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CASE REPORT

Mycobacterium tuberculosis of the temporal bone

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ABSTRACT

Tuberculous otitis media (TOM) is a rare manifestation of tuberculosis (TB) caused by *Mycobacterium tuberculosis*. A case of a 64-year-old female and challenges involved in arriving at the diagnosis of TOM is presented. The patient had surgery for suspected complicated cholesteatoma, but given intraoperative findings and clinical suspicion, investigations were performed to exclude multiple differential diagnoses, including TOM. Initial histopathological finding showing necrotising granulomata was suspicious for TB, but initial samples were culture negative. However, in the absence of alternative diagnoses and high pre-test probability the patient was commenced on empirical treatment. During therapy, a sample of ear cerumen was sent for mycobacterial culture and was found to be culture positive for *M. tuberculosis*, confirming the diagnosis. To our knowledge, this is the first case to report *M. tuberculosis* cultured from ear cerumen. The patient is being treated with six months of therapy and is showing improvement with resolution of symptoms.

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KEYWORDS
Tuberculous otitis media; temporal bone; ear wax

Background

Tuberculosis (TB) is an important and relevant communicable disease as it remains a major cause of morbidity and mortality globally [1]. In 2018, there were an estimated 1.7 billion people worldwide infected with *Mycobacterium tuberculosis* [2], of which it caused active disease in 10 million people, and the death of 1.5 million people [3]. Despite a decrease in incidence of 2% per year, TB is thought to have re-emerged in developed countries recently due to emigration from countries of a high incidence, immunodeficiency, and anti-TB drug resistance [4]. According to the World Health Organisation (WHO), in Australia the total TB incidence is estimated at 6.6 per 100,000 population [5]. TB is classified into either pulmonary or extrapulmonary TB (EPTB), and can theoretically affect all parts of the body [6]. The organ most commonly affected is the lung – with pulmonary TB accounting for 90% of presentations [7]. EPTB is less common. Ear, nose and throat (ENT) manifestations of TB, excluding cervical lymphadenopathy, only account for 2–6% of EPTB, and less than 1% of all TB cases [8]. In particular, TB of the ear or temporal bone is one of the rarest forms of TB. Tuberculous otitis media (TOM) is reported in approximately 0.05–0.9% of chronic middle ear infections [8–11].

This case demonstrates the diagnostic challenges involved in patients with TOM and describes the unusual way in which TB was formally diagnosed. There are several published case reports of TOM. However, on review of the literature, and to our knowledge, this is the first case to identify culture of *M. tuberculosis* from ear wax in a suspected patient.

Case presentation

A 64-year-old female presented with a five-month history of tinnitus in her left ear followed by otorrhoea, otalgia and hearing loss. She had no other systemic symptoms, such as cough, dyspnoea, sinonasal congestion, rash or joint pain. She denied any unintentional weight loss and there were no previous episodes of ear infections or ear surgery. Her only relevant past medical history was gastric oesophageal reflux disease which had been treated with pantoprazole. She had no known allergies. She was a non-smoker and was otherwise fit and well. The patient had migrated from the Philippines to Australia two

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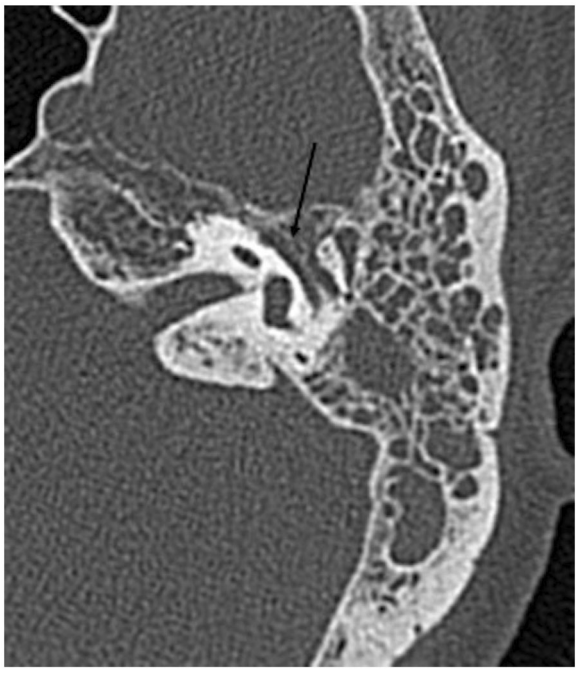

