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Title: A case of Chronic Otitis Media Caused by Mycobacterium abscessus

Abstract: The first case report of adult chronic otitis media (COM) caused by Mycobacterium abscessus (M. abscessus) is described here. A 61-year-old woman presented persistent otorrhea for 2 months, despite treatment with standard antimicrobial drugs. Physical examination revealed a small perforation of the tympanic membrane and edematous middle ear mucosa. Mycobacterial cultures and PCR yielded non-tuberculous mycobacteria (NTM); M. abscessus. Intravenous piperacillin/tazobactam and amikacin and oral clarithromycin were administered for 36 days. Computed tomography of the temporal bone showed improved aeration in the tympanic cavity, but soft tissue shadow remained unchanged in the mastoid 31 days after starting medication. She therefore underwent tympanomastoidectomy at 36 days. At surgery, inflammation remained in the middle ear, and edematous pale mucosal tissue was noted around the stapes and ossicular chain. Histopathologic examination showed inflammation and granulation tissue, but no caseating necrosis or acid-fast bacilli. After surgery the symptoms resolved and remained well without evidence of infection recurrence 12 months after the operation. Although it appears very uncommon in adult COM, M. abscessus should be considered as a possible cause of a chronically draining ear. Multi-antibiotic chemotherapy including high-dose clarithromycin can effectively treat adult COM caused by M. abscessus.
A case of Chronic Otitis Media Caused by Mycobacterium Abscessus

Hisashi Sugimoto, MD, PhD\(^1\), Makoto Ito, MD, PhD\(^1\) *, Miyako Hatano, MD, PhD\(^1\)\(^2\)
Yosuke Nakanishi, MD\(^1\)\(^3\), Yumiko Maruyama, MD, PhD\(^1\)\(^3\) and Tomokazu Yoshizaki, MD, PhD \(^1\)

1) Department of Otolaryngology-Head and Neck Surgery, Kanazawa University Graduate School of Medical Science, Kanazawa, Japan
2) Department of Otolaryngology, Tonami General Hospital, Tonami, Japan
3) Department of Otolaryngology, Kurobe Civic Hospital, Kurobe, Japan

*Address correspondence and reprint requests to: Dr. Makoto Ito, MD, PhD.
Department of Otolaryngology Head and Neck Surgery, Kanazawa University Graduate School of Medical Science, 13-1 Takaramachi, Kanazawa, Ishikawa 920-8640, JAPAN
Telephone: 76-265-2413, FAX: 76-234-4265
E-mail: makoto@med.kanazawa-u.ac.jp
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Although it appears very uncommon in adult COM, M. abscessus should be considered as a possible cause of a chronically draining ear. Multi-antibiotic chemotherapy including high-dose clarithromycin can effectively treat adult COM cases by M. abscessus. The first case report of adult chronic otitis media (COM) caused by Mycobacterium abscessus (M. abscessus) is described here. A 61-year-old woman presented persistent otorrhea for 2 months, despite treatment with standard antimicrobial drugs. Physical examination revealed a small perforation of the tympanic membrane and edematous middle ear mucosa. Mycobacterial cultures and PCR yielded non-tuberculous mycobacteria (NTM); M. abscessus. Intravenous panipenem/betamipron and amikacin and oral clarithromycin were administered for 36 days. Computed tomography of the temporal bone showed improved aeration in the tympanic cavity, but soft tissue shadow remained unchanged in the mastoid 31 days after starting medication. She therefore underwent tympano-mastoidectomy at 36 days. At surgery, inflammation remained in the middle ear, and edematous pale mucosal tissue was noted around the stapes and ossicular chain. Histopathologic examination showed inflammation and granulation tissue, but no caseating necrosis or acid-fast bacilli. After surgery the symptoms resolved and remained well without evidence of infection recurrence 12 months after the operation.

