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Ototoxicity due to Oxaliplatin in Adjuvant Setting for Colorectal Cancer

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***Abstract*—Oxaliplatin is a new platinum compound agent used in the treatment of many cancers, especially colorectal cancer (CRC).Neurotoxicity is the dose limiting toxicity and ototoxicity is very rare, less than 1% of patients.**

We present a case of hearing loss that occurred in a 52-year-old man receiving adjuvant chemotherapy based on the combination of oxaliplatin and capecitabine for stage IIIcolon cancer. The dose of oxaliplatin was stopped after 5 cycles

Discussion To the best of our knowledge, this is the sixth reported case of oxaliplatin ototoxicity. Although oxaliplatin ototoxicity is rare, physicians must be aware of this important adverse effect,and an audiometric evaluation must be performed when necessary.

***Index Terms*—ototoxicity,oxaliplatin,hearing loss.**

I. INTRODUCTION

Oxaliplatin is a third-generation diamine cyclohexane platinum derivative which mechanism of action involves the formation of DNA adducts and inhibition of the DNA synthesis [1].

The clinical development of oxaliplatin-based chemotherapy regimens started in the 1990s and along the years,several different combination regimens have been used in oncology [2].

Oxaliplatin is a platinum-derived agent used in the treatment of a variety of solid tumors. It is typically administered with fluorouracil for the treatment of colorectal cancer.

Platinum containing chemotherapeutic agents are known to be ototoxic [3].

Ototoxicity occurs in 7–72% of adults receiving cisplatin [4].Neurotoxicity is a frequent side effect of oxaliplatin (76%). In comparison, ototoxicity due to newer generation platinum-derived agents

Such as oxaliplatin is rare [5]. Less than 1% of patients who receive oxaliplatin develop ototoxicity characterized by hearing loss.[6]

II. CASE REPORT

A 52-year-old woman

having diabetes and high blood pressure as a medical history under treatment,no surgical or family history

The patient underwent a subtotal colectomy with ileo-rectal anastomosis followed by adjuvant chemotherapy based on capecitabine 2,000 mg/m2/day for 14 days every 3 weeks and oxaliplatin 130 mg/m2/day every 3 weeks for 6 months.

the patient complained bilateral hearing loss At the end of third cycle ,she noticed further difficulty in hearing.

The audiogram showed that the speech recognition threshold was 55

the dose of oxaliplatin was reduced to 50 percent and another audiogram was performed a month later and showed that the speech recognition threshold was decreased from 55 dB to 85 dB.

This change confirmed her to progress from moderate to profound hearing loss as depicted in Table 1.

For this, oxaliplatin was stopped after five cycles and xeloda is maintained alone for the last three cycles.

After 2 months, the patient reported improved hearing and the control audiogram demonstrated a bilateral slight improvement in hearing.

After 8 months,The audiograms showed a good evolution of the hearing with the last value of 25 dB which confirms that the toxicity is linked to oxaliplatin.

Table 1. The following table relates how loud a sound must be for a person to hear it (hearing thresholds) to the degree of hearing loss for adults.

Severity	Average loss	Symptoms
Mild	20-40 dB	• Difficulty with soft speech • Sustained attention sometimes difficult
Moderate	41-55 dB	• Difficulty with normal conversational speech • Moderate difficulty in group or noisy situations
Moderately-severe	56-70 dB	• Hears shouted speech only • Appears to not pay attention
Severe	71-90 dB	• Hears only amplified speech (with hearing aid or personal amplifier) • May distinguish vowel sounds but not consonant sounds
Profound	91+ dB	• Difficulty hearing even with amplification • Speech and language are distorted

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III. DISCUSSION

Oxaliplatin is one of the most-used agents for colorectal, pancreatic, and gastric cancers, and studies have also shown that oxaliplatin is active in many tumors. However, like other Chemotherapeutic agents Its most common side effects are nausea, diarrhea, myelotoxicity,and peripheral neuropathy.

Oxaliplatin is a third generation cisplatin analog, it is considered to be far less nephrotoxic, and ototoxic compared to cisplatin or carboplatin [2]. These agents damage the outer hair cells of the cochlea, causing hearing loss, vertigo, and tinnitus. Using animal models, Dammeyer et al.[7] reported that cisplatin and oxaliplatin are toxic to the cochlear outer hair cells, and both target thioredoxin reductase in organ of Corti cultures. Nevertheless, fewer than 1% of patients who undergo oxaliplatin treatment develop ototoxicity.[8]

Reddel et al. [8]reported that 72% of patients on cisplatin treatment suffer from ototoxicity. However, the data for oxaliplatin ototoxicity are limited.

To the best of our knowledge, this is the sixth case report of oxaliplatin-induced ototoxicity

Previously, Malhotra et al. have reported a case of acute unilateral ototoxicity following a single intravenous infusion of oxaliplatin that was minimally improved after 2 years of follow-up [9]. Vietor and George have described a case of oxaliplatin-induced ototoxicity and transient hepatotoxicity [10]. Sun Young Oh, Nawal Wasif et al reported a case of hearing loss following the third cycle of gemox [11] ,

Fatima Zahra Hijri , Samia Arifi et al reported a case of Oxaliplatin-Induced Ototoxicity in Adjuvant Setting for Colorectal Cancer after 8 cycles of xelox[12]

The last one is M. Güven Güvenç, Denizhan Dizdar et al they presented a case of Sudden hearing loss after third dose of folfox-cetuximab use in a patient with colon cancer[13]

Comparing the five cases reported in the literature; there is a female predominance in 4 cases/5, in 2 cases the damage was irreversible; and it appears that the ototoxicity occurs at lower cumulative dosage compare to neuropathy which occurs in 10-15% of patients after a cumulative dose of 780 to 850 mg/m2 [14]

IV. CONCLUSION

We believe that although oxaliplatin ototoxicity is rare, physicians must be aware of this important adverse effect, and an audiometric evaluation must be performed when necessary,and if hearing loss is detected, treatment should be stopped immediately.

Further studies of the effects of oxaliplatin on the inner ear are required to clarify the exact relationship between oxaliplatin and hearing loss.

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