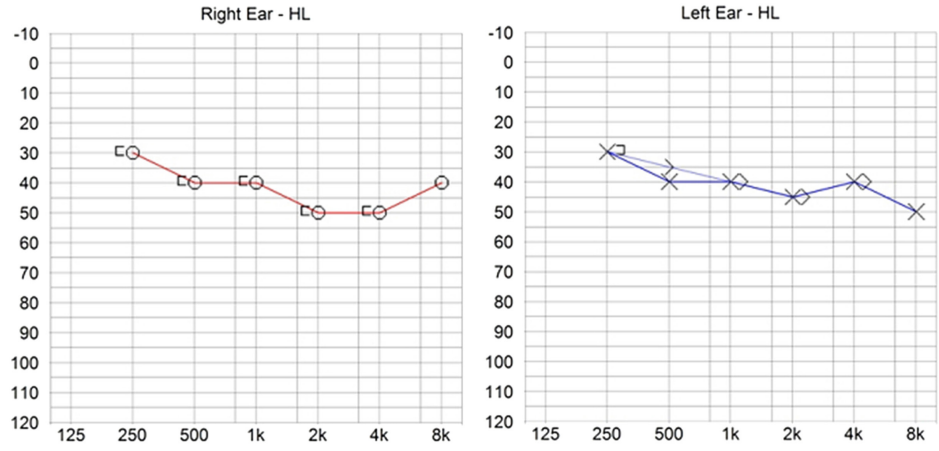

Figure 1. An initial pure tone audiometry shows 45 dB of sensorineural hearing loss on the right side (left panel) and 41 dB of sensorineural hearing loss on the left side (right panel).

that hearing loss and dizziness were substantially improved on the next day of treatment initiation. Because the patient's history was clear and the recovery was so quick, we did not perform an imaging study of the brain. A follow-up PTA was conducted on the seventh day, which showed no hearing loss on both sides (Figure 2A). No abnormal finding was observed in auditory brainstem response (Figure 2B) and distortion product otoacoustic emissions (Figure 2C). Video Frenzel Goggles examination demonstrated no nystagmus, and video HIT revealed normal gain values without catch-up saccades (Figure 2D).

Ethical committee approval was received from Konkuk University Medical Center (KUH_2021-06-021). Written informed consent was obtained from all participants who participated in this study.

DISCUSSION

Aspirin has antipyretic, anti-inflammatory, and analgesic effects and is one of the most commonly used pain reliever. Because aspirin is available without a prescription in most countries, it is exposed to the possibility of suicidal drug intoxication. Temporary sensorineural hearing loss with tinnitus has been reported as a consequence of acute aspirin intoxication.[2] Hearing loss observed in this condition was characterized by bilateral symmetric, mild-to-moderate sensorineural hearing loss involving all tested frequencies.[2] Our patient also showed bilateral symmetric sensorineural hearing loss of 41-45 dB, which was rapidly recovered after treatment. The severity of hearing loss in acute aspirin intoxication is known to be closely associated with plasma salicylate concentration.[6] Salicylate has long been known to impair cochlear function in a way that salicylate reduces

