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Original Article

Primary bilateral tuberculous otitis media with peripheral facial paralysis: a case report and literature review

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Abstract: Tuberculous otitis media (TOM) is a rare disease. This study presents our experience in the diagnosis and treatment of TOM. A 49-year-old female had repeated ear discharge, vertigo, and severe hearing loss for six years, and underwent mastoid surgery four times because she was misdiagnosed with chronic suppurative otitis media. The patient had left-sided facial paralysis for two weeks when she was admitted to our hospital and was managed with radical mastoidectomy and facial nerve decompression. After surgery, facial nerve function gradually improved from grade V to grade II, and the patient was diagnosed with an unusual primary bilateral TOM after tuberculosis smear culture, pathologic examination, and tuberculosis DNA testing by the PCR technique. After anti-tuberculosis therapy, the operative mastoid cavity in the patient was eventually epithelialized and dry. Therefore, this study suggests that, TOM should be actively excluded in patients with uncontrollable ear leakage, massive white granulation tissue and dead bone formation in the ear. Surgical decompression is recommended to prevent permanent facial paralysis, since opening the facial nerve sheath effectively relieves facial nerve compression and edema due to the TOM-induced persistent inflammation and granulation tissue formation.

Keywords: Tuberculous otitis media, mycobacterium tuberculosis, middle ear, facial paralysis

Introduction

Tuberculous otitis media (TOM) is a rare disease that accounts for 0.05%-0.9% of chronic otitis media cases [1, 2]. TOM is easily misdiagnosed because of its variable clinical signs and nonspecific manifestations compared to other types of chronic otitis media [3, 4]. Improper or delayed treatment due to misdiagnosis may lead to severe complications, such as facial paralysis, meningitis, irreversible hearing loss, and intracranial complications [3, 5-8]. In this study, an unusual case with primary bilateral TOM presenting with repeated ear discharge, vertigo, severe hearing loss, and facial paralysis was reported, and the patient underwent mastoid surgery four times due to the misdiagnosis of chronic suppurative otitis media. It was not necessary to obtain ethical approval for this case report; however, this patient gave our informed consent for report this case.

Case report

A 49-year-old female was diagnosed with left peripheral facial nerve paralysis and bilateral chronic otitis media, and admitted to our hospital. The patient experienced repeated bilateral ear discharge, vertigo, hearing loss, and headache for six years, and received three surgeries in her left ear and one in her right ear. The patient complained that the above symptoms were relieved for only a short time after surgery. Two weeks ago, the patient felt pain around her left ear and was unable to close her left eyelid. Under oto-endoscope, tough white new tissues and purulent secretions were found in the bilateral external auditory canals and mastoid cavities (**Figure 1**). The preoperative temporal bone CT revealed the presence of a massive soft tissue density, bone destruction, and dead bone formation in bilateral tympanums and mastoid cavities. There was also a horizontal semicircu-

