Invasive Aspergillus of the temporal bone

James L. Connolly, MD¹, Jeffrey D. Carron, MD*

Department of Otolaryngology and Communicative Sciences, University of Mississippi School of Medicine, Jackson, MS

Received 22 June 2006

Abstract

Although invasive fungal infections of the paranasal sinuses have been well described in immunocompromised patients, those affecting the ear and temporal bone are rare. Described is the case of invasive aspergillosis of the temporal bones after bone marrow transplant in an 8-year-old girl. The diagnosis and treatment of such infections are discussed.

© 2007 Elsevier Inc. All rights reserved.

1. Presentation of case

An 8-year-old girl was seen in consultation by an otolaryngologist for a 1-week history of bilateral otorrhea and otalgia, and a 1-day history of grade 6/6 House-Brackmann left facial paralysis. She had been using ofloxacin drops for a week without improvement. She had a history of bilateral tympanic membrane perforations since undergoing an adenoidectomy and bilateral pressure equalization tube placement at the age of 2 years. She was diagnosed with pancytopenia and myelodysplasia syndrome with monosomy 7 at the age of 6 years. She underwent a bone marrow transplant that she subsequently rejected. Two weeks before the current consultation, she had her second bone marrow transplant. She had been followed in the past in the otolaryngology clinic and noted to have 30% central tympanic membrane perforations bilaterally and mild-moderate conductive hearing loss. Physical examination revealed yellow foreign material in the left external auditory canal (EAC) with whitish yellow purulent drainage filling the middle ear with significant amount of canal edema. The right EAC was mildly edematous with white purulent drainage. Neither eardrum could be seen on bedside examination. A Weber’s test demonstrated lateralization to the left ear, with bone conduction better than air bilaterally on Rinne testing. Audiometry revealed a 50 to 60 dB conductive hearing loss bilaterally. Axial and coronal computed tomography (CT) of the temporal bones without contrast showed soft tissue vs fluid filling the entire middle ear and mastoid. There was no obvious bony erosion (Figs. 1 and 2). Laboratory studies were significant for a white blood cell count of 600/mm³, with a differential count of 30% segmented neutrophils and 14% banded neutrophils.

Because she was septic and medically unstable, an initial middle ear and EAC debridement was performed. She was also begun on intravenous filgrastim (granulocyte colony-stimulating factor) in an effort to raise her white blood cell count. Once her condition permitted, a modified radical mastoidectomy and facial nerve decompression were performed. A biopsy of the ear canal skin, tympanic membrane, and middle ear mucosa was performed, as well as a small biopsy from the necrotic facial nerve (Fig. 3). A facial nerve biopsy prepared with Gomori’s methenamine silver nitrate stain was done (Fig. 4).

Over the next several weeks, her condition deteriorated and her liver began to fail. A repeat examination under anesthesia was done, in which a bone of the promontory was curetted for biopsy. The bone showed a similar invasion process to the prior biopsies, and she died several days later of sepsis and hepatic failure.

Histologic evaluation revealed a 0.5 × 0.3 × 0.2-cm aggregate of tan-yellow friable tissue fragments, which when sectioned using hematoxylin-eosin, showed hyphae
with multiple septae at acute angles. The hyphae were embedded and surrounded by fibrin and squamous debris. The hyphae also appeared to infiltrate the fibrous tissue. The canal skin showed necrotic epithelium with hoards of delicate hyphae with septations and branches with acute angles as well. A culture of the material acquired through biopsy grew *Aspergillus fumigatus*.

