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# UNCOMMON ADVERSE DRUG REACTION OF CISPLATIN-INDUCED OTOTOXICITY IN AN ONCOLOGY PATIENT: A CASE REPORT

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## ABSTRACT

**Background:** Dose-dependent toxicities are associated with cisplatin, a widely used platinum-based chemotherapeutic agent. Among the adverse effects, ototoxicity is a major concern. Hearing loss is mainly sensorineural and often bilateral, severely affecting communication, social interaction, and quality of life. Early identification and intervention can prevent permanent auditory damage **Case Presentation:** We describe a patient who was on cisplatin-based chemotherapy and presented with progressive bilateral tinnitus and hearing impairment. Clinical and audiological evaluation revealed high-frequency sensorineural hearing loss, a typical presentation of cisplatin ototoxicity. Treatment consisted of drug discontinuation from temporary use of cisplatin, administration of corticosteroids and antioxidants, and regular audiological follow-up. Partial relief of symptoms and stabilization of hearing thresholds were observed. **Conclusion:** With cisplatin-induced ototoxicity still being a clinically relevant challenge in oncology practice, audiological testing at baseline and follow-up during chemotherapy would help with early identification. Early intervention, counseling of patients, and preventive measures should all be implemented to minimize the risk of permanent hearing impairment and better the prognosis of the patient.

**KEYWORDS:** Cisplatin, Ototoxicity, Sensorineural Hearing Loss, Chemotherapy, Audiological Evaluation.

## INTRODUCTION

Cisplatin is a platinum-based chemotherapeutic agent used to treat many malignancies such as head and neck, lung, and female genital cancers.[1] Despite its efficacy, cisplatin has been found to cause a wide spectrum of dose-limiting toxicities, including nephrotoxicity, neurotoxicity, and ototoxicity. Hearing loss is probably the most threatening

ototoxicity since it leads to permanent sensorineural hearing loss, thereby greatly diminishing patients' quality of life and the ability to communicate with others and socially interact with them.[2,3]

Cisplatin ototoxicity can be classified as a ROS-mediated toxic effect of cisplatin, with the reactive species of oxygen causing oxidative stress to kill the affected cochlear hair cells, the stria vascularis, and the spiral ganglion neurons.[4] The ototoxicity or hearing loss varies from patients to patients depending on the cumulative dose-, therapy-time-, and pre-occupational health factors. Usually, the symptoms begin with tinnitus and high-frequency hearing impairment; if undetected or untreated, it will progress to a bilateral, permanent sensorineural hearing impairment.[5,6]

Considering that the incidence of ototoxicity with cisplatin seems to be on the rise, prevention measures need to be taken. While monitoring hearing aids daily and possibly modification of dose, as well as the use of protective agents like antioxidants, will help avert ototoxicity.[7] This case report details the clinical presentation of ototoxicity induced by cisplatin, its diagnostic evaluation, approach towards management, and the outcome, focusing on the importance of multidisciplinary care in the oncology patient.[8]

## CASE PRESENTATION

**Patient Details:** A 54-year-old man, living in a semi-urban locality came to the outpatient department of oncology at the tertiary care teaching hospital. He was married, and no hereditary or congenital health disorders were known to his family. His weight was 68 kg and height 168 cm (BMI: 24.1 kg/m²).

**Chief Complaints:** The patient presented with:

- Gradual onset hearing difficulty in both ears, predominantly for high-pitched sounds, for 2 weeks.
- Associated persistent tinnitus (ringing sensation in the ears).
- Mild difficulty in communication in daily activities.

**History of Present Illness:** This patient was a known case of squamous cell carcinoma of the oropharynx (Stage III, T3N1M0), diagnosed 4 months previously on biopsy and imaging studies. A cisplatin-based concurrent chemoradiation regimen was instituted (cisplatin 100 mg/m² every 3 weeks with external beam radiotherapy).

- He tolerated the first cycle of chemotherapy with no significant adverse effects.
- Following the second cycle, he complained of intermittent tinnitus and mild hearing difficulty, which was initially overlooked as a possible symptom of chemotherapy-related fatigue.
- After the third cycle (cumulative cisplatin dose ~300 mg/m²), he had suddenly-onset bilateral hearing loss accentuated in the higher frequencies, accompanied by continuous tinnitus. There was no vertigo, imbalance, or ear discharge.
- He had no history of exposure to loud noise or use of headphones, nor had he suffered from ear infections.

**Past Medical History**

- No history of hypertension, diabetes mellitus, thyroid disease, or chronic renal disease.
- No history of prior auditory dysfunction.

**Surgical History**

- No past surgical interventions.

