CASE REPORT

# A Diagnostic Odyssey of Unusual Presentation of Left Concurrent TB and Fungal Otitis Media with Skull Base Osteomyelitis: A Case Report

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**ABSTRACT**

Concurrent tuberculosis and fungal otitis media complicated with skull base osteomyelitis is a rare and intricate clinical entity, particularly in well-controlled diabetes mellitus patients with unusual symptomatology. We present the case of an elderly gentleman with well-controlled type II diabetes mellitus who endured four months of chronic left ear pain, left-sided temporal headaches, and left ear pulsatile tinnitus, which persisted despite multiple courses of antibiotics. Initial investigations yielded conflicting suggestions, indicating the possibility of either an infection or the presence of a glomus tumor. However, intraoperative samples sent for microbiological and histological investigation revealed the presence of Aspergillus Niger and Mycobacterium complex. Treatment with antifungal and antituberculosis agents led to a remarkable improvement in the patient's clinical symptoms and radiological and biochemical markers.
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## INTRODUCTION

Skull base osteomyelitis (SBO) is a rare yet lethal clinical entity caused by osteomyelitis at the area of the skull base, which usually affects immunocompromised patients (1). This disease is usually caused by bacterial or fungal infections, with the former being more common (1). Tuberculous otitis media is a rare form of extrapulmonary TB, accounting for 0.04-0.9% of chronic suppurative otitis media (CSOM) (2). For fungal causes, *Aspergillus Fumigatus and Flavus* are amongst the most identified fungal species causing SBO. However, *Aspergillus Niger* is less commonly reported as a cause of the invasive disease (3)

## CASE REPORT

We present a case of a 66-year-old Malay gentleman with well-controlled Type 2 Diabetes Mellitus (T2DM) who presented to our center with a four-month history of persistent, severe, throbbing left ear pain. He rated the pain 'eight' on the pain scale, and the pain frequently awoke him from sleep. Accompanying symptoms included reduced hearing in the left ear, persistent pulsatile tinnitus, and a throbbing left-sided headache. He sought medical care at multiple healthcare centers and was prescribed numerous courses of antibiotics. However, his symptoms persisted. There was no history of ear discharge, vertigo, rhinosinusitis symptoms, diplopia, fever, persistent cough, recent sick contacts, or constitutional symptoms. Clinical examination revealed a normal left external auditory canal with an intact but dull, pulsatile tympanic membrane. Nasal and throat examinations were normal, and all cranial nerves were intact. Laboratory investigations revealed elevated inflammatory markers with raised erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) exceeding 140. Given the suspicion of SBO, commonly caused by *Pseudomonas*, the patient was empirically treated with ciprofloxacin. High-resolution computed tomography (HRCT), done in January 2023, revealed a soft tissue within the left middle ear cavity with an enhancing lesion at the jugular foramen region.

Opacification of mastoid air cells was observed with intact tegmen tympani and scutum. Radiologically, the image raised suspicions of a glomus tumor. Magnetic resonance imaging (MRI) of the brain and internal auditory meatus was done to further assess the lesion. Apart from enhanced lesions within the left middle ear cavity (Fig.1 and Fig. 2) and parapharyngeal space, marrow changes were observed over the skull base region (clivus, petrous apex, and occipital condyle), which were suggestive of SBO or pseudotumor. Pure tone audiometry (PTA) showed asymmetrical hearing loss where there was moderate to profound mixed hearing loss of the left ear with mild to severe sensorineural hearing loss of the right ear (Fig. 3). We performed a left exploratory tympanotomy, revealing only mucoid fluid within the middle ear without mucopus, granulation tissue, mass, or keratin. The ossicles were found to be intact. Subsequently, a grommet tube was inserted to drain any residual fluid. Additionally, an endoscopic biopsy was conducted over the left parapharyngeal region due to enhancing lesions as reported on MRI and CECT neck. Post-operatively, the patient continued to experience left ear pain, but tinnitus resolved. Oral ciprofloxacin was continued for a total duration of six weeks while waiting for the intraoperative sample results. Microbiological analysis of middle ear fluid revealed *Aspergillus Niger*, while fluid acid-fast bacilli (AFB) was negative. Middle ear fluid for cytology showed no evidence of malignancy. The histological analysis of the left parapharyngeal tissue biopsy was negative for malignancy, but tissue culture and sensitivity from the left parapharyngeal region revealed non-sporulating hyaline dematiaceous organisms. As the fungal culture yielded *Aspergillus Niger*, we consulted with an Infectious Disease (ID) physician, prompting the initiation of oral itraconazole therapy for six weeks. Clinically, the patient became asymptomatic upon completion of antifungal treatment, and there was a marked improvement in ESR and CRP levels. A follow-up HRCT temporal and CECT neck after completion of six weeks of antifungal demonstrated the absence of previously observed enhancing lesions in the left middle ear cavity and jugular fossa (Fig. 4) with resolving left parapharyngeal soft tissue enhancing lesion seen in the previous CT scan.

