

A Side Effect You've Never Heard of: Ototoxicity Associated With Mirtazapine

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Mirtazapine is an antidepressant approved for the treatment of major depressive disorder but commonly prescribed off label for insomnia and anxiety because of its relatively benign safety profile and broad range of effects. It is a tetracyclic antidepressant drug that antagonizes the 5-hydroxytryptamine (5-HT_{2A}), 5-HT_{2C}, and 5-HT₃ serotonin receptors along with α -2 adrenergic auto/heteroreceptors, leading to an overall increase in adrenergic and serotonin activity.¹ Side effects such as weight gain, drowsiness, constipation, and dry mouth are common.² Ototoxicity is incredibly rare. It can manifest as a variety of symptoms, including hearing loss, tinnitus, or auditory hallucinations. It has only been reported twice in the literature, and the aforementioned triad was not fully present in either case.^{3,4} Furthermore, in both cases,^{3,4} ototoxic symptoms began shortly after initiation of the medication.

Here, we present the case of a patient suffering from hearing loss, tinnitus, and musical hallucinations following several months of mirtazapine use. Given the widespread use of mirtazapine, prescribers need to know how to manage medication-induced ototoxicity. Indeed, of drugs associated with ototoxicity, the second largest class is psychotropics.⁵

Case Report

The patient is a 57-year-old woman with a history of type II diabetes, anxiety treated with mirtazapine (45 mg nightly) started 7 months ago, opioid use disorder on methadone, and alcohol use disorder, who presented to the hospital with bilateral hearing loss that is worse on the left side. She was admitted to the medicine service for treatment of uncontrolled type II diabetes and hyperglycemic hyperosmolar state with polyuria and polydipsia. She has had hearing loss for 1 week, associated with new-onset tinnitus and auditory hallucinations (“like music in my ear”). The patient has no past or family history of hearing loss. She denies any vertigo, headaches, or trauma/infections preceding her symptoms. Besides electrolyte values and glucose levels consistent with hyperglycemic hyperosmolar state, the rest of the patient’s medical workup (including vitals, complete blood count, kidney function, and drug levels) was unremarkable. The patient was not receiving any known ototoxic medications besides mirtazapine. Ear, nose, and throat consultation suggested this was the likely culprit, and audiograms were requested.⁵ Mirtazapine was discontinued, and a 15-day steroid taper was started. The steroids were discontinued after 6 days due to worsening paranoia, hallucinations, and agitation

that were suspected to be secondary to steroid-induced psychosis. Initial and final audiograms showed that her hearing loss and associated symptoms largely resolved even with this partial treatment (Table 1).

Discussion

This is the first report, to our knowledge, of mirtazapine-induced ototoxicity where the complete triad of hearing loss, tinnitus, and auditory hallucinations was present. Medication-induced ototoxicity is posited to be due to various factors, including disruption of blood flow, damage to hair cells, and degeneration of the vestibulocochlear nerve.⁶ For mirtazapine, the specific mechanism is unknown. The treatment for all medication-induced ototoxicity is largely the same: discontinuation of the offending agent and then, depending on the severity, a short steroid course.⁷ Here, because of the debilitating nature of the patient’s symptoms, the latter was opted for. Interestingly, a prior report⁴ described this hearing loss as being “irreversible,” whereas our patient’s symptoms did improve. Additionally, this case was unique in that the symptoms started some months following initiation of the medication rather than immediately. This is surprising, as there would have been expected to be a progression of hearing-related symptoms following mirtazapine initiation or some

Table 1.
Audiogram Before and After Steroid Treatment and Mirtazapine Discontinuation

	Left ear results	Right ear results
Audiogram before discontinuation of mirtazapine	Severe rising to moderate mixed hearing loss at 250–8,000 Hz	Moderate most likely mixed hearing loss at 250–500 Hz, mild sensorineural hearing loss at 1,000–2,000 Hz, hearing within normal limits at 4,000–8,000 Hz
Audiogram following discontinuation of mirtazapine and partial steroid course	Left ear: Mild hearing loss at 250–8,000 Hz	Hearing essentially within normal limits at 250–8,000 Hz with the exception of a mild hearing loss at 500 Hz

additional environmental trigger such as trauma or infection causing sudden onset. Further investigation is warranted, potentially involving animal or in vitro models to better understand the pathogenesis of this process given the lack of research into the mechanism of mirtazapine-related ototoxicity. In the meantime, clinicians should add mirtazapine to the existing list of psychotropics that can cause ototoxicity and lend caution to its use in patients at high risk for developing hearing impairment.

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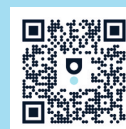
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References

1. Alam A, Voronovich Z, Carley JA. A review of therapeutic uses of mirtazapine in psychiatric and medical conditions. *Prim Care Companion CNS Disord*. 2013;15(5):PCC.13r01525.
2. Anttila SA, Leinonen EV. A review of the pharmacological and clinical profile of mirtazapine. *CNS Drug Rev*. 2001;7(3):249–264.
3. Lee GH, Stewart JT. A case of musical hallucinations related to mirtazapine. *Clin Neuropharmacol*. 2018; 41(6):222–223.
4. Dursun E, Akpinar A, Battal B. Sudden hearing loss associated with mirtazapine therapy: a case report. *Klin Psikofarmakol Bul*. 2009;19(4):417–419.
5. Rizk HG, Lee JA, Liu YF, et al. Drug-induced ototoxicity: a comprehensive review and reference guide. *Pharmacotherapy*. 2020;40(12):1265–1275.
6. Ganesan P, Schmiedge J, Manchaiah V, et al. Ototoxicity: a challenge in diagnosis and treatment. *J Audiol Otol*. 2018;22(2):59–68.
7. Hammill TL, Campbell KC. Protection for medication-induced hearing loss: the state of the science. *Int J Audiol*. 2018;57(suppl 4):S67–S75.

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