Figure 1. High-resolution axial CT scan of the left temporal bone showing an opacified middle ear, antrum and mastoid with no ossicular erosion or erosion of the cortical bone. Arrow indicates the tympanic segment of the facial nerve.

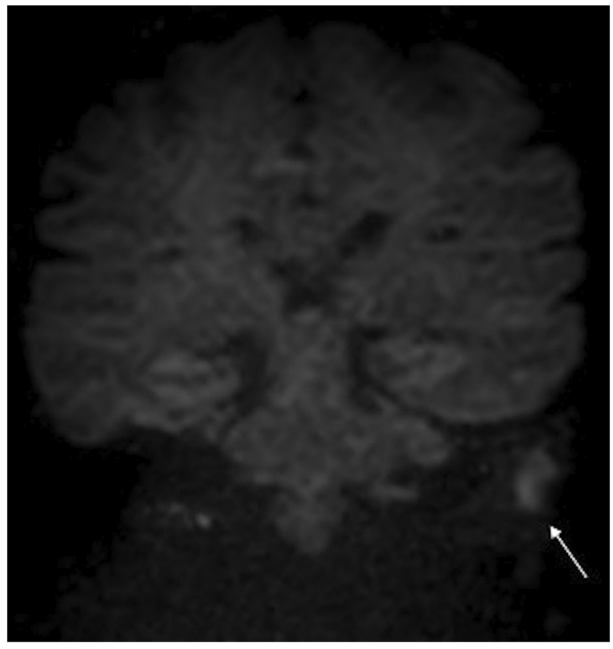

Figure 2. Diffusion-weighted imaging (DWI) MRI scan of the brain showing a 16 mm area of diffusion restriction in the region of the left temporal bone (arrow). This was initially suggestive of a possible cholesteatoma.

years prior to presentation with no other recent travel history. She was a volunteer at a residential aged-care facility.

She was initially assessed by her general practitioner who prescribed oral antibiotics and antibiotic ear drops for a presumed otitis media, with a further course of oral antibiotics after showing no symptomatic improvement. She was subsequently referred onto an ENT Specialist who assessed her clinically. She was noted to have an unusually opacified tympanic membrane that was bulging and thickened but intact, and her audiogram showed a profound sensorineural hearing loss (SNHL). There was no attic retraction, granulation or purulent debris. Her facial nerve function was normal, as was her vestibular examination.

Investigations and treatment

A high-resolution CT scan of the temporal bone and magnetic resonance imaging (MRI) was performed. The CT scan showed complete opacification of the left middle ear and mastoid, thought to be due to a combination of both mucosal thickening and fluid (Figure 1). The MRI scan showed a 16 mm focus of diffusion restriction within the posterosuperior epitympanum, mastoid aditus and antrum, suggestive of a possible cholesteatoma (Figure 2). The MRI scan also showed involvement of the eustachian tube (Figure 3). The CT scan of the temporal bones, however, showed no evidence of ossicular or scutal erosion typically seen in patients with cholesteatoma or chronic suppurative otitis media.

Given the profound SNHL and the possibility of complicated cholesteatoma, the patient underwent an urgent left intact canal wall mastoidectomy and tympanoplasty. Intraoperatively there was extensive granulation tissue in the left mastoid cavity extending into the antrum and middle ear, with a well-pneumatised mastoid cavity. Anterosuperior and anteroinferior tympanic membrane perforations were present together with dehiscence of the tympanic segment of the facial nerve which was stimulating normally. The long and short processes of the incus were eroded and the stapes superstructure was intact but surrounded by granulation tissue. Intraoperative tissue samples, including granulation tissue of middle ear and mastoid, were sent for histopathology, cytology, immunophenotyping and microbiological testing. The patient's postoperative course was uncomplicated.