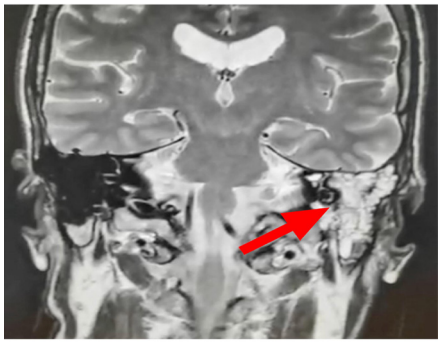

**Fig. 1: Coronal view of T2 weighted MRI image showing hyperintense signal within the left middle ear cavity (red arrow).**

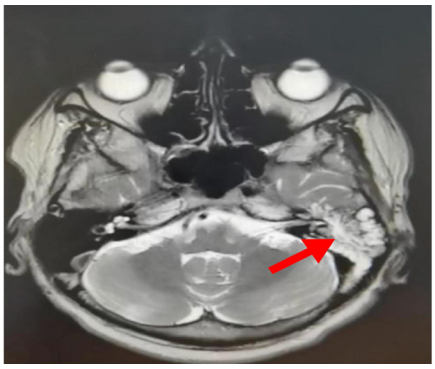

**Fig. 2: Axial view of T2 weighted MRI image showing hyperintense signal within the left mastoid region (red arrow).**

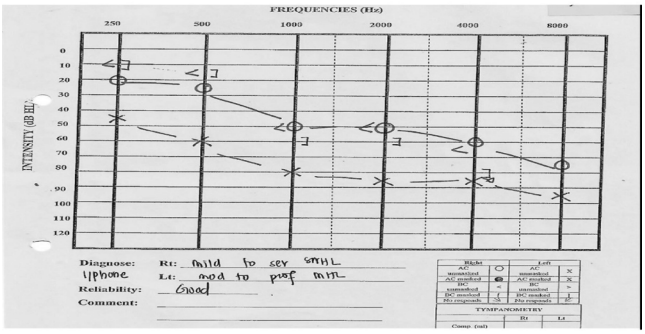


**Fig. 3: PTA during the patient's initial presentation. The right ear showed mild to severe sensorineural hearing loss, while the left ear showed moderate profound mixed hearing loss. Conductive hearing loss over the left ear can be seen from 250Hz to 2000Hz.**

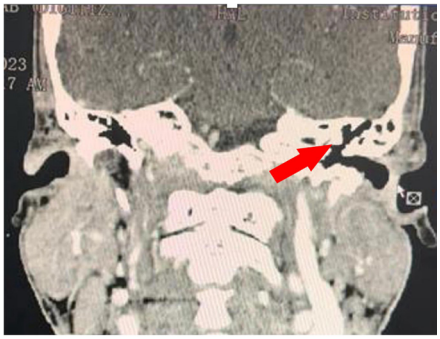

**Fig. 4: Coronal view from follow-up HRCT temporal showed clear left middle ear cavity (red arrow).**

There was also a marked reduction in the heterogeneous lesion over the left parapharyngeal space, with irregularities noted over the cortical part of the petrous apex. After Discussion with the infectious disease team (ID physician), oral Itraconazole was continued for a total duration of three months to treat the fungal SBO. Three months after the initial evaluation, the left middle ear fluid and left parapharyngeal tissue samples sent for TB PCR returned positive for Mycobacterium complex, leading to a referral to the respiratory team for anti-TB treatment. Other TB investigations, including CXR, Mantoux test, and sputum AFB, were all negative for TB (Table I). Due to positive TB PCR, the patient was started on an anti-TB regimen together with the ongoing oral itraconazole regime. He is planned for two months

intensive phase and six months maintenance for TB treatment. The patient is still having ongoing follow-up. As of now, the most recent HRCT temporal and CECT neck scans, following the completion of the intensive phase of the anti-TB regimen, revealed remarkable radiological improvement. The left middle ear cavity and jugular fossa appeared clear, and the left parapharyngeal space looked normal. Furthermore, his symptoms have completely resolved, and biochemical results are now within the normal range (Table II).

