Fungal Osteomyelitis of the Temporal Bone: A Review of Reported Cases

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Introduction
Otopathogenic fungal infections of the temporal bone are rare and often represent a diagnostic challenge. A summary review of the literature divulged only eight cases of fungal osteomyelitis of the temporal bone. The authors add a recent case of their own, which illustrates the difficulty in distinguishing this rare disease from the more common bacterial necrotizing external otitis. Both conditions present with deep ear pain and persistent otorrhea. Imaging studies show similar findings in both conditions. Bone scans show evidence of bone infection, computerized tomography (CT) scans reveal bone destruction, magnetic resonance imaging (MRI) demonstrates soft tissue inflammation.

Bacterial necrotizing external otitis is caused usually by Pseudomonas invasion of the bony external canal in elderly diabetic patients, while fungal osteomyelitis is caused usually by Aspergillus invasion of the bony middle ear in immunocompromised patients. Early diagnosis of a fungal etiology depends on a high index of suspicion. Lack of definitive bacterial cultures and inadequate response to antipseudomonal therapy should raise the possibility of mycotic infection. This case report and literature review of similar cases illustrate the management dilemma which rare temporal bone fungal infections can cause.

Case Report
A 51-year-old, diabetic man saw his otolaryngologist with a 2-month history of right ear pain. He was given oral antibiotics for approximately 4 weeks without improvement. He was then admitted to an outside facility where he received intravenous (IV) antipseudomonal antibiotics for 7 days. Cultures from the right ear grew Staphylococcus epidermidis and diphtheroids. He was discharged home on oral antibiotics for 3 weeks, again with no response. He was referred to our facility for evaluation and further management with a presumptive diagnosis of necrotizing external otitis. On presentation, he was complaining of intermittent right otalgia and right hearing loss. On examination, the right external auditory canal was diffusely swollen, more so in the posterior superior portion. There were no granulations, ulcers or discharge. His tympanic membrane appeared normal. Mild trismus, tenderness over the right temporomandibular joint

![Diagram](https://example.com/diagram.png)

Figure 1. Audiogram showing moderate to profound mixed hearing loss on the right and severe high frequency sensory neural hearing loss on the left with fairly good speech discrimination bilaterally.

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Figure 2. Tc bone scan showing increased uptake in the right temporal bone consistent with osteomyelitis.

Figure 3. CT scan axial view of the temporal bone showing opacification of the mastoid and middle ear.

Figure 4. MRI with contrast (gadolinium) showing opacification and enhancement of the middle ear and mastoid consistent with otomastoiditis.

Figure 5. Coronal view showing bone erosion of the glenoid fossa with lateral displacement of the mandibular condyle.

(TMJ), and preauricular fullness were evident. Facial nerve function was normal. His audiogram is shown in Figure 1. A workup included a bone scan and CT scan of the temporal bone (Figures 2 and 3), and MRI with contrast was also done (Figure 4). Biopsy of the external canal skin was negative for tumor. Except for a sedimentation rate of 76 mm/1st hour and a C-reactive protein of 8.2, his blood picture and chemistry were within normal limits. His blood sugar was under good control with insulin. A repeat ear culture showed Colegatus negative staphylococci and yeast. He was admitted to the hospital and was treated with IV antipseudomonal antibiotics for 2 weeks with mild improvement. He was discharged and kept on home IV antibiotics.

One week later, he developed worsening ear pain and increased preauricular induration and tenderness. The ear canal was dry and the tympanic membrane intact. A repeat CT scan showed erosion of the glenoid fossa with lateral displacement of the mandibular condyle (Figure 5). Fine needle aspiration (FNA) of the TMJ and preauricular region was inconclusive. It was felt that a deep-seated malignancy masquerading with ear pain should be ruled out. Accord-
ingly, exploration of the right preauricular region, right superficial parotidectomy and intraoperative FNA of TMJ were done. Histopathology of surgical specimens revealed no evidence of neoplasia. Postoperatively he continued to complain of severe pain in and around the ear, and 1 week later he underwent a modified radical mastoidectomy. At surgery the external canal skin was diffusely thickened. In the middle ear there was evidence of mucosal thickening with diffuse osteitis, erosion of the anterior canal wall and glenoid fossa to egg-shell thickness. Moreover, there was debris that the tympanic segment of the facial nerve and dentotens high-riding jugular bulb; there was no evidence of mastoid disease. A generous meatoplasty was performed at the end of the procedure. Histopathology of tissue specimens showed evidence of chronic inflammation and no evidence of neoplasia. Cultures from surgical specimens showed *Aspergillus flavus* in one out of two culture media and *Candida ciferri* in the other. The results were considered inconclusive and the patient was still maintained on antipseudomonal antibiotics.