The initial samples showed no evidence of malignancy or lymphoproliferative disorder. In addition, there were no bacteria, acid-fast bacilli (AFB) or fungal organisms identified. However, histology of the specimens showed necrotising granulomatous inflammation. An autoimmune and inflammatory screen including the antinuclear cytoplasmic antibody (ANCA), antinuclear antibody (ANA), anti-double

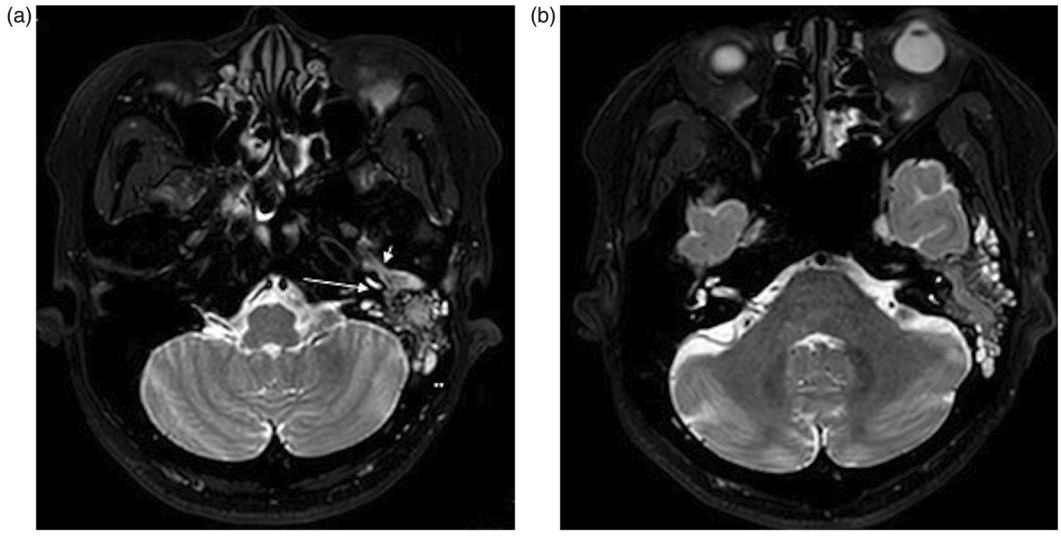

Figure 3. (A) Axial T2-weighted MRI scan showing abnormal signal along the left Eustachian tube (short arrow). The long arrow indicates the basal turn of the cochlea. There is also abnormal signal within the mastoid air cells (**). (B) This shows the view of the right ear to demonstrate a comparable normal anatomy. Unfortunately, the patient was rotated in the scanner, which does not allow one axial image to capture appropriate alignment of the left and right cochlear for comparison.

stranded antibody (dsDNA) and extractable nuclear antigen (ENA) were normal, as was a serology for HIV and syphilis. A CT scan of the paranasal sinuses demonstrated no evidence of sinus disease. A diabetic screen was negative, and a chest x-ray revealed subtle right apical scarring, possibly from previous pulmonary TB. A repeat Quantiferon test was positive which indicated previous exposure to TB and sputum samples were smear negative and culture negative for *M. tuberculosis*.