2. Discussion

External auditory canal infections can be credited to viral, bacterial, or fungal pathogens. Of these, the most deadly is necrotizing or “malignant” otitis externa, which is most commonly seen in the immunocompromised patient with poorly controlled insulin-dependent diabetes mellitus. The microorganism is usually *Pseudomonas aeruginosa*, but invasive fungal osteomyelitis should not be forgotten. This disease is often aggressive and can extend through soft tissue and vascular planes into the adjacent structures. If uncontrolled, multiple cranial neuropathies and septic thromboembolism can occur resulting in death [1-7]. The cardinal rules to management of invasive temporal bone infections are timely identification followed by prolonged antimicrobial therapy and early surgical debridement. In the routine work-up of malignant otitis externa, a technetium 99 bone scan, in which the technetium tracer is taken up by osteoblasts and remains positive in bone undergoing repair, is very sensitive. A gallium 67 citrate scan, in which the tracer is taken up by macrophage lysosomes during the inflammatory response, can also be used in following the course of the disease. Computed tomography can reveal evidence of bone destruction and soft tissue filling defects. However, definitive diagnosis of invasive fungal osteomyelitis requires biopsy for pathologic illustration of tissue invasion.

Mucormycosis, or zygomycosis, is a saprophytic fungal vascular infection that is propagated by vascular thrombosis and tissue infarction and is caused by fungi of the class Zygomycetes; the fungus grown in the reported case, *A. fumigatus*, is of the class Eurotiomycetes. It is characterized by a centrifugally disseminating necrosis,
which frequently exhibits a notorious black eschar plaque. It usually occurs in the immunocompromised patients because of cancer, immunosuppressive therapy, poorly controlled diabetes mellitus, blood dyscrasia, or protein-energy malnutrition. Invasive fungal infection has been widely reported in the rhinologic literature, but sparsely reported in the otologic literature. Review of the literature revealed 14 reported cases of invasive fungal osteomyelitis of the temporal bone [1-8]. Because of the rarity of invasive fungal infection of the temporal bone, nearly all prior reported cases had a delay in diagnosis subsequent to the misdiagnosis of bacterial induced malignant otitis externa.

Of the 14 cases of invasive temporal bone fungal infection reviewed, 6 patients were known to have died from their fungal infections at the time of publication, and the remainder had significant morbidity, including hearing loss, disequilibrium, and facial nerve paralysis. All prior reported cases required prolonged systemic antifungal therapy and radical surgical debridement, with or without adjuvant therapy. Because of the rarity of the disease, the therapy for temporal bone fungal infections has been extrapolated from the literature on sinonasal infections. Although topical antifungals have been used for sinonasal mucormycosis, high-dose intravenous lipid amphotericin B is the only proven medical therapy [8]. Adjuvant therapies such as interferon γ, colony-stimulating factors, autologous peripheral blood stem cell transplantation, and hyperbaric oxygen have also been reported in overall combined therapeutic approach to the treatment of invasive fungal infection of the paranasal sinuses [8-12].

Risk factors for invasive fungal infection of the temporal bone in immunocompromised patients are not well documented; however, it can be assumed that they are similar to risk factors for invasive fungal sinusitis. Otitis media and sinusitis have a similar pathogenesis, and invasive fungal sinusitis in bone marrow transplant patients is more common with granulocytopenia [13,14]. The rarity of invasive fungal otitis as compared with sinusitis in this patient population may be explained by the usual barrier of the tympanic membrane and lack of direct exposure of the eustachian tube orifice to inhaled fungal spores, compared with the proximity of the sinus ostia with the middle turbinates and ostiomeatal complex, where much inhaled debris is deposited. In the patient presented herein, her preexisting otorrhea with perforations had been treated with chronic administration of ototopical drops, which have been shown to predispose to fungal infection as well [15]. She did have a low granulocyte count at the time of diagnosis, and granulocyte colony-stimulating factor was instituted immediately, with a modest response shown in complete blood count with differential.

In summary, diagnosis of invasive fungal temporal bone infection requires a high index of suspicion, because it is often misdiagnosed as malignant otitis externa. It is almost always associated with a neutropenic immunocompromised state. Aggressive debridement, antifungal therapy, and restituation of an immunocompetent state are the recommended therapies. Without these interventions, death is likely, and even after the recommended therapy, mortality and morbidity related to facial nerve palsy, hearing loss, and balance problems are common.

References


