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MANAGEMENT OF HEARING LOSS IN A PATIENT WITH MULTIDRUG-RESISTANT TUBERCULOSIS (MDR-TB)

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ABSTRACT

Background: Multidrug-resistant tuberculosis (MDR-TB) remains a major global health concern requiring prolonged treatment with second-line drugs. Aminoglycosides such as kanamycin are still widely used but carry a high risk of ototoxicity that may result in permanent hearing loss. **Case Presentation:** We report a 39-year-old female with rifampicin-resistant pulmonary tuberculosis who developed bilateral progressive hearing loss after two weeks of kanamycin therapy. Otoscopy and tympanometry were normal, but otoacoustic emission (OAE) showed bilateral refer results. Pure tone audiometry revealed severe bilateral sensorineural hearing loss. Kanamycin was discontinued and replaced by an injection-free regimen, and the patient was fitted with bilateral hearing aids to support communication. **Conclusion:** This case emphasizes the importance of baseline and regular audiological monitoring during MDR-TB treatment to detect early ototoxic effects and to allow prompt regimen modification to minimize permanent disability.

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INTRODUCTION

Tuberculosis (TB) remains one of the most significant infectious diseases worldwide, with an estimated 10.6 million new cases and 1.6 million deaths reported in 2021, making it the second leading cause of death from a single infectious agent after COVID-19.[1] Multidrug-resistant tuberculosis (MDR-TB), defined as resistance to at least isoniazid and rifampicin, poses a particular challenge due to its limited treatment options, prolonged duration of therapy, and high toxicity of second-line drugs.[2] The World Health Organization (WHO) estimated that globally there were about 450,000 new cases of MDR-TB in 2021, with Indonesia among the high-burden countries.[3]

Treatment of MDR-TB requires a combination of second-line drugs that are generally less effective and more toxic compared to first-line regimens. Among these, aminoglycosides such as kanamycin and amikacin have been widely used as core injectable agents in many national TB programs.[4] However, their use is strongly associated with ototoxicity, which may lead to irreversible sensorineural hearing loss.[5] The mechanism involves drug accumulation in the inner ear, oxidative stress, mitochondrial dysfunction, and apoptosis of cochlear hair cells.[6]

The prevalence of aminoglycoside-induced ototoxicity varies across regions but remains high. A scoping review from Indonesia reported that 39.3% of MDR-TB patients receiving injectable drugs developed ototoxicity, with kanamycin most frequently implicated.[7] Similarly, international studies have documented hearing loss in up to 41% of MDR-TB patients treated with aminoglycosides.[8,9] Prospective data from Bangladesh even showed that more than 75% of patients developed new hearing loss during kanamycin therapy, often within the first two months.[10]

While most cases of ototoxicity are detected after weeks to months of therapy, early-onset cases are less frequently reported.[3,10] This case highlights an unusual and rapid onset of bilateral sensorineural hearing loss occurring after only two weeks of kanamycin therapy, underlining the importance of baseline and regular audiological monitoring during MDR-TB treatment.

The purpose of this study is to present a case of early-onset bilateral sensorineural hearing loss

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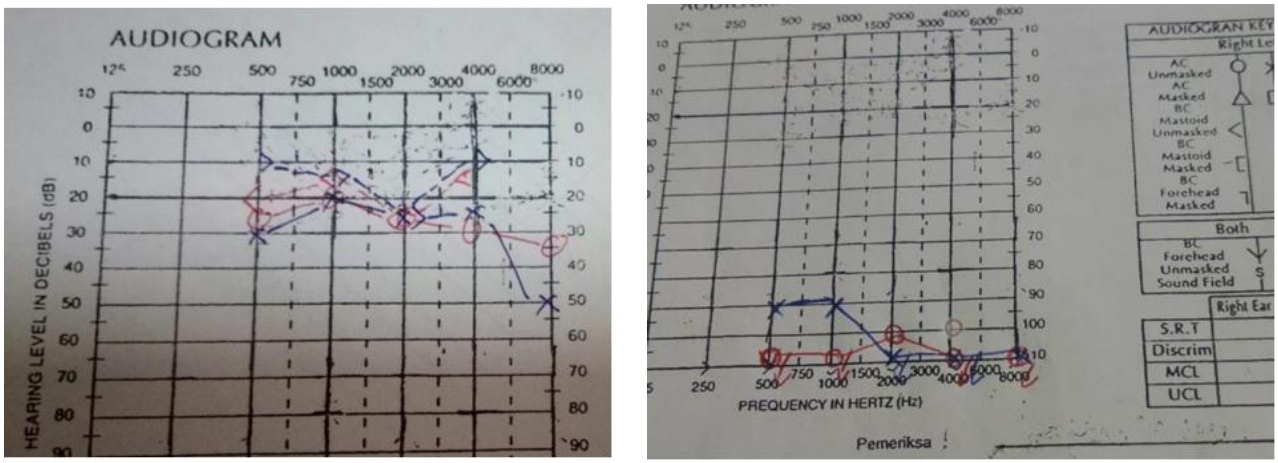
induced by kanamycin in a patient with MDR-TB and to emphasize the importance of baseline and regular audiological monitoring in preventing irreversible disability.