Approximately, one month after surgery, the patient had persisting left-sided otalgia and was noted to have an anteroinferior pars tensa perforation. Pure tone audiometry revealed a persisting profound SNHL in the left ear with a type B tympanogram (Figure 4). The patient continued to have persistent left-sided otalgia, even after five-month following surgery. At this time, hard wax noted in the EAC on examination was removed. There was no otorrhoea and the tympanic membrane perforation was healing well. The ear wax was sent for microscopy and mycobacterial culture. No AFB were identified on the initial results, although the sample continued to be cultured for the standard incubation period for mycobacterial cultures. Despite the negative TB tests thus far, a decision was made to treat the patient with anti-tuberculous treatment given TB was deemed the most likely aetiology with the presence of granulomatous inflammation. Treatment with the WHO standard regimen for drug-sensitive TB, 2HRZE/4HR was commenced – this involved two months of isoniazid (H) with pyridoxine supplementation, rifampicin (R), pyrazinamide (Z)

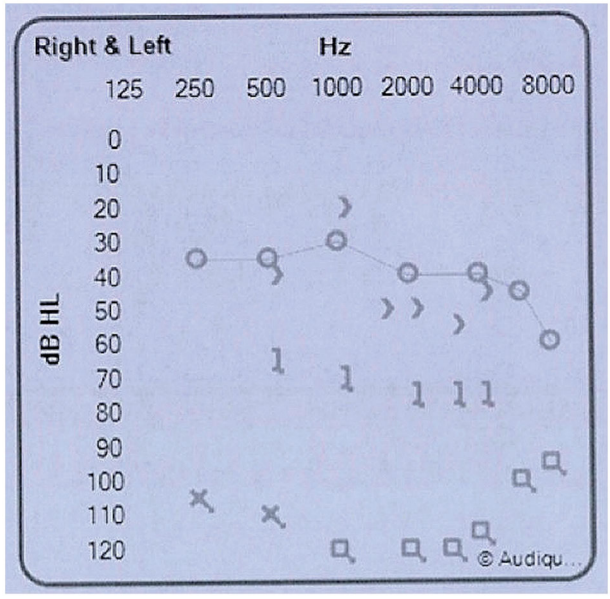

Figure 4. Pure tone audiogram showing profound left-sided sensorineural hearing.

and ethambutol (E) followed by four months of H and R, with a plan to review the patient's response for consideration of extension of treatment, if required.

After three months of incubation (approximately nine months after the initial surgery, and over one year from the initial presentation), *M. tuberculosis* was isolated from the ear wax growth; during which time the patient had been on the anti-TB treatment and symptoms were gradually improving. The cultured *M. tuberculosis* was fully susceptible to the first-

line drugs prescribed. At the time of writing this report, the patient's ear pain had settled but there was no improvement to her hearing. Her tympanic membrane was dull but intact and not inflamed.

Differential diagnosis

There are several differential diagnoses of chronic otorrhoea that are non-responsive to conventional medical and surgical therapy. These include syphilis, fungal infection, malignant otitis externa, histiocytosis X, cholesteatoma, lymphoma, sarcoidosis or granulomatosis with polyangiitis (GPA) [2,12–14]. These differentials were considered throughout the case presented; each one excluded by the wide range of blood tests, imaging and tissue samples, as well as patient history and clinical picture.

Outcome and follow-up

The patient is continuing to be followed up, with a planned MRI for after completion of six months of anti-TB treatment. She is currently well, with no otorrhoea, tympanic perforations or otalgia. Management of her hearing loss is currently non-surgical. She has opted not to have a contralateral routing of signal (CROS) device for the time being. Cochlear implantation was not considered an option given the presence of active TB treatment.

Discussion

TOM is rare – accounting for <1% of chronic ear infections [8–11]. The mechanism of infection to the otomastoid region has been postulated to occur by three mechanisms: a haematogenous spread, direct invasion *via* a tympanic perforation, or reflux through the Eustachian tube [15]. We are unable to determine the mechanism of spread in the case discussed, but there were both tympanic perforations evident as well as indication of eustachian tube involvement on imaging. The patient's country of origin and suspicious chest x-ray findings suggest a possibility of haematogenous spread from latent pulmonary TB infection.