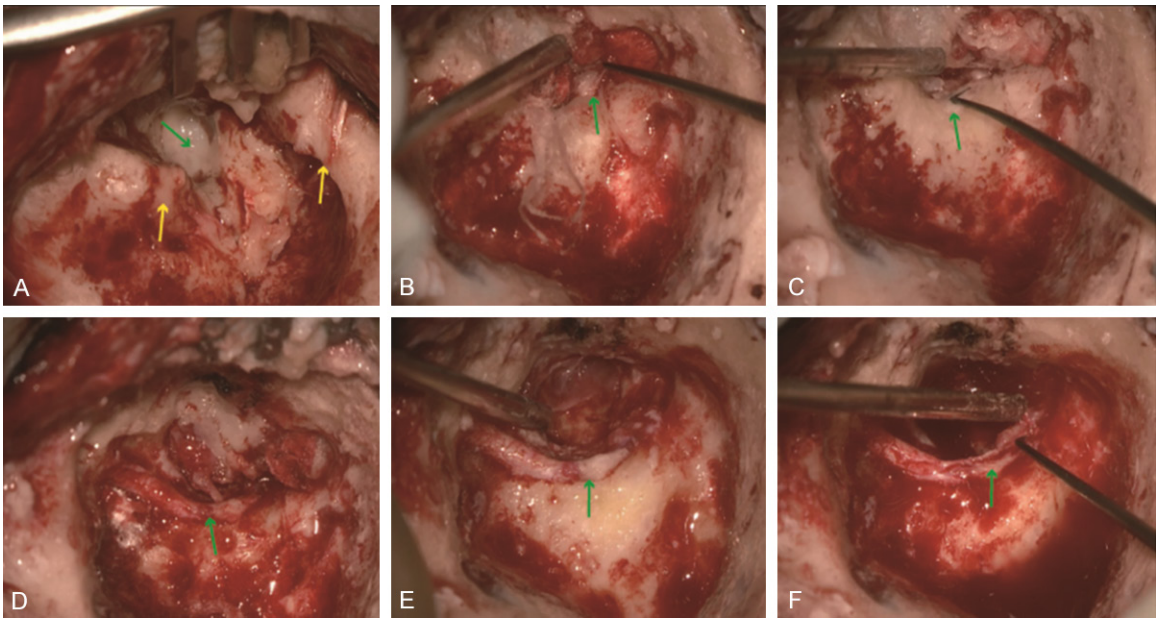

Figure 1. The procedures of radical mastoidectomy and left facial nerve decompression are demonstrated. A. White granulation tissue and necrotic fibrous tissue in the tympanomastoid cavity (green arrow) and the protruding superior and posterior wall of the external auditory canal (yellow arrows) were seen before operation. B. The facial nerve was compressed in the conic segment of facial nerve bone tube (green arrow). C-E. Facial nerve was decompressed from the geniculate ganglion to the stylomastoid foramen (green arrows). F. The sheath of the facial nerve was cut open (green arrow).

lar canal fistula and the facial nerve was exposed in the left ear, since the bony canal around the facial nerve and the semicircular canal were impaired. The superior and posterior wall of the external auditory canal obviously protruded (**Figure 2**). As discovered by electrical audiometry, the patient had bilateral mixed deafness, the average air conduction hearing threshold in 250-1000 HZ was 90 dB, the average air-bone conduction gap was 70 dB, and the average 2000-4000 HZ bone conduction hearing threshold was 75 dB. At the same time, the thresholds of auditory brainstem response (ABR) were 95 dB in the right ear and 85 dB in the left ear, respectively. Facial nerve function was assessed as grade V according to the House Brackmann guideline (**Figure 3**). Thus, radical mastoidectomy and left facial nerve decompression under general anesthesia were performed in the left ear. Under microscopy, a massive white and tough neoplasm, incomplete calcified new bone formation, incarceration and compression of the facial nerve in the left tympanic cavity and mastoid cavity were observed. Thereafter, the neoplasm and overhanging bone were excised, and the mastoid cavity and the tympanic segment of facial nerve were outlined, then the sheath of facial nerve was cut open for decompression and covered with the temporal muscle fascia for protection (**Figure 1**). After surgery, function of the left facial nerve gradually improved from grade V to grade II (**Figure 3**), but the soft tissue was obviously hyperplastic on the bone surface with persistent inflammatory exudate, leading to a gradually shrinking operative cavity. Four months after surgery, the mastoid cavity was transiently dry after applying the antibiotic auristilla and cleaning the surgical cavity intermittently (**Figure 4**). Three months after surgery, temporal bone CT revealed that the mastoid cavity was outlined, with no obvious soft tissue proliferation, bone destruction, or dead bone formation in the left ear. There was no obvious change in the right ear. One year after surgery, bone destruction and new dead bone formation were observed in the superior and anterior wall of the external auditory canal, along with soft tissue proliferation in the operative mastoid cavity, but there was no significant change in the right ear (**Figure 2**). Nineteen months after surgery, the patient suffered from severe pain in the left ear, which affected her sleep at night. Upon examination, the cartilage

