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Case Report

Iatrogenic invasive otomycosis

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ABSTRACT

Otomycosis usually develops in hot humid climates, and patients with otomycosis generally show a good response to medical treatment. However, invasive otomycosis is rarely observed in immunocompetent patients. The predisposing factors for invasive otomycosis include malignant neoplasms and increased use of steroids and broad-spectrum antibiotics. We report a unique case of iatrogenic invasive otomycosis in a 35-year-old woman who had been given ofloxacin eardrops over a long period, which led to an invasive fungal infection. The patient showed no response to general antifungal agents, but the infection was successfully controlled with voriconazole.

1. Introduction

Otomycosis is commonly observed in otolaryngology practice. In this disease, the most common fungal species isolated in culture are *Aspergillus* and *Candida*. However, cultures of the discharge are not routinely obtained because the condition is rapidly responsive to treatment with topical antifungal agents. An erroneous diagnosis of otomycosis and lack of caution in the administration of ototopical antibiotics may change the normal acidic environment of the external ear canal and the clinical process of otomycosis.

2. Case report

A 35-year-old woman with a history of right otalgia and headache for 2 months visited our otolaryngology clinic. She had developed right otalgia after an episode of acute pharyngitis and had visited a local otolaryngologic clinic 2 months previously. At the local clinic, she was diagnosed with acute otitis media and was administered empirical oral antibiotics (amoxicillin 500 mg four times a day) for 1 week. Because the otalgia and otorrhea persisted, she visited another otolaryngology clinic for a second opinion, where she was diagnosed with acute otitis media and otitis externa. Empirical oral antibiotics (amoxicillin and clabulanate potassium [Augmentin] 1 g two times a day) and ototopical drops (ofloxacin) were prescribed for 4 weeks. However, the otorrhea and otalgia, which were accompanied by headache, became more severe, and necrotizing otitis externa was suspected. Therefore, she was referred to our hospital for further evaluation and treatment.

Her medical history was unremarkable, and she was afebrile without any neurological deficit. The right external ear canal was injected and swollen with a purulent discharge. The ear discharge was thick and cheesy, and some pepper-like colonies were observed in the external ear canal. We also observed granulation tissue and bony destruction in the posterior wall of the external ear canal along with 20% perforation of the tympanic membrane (Fig. 1). Pure tone audiometry showed right conductive hearing loss (air-bone gap: 25 dB). High-resolution computed tomography scan of the temporal bone (Fig. 2) revealed increased soft tissue in the right middle ear cavity and the external ear canal.

The diagnosis of necrotizing otitis externa was made and we administered empirical intravenous antibiotics (amoxicillin and clabulanate potassium [Augmentin] 1200 mg every 8 hours and gentamicin 160 mg once a day [qd]); however, these antibiotics were discontinued 3 days later because the culture of the discharge yielded fungi instead of bacteria. However, the definite fungus species could not be identified initially in our laboratory. We performed a biopsy of the granulation tissue in the right external ear canal to rule out malignancy, and pathological examination revealed fibrous tissue with moderate infiltration of lymphocytes. We administered oral ketoconazole (400 mg qd) on the basis of a diagnosis of invasive otomycosis and performed daily clearing of

Conflict of interest: none.

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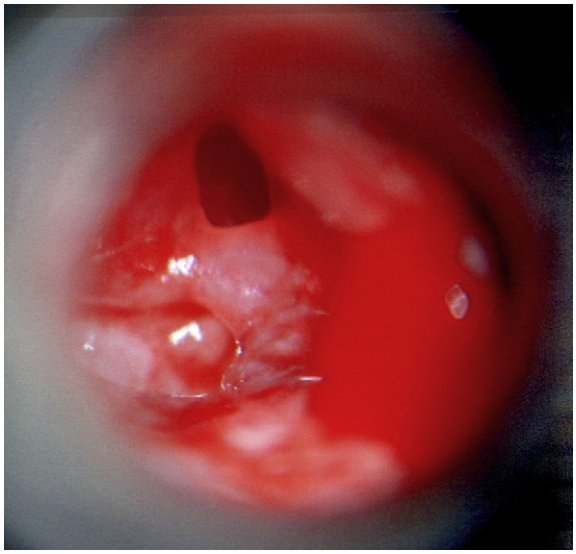

Fig. 1. Granulation tissue and bony destruction in the posterior wall of the external ear canal with 20% perforation of the tympanic membrane.

the ear discharge. The patient's headache and otalgia gradually subsided, and she was discharged 2 weeks later.