The classical TOM signs first identified in 1853 describe a triad of painless otorrhoea, multiple tympanic membrane perforations and associated facial nerve palsy [15]. However, the clinical presentation is in fact variable and often non-specific – ranging from painless to significant otalgia, serous or purulent discharge, sensorineural and/or conductive hearing loss [4]. Examination findings often reported include one or more tympanic perforations, thickened tympanic membranes, pale appearance and granulation tissue in the middle ear and mastoid [16]. Notably, TOM frequently presents as a unilateral chronic otorrhoea which is unresponsive to conventional antimicrobial treatment, and patient symptoms disproportionate to examination [12,17]. This is comparable to our case presented . However, in particular, the patient did not exhibit a facial nerve palsy. Similarly, in a retrospective analysis of 52 patients with TOM, Cho et al. found that only 9.6% of cases had facial palsy, varying from the previously reported 20% [10]. It is possible that this did not occur in our patient due to the acute nature of the presentation and prompt treatment despite the presence of tympanic facial nerve dehiscence.

Otological TB is diagnostically challenging for several reasons. It often mimics other forms of otological conditions [13]. Additionally, given it is a rare entity, there is unfamiliarity with the disease and low suspicion especially in countries where active TB is rarely encountered [4,14]. Subsequently, TB tests are not routinely ordered and even when requested, microbiological tests can give false negatives [14], explained by presence of other bacteria in the sample or masking from topical antibiotic therapy [18]. Smears for AFB in EPTB have a low yield, with only a small percentage testing positive [6]. Of 12 cases reviewed by Jesic et al., only one had a positive Ziehl-Neelsen staining [19]. Additionally, TB is a paucibacillary disease, and therefore in TOM the small amount of sample available for testing makes identification of the organism difficult – only 20–30% of cases are microbiologically confirmed using ear secretion cultures [2,8]. Despite histopathology being recognised as the most reliable diagnostic tool [11,17], in our case the histopathology for the operative biopsies only identified the presence of necrotising granulomatous inflammation. TB was only confirmed once *M. tuberculosis* had been cultured from an ear cerumen sample taken at a post-operative review. Comparably, a retrospective review of 10 TOM patients by Vaamonde et al. found aural exudate to be more effective than tissue biopsy in diagnosis [8]. However, the aural exudate was specified as otic discharge. In fact, all TOM cases in the literature that have been reported as culture-positive are either from a tissue biopsy or ear discharge. There is no other case published that has a diagnosis of TB from the culture of ear cerumen. This case suggests that opportunistic sampling of all material from the ear should continue to occur at every clinical encounter to improve the ability to detect *Mycobacteria*.

Although the patient was started on the correct treatment before the confirmed diagnosis of *M. tuberculosis* was made – due to prolonged incubation time, it is important to acknowledge there was still a delay in treatment from presentation. The late recognition of TOM is widely recognised in the literature [19]. Delay in appropriate treatment can increases the risk of complications, such as mastoiditis, labyrinthitis, osteomyelitis, fistulae, abscesses, facial nerve palsies, profound hearing loss and intracranial spread [1,13].

Standard management of TOM is anti-tuberculous medications for at least six months [20]. Surgery is reserved for complications, but given the challenge in identifying the disease, the diagnosis is often made peri- or post-operatively [10]. Varied versions of diagnostic-management algorithms of TOM have been suggested [10,12,14], but the underlying theme is that repeated samples for histopathology and microbiological testings are often required. Negative tests do not necessarily exclude TB; even without positive culture results, commencing empirical treatment is recommended based on clinical grounds and suspicion [17].

Learning points

- TOM can mimic other causes of chronic ear disease, and several differential diagnoses need to be considered.
- TOM is diagnostically challenging.
- Given it is a paucibacillary condition and the insidious disease process, clinical suspicion plays an important role in diagnosis and avoiding delayed treatment in EPTB secondary to *M. tuberculosis*.
- To the best of our knowledge, this case is the first to demonstrate positive culture from an ear cerumen sample. Therefore, this case suggests that opportunistic sampling of all material from the ear should continue to occur at every clinical encounter to improve the ability to detect AFB.

Informed consent statement

Informed consent was obtained to publish this case report.

Disclosure statement

The authors report no conflict of interest.

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