Key words: non-tuberculous mycobacteria, *Mycobacterium abscessus*, chronic otitis media, multi-antibiotic chemotherapy, surgery
Introduction

Most cases of infectious diseases caused by non-tuberculous mycobacteria (NTM) are resistant to antibiotic therapy. Among NTM, *Mycobacterium abscessus* (*M. abscessus*) is the most pathogenic and chemotherapy-resistant, and the most rapidly growing [12]. It is therefore a problematic infection requiring specific diagnosis and treatment. Ear, nose, and throat (ENT) infections caused by *M. abscessus* are very infrequent now, and most are cervico-facial lymphadenitis [14-16]. Only 10 cases of chronic otitis media (COM) caused by *M. abscessus* have been reported in the literature and all of them were intractable cases in children [5-8,10]. To the best of our knowledge, we present here the first case report of adult COM caused by *M. abscessus*. Multi-antibiotic chemotherapy including high-dose clarithromycin is potentially effective for adult *M. abscessus* otitis media.

Case Report

A 61-year-old woman presented with recurrent right-sided otorrhea for seven years, and perforation of the tympanic membrane was diagnosed. In the episode in which she presented she had experienced right ear fullness and persistent otorrhea for two months, despite treatment with standard antimicrobial drugs. She did not have undue susceptibility to infections other than otitis media. Otoscopy revealed a small perforation of tympanic membrane with copious, serous otorrhea. The tympanic membrane and mucosa of the tympanic cavity showed edematous swelling (Fig.1). Initial cultures did not yield any bacteria. Computed tomography (CT) showed a soft tissue shadow occupying the middle ear and the mastoid cavity but no bone destruction (Fig.2). Laboratory studies revealed a normal white blood cell count and CRP. We
suspected middle ear tuberculosis, and acid-fast bacillus stains revealed mycobacteria (Gaffky 3). However, polymerase chain reaction (PCR) for \textit{M. tuberculosis} was negative. Eventually mycobacterial cultures and PCR yielded \textit{M. abscessus}, a type of NTM. Chest CT revealed no evidence of lung mycobacterial infection. Audiometry revealed right conductive hearing loss (Fig.3).

She received treatment with multiple antibiotics (600 mg/day oral clarithromycin, 200 mg/day intravenous amikacin, and 0.5 g/day intravenous panipenem/betamipron) for 36 days. The otorrhea stopped after 25 days of chemotherapy. CT of the temporal bone showed improved aeration in the tympanic cavity, but the soft tissue shadow remained unchanged in the attic and mastoid cavity 31 days after starting medication. Hence tympano-mastoidectomy was performed 36 days after starting medication. At operation, although serous otorrhea had already stopped, inflamed tissue remained in the middle ear cavity, and edematous pale mucosal tissue was noted around the stapes and ossicular chain. Histopathologic examination showed inflammation and granulation tissue, but no caseating necrosis or acid-fast bacilli.

After surgery the symptoms resolved and the right ear remained dry. She remained well without evidence of infection recurrence 12 months after the operation. Follow-up audiometry revealed improvement of the conductive hearing loss (Fig.4). Follow-up CT demonstrated good aeration in the tympanic cavity (Fig.5).

**Discussion**

Runyon first classified NTM into 4 groups based on growth rate and pigment production [2] and \textit{M. abscessus} belongs to the rapidly growing group (visible colony formation within 7 days of subculture) [11]. To become infected with NTM, it is
necessary to aspirate the organism or become inoculated with it from a natural reservoir; so far there is no evidence of transmission from one human to another [12]. *M. abscessus* was first recognized by Moore and Frerichs in 1953 [13]. It is a ubiquitous organism that is commonly found in soil and water. *M. abscessus* can cause disseminated disease in immunocompromized individuals but is not as serious in immunologically normal hosts. Previously reported patterns of *M. abscessus* infection include pulmonary disease, lymphadenitis, and ulcerative skin lesions. *M. abscessus* infections typically follow surgery, or penetrating trauma, particularly that causing retained foreign bodies.

ENT infections caused by NTM, particularly *M. abscessus*, are very infrequent. The most common ENT manifestation of NTM infections is cervico-facial lymphadenitis [14-16]. We found only 10 cases of COM caused by *M. abscessus* in the literature. Most of these patients were systemically well children who presented with painless chronic otorrhea that failed to settle with aural toilet and antimicrobial chemotherapy. To the best of our knowledge, we herein report the first case of *M. abscessus* COM in an adult.