However, 3 days later, she was rehospitalized because of recurrent severe headache and otalgia. She again had an injected right external ear canal with purulent and cheesy discharge and some pepper-like colonies. The patient initially received intravenous fluconazole (200 mg qd) and gentamicin (160 mg qd) for 3 days after which these antibiotics were replaced by amphotericin B (30 mg qd) and piperacillin and tazobactam (Tazocin) (2.25 g every 8 hours) for 4 days. The patient's condition did not improve despite the treatment, and the fungal culture yielded *Aspergillus niger* (Fig. 3); therefore, we prescribed intravenous voriconazole (loading dose, 300 mg every 12 hours for 1 day; maintenance dose, 200 mg every 12 hours for 5 days), whereby her condition improved. Oral voriconazole (200 mg two times a day) was administered for another 5 days, and then the patient was discharged.

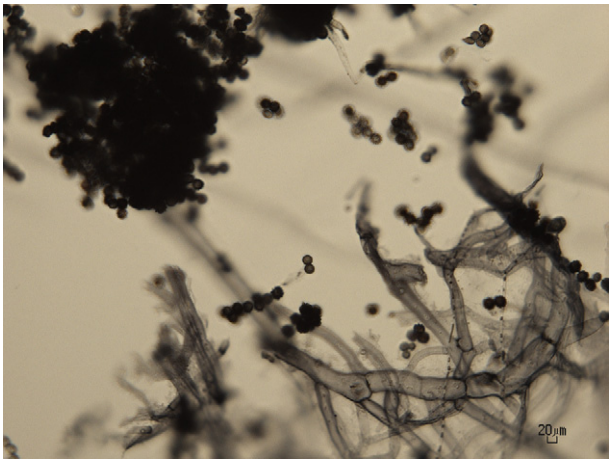

Fig. 3. Microscopic examination reveals condensed aggregation of vesicles and hyphal forms of *Aspergillus niger* (1,000× oil immersion).

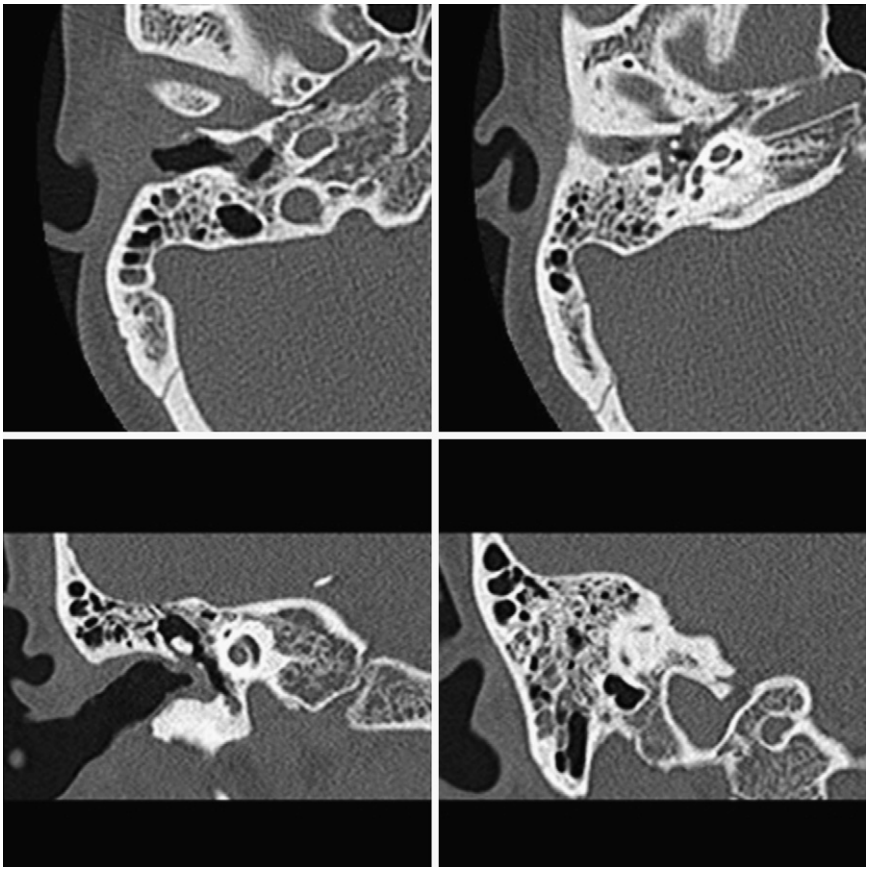

Fig. 2. CT scan of the temporal bone showing increased soft tissue in the right middle ear cavity, the external ear canal and the mastoid cavity. CT = computed tomography.