Six weeks later he developed acute right facial paralysis for which he underwent re-exploration of the right ear. The previous meatoplasty had totally stenosed and an abscess was found in the middle ear and mastoid amidst scar tissue. The previously noted debris of the facial nerve canal was identified and the nerve was found to be diffusely edematous and inflamed. The nerve sheath was incised longitudinally for decompression. Cultures from surgical specimens revealed *Candida parapsilosis*, *albicans* and *glabrata*. The patient was started on oral Diflucon with temporary relief. Two months later, the patient came in with recurrent otalgia and his revision meatoplasty was completely closed with scar tissue. He was started empirically on IV Amphotericin B. Two weeks later, he underwent revision meatocanaloplasty using split-thickness skin graft as well as exploration of the middle ear, mastoid and intratemporal fossa. There was no evidence of inflammation, pus or granulation tissue. Cultures grew *Aspergillus flavus*. The patient was maintained on Amphotericin B for a total dose of 3 gm with marked relief of his otalgia and a clean, dry ear with wide open meatoplasty. His facial nerve function has completely recovered.

**Discussion**

A brief, incomplete review of the literature detected 8 cases. These 8 cases and the authors' own case will be discussed. (Figure 6). Fungal infections of the temporal bone represent a rare clinical entity. Secondary mycosis of the temporal bone could be of meningogenic, hematogenic or rhinogenic origin. The causative agents included cryptococcus, candida, blastomyces or mucor. Primary osteogenic fungal infection of the temporal bone is almost always caused by *Aspergillus fumigatus and less commonly by Aspergillus flavus*. *Aspergillus niger* which is responsible for noninvasive otomycosis has not been implicated in fungal temporal bone infections. The clinical picture of fungal skull base osteomyelitis (SBO) includes intractable deep ear pain, persistent otorrhea, and progressive cranial nerve paralysis. The facial nerve being the most commonly involved. More extensive cases may also present with jugular foramen syndrome with paralysis of cranial nerves IX, X and XI. This clinical presentation closely resembles that of bacterial necrotizing external otitis (NEO). All reported cases of fungal SBO (except one) were initially misdiagnosed as NEO.

Unlike NEO, fungal SBO has not shown a strong correlation with diabetes mellitus. However, most patients with fungal SBO were immunocompromised. This was mostly due to neutropenia secondary to chemotherapy for lymphomas, leukemias or other myelodysplastic syndromes. Most patients were advanced in age and the only young patient (27 years old) had AIDS.

There are two levels of defense against Aspergillus invasion. Macrophages are considered the primary or first line of defense and are instrumental in preventing tissue invasion by the conidial forms. Polymorphonuclear leukocytes (PMNs) constitute the second barrier and play a key role in protection against mycelial forms. Both lines of defense must be breached before the fungus can establish progressive infection.

The pathogenesis of invasive *Aspergillus* seems to involve: 1) deficiency of the immune barriers against the organism; 2) local point of entry for the fungus; and 3) disruption of the normal bacterial flora by recent or concurrent therapy with broad spectrum antimicrobial agents. These predisposing factors are evident in the collective group of patients reported to have otogenic fungal SBO. Almost all patients had received broad spectrum antibiotics for prolonged periods of time for a presumed NEO, and

![Figure 6. Characteristics of 9 patients with fungal osteomyelitis of the temporal bone.](entimagazine.com/images/figure6.png)
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Almost half the patients had a previous history of chronic sinus media. It is possible that these two factors have led to fungal overgrowth and when the immune system was compromised, the opportunistic fungus gained access to the bone with tissue invasion.