**Table I: Intraoperative sample results**

| Intraoperative Samples (9/5/2024) | | |
|---|---|---|
| **Middle Ear Fluid** | Fluid C&S | Bacilus sp |
| | Fungal C&S | Aspergillus niger |
| | MTB C&S | negative |
| | TB PCR | Mycobacterium tuberculosis complex detected |
| | Fluid AFB | negative |
| | Fluid for cytology | no malignancy seen |
| **Nasopharynx Tissue (Left Fossa Of Rosenmuller)** | tissue C&S | Non Sporulating hyaline/ dematiceous mold isolated |
| | Tissue Fungal PCR | negative |
| | Tissue MTB C&S | negative |
| | Tissue TB PCR | Mycobacterium tuberculosis complex detected |
| | Tissue for HPE | No malignancy, granuloma or fungal body seen |

**Table II: Investigation results**

| Investigation Results | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Types Of Investigations** | **Date** | 11-Jan | 07-May | 08-May | 14-May | 16-May | 17-May | 21-May | 22-May | 30-May | 12-Jun | 25-Jun | 20-Jul | 25-Jul | 26-Jul | 27-Jul | 07-Aug | 24-Aug |
| Full Blood Count | Haemoglobin | | 12.3 | | | | | | | | | | | | | | | 12.3 |
| | Total White Count | | 9.4 | | | | | | | | | | | | | | | 7.6 |
| | Platelet | | 306 | | | | | | | | | | | | | | | 295 |
| Renal Profile | Urea | | 3.8 | | 3.3 | | 3.4 | 4 | | | | | | | | | | 2.5 |
| | Sodium | | 147 | | 139 | | 137 | 137 | | | | | | | | | | 140 |
| | Potassium | | 4.9 | | 3.5 | | 3.7 | 4.1 | | | | | | | | | | 4.1 |
| | Creatinine | | 67 | | 64 | | 56 | 70 | | | | | | | | | | 87 |
| Liver Function Test | Albumin | | | | | | | | | 30 | 31 | 33 | 36 | | | | 37 | |
| | ALP | | | | | | | | | 78 | 90 | 83 | 92 | | | | 102 | |
| | ALT | | | | | | | | | 9 | 15 | 20 | 14 | | | | 18 | |
| Glucose | HbA1C | | | 11 | | | | | | | | | | | | | | |
| Inflammatory Markers | ESR | >140 | >140 | | 86 | | | | 102 | | 82 | 31 | 52 | | | | | |
| | CRP | 40 | 38.5 | | 30.3 | | | | 24.4 | | 13.8 | 2.4 | 1.4 | | | | | |
| Microbiological Investigations | Sputum For AFB | | | | | | | | | | | | | x1: negative | x2: negative | x3: negative | | |

## DISCUSSION

This case report presents a rare infection involving concomitant fungal and tuberculous otitis media with SBO. The clinical presentation of this entity was also atypical, which led to difficulty in establishing the diagnosis. Tuberculosis of the middle ear, a seldom reported entity, usually presents as painless otorrhea, multiple tympanic perforations, abundant granulation tissue, bone necrosis, and severe hearing loss (2). Diagnosing this infection via ear discharge for acid-fast bacilli (AFB) smear positivity is challenging. Based on Alli O et al., it is found that the Polymerase Chain Reaction (PCR) assay is more sensitive (75.5%) and specific (94.8%) than microscopy in detecting Mycobacterium tuberculosis complex from clinical samples (4). This is demonstrated in our case, where all TB investigations except for TB PCR were negative.

SBO is an inflammatory process that affects the bone of the skull base, often resulting from adjacent infections in the middle ear, mastoid, and sinuses (1). Early SBO symptoms are nonspecific. Patients may present with headaches, cranial nerve palsies, meningitis, and signs of intracranial pressure of venous thrombosis (1). Notably, our patient did not present with cranial nerve palsy or typical tubercular otitis media symptoms, highlighting the importance of considering tubercular SBO in cases without typical tubercular otitis media symptoms and refractory to medical therapy.

*Aspergillus* is amongst the most identified fungal species causing SBO with considerable high morbidity and mortality up to 50%, in which most infections are attributed to *Aspergillus fumigatus, Aspergillus Flavus*, and *Aspergillus Terreus. Aspergillus Niger* is less commonly reported as a cause of invasive cases (3). Discussion with the ID team led to the commencement of Itraconazole, to which the patient responded, thus supporting our diagnosis.

Radiological evaluation plays a critical role in the diagnosis of SBO. In our case, the initial HRCT temporal was suggestive of a glomus tumor, adding to the complexity of the diagnosis. However, despite being radiologically suggestive, we did not completely rely on HRCT findings for diagnosis as we would not expect elevated acute phase reactants with benign neoplasm.

While the standard diagnostic procedure for SBO involves biopsy to rule out malignancy and histopathologic confirmation, this is often challenging due to the proximity of the involved bone with vital neurologic structures. In our case, the conflicting symptoms and radiological findings necessitated an accurate microbiological and histological diagnosis.

## CONCLUSIONS

Concomitant fungal and tubercular otitis media with SBO is rare. It can be challenging to diagnose; thus, histopathology samples taken must include TB and fungal workup, especially after failure of multiple courses of antibiotics. The management may require a combination of appropriate antibiotic, antifungal, and antitubercular therapy, along with surgical intervention, such as surgical drainage of abscesses and sometimes surgical debridement of infected bone, when necessary.

## ACKNOWLEDGEMENTS

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