NTM and *M. tuberculosis* infections of the ear have similarities in their clinical presentation, such as edematous tissue in the middle ear and chronic otorrhea that fails to settle with antimicrobial chemotherapy. On the other hand, *M. Tuberculosis* causes necrosis of the tympanic membrane and skin of the external auditory canal and can result in facial paralysis and necrosis of the nasopharynx, while NTM is less pathogenic and does not cause such destructive changes. CT of the temporal bone cannot differentiate NTM from other forms of otitis media or granulomatous disease but is generally performed to rule out bone erosion and intracranial complications [13,17,18].
Differentiation from other granulomatous diseases is performed by biopsy of the granulations and by culture looking specifically for NTM [9,18]. The diagnosis of *M. abscessus* infection is generally straightforward, i.e., the organism is an acid-fast, Gram-positive rod that resembles diphtheroid group on a Gram-stained smear. *M. abscessus* grows well on routine bacterial culture media. The cultures must be maintained for more than 4 days to allow sufficient time for growth of the organism [1,5]. In recurrent or persistent COM with otorrhea, mycobacterial cultures should be obtained to diagnose NTM and tuberculosis.

Until recently the treatment of *M. abscessus* was considered difficult. Rapidly growing mycobacteria are routinely resistant to standard anti-tuberculous drugs, and *M. abscessus* is particularly drug resistant. Spontaneous recovery is accordingly rare in these infections. Therapy consists of surgical debridement, removal of all foreign bodies, and long-term multi-antibiotic chemotherapy [4]. In the literature, surgical excision of the infected tissue is recommended for *M. abscessus* COM and long term antimycobacterial chemotherapy with clarithromycin and amikacin is also recommended for *M. abscessus*. Clarithromycin should be given at high doses (600-800 mg/day) and the chief disadvantage of multi-antibiotic chemotherapy is gastrointestinal symptoms due to high-dose clarithromycin. When performing surgical debridement, as much infected tissue must be removed as possible to avoid multiple surgical interventions, because one study showed that almost 50% of all cases needed multiple surgical debridements before the infection resolved [5,7,9,10].

In the present adult case, the infection was successfully eradicated with multi-antibiotic treatment and tympano-mastoidectomy. Multi-antibiotic chemotherapy including high-dose clarithromycin was very effective, and no bacteria including NTM
or residual suppuration were observed in the middle ear on the day of surgery. On the basis of our experience with this case, we recommend multi-antibiotic chemotherapy including high-dose clarithromycin for the initial treatment for adult cases of COM caused by *M. abscessus*.

*M. abscessus* otitis media is usually found in well children presenting with painless chronic otorrhea. Although it appears very uncommon in adult otitis media, *M. abscessus* should be considered as a possible cause of a chronically draining ear in an adult. It is important to obtain mycobacterial cultures to diagnose *M. abscessus* infection.

**Acknowledgement**

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Figure 5. Computed tomography on August 29, 2008 demonstrated good aeration in the tympanic cavity.
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<th>Authors</th>
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<td>Tympanomastoidectomy</td>
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<td>residual 30-dB conductive hearing loss</td>
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Fig 2 CT scan showed soft tissue shadow occupied in the middle ear and the mastoid cavity.
Fig3 audiogram revealed right conductive hearing loss
Fig 4 Two months after the operation. Improvement of conductive hearing loss.
Fig5  Three months after operation. Good airation in the tympanic cavity.
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Dear, Editor-in-Chief

ANL

Thank you for sending me the editorial response. We agree with removing “The first case report of” from the title. Thank you.

With best regards,
Makoto Ito, MD, PhD

Department of Otolaryngology, Clinical Neuroscience, Kanazawa University
Graduate School of Medical Science
TEL; 76-265-2413
FAX; 76-234-4265
makoto@med.kanazawa-u.ac.jp

On 2010/01/25, at 13:54, Auris Nasus Larynx wrote: