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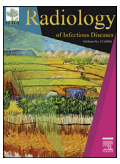

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Case Report

Rediscovering tuberculosis of the middle ear

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Abstract

Tuberculous otitis media (TOM) has no specific clinical presentation. Early diagnosis is necessary in order to avoid serious complications. The aim of this paper is rediscovering this rare forgotten disease that can re-emerge in a globalized society.

A case of a 37 year-old woman with persistent unilateral otitis media with ear discharge and deafness since two years is presented. Systemic and topic antibiotic therapy was not effective. She underwent surgery twice with no improvement. As clinical conditions worsened, she was hospitalized. Histological examination and culture for mycobacteria detection revealed *Mycobacterium tuberculosis* complex infection.

The patient was treated with anti-tuberculosis medical therapy for 9 months with clinical improvement.

TOM is a diagnostic challenge and is often treated late because not suspected. Chronic otitis media not responding to common antibiotics should be investigated for tuberculous infection.

Keywords: Tuberculosis; Otitis media; Atypical tuberculosis

1. Introduction

Tuberculous otitis media (TOM) is a rare atypical extrapulmonary localization of *Mycobacterium tuberculosis*. Incidence of middle ear tuberculosis is reported as 0.05−0.9% of infections of the middle ear [1]. TOM still remains a significant diagnostic challenge in low-incidence tuberculosis country, because suspicion is very low, clinical signs are variable and not-specific, standard microbiological and histological tuberculosis tests can give false negative [2]. Otolaryngologists should rediscover this type of chronic otitis media, in particular in Countries characterized by immigration from Countries with high prevalence of tuberculosis infection. Early diagnosis is necessary in order to avoid serious complications. Patients with chronic middle-ear infection unresponsive to standard antibiotic therapy should be suspected for TOM. A case is presented.

2. Case report

2.1. Informed consent was not required since the face of the patient is not visible in all figures

A case of a 37-year-old woman with chronic left middle ear otitis with discharge in the last two years is reported. She was born in Moldova and had been living in Italy for ten years. She was treated with antibiotic therapy for several months. She had undergone tympanoplasty twice. During first surgery, white tissue occupying the tympanic cavity suggestive for cholesteatoma was removed; ossicular chain was eroded, residual malleus and incus were removed, stapes was intact. Revision surgery was performed after six months, crura of the stapes were eroded, platina of the stapes was intact, inflammatory tissue occupying the tympanic cavity was removed. Tissue

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removed from tympanic cavity was visually described as cholesteatoma, but histological examination was not performed because other causes of chronic inflammation were not suspected.

Patient was hospitalized in Otolaryngology department because of persistent left ear discharge, earache, hearing loss, headache and vertigo. Audiometry revealed complete deafness on the left side (Fig. 1). She had no facial paralysis nor temporo-mandibular joint impairment. Otoscopy revealed purulent ear discharge and inflammatory tissue occupying the external auditory canal with erosion of tragal cartilage and complete perforation of tympanic membrane (Fig. 2). Ear

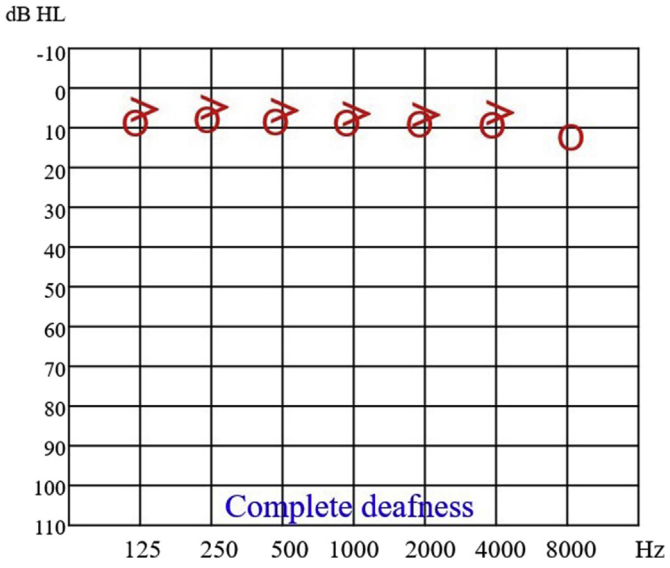

Fig. 1. Audiogram showing complete deafness on the left side and normal hearing thresholds on the right side.

