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Case Report

Primary Bilateral Tuberculous Otitis Media After Kidney Transplantation: A Case Report

Jeon Mi Lee[1*], Keun-Woo Jung[1*], Ki-Won Kim[1], Gilmoon Lee[1], Han Seong Kim[2]

[1]Department of Otorhinolaryngology, Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea
[2]Department of Pathology, Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea

ORCID iDs of the authors: J.M.L. 0000-0003-2793-9045, K.-W.J. 0000-0002-6092-7348, K.-W.K. 0000-0002-8107-3409, G.L. 0009-0005-3334-0145, H.S.K. 0000-0003-3740-0588.

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We report a case of primary bilateral tuberculous otitis media in a patient who underwent kidney transplantation. This case presents unusual clinical features and histopathology from those of classical tuberculous otitis media. A 75-year-old woman presented at the clinic with purulent ear discharge and hearing loss in both ears. She had undergone kidney transplantation 6 years prior and had been taking immunosuppressant medications. Otoscopic examination and imaging studies suggested acute otitis media, which was irresponsive to antibiotics. The patient underwent surgery to eradicate the disease, and histopathologic examination revealed multifocal granulomas with Langhans giant cells without caseous changes. Ziehl–Neelsen staining and polymerase chain reaction confirmed the diagnosis of tuberculous otitis media.

While tuberculous otitis media is a very rare manifestation of extrapulmonary tuberculosis, this case is more noteworthy in that it occurred as a primary infection rather than as a reactivation of a prior infection. In addition, it did not show the classical triad of clinical manifestations, which occurred bilaterally, and its histopathology was different from those of classical tuberculous otitis media. This case presents a new clinical variation in tuberculous otitis media.

KEYWORDS: Tuberculosis, extrapulmonary tuberculosis, suppurative otitis media, immunocompromised patients, mixed hearing loss

INTRODUCTION

Tuberculosis (TB) is a major health threat worldwide. Immunocompromised patients, including those who undergo organ transplantation, are at a high risk of TB. The prevalence of TB among organ transplant recipients is up to 15%,[1] and the mortality rate is up to 30%.[2] The most common cause of posttransplant TB is reactivation of a prior infection. Rarely, it can be acquired from a donor organ, or opportunistically acquired in TB endemic regions. The most common presentation is pulmonary involvement, but the proportion of extrapulmonary manifestations is higher in transplant recipients than in the general population.[3] Among those, tuberculous otitis media (TOM) is a very rare manifestation.

The classical triad of TOM includes painless otorrhea, multiple tympanic perforations, and facial palsy, but recent reviews emphasize that clinical features are more variable than the triad. Moreover, due to low mycobacterial counts in extrapulmonary TB, the positivity for TB from ear discharge culture is 5%-44%.[4] Temporal bone computed tomography (TBCT) is also not diagnostic, as it is hardly different from common otitis media.[5] Due to its rarity and variable clinical presentation, diagnosis of TOM is often delayed. This can lead to severe complications, such as permanent hearing loss, facial palsy, meningitis, and labyrinthitis.[6] An immunocompromised state can make the symptoms ambiguous, thus complicating the diagnosis.

Herein, we report a case of primary bilateral TOM in a patient who underwent kidney transplantation. This case presents unusual clinical features and histopathology from those of classical TOM. This report may serve as a new clinical variation in TOM.

CASE PRESENTATION

This study was approved by the Institutional Review Board of Inje University Ilsan Paik Hospital (ISPAIK 2022-11-002), and informed consent was obtained prior to the writing of this case report.

*These authors contributed equally to this work.
Corresponding author: Jeon Mi Lee, e-mail: entmeowmiya@gmail.com

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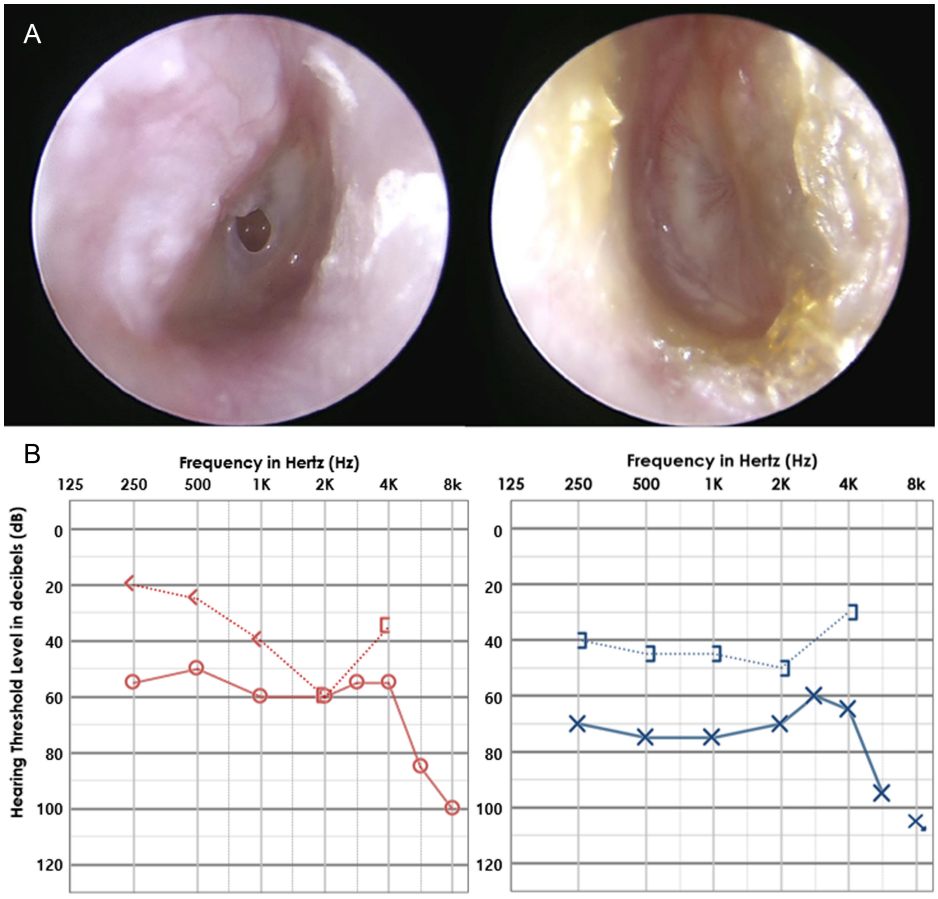

Figure 1. Preoperative findings. (A) Otoscopic examination shows a small perforation with pumping otorrhea on the right eardrum and a bulging left eardrum. (B) Pure-tone audiometry testing revealed mixed hearing loss on both sides.

A 75-year-old woman presented with purulent discharge from the right ear and hearing loss in both ears for a month. She had no history of chronic otitis media or evidence of eardrum perforation prior to the event. She had hypertension and diabetes and underwent kidney transplantation 6 years prior. The tuberculin test performed before transplantation was negative. She had been taking immunosuppressants since transplantation.

Otoscopic examination revealed a small central perforation of the right tympanic membrane (TM) with pumping otorrhea and a bulging left TM (Figure 1A). Pure-tone audiometry indicated moderate mixed hearing loss on both sides (Figure 1B). Her previous hearing level was normal bilaterally. TBCT demonstrated soft tissue density on both sides of the middle ear space and mastoid cavity, indicating acute mastoiditis. The bacterial culture test from the middle ear revealed methicillin-resistant *Staphylococcus epidermidis* and *Corynebacterium*; therefore, the patient was admitted for intravenous vancomycin injection with regular ear cleansing.

MAIN POINTS

- We present a rare instance of primary bilateral tuberculous otitis media (TOM).
- Unusual clinical features and histopathology can be found in immunocompromised patients.
- When acute otitis media is unresponsive to standard antibiotic therpy, clinical vigilance for TOM is essential, especially in immunocompromised patients.

One day after admission, the left ear developed a small central perforation and was discharged. The patient did not respond to the 1-week-administration of vancomycin. For the following 2 weeks, ceftazidime and fluconazole were added; however, the symptoms persisted, and serial TBCT revealed no changes. The hearing level on the left side further decreased, and the patient decided to undergo a left-sided mastoidectomy to surgically eradicate the disease. During the surgery, pale granulation was noted in the mesotympanum and mastoid cavity, which was sent to the pathology department for histopathological analysis. Ossicles were surrounded by granulation. After all the granulation was removed, it was confirmed that the incus–stapes were dislocated due to the erosion of the lenticular process of the incus. The incus and malleus head were removed and the ossicle chain was reconstructed using a partial ossicular replacement prosthesis. The perforated TM was repaired with the deep temporalis muscle fascia using the underlay technique. Harvested tragal cartilage was interposed between the prosthesis and TM to discourage extrusion. After packing the ear canal with gel foam, the operation ended.

Histopathological examination revealed multifocal granulomas with Langhans giant cells, without caseous changes (Figure 2A).

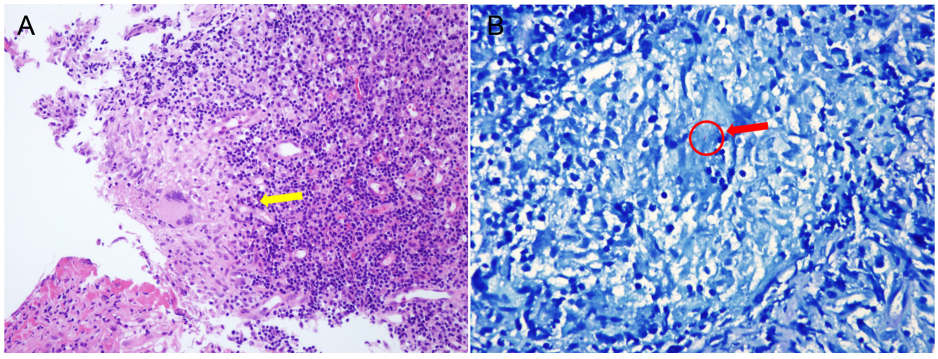

Figure 2. Histopathological examination findings. (A) Granuloma with Langhans giant cells is observed under a light microscope (arrow, H&E, ×200). (B) Acid-fast bacillus is noted in the granulomatous lesion (arrow, ×400, Ziehl–Neelsen stain).

Ziehl–Neelsen staining of the biopsy material revealed scanty acid-fast bacilli in the granulomatous lesions (Figure 2B), and polymerase chain reaction identified *Mycobacterium tuberculosis*, leading to the diagnosis of acute TOM. Chest x-ray imaging and sputum culture were performed to determine the involvement of other organs, such as the lungs, which were all unaffected.

The patient commenced anti-tuberculosis therapy while continuing to take immunosuppressants. She started with the HERZ regimen (isoniazid 300 mg, ethambutol 800 mg, rifampin 500 mg, and pyrazinamide 25 mg daily), but due to severe abdominal pain and nausea, she was switched to the HR regimen (isoniazid and rifampicin) at 1 month. After 2 months of administration, the patient clinically improved with no ear discharge from the right side. However, in the third month of drug administration, multiple perforations were newly developed on the left side without ear discharge (Figure 3A). Anti-tuberculosis therapy was discontinued after 6 months of drug administration. The perforations of both TMs persisted without ear discharge, and the hearing level hardly changed from the initial evaluation (Figure 3B). Tympanoplasty was recommended to improve hearing and prevent infection, but the patient refused and used a hearing aid.

DISCUSSION

This is a case report of TOM in a patient who underwent kidney transplantation. While TOM is a very rare manifestation of extrapulmonary

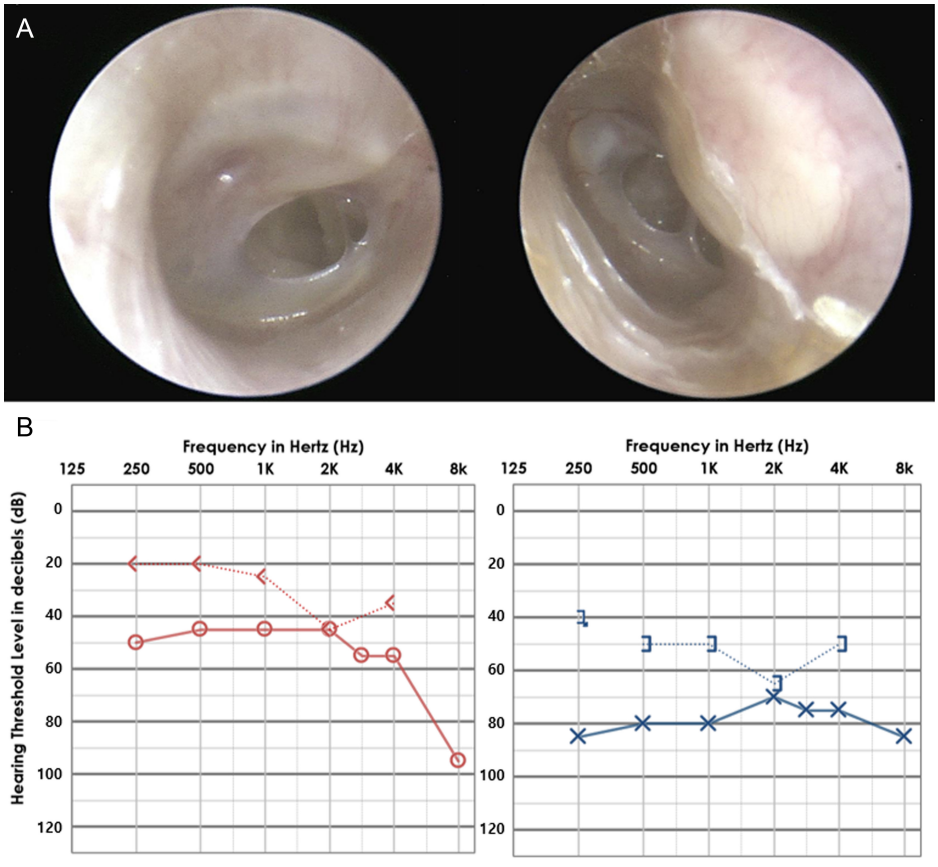

Figure 3. Postoperative findings. (A) Multiple perforations were newly developed on the left side without ear discharge. (B) Hearing level hardly changes from the initial evaluation.

TB, this case is more noteworthy in that it occurred as a primary infection rather than as a reactivation of a prior infection. In addition, it presented bilaterally with unusual clinical features and histopathology compared to those of classical TOM. Only a little information is available for bilateral TOM, and the reported cases have a variety of aspects. It occurs in immunocompromised patients,[7] as well as in healthy young patients.[8] It not only develops severe clinical manifestations, such as bilateral facial palsy or meningitis,[9,10] but also presents as minor symptoms, such as conductive hearing loss with otorrhea.[11] Although the number of cases is too small to elucidate the general characteristics of bilateral TOM, it should be recognized that TOM can appear in a bilateral form.

Histopathological findings were also notable. In this case, the multifocal granuloma consisted of epithelioid and lymphoid cells with Langhans giant cells, without caseous necrosis. TB lesions are usually characterized by typical caseous necrotic granulomas. We suggest 3 hypotheses to explain this atypical pathological finding. First, the administration of immunosuppressants may have induced an insufficient immune reaction to form necrosis. This could be supported by Kumer, who suggested a relationship between necrotic changes in TB granulomas and immune reactions based on the fact that myeloid-derived suppressor cells increased in non-necrotic TB granulomas compared to necrotic TB granulomas.[12] As in this case, non-caseous necrosis has been reported in a biopsy of a patient infected with TB after kidney transplantation.[13] One study reported that a patient with human immunodeficiency virus-1 (HIV-1) and pulmonary TB showed the presence of fewer necrotic granulomas and less pulmonary cavitations.[14] On the other hand, completely opposite results have been reported that HIV-1 and TB co-infected patients have more poorly formed and necrotic lymph nodes than HIV-1 negative patients. This discrepancy may be due to different stages of immunosuppression. Although it is recognized to some extent that the granulation formation pattern varies according to immunity, further research is needed on the exact mechanism. Second, the size of the granuloma is limited in the middle ear compared to the lung. As the size of the granuloma increases, the blood supply into the granuloma decreases thus leading to caseous necrosis.[12] Therefore, the middle ear might not be anatomically prone to caseous necrosis. In a study of 10 cases of TOM, only 5 cases showed necrotic patterns.[15] This is in contrast to a report on TB lymph node pathology in 100 immunocompetent patients, where 73% of cases showed caseous necrosis; as a result, the proportion for non-caseous necrosis is thought to be much higher in TOM.[16] However, many cases of TOM have also reported caseous changes in pathology. Furthermore, there is no evidence that non-caseous necrosis is more common in TB infections that occur in confined spaces such as the paranasal sinuses or nasal cavities. Further research on pathological differences according to anatomy should be considered. Third, it is possible that caseous necrosis had not yet occurred. The time from the onset of symptoms to diagnosis was 3 months. This might not be sufficient time for necrosis to occur.

This case presents a new clinical variation in TOM. It did not show the classical triad of clinical manifestations, which occurred bilaterally, and its histopathology was different from those of classical TOM. This case also highlights the diagnostic challenge of TOM due to the rarity of the disease, nonspecific clinical manifestations, and low sensitivity of microbiological tests for ear discharge. When acute otitis media is unresponsive to standard antibiotic therapy, clinical vigilance for TOM is essential, especially in immunocompromised patients.

Ethics Committee Approval: This study was approved by the Institutional Review Board of Inje University Ilsan Paik Hospital (IRB number: ISPAIK 2022-11-002)

Informed Consent: Informed consent was obtained from the patient who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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Declaration of Interests: The authors have no conflicts of interest to declare.

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