Case Report

A Case Report of Cisplatin Induced Ototoxicity and Brief Review of Literature

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ABSTRACT

Ototoxicity refers to the hearing disorder those results from the temporary or permanent inner ear dysfunction after treatment with an ototoxic drug. Those of serious concern for permanent effects are the aminoglycoside antibiotics and the anticancer drug cisplatin. Cisplatin is a platinum coordination compound, which is used as first line drug in many cancers. Cisplatin ototoxicity can produce permanent hearing loss which can negatively affect the quality of life of a cancer patient. It is therefore important for health care professionals managing these patients to be aware of cisplatin ototoxic properties. This case of cisplatin induced ototoxicity points out the need of proper screening and audiological rehabilitation of patients with ototoxicity.

Keywords: *Cisplatin, Ototoxicity, Chemotherapy*

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INTRODUCTION

Ototoxicity[1] is a condition characterised by a temporary or permanent malfunction of the inner ear that occurs as a result of treatment with a substance that has toxic effects on the ear.

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There are around 200 medications. that have been classified as ototoxic. The aminoglycoside antibiotics and the anticancer medication cisplatin are particularly worrisome due to their potential for causing long-lasting damage. Cisplatin is a platinum-based coordination molecule that serves as a primary chemotherapy treatment for several types of cancer. Cisplatin possesses ototoxic properties, hence posing a risk of auditory impairment to cancer patients undergoing this therapy.[2] Hence, it is crucial for healthcare

personnel responsible for the care of these patients to possess knowledge regarding the ototoxic qualities of cisplatin and its associated clinical indicators, to effectively identify individuals who are susceptible to developing hearing impairments. Nevertheless, Malhotra[3] stated that the majority of oncologists in India do not refer patients receiving cisplatin for audiological examinations. This instance of cisplatin-induced ototoxicity highlights the necessity of conducting thorough screening for ototoxicity in patients at high risk.

CASE REPORT

A 37-year-old female patient visited the outpatient ENT department at AIIMS Bhopal in November 2021, reporting tinnitus that had been present for the past 2 weeks. From May 2021 to October 2021, she had salvage chemotherapy using the GDP regimen, which includes gemcitabine, dexamethasone, and cisplatin, to treat her non-Hodgkin's lymphoma that was not responding to previous treatments. Three GDP cycles were provided with a three-week break between each. The administration of cisplatin and gemcitabine was performed intravenously, with a dosage of 25 mg/m2 and 100 mg/m2 of body surface area, respectively. Dexamethasone was administered at a dosage of 40 mg per day for a duration of 5 days in each cycle. Following the completion of her second session of chemotherapy, she experienced the onset of tinnitus. In order to prevent ototoxicity, cisplatin was substituted with carboplatin. The patient has a preexisting medical history of Meniere's illness. She had examination and investigation by an otorhinolaryngologist. She received an audiogram test that revealed sensorineural hearing loss. The otorhinolaryngologist recommended that she have an intratympanic injection of dexamethasone, but she declined the treatment. The tinnitus steadily diminished over the course of one month.

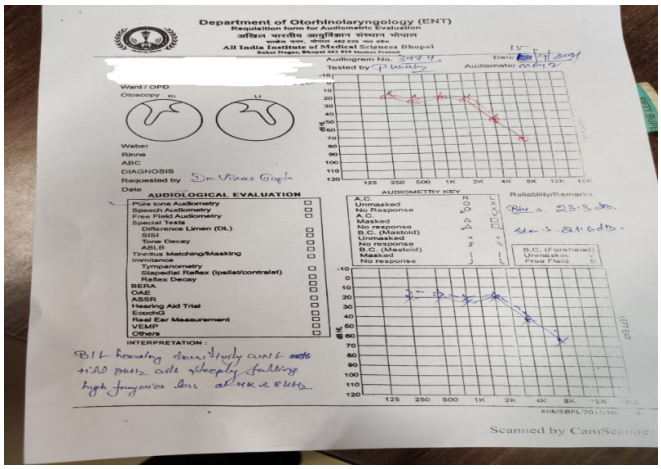

Figure 1: Audiogram showing loss of higher frequencies.

DISCUSSION

The occurrence of ototoxicity, a negative medical event, was reported to the adverse event monitoring centre (AMC) at AIIMS Bhopal. Subsequently, a causality assessment was undertaken according to the causality assessment guidelines established by the World Health Organisation (WHO). According to the causation evaluation criteria of the World Health Organisation (WHO), adverse events are categorised as certain, probable, possible, unlikely, unclassified, and unclassifiable. The connection was deemed "probable" according to the causality evaluation criteria[4] set by the World Health Organisation (WHO). The Schumock and Thornton scale[5] was utilised for the assessment of preventability. Adverse occurrences in this scale are categorised as definitely preventable, maybe preventable, or non-preventable, based on their aetiology. This adverse incident falls under the classification of a "Definitely Preventable" adverse event. Due to the patient's pre-existing history of Meniere's Disease, this medicine was unsuitable for the patient's clinical state.