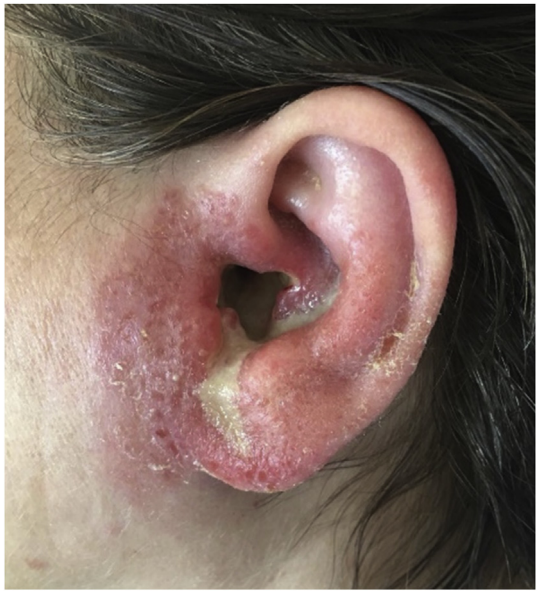

Fig. 2. Examination of the patient: inflammation of the external ear with extension to the surrounding soft tissues. Dense purulent yellow secretion occupies the external auditory canal. Erosion of the tragus can be noticed.

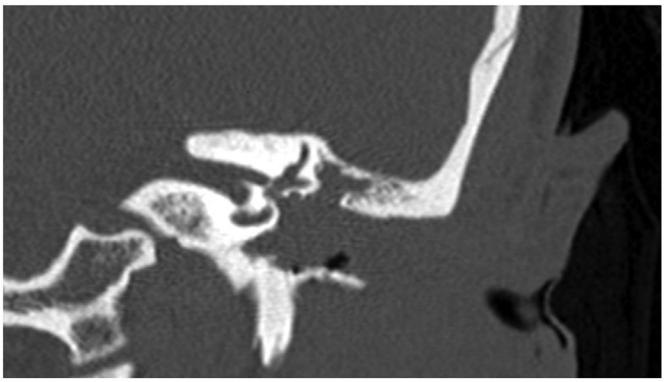

Fig. 3. Left ear computed tomography scan, coronal section. Soft tissue occupies tympanic cavity. Ossicles and scutum are absent. Bone erosion of external auditoy canal can be noticed.

secretion sample was negative for most common bacteria and fungi. Serology for Syphilis (Liason® Treponema screen, DIaSorin, Italy) and HIV test (Vikia® HIV1/2, Biomérieux, Italia) were negative.

A computed tomography scan of the middle ear revealed opacification of tympanic cavity, antrum and mastoid, bone erosion of anterior and posterior walls of external auditory canal; lateral epitympanic wall and ossicular chain were absent (Fig. 3).

Magnetic resonance imaging (MRI) revealed inflammatory tissue occupying the middle ear, with disomogeneous contrast enhancement with cystic and necrotic areas. Periauricular tissues, external auditory canal walls, tympanic bone and temporo-mandibular joint showed contrast enhancement (Fig. 4).

Chest radiography revealed bilateral apical nodular lesions. Computed tomography scan of the chest revealed right apical fibro-nodular lesions of 6 mm of diameter. Micronodular

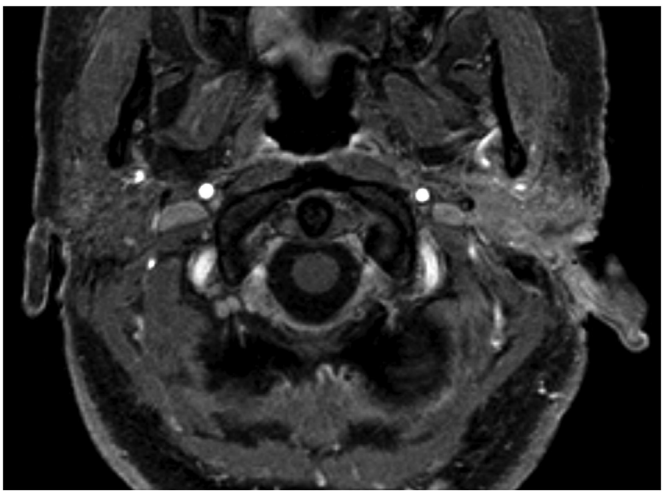

Fig. 4. Cerebral MRI with contrast. Left middle ear cavity is occupied by tissue with disomogeneous signal and contrast enhancement, with extension to periauricular soft tissues, external auditory canal walls and anterior pericondilar tissues. Cystic and necrotic aspects can be noticed. Tissue is described as inflammatory as first hypothesis.

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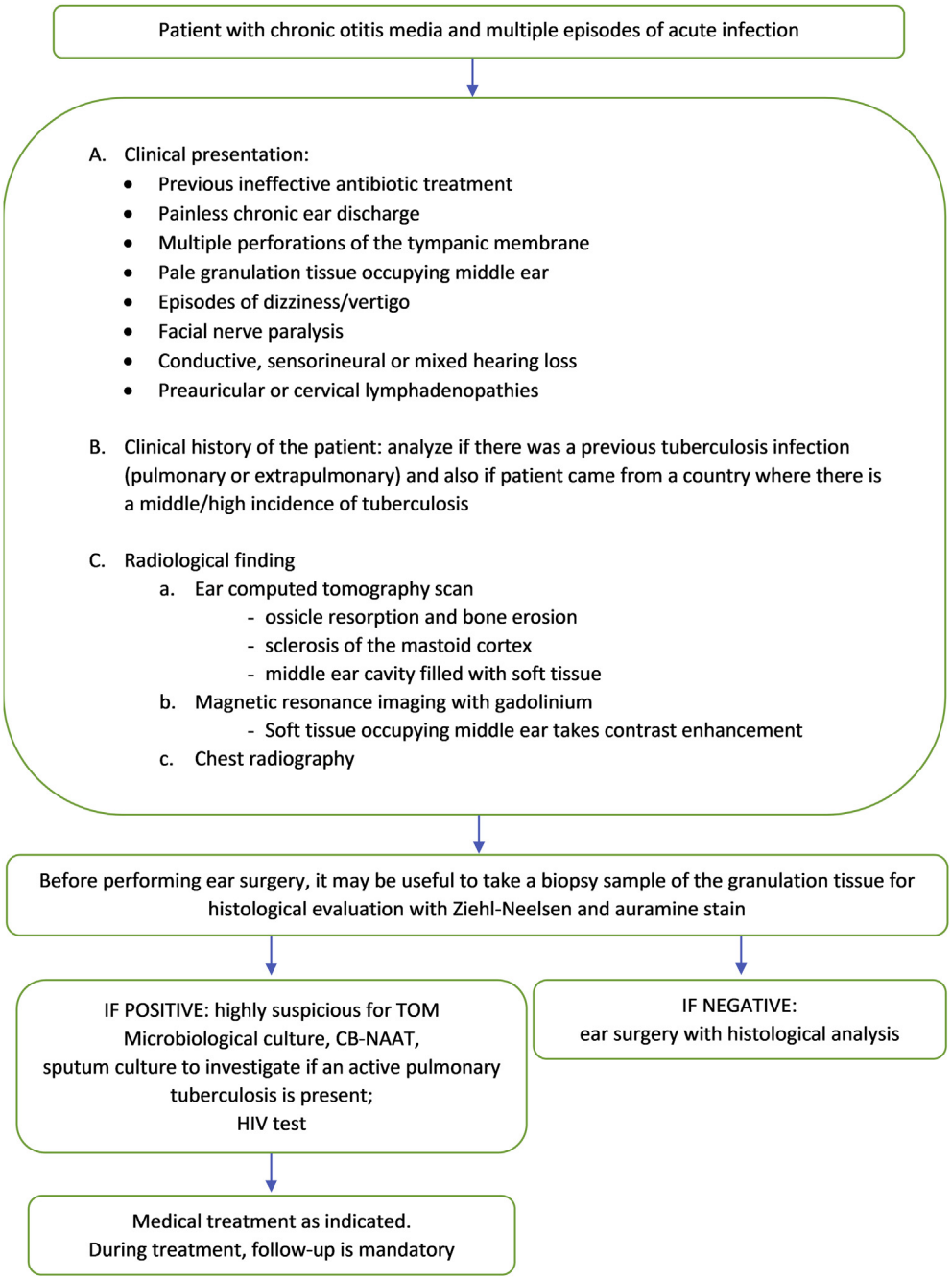

Fig. 5. Diagnostic-therapeutic algorithm of TOM.

peribronchial lesions were present at middle lobe and inferior right lobe. An apical calcific nodular lesion was also present on the left side.

Quantiferon test (QuantiFERON® - TB Gold, QIAGEN® Group, Germany) was positive for tuberculosis. Biopsy samples of the inflammatory tissue in the external auditory canal evidenced the presence of mycobacteria at Ziehl-Neelsen stain and necrotic material. Ear secretion sample was positive for *M. tuberculosis* complex.