CASE REPORT

A 39-year-old female was diagnosed with rifampicin-resistant pulmonary tuberculosis and was initiated on a kanamycin-based MDR-TB regimen. She had no prior history of ear infections, head

trauma, noise exposure, or use of other ototoxic medications. After two weeks of therapy, the patient reported progressive bilateral hearing loss accompanied by low-frequency tinnitus, which interfered with her daily communication. She denied vertigo, otalgia, or otorrhea. On physical examination, the external auditory canals were clear and tympanic membranes were intact bilaterally. Tuning fork tests revealed Rinne positive bilaterally and Weber test did not lateralize. Tympanometry showed type A curves on both sides, suggesting normal middle ear function. Baseline audiometry performed before treatment had demonstrated normal hearing thresholds across all frequencies.

Follow-up audiological evaluations after two weeks of kanamycin therapy revealed early evidence of ototoxicity. Otoacoustic emission (OAE) testing showed bilateral “refer” results, raising suspicion of cochlear dysfunction. Subsequent pure tone audiometry confirmed severe bilateral sensorineural hearing loss involving both high frequencies and speech frequencies. The antituberculosis regimen was promptly modified by discontinuing kanamycin and switching to an injection-free combination of second-line drugs including moxifloxacin, clofazimine, ethionamide, para-aminosalicylic acid, pyrazinamide, and linezolid. The patient received counseling regarding her condition and was fitted with bilateral hearing aids to support daily communication and quality of life.



(a) (b)

Figure 1. Pure tone audiometry before and after therapy.(a) Baseline audiometry prior to initiation of kanamycin therapy showing normal bilateral hearing thresholds. (b) Follow-up audiometry after two weeks of kanamycin therapy demonstrating severe to profound bilateral sensorineural hearing loss, predominantly at high frequencies and extending into the speech frequency range.

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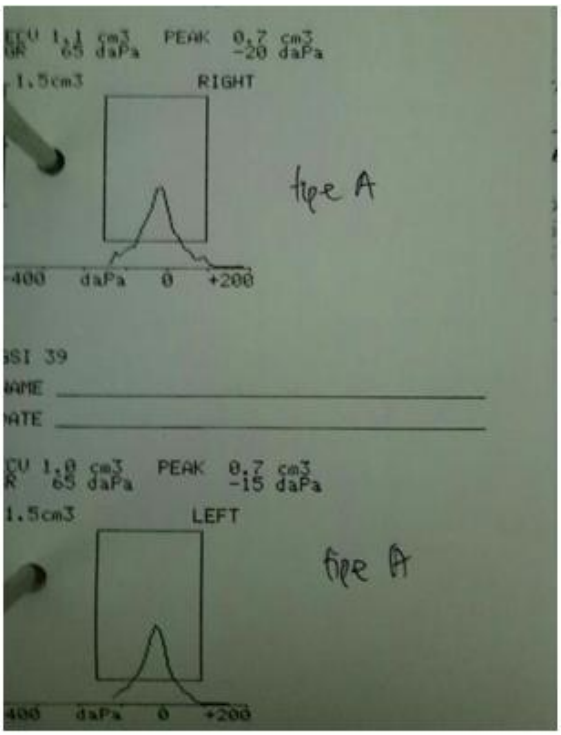


Figure 2. Tympanometry results. Tympanograms of the right and left ear showed a type A curve bilaterally, indicating normal middle ear function.