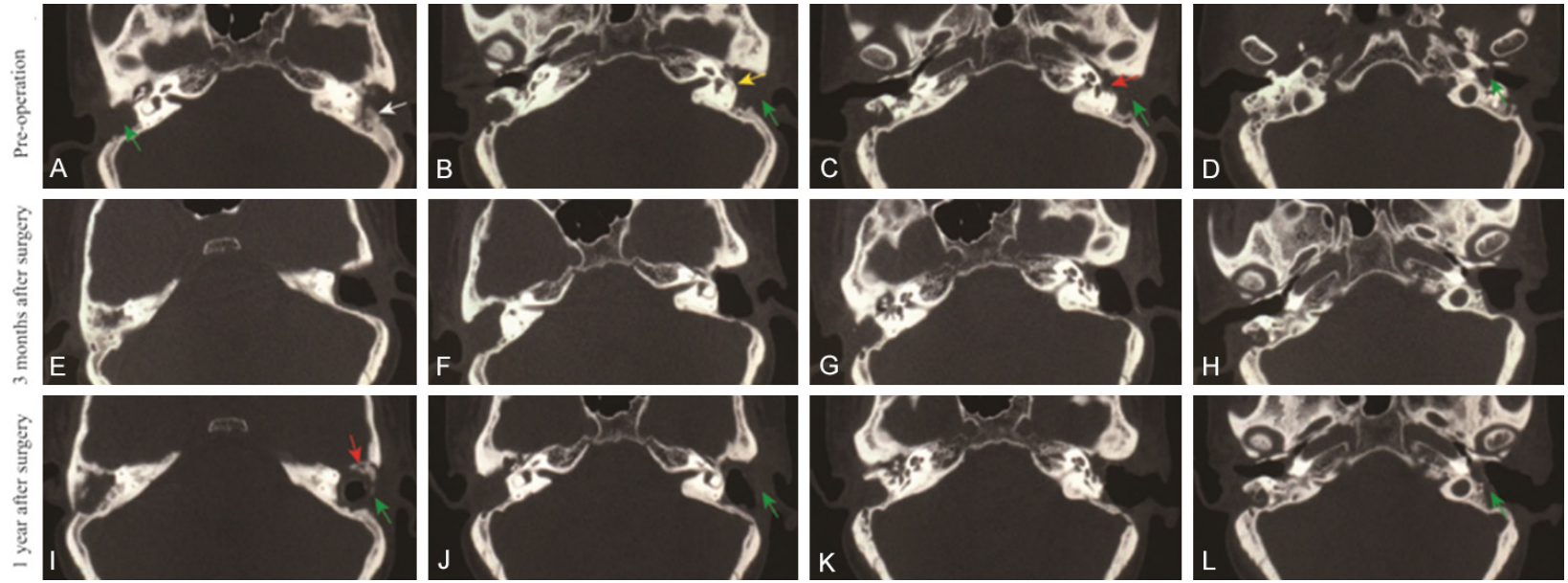

Figure 2. Temporal bone CT was followed up to demonstrate the changes in both ears. A-D. The preoperative CT revealed a proliferation of massive soft tissues in the bilateral tympanum and mastoid cavity (green arrows), and bone destruction with dead bone formation was observed around the labyrinth and in the mastoid cavity of the left ear (white arrows). There was a horizontal semicircular canal fistula (yellow arrows) and the facial nerve was exposed (red arrows) in the left ear. E-H. Three months after surgery, the temporal bone CT showed that the mastoid cavity was outlined, with no obvious soft tissue proliferation, bone destruction, or dead bone formation in the left ear. I-L. One year after surgery, new bone destruction and dead bone formation appeared again in the superior and anterior wall of the external auditory canal (red arrow), and soft tissue proliferation was observed in the operative mastoid cavity (green arrows).