Smear and culture of sputum were positive for *M. tuberculosis* too. The patient began specific systemic therapy with isoniazid, rifampicin, pyrazinamide and ethambutol (HRZE scheme). She was discharged after 9 days and continued antibiotic therapy with HRZE/daily till 2 months after discharged and with isoniazid and rifampicin only (HR scheme). After 9 months of therapy, sputum culture was negative for *M. tuberculosis*, chest radiography was negative, ear discharge and inflammatory tissue in middle ear cavity were no longer present, tragal cartilage was absent because of complete erosion due to previous infection. Hearing loss was unchanged. She did not need further surgical therapy.

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Table 1
Recommended doses of first line anti-tuberculosis drugs for adults [11]. *Patients aged over 60 years may not be able to tolerate more than 500−750 mg daily, so some guidelines recommend reduction of the dose to 10 mg/kg per day in patients in this age group (2). Patients weighing less than 50 kg may not tolerate doses above 500−750 mg daily.

Drug	Daily		Three times per week	
	Dose and range (mg/kg body weight)	Maximum (mg)	Dose and range (mg/kg body weight)	Maximum (mg)
Isoniazid	5 (4−6)	300	10 (8−12)	900
Rifampicin	10 (8−12)	600	10 (8−12)	600
Pyrazinamide	25 (20−30)	–	35 (30−40)	–
Ethambutol	15 (15−20)	–	30 (25−35)	–
Streptomycin*	15 (15−18)		15 (12−18)	1000

3. Discussion

The incidence of tuberculosis in Italy has decreased over the last century; however, it is becoming again a matter of public health concern because of recent immigration from high incidence areas of tuberculosis.

Extra-pulmonary localizations of tuberculosis in head and neck area have been reported [3]. TOM is extremely rare [1].

There are different hypothesis of pathogenetic mechanism of infection [2]: (1) tuberculosis bacilli spread to the middle ear via the Eustachian tube by coughing up sputum laden with bacilli especially in new-born/children who have shorter and large-bored Eustachian tube; (2) direct implantation from the external auditory canal contracted via infected sputum through perforation of the tympanic membrane; (3) via haematogenous spread from other tuberculous foci like pulmonary one.

Tuberculous mastoiditis was first described by Jean Louis Petit in the 18th century and the clinical signs of tuberculosis of the ear were first reported by Wilde in 1853 [4]. In 1882 Koch discovered bacillus responsible for tuberculosis and in the same year Ménière described the effect of this infection on the tympanic membrane [2]. The classic clinical features of TOM were then described again in 1953 by Wallner [4]: painless ear discharge, multiple tympanic membrane perforations, pale granulation tissue, ipsilateral facial nerve paralysis, early severe hearing loss and bone necrosis, including sequestrum formation. However, combination of all these characters is rarely observed today, indeed the most frequent presentation of TOM is characterized by moderate/severe hearing loss, painless ear discharge, single perforation of the tympanic membrane, hyperemic middle ear mucosa with some pale granulation [2]. Hearing loss occurs early and is usually found in almost all cases nowadays, while it was not reported as a main clinical presentation by Wallner. Conductive hearing loss is due to granulation tissue occupying middle ear, then severe sensorineural or mixed hearing loss can occur. Sensorineural hearing loss can be attributed to vasculitis of the cochlear veins, immunocomplex deposits in the cochlea or the presence of granulomatous tissues affecting the acoustic nerve [5]. The tubercular infection causes a hyperemic mucosa, rather than only pale granulation tissue, as previously described as a diagnostic criteria. There is usually a single tympanic membrane perforation, while multiple perforation are encountered rarely. Facial nerve paralysis has been reported in only 30−45% of cases [6]. The patient presented atypical presentation, that is more similar to most recent diagnostic criteria than to those originally reported by Wallner: she had earache, hearing loss, a single large tympanic membrane perforation and she had not facial palsy. Some major complications of untreated TOM are osteomyelitis, labyrinthitis, petrositis, lateral sinus thrombophlebitis and thrombosis, subperiosteal abscess, meningitis, brain abscess and tuberculoma of the brain [7].

The typical radiological findings of TOM at computed tomography scan are ossicle resorption, sclerosis of the mastoid cortex, middle ear cavity filled with soft tissue and bone resorption [8]. Diffuse temporal bone destruction on computed tomography scan or presence of facial palsy in absence of cholesteatoma should raise the suspicion of TOM. Clinical presentation and radiological findings can be mistakenly interpreted as chronic otitis media and treated with common antibiotics or surgical therapy, without benefit [8].