DISCUSSION

Aminoglycoside-induced ototoxicity remains one of the most serious and feared adverse effects of multidrug-resistant tuberculosis (MDR-TB) treatment. MDR-TB itself continues to be a global health challenge, with approximately 450,000 new cases reported in 2021, and Indonesia is listed among the high-burden countries by the World Health Organization (WHO).[1] Aminoglycosides such as kanamycin and amikacin, although effective in suppressing Mycobacterium tuberculosis, have been consistently linked to irreversible sensorineural hearing loss due to their ototoxic potential.[2] The ototoxic effect is primarily explained by drug accumulation in the cochlea, oxidative stress, mitochondrial dysfunction, and apoptosis of outer hair cells, particularly at the basal turn of the cochlea, resulting first in high-frequency loss which can progress into the speech frequency range.[4-6]

In this case, ototoxicity developed unusually early, within only two weeks of kanamycin initiation, whereas most reported cases occur after one to three months of treatment.[3] Early-onset case, though rare, have been described in Bangladesh and other high-burden settings, especially where kanamycin is part of the initial regimen.[3] A scoping review in Indonesia showed that the prevalence of aminoglycoside-induced ototoxicity ranged between 20–46%, most frequently associated with kanamycin use.[7,10] Similarly, studies from South Africa and Namibia confirmed high ototoxicity rates, especially in patients with HIV co-infection or renal impairment.[8,9]

A systematic review reported by Dillard et al. estimated that globally around 40% of MDR-TB patients exposed to aminoglycosides develop some degree of hearing loss[2]. Several risk factors contribute to the severity and likelihood of ototoxicity. These include cumulative dose, prolonged treatment duration, renal dysfunction, advanced age, HIV co-infection, and genetic susceptibility, such as mitochondrial mutations.[5,6,11] In this patient, despite the absence of overt comorbidities, severe bilateral hearing loss still occurred rapidly, highlighting that even short exposure can be sufficient to trigger toxicity. Harris et al. emphasized that HIV-positive patients had a higher risk of aminoglycoside-related hearing loss compared to HIV-negative counterparts.[8] Moreover, studies in other resource-limited settings have demonstrated that inadequate audiological monitoring programs significantly delay detection and intervention, further worsening outcomes.[12,13]

There is currently no proven therapy to reverse aminoglycoside-induced ototoxicity, making prevention and early detection crucial. Recommended strategies include baseline audiometry, high-frequency audiometry, and otoacoustic emission prior to therapy, with regular monitoring throughout treatment.[4,14] WHO now advocates for all-oral MDR-TB regimens, prioritizing bedaquiline, linezolid, and delamanid, thereby avoiding aminoglycosides and reducing ototoxic risks.[1,15] Supportive management with hearing aids or cochlear implants is often necessary once damage has occurred.[16] Experimental approaches, such as antioxidant supplementation and intratympanic therapies, are being studied but remain investigational.[17,18] Strengthening ototoxicity monitoring programs, particularly in high-burden countries such as Indonesia, is critical to minimize permanent disability and improve the quality of life for MDR-TB patients.[7,19,20]

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CONCLUSION

Kanamycin can cause rapid onset irreversible sensorineural hearing loss even within weeks of initiation. This case emphasizes the need for early baseline audiological evaluation and regular monitoring during MDR-TB treatment. Timely modification of therapy is critical to prevent permanent disability and improve quality of life. This case highlights the importance of routine audiological monitoring and provides evidence of early-onset ototoxicity in MDR-TB therapy in Indonesia.

ETHICAL APPROVAL

This study is a case report and did not involve any experimental intervention or data collection from human subjects beyond routine clinical care. Therefore, ethical approval was not required. Patient consent for publication of anonymized clinical information and audiological findings was obtained.

CONFLICTS OF INTEREST

The authors declare no conflict of interest related to the materials, methods, or findings of this study. No personal or financial relationships could be perceived as influencing the interpretation of the results.

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AUTHOR CONTRIBUTIONS

Conceptualization: I.G.A.M. Danastri and K.T.M.N. Pinatih; Methodology: I.G.A.M. Danastri; Data curation: I.G.A.M. Danastri; Writing—original draft preparation: I.G.A.M. Danastri; Writing—review and editing: K.T.M.N. Pinatih; Supervision: K.T.M.N. Pinatih. All authors have read and approved the final manuscript.

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