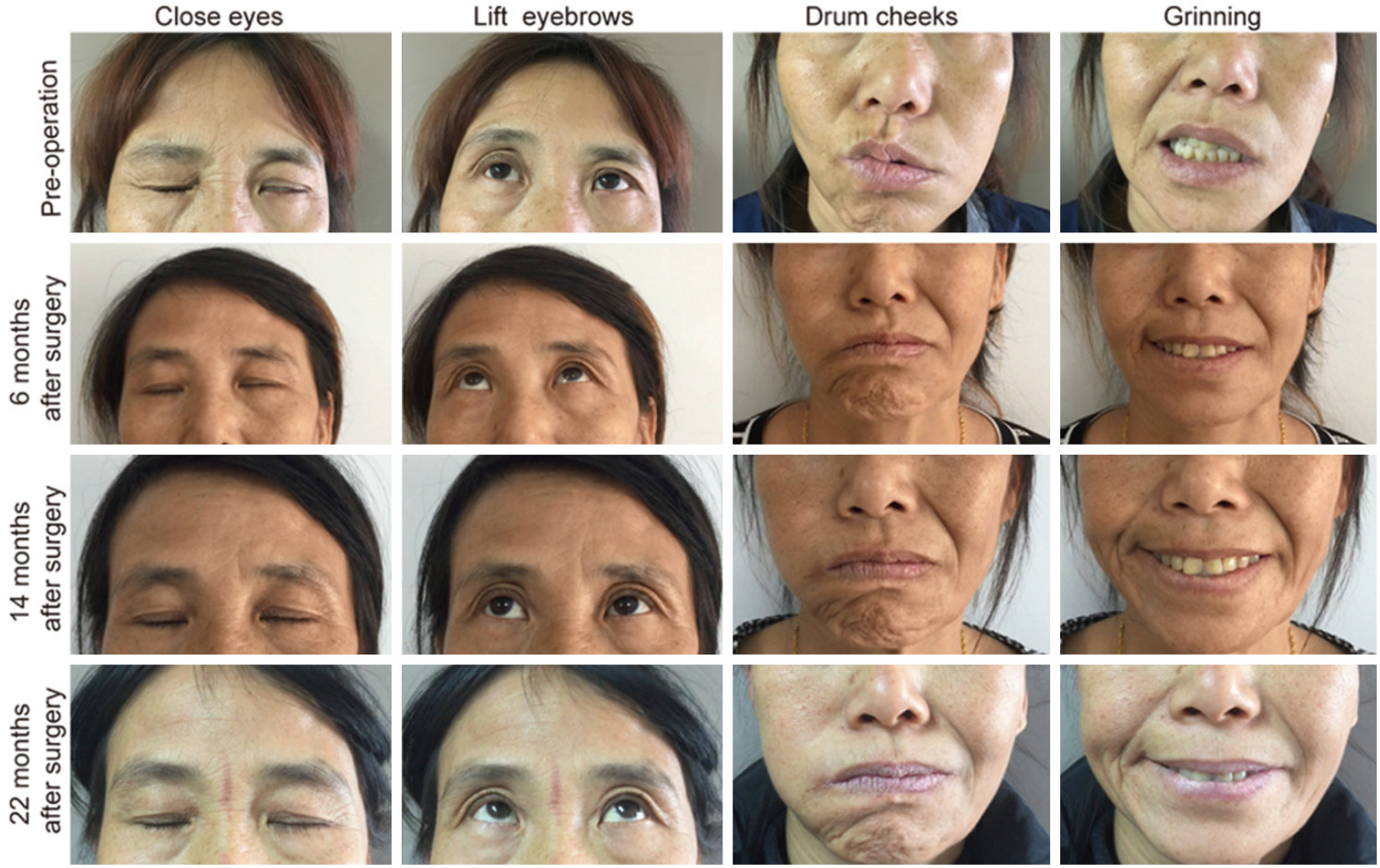

Figure 3. Facial expressions were followed up to show the improvement in left facial nerve function. The grade of left facial nerve function of pre-operative, 6, 14 and 22 months after surgery was grade V, II, II, and II respectively.

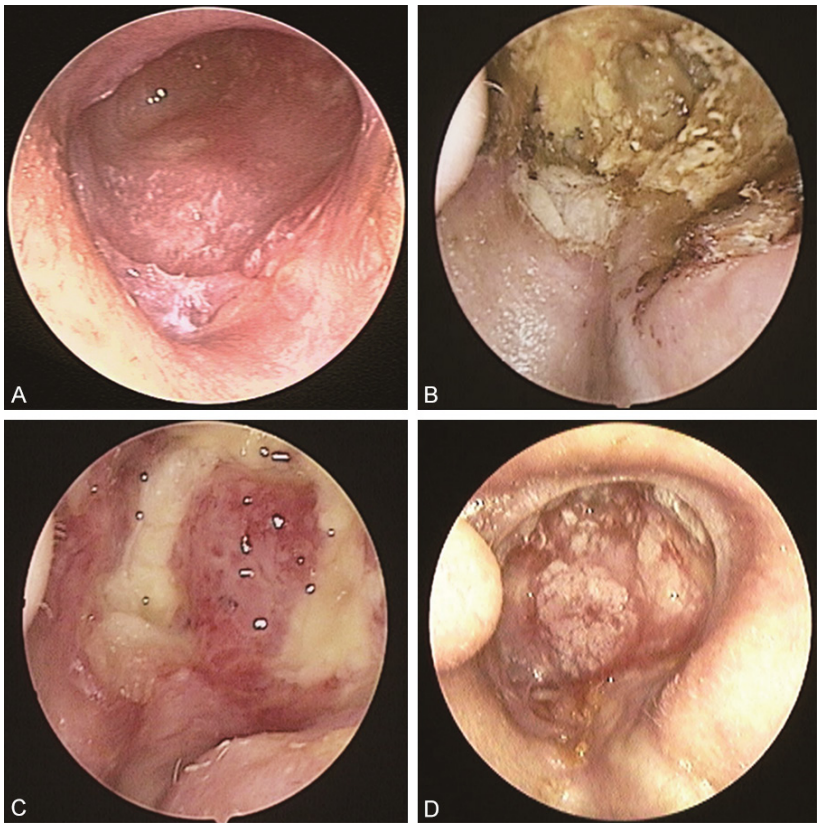

Figure 4. Otoscopic images were followed up to display the changes in left postoperative mastoid cavity. A. Four months after surgery, soft tissue proliferated in the operative cavity. B. Nineteen months after surgery (two weeks before anti-tuberculosis therapy), the hyperplastic tissue became necrotic fibrous tissue. C. Two weeks after anti-tuberculosis therapy, the necrotic tissue in the left ear was replaced by fresh granulation tissue. D. Two months after anti-tuberculosis therapy, the granulation tissue was epithelialized and the operative cavity was dry.

in the left auricular concha was partially necrotic and covered with pus scabs, and thin purulent secretions were observed on the soft tissue surface in the operative cavity (**Figure 4**). Pseudomonas aeruginosa and fungal infections were detected after bacterial and fungal culture, which were sensitive to vancomycin and imipenem. The erosive ulcer was further biopsied, and the pathologic results showed that there were necrotic tissues with positive acid-fast bacilli detected by specific staining. Additionally, mycobacteria were discovered by auricular secretion smear (**Figure 5**). Furthermore, automated real-time nucleic acid amplification technology for the rapid and simultaneous detection of Mycobacterium tuberculosis and rifampicin resistance (Xpert MTB/RIF) was applied, which disclosed that the MTB complex was positive and sensitive to rifampicin. Thus, the diagnosis of TOM with peripheral facial paralysis was made by the following diagnostic criteria: (A) The patient suffered from recurrent otorrhea, vertigo, severe hearing loss, headache, and left peripheral facial nerve paralysis, even though she received three mastoid surgeries in her left ear and one mastoid surgery in her right ear. (B) Under microscopy, it was found that the tympanic cavity and mastoid cavity were filled with inflammatory granulation tissue and necrotic fibrous tissue. (C) CT showed typical features of TOM, including massive soft tissue proliferation in bilateral tympanic cavities and mastoid cavities, and bone destruction with dead bone formation around the labyrinth and in the mastoid cavity. (D) Histopathologic findings included extensive caseous necrosis with positive acid-fast bacilli detected by specific staining. (E) Acid-fast staining of routine pathologic sections and microbiological secretion smears found mycobacteria. (F) Xpert MTB/RIF found that the MTB complex was positive and sensitive to rifampicin. The patient was treated with anti-tuberculosis therapy (including isoniazid, rifampicin, pyrazinamide and ethambutol) in combination with mastoid cavity cleaning with hydrogen peroxide. Two weeks after anti-tuberculosis therapy, the necrotic tissue in the left ear was gradually replaced by fresh granulation tissue, the discharge of inflammatory secretion from the ear canal was significantly improved, and the ear pain disappeared. Also, the white tough granulation tissue in the tympanic cavity of the right ear shrunk. Two months after anti-tuberculosis therapy, the granulation tissue was epithelialized and the operative cavity was dry (**Figure 4**).

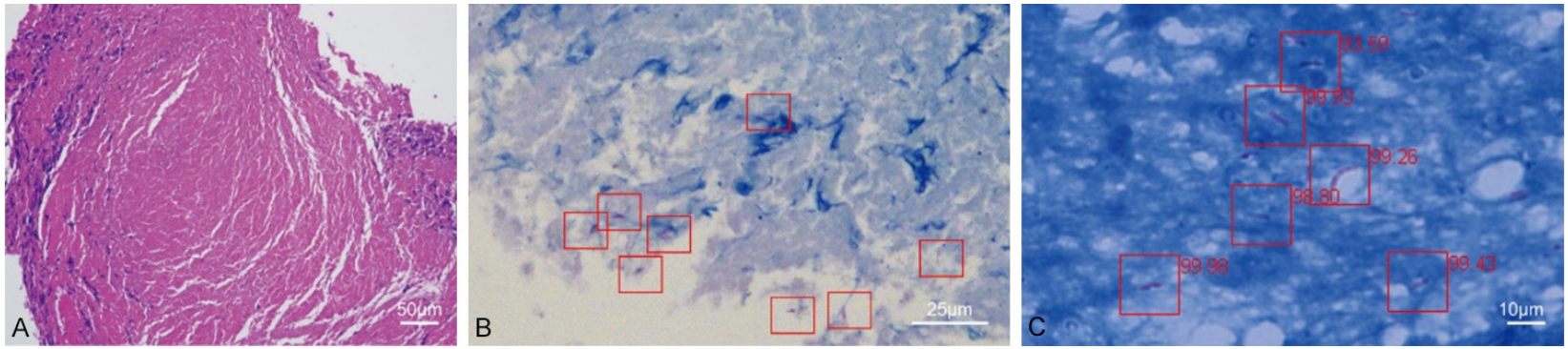

Figure 5. A. Histopathologic findings showed that extensive caseous necrosis was rimmed by inflammatory cells and epithelioid cells (H&E stain, 400×). B. Acid-fast staining of histologic sections showed acid-fast, pink bacilli (800×). C. Tuberculosis smear examination and acid-fast bacillus staining showed acid-fast, pink bacilli (1000×).

Discussion

It is reported that TOM is a rare infectious disease that can be divided into primary and secondary types, with secondary TOM being more common while primary TOM being rare [4, 9]. 52%-65% of secondary TOM patients are associated with lung tuberculosis or tuberculosis in other parts, like nasopharyngeal tuberculosis and laryngeal tuberculosis [10]. The infection route of TOM can be classified into a hematogenous pathway and a eustachian tube pathway, and the latter is more common [11]. In our case, as no tuberculosis focus was found in other parts of the body, Mycobacterium tuberculosis was less likely to infect the middle ear hematogenously. Thus, the patient was suspected to have primary TOM, and Mycobacterium tuberculosis was more likely to enter the middle ear cavity through the eustachian tube.

The typical symptoms of TOM are painless otorrhea, multiple tympanic membrane perforations, and massive pale granulation tissue in the mastoid cavity of the external auditory canal [2, 12, 13]. Severe hearing loss and peripheral facial paralysis in early stage are more common in TOM than in purulent otitis media [3, 7, 14]. In our case, the patient suffered from recurrent otorrhea, vertigo, severe hearing loss, headache, and left peripheral facial nerve paralysis, even though she received three mastoid surgeries in her left ear and one mastoid surgery in her right ear. Moreover, her facial nerve function was seriously impaired and assessed as House Brackmann grade$\mathrm{V}$. Under microscopy, it was found that the tympanic cavity and mastoid cavity were filled with inflammatory granulation tissue and necrotic fibrous tissue; meanwhile, facial nerve edema and compression in the conic segment of facial nerve bone tube were also observed. However, the typical characteristics of middle ear tuberculosis, like painless otorrhea and multiple tympanic membrane perforations, disappeared.

It is difficult to make a definite diagnosis of primary TOM, which usually takes 1 month to 1.5 years after the patients seek for medical assistance [15]. Tuberculosis culture and smear examination are the essential tests for the diagnosis of TOM, as recommended by the European guidelines [16]. Mycobacterium tuberculosis is only one of the mycobacteria. Sometimes, tuberculosis DNA testing using PCR technique is necessary to exclude other types of mycobacteria, especially in rare sites such as the middle ear [17]. Garg et al. for example, reported that PCR was more sensitive than histopathology and AFB smear in detecting MTB in fistula-in-ano [18]. Xpert MTB/RIF test is a PCR-based assay, which can detect the presence of MTB DNA (rpoB gene), with a sensitivity of 131 MTB colony forming units/mL in 2 h, and it also gives an idea about resistance to rifampicin [19-22]. Xpert MTB/RIF was an effective tool to rapidly diagnose extrapulmonary tuberculosis [23, 24]. In this case, acid-fast staining of routine pathological sections and microbiological secretion smears was positive, and the Xpert MTB/RIF test was also utilized to confirm the diagnosis of TOB.

The diagnosis of tuberculosis also depends on the pathologic examination of granulation tissue in the middle ear [6], which shows granuloma formation with caseous necrosis, epithelioid cells, and Langhans giant (multinucleated) cells. These also rule out cholesteatoma, tumor, and other granulomatous diseases such as Wegener's gramulomatosis and eosinophilic granuloma. Sebastian et al. suggested that histopathologic analysis along with AFB staining of tissue collected from the middle ear cleft confirmed 90% of tuberculosis cases [3]. In the T-SPOT examination, the enzyme-linked immunospot (ELISPOT) methodology is employed to enumerate the MTB-sensitized T cells, which respond to stimulation by the MTB antigens ESAT-6 and CFP 10 by capturing interferon gamma (IFN-γ) around T cells in human whole blood. The positive results of T-SPOT suggest the presence of MTB-specific effector T cells and tuberculosis infection in the patients. However, tuberculosis infection includes both the latent and active types. Latent tuberculosis infection refers to the presence of MTB in the body, with no clinical symptoms or imaging findings, and a small number of people may develop active tuberculosis. Notably, the positive results in T-SPOT cannot be used as the only basis for the diagnosis of active tuberculosis. In our case, the patient had negative results by T-SPOT examination.

Temporal bone CT plays an important role in the diagnosis of TOM. Typically, soft tissue density shadow and bone destruction, especially

dead bone formation in the tympanic cavity and mastoid cavity, are the representative characteristics of TOM. In our case, the preoperative CT showed typical features of TOM, including massive soft tissue proliferation in bilateral tympanic cavities and mastoid cavities, and bone destruction with dead bone formation around the labyrinth and in the mastoid cavity. Although radical mastoidectomy was performed previously, the CT conducted at one year after surgery showed that bone destruction and dead bone formation appeared again in the superior and anterior wall of the external auditory canal, with significant soft tissue proliferation in the anterior walls of the sigmoid sinus and the external auditory canal.