Concomitant pulmonary lesions are present in 50% of patients with TOM [8]. Gold standard to make diagnosis of TOM is the identification of acid-alcohol-resistant bacilli of *Mycobacterium complex* by microscopy and culture, however, the presence of other bacteria can slow down *M. tuberculosis* growth and interfere with microbiological investigations [9]. Acid-fast staining (auramine and Ziehl-Neelsen) of ear discharge is strongly suggestive for TOM [8]. Tuberculin (Mantoux) and Quantiferon tests have very low specificity with false positive results in cases of previous infection or vaccination. Ideally, CB-NAAT (Cartridge Based Nucleic Acid Amplification Test) for the rapid, simultaneous detection of tuberculosis and rifampicin resistance (GeneXpert MTB/RIF assay) should be performed in all adults and children with suspected TOM [2].

TOM goes into differential diagnoses with chronic otitis media, cholesteatoma, malignant external otitis, fungal infection, malignant tumor, Wegener's disease, Lyme disease, syphilis, sarcoidosis, nocardiosis, lymphoma [5]. A management algorithm for future patients is proposed in Fig. 5.

Early treatment is essential in preventing possible complications. As indicated in the last edition of the World Health Organization's guidelines [10], both pulmonary and extrapulmonary disease should be treated with the same regimens of antitubercular therapy: a four-drug daily regimen with isoniazid, rifampicin, pyrazinamide and ethambutol (HRZE

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Table 2
Common adverse effects of anti-tuberculosis drugs and their management.

Side Effect	Drugs	Management
MAJOR		*STOP responsible drugs and refer to clinician urgently*
Skin rash with/without itching	Streptomycin Isoniazid Rifampicin Pyrazinamide	Antihistamine Drugs (under clinician control) STOP anti-TB drugs
Deafness	Streptomycin	STOP Streptomycin
Dizziness, vertigo and nystagmus	Streptomycin	STOP Streptomycin
Jaundice (other causes excluded) Hepatitis Acute liver failure	Isoniazid Pyrazinamide Rifampicin	STOP anti-TB drugs
Visual impairment (other causes excluded)	Ethambutol	STOP Ethambutol
Shock, purpura Acute renal Failure	Rifampicin	STOP Rifampicin
Decreased urine output	Streptomycin	STOP Streptomycin
MINOR		*Continue anti-tuberculosis drugs; check drug doses*
Anorexia, nausea, Abdominal pain	Pyrazinamide Rifampicin Isoniazid	Take drugs with small meals or just before bedtime Id symptoms persist or worsened, with protracted vomiting or hemoptysis consider a major side effect and refer to clinician
Joint pains	Pyrazinamide	NSAID (non-steroidal anti-inflammatory drugs) or paracetamol
Burning, numbness or tingling sensation in the hands or feet	Isoniazid	Preventive treatment with pyridoxine
Drowsiness	Isoniazid	Reassurance. Give drugs before bedtime
Orange/red urine	Rifampicin	Reassurance. It is normal
Flu syndrome (fever, chills, malaise, headache, bone pain)	Rifampicin give with intermittent dosing	Chance administration

scheme) for the first 2 months, followed by two drug daily regimen with isoniazid and rifampicin (HR scheme) for 4 months. During the follow-up period, signs and symptoms should be investigated and monitored, and remission of symptoms will indicate a positive therapeutic response [8]. The dosage of drugs is reported in Table 1. Most patients complete the treatment without any significant adverse drug effect. However, a few patients can show adverse effects. Therefore all patients must be clinically monitored during treatment, so that adverse effects can be detected and managed properly. The most common adverse effects of anti-tubercular drugs can be divided in major and minor categories [11]. They are reported in Table 2. Patient who develop minor adverse effects should continue the anti-tubercular treatment and should be given symptomatic treatment. Patients with major adverse reactions should be treated in hospital.

The role of surgery is still debated [6]. Tympanoplasty without antitubercular therapy is not curative, as surgery alone may be effective in the short term but the infection can relapse and get worse in 6−12 months. Surgery could be needed in order to obtain histological or biological samples, to treat complications, for functional reconstruction or facial nerve decompression.

4. Conclusion

All patients with chronic middle-ear infection unresponsive to standard antibiotic therapy should be suspected for TOM. The usefulness of microbial culture, serological tests, polymerase chain reaction and histological analysis depend on the availability of the test within a hospital's laboratory services. Early diagnosis and treatment of TOM is important to avoid complications.

Acknowledgments

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