The main cause of cisplatin-induced ototoxicity is the generation of reactive oxygen species (ROS) in the cochlea.[6] Another method involves the involvement of the NOX3 isoform of nicotinamide adenine dinucleotide phosphate oxidase in the production of reactive oxygen species in the cochlea, which occurs when cisplatin activates it. Additionally, the transient receptor potential vanilloid 1 (TRPV1) channel is also activated. The ototoxicity caused by cisplatin is directly proportional to the dosage administered. Increasing the number of treatment cycles with cisplatin will result in a higher incidence of ototoxicity. Additional risk factors for ototoxicity include advanced age, impaired kidney function, simultaneous administration of ototoxic medications, previous ear conditions, exposure to loud noise, and genetic predisposition.[7]

Cisplatin-induced ototoxicity typically presents as bilateral, high-frequency sensorineural hearing loss with tinnitus, which is usually irreversible and progressive. Tinnitus can manifest with or without auditory impairment and can be either permanent or temporary. Although the majority of cases of hearing loss are permanent, occasional and incomplete recovery may occur. In addition, there have been reports of infrequent instances of unilateral hearing loss.The structures of the inner ear are highly vulnerable to damage caused by cisplatin chemotherapy, particularly resulting in apoptotic degradation of the hair cell in the Organ of Corti. The outer hair cells located in the basal turn of the cochlea are primarily impacted. As a result, there is an initial increase in the thresholds for high-frequency hearing tests, which is then followed by a gradual decrease in hearing ability for lower frequencies as therapy continues. The symptoms of ototoxicity are also influenced by the location of the affected area. If the cochlea is largely injured, patients typically report with symptoms of tinnitus and sensorineural hearing loss. If the vestibulum is largely damaged, the patient typically exhibits symptoms such as vertigo, ataxia, light headedness, imbalance, and nystagmus.

Almost all otoprotective medicines are antioxidants that contain sulphur or sulfhydryl groups (SH).[6] These substances are alternatively referred to as thio compounds. Some examples of substances are N-acetylcysteine, melatonin, amifostine, vitamin E, dexamethasone, methionine, and lipoic acid. Nevertheless, none of these

drugs have been conclusively proven to be advantageous in avoiding cisplatin-induced hearing loss, and there is currently no agent that is indicated for regular usage.

Ototoxicity is a significant challenge for cancer patients, as the administration of cisplatin chemotherapy can have a detrimental impact on their quality of life. Everyday tasks that people with normal hearing consider easy may become difficult and irritating for individuals with hearing loss, potentially leading to psychosocial and physical health issues, including depression and social isolation.[5] Therefore, hearing loss, commonly known as the imperceptible ailment, significantly impacts the overall well-being of individuals who experience it. Infants and young children who are at a key stage of their speech and language development may experience a more significant impact from an ototoxic hearing loss.[6] Ototoxicity can result in impaired communication, learning challenges, cognitive deterioration, sadness, and stress. Ototoxicity can also result in occupational restrictions, diminished quality of life, reduced income, social isolation, and safety concerns.[8]

Should a cisplatin-induced hearing impairment lead to challenges in communication, it becomes the ethical duty of the audiologist to initiate or suggest aural rehabilitation. Individuals experiencing sensorineural hearing loss as a result of cisplatin usage can derive advantages from employing assistive listening devices, such as hearing aids or cochlear implants. Children who have ototoxic hearing loss may also need to utilise remote microphone technology in order to enhance the ratio of the desired sound to background noise in the classroom. The "Guidelines for the Audiological Management of Individuals receiving cochleotoxic Drug Therapy" developed by the American Association of Speech-Language-Hearing Association (ASHA)[9] can assist audiologists in implementing a programme to monitor ototoxicity. The ototoxicity monitoring regimen suggested by ASHA is a proactive and optimal method for monitoring ototoxicity. The audiological tests used to assess ototoxicity include high frequency audiometry (HFA), Otoacoustic Emissions (OAE), pure tone audiometry, Distortion product otoacoustic emission (DPOAE), and auditory Brainstem Response (ABR). Prior to the initiation of cisplatin chemotherapy, it is recommended to provide intervention in accordance with ASHA standards.[10] It is important to implement aural rehabilitation treatments, such as speech reading and counselling on compensatory communication strategies. Children who have ototoxic hearing loss may also need to use personal frequency modulated systems in the classroom. Hearing aids and cochlear implants are viable options for auditory rehabilitation.

CONCLUSION

This case report emphasises that cisplatin ototoxicity is a prevalent and avoidable side effect of cisplatin chemotherapy, which can have a detrimental impact on the well-being of cancer patients. Cisplatin ototoxicity can be mitigated by doing a thorough clinical history, examination, and identifying patients who are at risk of developing hearing impairments. Carboplatin or oxaliplatin can be used as alternatives to cisplatin in individuals with pre-existing ear disease or high-risk patients due to their lower ototoxicity. An audiological monitoring programme, consisting of a team of oncologists and otorhinolaryngologists who are well-informed on cisplatin ototoxicity, could enhance the provision of evidence-based services to these patients.

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