**Medication History**

- Currently on cisplatin chemotherapy (as per oncology protocol).
- Received ondansetron and dexamethasone as antiemetic prophylaxis.
- Received IV hydration with normal saline during chemotherapy cycles.
- No history of aminoglycoside antibiotics, loop diuretics, or other known ototoxic medications.
- No history of alternative or herbal medications.

**Personal History**

- Non-smoker and non-alcoholic.
- Normal dietary habits, with no history of substance abuse.
- Sleep and appetite were reported as normal.
- No occupational exposure to heavy metals, solvents, or industrial noise.

**Examination Findings**

**General Examination**

- The patient was conscious, oriented, and cooperative.
- Well-nourished, moderately built.
- No pallor, icterus, cyanosis, clubbing, pedal edema, or lymphadenopathy.
- No signs of dehydration or cachexia.

**Vital Signs**

- Temperature: 98.4°F
- Pulse: 82 beats/min, regular rhythm
- Blood pressure: 126/78 mmHg
- Respiratory rate: 18 cycles/min
- Oxygen saturation: 98% on room air

**Head and Neck Examination**

- No cranial nerve deficits other than auditory complaints.
- No cervical lymphadenopathy.
- Oral cavity: presence of mild mucositis related to radiotherapy, no active bleeding or ulceration.

**Ear, Nose, and Throat (ENT) Examination**

- **External ear:** No swelling, lesions, or discharge.
- **Ear canal:** Clear bilaterally.
- **Tympanic membranes:** Intact, normal light reflex, no signs of perforation or fluid.
- **Hearing tests**
  - Rinne’s test: Negative bilaterally (suggestive of sensorineural hearing loss).
  - Weber’s test: Sound lateralized to the right ear.
  - Absolute bone conduction (ABC): Reduced bilaterally.
- **Nasal and throat examination:** Within normal limits except for radiation-related mucositis.

**Systemic Examination**

- **Cardiovascular system:** Normal S1 and S2, no murmurs.
- **Respiratory system:** Bilateral clear lung fields, no added sounds.
- **Abdomen:** Soft, non-tender, no hepatosplenomegaly and bowel sounds present.
- **Neurological system:** Higher mental functions intact; cranial nerves normal except VIII (auditory nerve) involvement; no motor or sensory deficits; reflexes normal.

**Laboratory Investigations**

| Parameter | Result | Normal Reference Range |
|---|---|---|
| **Complete Blood Count (CBC)** | | |
| Hemoglobin | 13.6 g/dL | 13–17 g/dL |
| Total Leukocyte Count | 6,800 /mm³ | 4,000–11,000 /mm³ |
| Differential Count | N 62%, L 30%, E 4%, M 3%, B 1% | N 40–70%, L 20–40%, E 1–6%, M 2–10%, B 0–1% |
| Platelet Count | 2.1 lakh /mm³ | 1.5–4.5 lakh /mm³ |
| **Renal Function Tests (RFTs)** | | |
| Blood Urea Nitrogen (BUN) | 14 mg/dL | 7–20 mg/dL |
| Serum Creatinine | 0.9 mg/dL | 0.6–1.2 mg/dL |
| Sodium | 139 mmol/L | 135–145 mmol/L |
| Potassium | 4.1 mmol/L | 3.5–5.1 mmol/L |
| Chloride | 103 mmol/L | 98–107 mmol/L |
| **Liver Function Tests (LFTs)** | | |
| Total Bilirubin | 0.7 mg/dL | 0.2–1.2 mg/dL |
| AST (SGOT) | 28 U/L | 10–40 U/L |
| ALT (SGPT) | 32 U/L | 7–56 U/L |
| Alkaline Phosphatase | 85 U/L | 44–147 U/L |
| Total Protein | 7.2 g/dL | 6.0–8.3 g/dL |
| Albumin | 4.3 g/dL | 3.5–5.5 g/dL |
| **Other Tests** | | |
| Fasting Blood Glucose | 92 mg/dL | 70–100 mg/dL |
| Thyroid Profile | Normal | — |
| Viral Markers (HBsAg, HCV, HIV) | Negative | — |

**Audiological Evaluation**

As the patient described progressive bilateral hearing loss following cisplatin-based chemotherapy, a full audiological evaluation was considered necessary. This evaluation encompassed pure-tone audiometry, speech audiometry, and tympanometry, while also considering otoacoustic emissions (OAE) for the objective evaluation of cochlear function.