Further, close observation and follow-up with video endoscope are useful for the diagnosis of TOB. Massive white granulation and necrotic fibrous tissues were seen in the tympanomastoid cavity and external auditory canal in our patient before surgery. After surgery, the operative cavity healed slowly, and the ear was dry for a short period at four months after surgery, but the gradual proliferation of soft tissue in the operative cavity led to obvious shrinking. Then, the hyperplastic tissue became necrotic fibrous tissue, and an inflammatory exudate was observed. Subsequently, secondary resistant bacterial and fungal infections were discovered, and local necrosis of auricular cartilage appeared. After two weeks of anti-tuberculosis therapy, the necrotic tissue in the left ear was replaced by fresh granulation tissue. Two months after anti-tuberculosis therapy, the granulation tissue was epithelialized and the operative cavity was dry.

Systemic anti-tuberculosis therapy combined with mastoidectomy should be the preferred choice for the treatment of middle ear tuberculosis, as recommended by American guidelines [25]. Generally, quadruple agents, such as isoniazid, rifampicin, pyrazinylamine, ethambutol or streptomycin, are applied in anti-tuberculosis therapy for 6 months; meanwhile, vitamin B, vitamin A and calcium lactate are also administered to reduce toxic reactions and protect the liver [10, 26]. The discharge of inflammatory secretion in the affected ears may stop within 2 months in most patients after drug therapy, but the course of anti-tuberculosis therapy should be extended for at least one year. Recent studies have shown that, compared with anti-tuberculosis therapy alone, a higher rate of dry ear is achieved when surgery is performed prior to anti-tuberculosis therapy [6, 27]. In our case, after mastoidectomy and facial nerve decompression at our hospital, the facial nerve function recovered to grade II, and after middle ear tuberculosis was diagnosed, the patient was treated with anti-tuberculosis drugs combined with mastoid cavity cleaning. At one week later, the mastoid cavity was gradually covered with new granulation tissue, the discharge of inflammatory secretion from the ear canal was significantly improved, and ear pain disappeared.

Facial nerve decompression plays a key role in the management of TOM-induced peripheral facial paralysis. In our case, the patient underwent three mastoid surgeries in her left ear, but the postoperative inflammation was poorly controlled by conventional antimicrobial agents, and she suffered from peripheral facial paralysis for 2 weeks. Persistent discharge of inflammatory secretion, abnormal hyperplasia of granulation, and necrotic fibrous tissues and drug-resistant bacterial and fungal infections were detected in the mastoid cavity. The facial nerve function was severely impaired and assessed as House Brackmann grade V. Thus, radical mastoidectomy combined with left facial nerve decompression was performed. It was found that the tympanic cavity and mastoid cavity were filled with inflammatory granulation and necrotic fibrous tissues; meanwhile, facial nerve edema and compression in the conic segment of facial nerve bone tube were also observed. Therefore, the facial nerve was decompressed from the geniculate ganglion to the stylomastoid foramen, and the nerve function gradually recovered from grade V to grade II after operation, suggesting that surgery was effective in treating the TOM-induced facial paralysis. Due to persistent inflammation and granulation tissue formation in middle ear tuberculosis, anti-inflammatory treatment is ineffective in alleviating facial nerve edema, while facial nerve decompression relieves facial nerve incarceration and edema. Consequently, once peripheral facial paralysis induced by middle ear tuberculosis is diagnosed, surgical decompression is recommended as soon as possible to improve the recovery of facial nerve function.

Conclusions

It is suggested in this study that TOM should be actively excluded when patients show clinical manifestations including: continuous ear leakage that cannot be controlled by antibiotics, massive white granulation or tough fibrous tissue in the tympanomastoid cavity that can quickly proliferate after surgical removal, and dead bone formation in the external and middle ear demonstrated on the temporal bone CT. Surgical decompression is recommended to prevent permanent facial paralysis, since opening the sheath of the facial nerve effectively relieves the facial nerve compression and edema induced by the TOM-caused persistent inflammation and granulation tissue formation.

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Disclosure of conflict of interest

None.

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