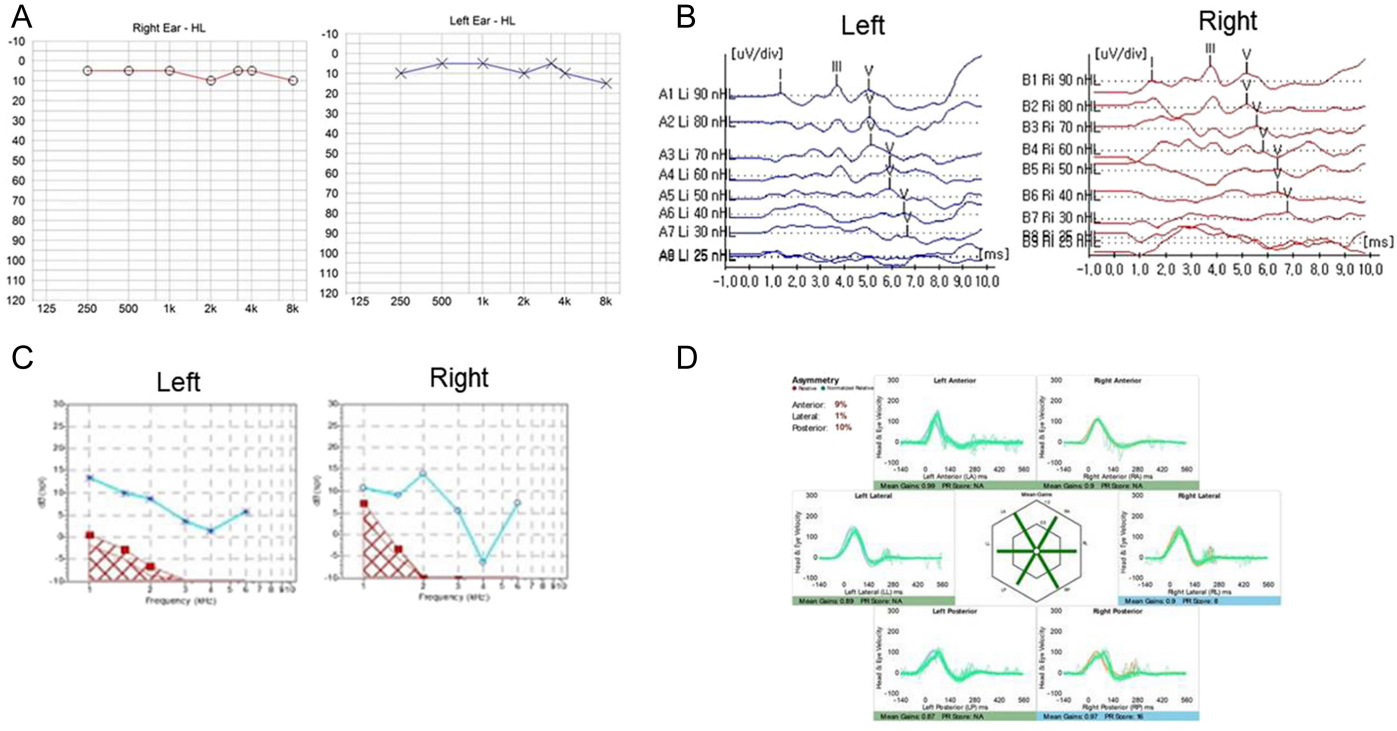

Figure 2. a-d. (a) A pure tone audiometry on the seventh day shows normal hearing on both sides. (b) Auditory brainstem response, which was conducted on the seventh day, demonstrates hearing threshold of 30 dB on both sides. (c) Distortion product optoacoustic emissions, which were conducted on the seventh day, show normal response on both sides. (d) A video head impulse test, which was conducted on the seventh day, shows normal gain values in all six semicircular canals.

cochlear sensitivity by depressing outer hair cell electromotility and decreases the neural output of the cochlea.[3] Salicylate has been reported to directly deteriorate the function of prestin by competing with chloride for the anion-binding site in prestin.[7] A human temporal bone autopsy of a 77-year-old woman, who had experienced a temporary hearing loss after chronic salicylate intake, showed that while the loss of spiral ganglion cells and atrophy of the stria vascularis were observed, the eighth nerve in the internal auditory canal and maculae of the saccule and utricle and crista of the semicircular canal were intact.[8] An animal histopathologic study of chinchillas with acute salicylate intoxication demonstrated that although temporary hearing loss was observed after acute salicylate intoxication, no morphological correlation was seen in scanning electron microscope or transmission electron microscope examination.[9] In addition to cochlear impairment, evidences for its effect on the central nervous system have been recently reported. Animal studies showed that high-dose salicylate enhances sound-evoked neural responses at high stimulus levels.[3]

To the best of our knowledge, nystagmus findings have not been reported in acute aspirin intoxication. In our patient, who complained of bilateral sudden hearing loss and vertigo, downbeat nystagmus was observed. Downbeat nystagmus is a frequent ocular motor sign in patients with lesions in the cerebellum or brainstem.[5,10] Other causes of downbeat nystagmus including amyotrophic lateral sclerosis, multiple sclerosis, encephalitis, heatstroke, hydrocephalus, and toxic-metabolic encephalopathy by anticonvulsant medication, lithium intoxication, alcohol intoxication, Wernicke's encephalopathy, magnesium depletion, amiodarone, opioids, vitamin B_{12} deficiency, toluene abuse, and ciguatera-fish poisoning have been reported.[5] Selective activation of bilateral anterior semicircular canal or inhibition of bilateral posterior semicircular canal can be considered if the cause of downbeat nystagmus originated from peripheral vestibular organs in our patient. However, selective damage in the part of the inner ear structure is unlikely to occur, and dysfunction in the central nervous system, especially vestibulocerebellum, by salicylate intoxication may be a more plausible explanation. Du et al[11] reported that salicylate administration changed the excitability of the paraflocculus, which is a part of the vestibulocerebellum, possibly by modulating the level of glutamic acid. Other animal studies reported that acute salicylate intoxication may induce cerebral white matter damage and the reduction of gamma aminobutyric acid (GABA) receptor expression in the central nervous system.[12]

The intensity of downbeat nystagmus was increased in bowing and leaning positions in our patient. Downbeat nystagmus may be influenced by gravity, and it has been reported to be often precipitated or increased when patients are placed in either a "head-hanging" or prone position.[5,10,13] The influence of gravity on downbeat nystagmus may be explained by dysfunction in the otolith-ocular pathways by salicylate intoxication or modulation of vertical vestibulo-ocular reflexes by otolith signals.[14,15] Another interesting finding was transient nystagmus with fast components beating toward the direction of former gaze when the patient returned the eyes to the neutral position from the lateral eccentric gaze. The direction of this nystagmus is opposite to that of the so-called "rebound nystagmus," in which transient nystagmus beats against the direction of the former gaze when returning the patient's eyes to the neutral position.[5] This characteristic nystagmus may suggest a shift of the null in the direction of prior eccentric gaze,[5] and further research is needed to understand the mechanism underlying this nystagmus.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Konkuk University Medical Center (approval number: KUH_2021-06-021).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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Supplementary Video 1: https://youtu.be/rq99R0gldlg.

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