**Pure-Tone Audiometry (PTA)**

- The audiological evaluation showed equal bilateral sensorineural hearing loss in the high frequencies, with deafness more severe in the frequency range of 4–8-kHz range, quite compatible with cisplatin-induced ototoxicity.
- Thresholds at low to mid frequencies (250–1000 Hz) were in near-normal limits, with the major decrement in higher frequencies (≥4000 Hz).
- **The patient's average pure-tone thresholds were**
  - **Right ear:** 35 dB HL at 4 kHz, 55 dB HL at 8 kHz
  - **Left ear:** 40 dB HL at 4 kHz, 60 dB HL at 8 kHz

**Speech Audiometry**

- **Speech Reception Threshold (SRT):** Mildly elevated, correlating with PTA findings.
- **Speech Discrimination Scores (SDS):** Normal scores at soft intensities but considerably decreased at high intensities, reflecting difficulty in understanding speech, mainly in noisy environments.

**Tympanometry**

- Tympanometry yielded Type A tympanograms bilaterally, thus confirming the middle ear's normal functional state and ruling out a possibility of conductive pathology.

**Otoacoustic Emissions (OAE)**

- **Distortion Product OAE (DPOAE):** High-frequency responses (≥ 4 kHz) were absent bilaterally, indicative of outer hair cell dysfunction from cisplatin cochlear toxicity.
- Low-frequency emissions were present, reaffirming the pattern of high-frequency selective damage.

**Final Diagnosis**

After thorough evaluation, a diagnosis of cisplatin-induced ototoxicity was made. The clinical picture was one of persistent tinnitus and progressive bilateral hearing loss, paroxysmal with chemotherapy cycles. With uneventful otoscopy and systemic examination, middle ear pathology was ruled out. Blood investigations within the normal range ruled out the metabolic causes. The audiological examination proved bilateral symmetrical high-frequency sensorineural hearing loss unique to drug-induced cochlear toxicity. No prior exposure to loud noises, no family history, and no infectious cause ruled out auditorily pertinent etiology. By exclusion of all other differential diagnoses and consideration of the temporal relations with cisplatin administration, the final clinical diagnosis was made: cisplatin-induced ototoxicity.

**Treatment and Management**

**Day 1: Initial Measures**

On the first day of symptoms, chemotherapy with cisplatin was immediately withheld to prevent further auditory toxicity. Admission was done at the hospital for close observation and supportive management. Intravenous fluids with electrolytes were kept to promote renal clearance of cisplatin metabolites and minimize systemic toxicity. Basic laboratory investigations, renal function, and electrolytes were done in the present case scenario to implement supportive therapy safely. A thorough audiological assessment was conducted, which confirmed the bilateral high-frequency sensorineural hearing loss. This assessment served as the baseline for the detection of successive hearing alterations during the course of management.

**Day 2–3: Antioxidant Therapy**

From the second day onward, antioxidant therapy was initiated for preventing ongoing oxidative stress and cochlear injury. The patient had received intravenous N-acetylcysteine while states that it is a strong free-radical scavenger for reactive oxygen species (ROS) generation by cisplatin. Follow-up prescription included high doses of Vitamin C and Vitamin E to give further antioxidant support and stabilize cochlear cell membranes. On the other hand, oral zinc was added to the therapies because of its ability to boost antioxidant mechanisms and promote repair in the cochlea. Symptomatic treatments remained the focus, which involved reassurance about tinnitus and advice on hydration and adequate rest.

**Day 4–5: Anti-inflammatory Management**

On the fourth day, the patient experienced clinical persistence of tinnitus and hearing impairment. Systemic steroids were thus considered to reduce inflammatory edema of the cochlea, starting as oral prednisolone on tapering doses. The goal was to suppress pro-inflammatory cascades that could aggravate cochlear damage. The patient was extensively counseled during this period on hearing conservation techniques, avoiding loud noises, using ear protection in noisy environments, and strict avoidance of other ototoxic drugs such as aminoglycosides or loop diuretics. Renal function and auditory symptoms remained under close inspection.

**Day 6–7: Monitoring and Modification of Therapy**

On the sixth and seventh days, a repeat audiogram was performed to check on the intervention. Persistent sensorineural hearing loss with a mild degree of improvement in tinnitus intensity became evident, indicating that the ototoxicity had reached stabilization. Following various medical discussions between the oncology and ENT teams, the chemotherapy regimen was altered to replace cisplatin with carboplatin, which has a relatively lower toxic potential on the ear. This prevented any further deterioration due to cancer treatment. Plans were set for later hearing rehabilitation, including the possibility of fitting hearing aids to enhance communication and, ultimately, their quality of life. The patient was instructed to regularly follow-up with audio logical assessments.