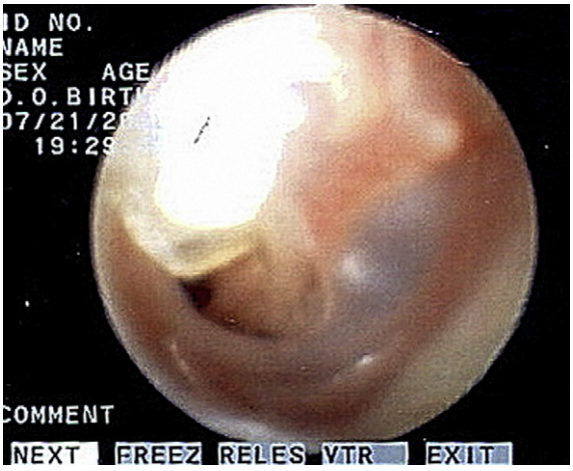

Fig. 4. The right tympanic membrane with 20% perforation.

The patient did not develop headache, otalgia, or otorrhea subsequently, but 20% perforation of the right tympanic membrane was still observed (Fig. 4). The patient underwent a Type I tympanoplasty 3 months later, and the postoperative course was uneventful.

3. Discussion

Otomycosis, also known as fungal otitis externa, is a fungal infection of the external auditory canal, and it commonly develops in hot humid climates, such as that found in Taiwan. The diagnosis of otomycosis is based on common presenting symptoms, including otalgia, otorrhea, and pruritus [1] and local examination findings, including an injected external ear canal with a fluffy white discharge. The treatment involves cleaning of secretions and debris in combination with application of topical antifungal agents. Cultures of the discharge are not routinely obtained because patients generally respond rapidly to treatment. Nevertheless, in cultures, *Aspergillus* and *Candida* are the most common fungal species isolated.

Otomycosis rarely results in serious complications. Chen et al. [2] classified fungal infections of the ear and temporal bone infections into four types according to extension of the disease process and treatment (Table 1).

The predisposing factors in invasive fungal infection include immunocompromised status, malignant neoplasms, and increased use of steroids and wide-spectrum antibiotics [3,4]. Widespread use of ototopical antibiotics has become a major concern because they may increase the risk of otomycosis [1,4,5]. Physicians often choose ofloxacin eardrops as the first-line therapy for otitis media and otitis externa because common pathogens can be eliminated with this treatment. However, ofloxacin may alter the homeostasis maintained by the normal flora in the external ear canal [4]. The recurrent and prolonged use of ofloxacin eardrops (pH 7), which changes the normal acidic environment of the external ear canal (pH 3–4), may lead to fungal proliferation and suppress the growth of competing bacteria, thereby contributing to a more severe bacterial infection or fungal proliferation.

In our patient, bacterial otitis externa was initially suspected at the other otolaryngologic clinics, but the patient showed a poor response to treatment. We hypothesize that otomycosis was not diagnosed at any of the previous clinics. Furthermore, the prolonged treatment with ofloxacin eardrops may have led to an invasive fungal infection. Furthermore, during the first hospitalization, the patient had a good response to oral ketoconazole treatment in the first 2 weeks. We presume that the use of ketoconazole masked the symptoms and the signs of invasive otomycosis. It may be the reason why she was rehospitalized 3 days later when she stopped oral ketoconazole. In addition, the main pathogenetic species of *A niger* is resistant to general antifungal agents but is sensitive to voriconazole.

Table 1
Classification of fungal infection of the ear and temporal bone by Chen et al. [2]

Type	Extent of the disease
I	Limited otitis externa
II	Otitis externa with extension into the mastoid cavity/mastoiditis
III	Invasive mastoiditis with nerve VII palsy
IV	Invasive mastoiditis, nerve VII palsy, and skull base osteomyelitis

To date, the common antifungal agents for the treatment of otomycosis include cresylate otic drops and topical azole antifungal agents (fluconazole, ketoconazole, and clotrimazole) [1,5]. However, recent reports have shown an increase in fungal resistance to these agents *in vitro* [6,7]. Because our patient showed a poor response to systemic ketoconazole, fluconazole, and amphotericin B, we chose voriconazole, which is used for the treatment of serious and invasive fungal infections [8]. Her clinical condition improved after administration of systemic voriconazole.

In Taiwan, ofloxacin eardrops are widely used in otolaryngology clinics for the treatment of otorrhea. Some clinics even prescribe eardrops containing steroids for the treatment of pruritus. Because our patient was immunocompetent and had not undergone surgery, we presume that the delayed diagnosis of otomycosis and the prolonged use of fluoroquinolone ototopical drops may have contributed to the iatrogenic and invasive fungal infection. Subsequently, the disease became invasive and extended to the middle ear cavity, and the pathogen developed resistance to general antifungal agents. In conclusion, it is emphasized that ototopical antibiotics be used cautiously by otolaryngology clinics. If persistent otorrhea is detected, especially after treatment with ototopical antibiotic agents, otomycosis should be considered. If otomycosis is diagnosed, then the fungal agent should also be identified as soon as possible, and optimal antifungal treatment must be given immediately.

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