| Date/Day | Treatment/Medication | Dose & Route | Frequency | Indication/Rationale |
|---|---|---|---|---|
| **Day 1** | Cisplatin discontinued | — | — | To prevent further ototoxicity |
| | IV Normal Saline | 1000 ml IV | Once daily | Hydration to enhance drug clearance |
| **Day 2** | IV Electrolytes (KCl, $MgSO_4$ as required) | Based on labs | Once daily | Correct electrolyte imbalance |
| | IV N-acetylcysteine | 600 mg IV | OD | Antioxidant, cochlear protection |
| **Day 3** | Vitamin E (Oral) | 400 IU PO | OD | Antioxidant protection |
| | Prednisolone (Oral) | 1 mg/kg PO | OD (tapering) | Reduce cochlear inflammation |
| **Day 4** | Audiology evaluation | — | — | Assess baseline hearing deficit |
| **Day 5** | Hearing aid trial & counseling | — | — | Rehabilitation support |
| **Day 6** | Chemotherapy modified (Carboplatin instead of Cisplatin) | As per oncology protocol | Cyclical | Avoid ototoxic agent |
| **Day 7** | Follow-up plan (ENT + Audiology) | — | Every 2 weeks | Long-term monitoring |

**Outcome**

The treatment outcome was good. After stopping Cisplatin and starting antioxidant therapy made up of N-acetylcysteine and Vitamin E, the patient had a dramatic diminution of tinnitus in a matter of days. An audiological reassessment four weeks later documented stabilization of thresholds of hearing with no further progression of sensorineural hearing loss. Replacement of Cisplatin with Carboplatin permitted continuation of the chemotherapy without additional ototoxic effects. Fitting of hearing aids improved speech recognition and quality of life. In a nutshell: the patient improved clinically, was able to maintain cancer treatment, and was functionally rehabilitated-an affirmation of timely intervention and audiological support in cisplatin-induced ototoxicity.

## DISCUSSION

Cisplatin serves as an exceptionally active platinum chemotherapeutic agent and is truly essential in the treatment of many solid tumors, including lung, ovarian, testicular, and head and neck cancers. This agent cannot be given a broader clinical usage due to toxicities that are dose-dependent, affecting chiefly the kidneys, nerves, and ears. In fact, this ototoxicity is characterized by a bilateral high-frequency sensorineural hearing loss, with tinnitus often accompanying it. ROS generation and apoptosis of cochlear hair cells, as well as vascular injury in the stria vascularis, have been implicated in the pathogenesis. The accumulation of Cisplatin inside cochlear tissues finally contributes to irreversible hearing loss; hence the importance of prompt diagnosis.[9]

This case highlights the need for monitoring hearing function in patients during Cisplatin therapy. The patient developed tinnitus and hearing loss soon after several cycles of Cisplatin-I, a fact that correlates with literature reports showing cumulative dosing as a major risk factor. Ototoxicity may compromise the quality of life, and treatment discontinuation may be one of its consequences, which endangers oncological outcome. Hence, this case stresses the need for baseline and periodic audio testing along the course of chemotherapy, especially in high-risk populations such as the elder and those with comorbidities.[10]

There may be several causes of hearing loss within oncology patients, such as presbycusis, chronic otitis media, noise exposure, and concurrent use of other ototoxic reagents like aminoglycosides. However, this particular patient was determined to have drug-induced ototoxicity as there had been no previous complaint of auditory problems, the otoscopic examination was normal, and the temporal occurrence of hearing loss was just after Cisplatin administration. The diagnosis was established based on audiometric confirmation of high-frequency sensorineural hearing loss. This highlights the importance of a thorough history taking, examination, and targeted audiological investigations to distinguish Cisplatin-induced ototoxicity from other causes.[11]

The treatment of ototoxicity caused by Cisplatin is challenging since the damage is quite often irreversible. In this particular case, recognition of the ototoxicity and drug withdrawal were crucial to avoid further deterioration. Substitution with Carboplatin allowed chemotherapy to continue with less ototoxic risk. Antioxidants such as N-acetyl-cysteine and Vitamin E were used as supportive therapy, whereas audiological rehabilitation through hearing aids was essential for improving the functional outcomes for the patient. This case underlines how important this multidisciplinary approach is between oncologists, audiologists, and pharmacists to ensure an effective cancer therapy while preserving auditory health. ND proactive monitoring and patient education tremendously help to minimize the long-term outcome disability associated with Cisplatin-induced ototoxicity.[12]

## CONCLUSION

An uncommonly seen adverse drug reaction but life-threatening is highlighted under this case with regard to cisplatin-induced ototoxicity in an oncology patient. Early identification of symptoms such as tinnitus and high-frequency hearing loss with proper and timely diagnosis played an important role in preventing irreversible damage. Replacement of cisplatin with carboplatin, antioxidant therapy, and audiological rehabilitation avoided further deterioration and hence led to the improvement of the patient's quality of life. This case stresses the need to monitor for ototoxicity in a vigilant manner in patients treated with cisplatin and stresses the collaboration between oncologists, audiologists, and pharmacists for safe and effective cancer treatment.

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