With the exception of one case, the diagnosis of fungal SBO was delayed for several weeks or months. Patients received IV antipseudomonal antibiotics for an average of 6 weeks. The lack of adequate clinical response as manifested by improved otalgia or otorrhea makes the diagnosis of NOE doubtful. Routine cultures from ear discharge were non-conclusive and failed to reveal a specific pathogen in any of the reported cases. Laboratory tests were generally non-diagnostic. An elevated ESR and C-reactive protein, although non-diagnostic, could be helpful in monitoring the clinical course of the disease. A variety of serologic tests for detecting antibodies in patients with Aspergillosis have been reported. Such antibodies are generally uncommon in sera from healthy personnel. The tests that appear to be most reliable are the immunodiffusion and ELISA. These have been positive in 70-80 percent of patients with invasive pulmonary aspergillosis. Unfortunately, in immunocompromised patients, these tests appear to have limited value because these patients have little capacity to elaborate antibodies. The imaging studies were generally non-specific. Technetium 99m bone scans accumulate at sites of osteoblastic activity secondary to an inflammatory or neoplastic process, including necrotizing external otitis, temporal bone malignancy, TMJ disorders, and recent or old fractures (low-specificity). A mere 10 percent increase in osteoblastic activity will turn a scan positive (high sensitivity). However, it remains positive for several weeks after clinical resolution, and therefore, is not particularly useful in monitoring the course of the disease. Gallium scanning may have a better role in monitoring the response to therapy. Gallium citrate is incorporated into granulocytes and localizes in areas of inflammation in soft tissue and bone. It is highly sensitive (80-100 percent). However, like 99mTc bone scans, it has very low specificity and can be positive in cases of simple external otitis or any inflammatory conditions of the middle ear cleft. Both technetium 99m and gallium scans have the disadvantage of imprecise anatomic localization of disease. CT scans and MRI are the current modalities of choice for defining the anatomic extent of the disease. While CT is more superior for bone detail, MRI is especially useful in delineating soft tissue abnormalities. Although both CT and MRI remained abnormal several months after clinical resolutions, it seems that serial scans help to monitor the clinical course of the disease.

The diagnosis of fungal SBO depends on the identification of pathogenic fungal forms. The mere presence of Aspergillus species on culture from ear discharge does not necessarily indicate a causal role in the disease. Suspicion should be heightened when either Aspergillus fumigatus or less commonly Aspergillus flavus is identified. The definitive diagnosis rests most securely on the demonstration of invasive Aspergillus in tissues obtained from surgical specimens. Tissue specimens should be placed in sterile, screw top bottles containing a drop of saline for moisture. The specimen may be examined directly with a 10-20 percent KOH fresh preparation. Aspergillus can be identified in tissues by its classic morphologic appearance. This includes septate hyphae, with dichotomous branching at approximately 45 degrees, and a uniform diameter of 3-4 μm. Special staining and immunofluorescence may help to type the organism.

After the diagnosis of fungal SBO is firmly established, the treatment of choice is IV Amphotericin B. The optimal dose and duration of therapy are unknown. However, high doses early in the course of the disease may be curative even in immunocompromised patients. The usual dosage for invasive aspergillosis infections is approximately 3 gm given over many weeks. The selection of an arbitrary duration of therapy (for e.g. 6 weeks) is discouraged. Early cessation of therapy is associated with a high recurrence rate and greater morbidity and mortality. The most serious and potentially fatal side effect of Amphotericin B is nephrotoxicity. Serum creatinine and BUN should be carefully monitored and the dosage adjusted accordingly. This may require smaller daily doses and/or longer time intervals between successive doses which prolongs the total duration of therapy. Consultation with infectious disease specialists is most helpful in this respect. The role of surgery is primarily diagnostic. In patients with non-specific cultures, exploration of the mastoid and middle ear may provide material for culture and histologic examination essential for accurate diagnosis. Debridement of necrotic tissue may be indicated when the disease either progresses or reaches a plateau on appropriate antifungal therapy.

Conclusions
1. Fungal SBO has deep ear pain, purulent otorrhea and progressive cranial nerve paralysis, mostly the facial nerve, simulating bacterial NEO.
2. Unlike NEO, there is no clear correlation between fungal SBO and diabetes mellitus.
3. Predisposing factors for fungal SBO include immunodeficiency and advanced age.
4. The diagnosis of fungal SBO should be suspected in the absence of definitive bacterial cultures and the lack of an
adequate response to IV antipseudomonal therapy.  

5. Definitive diagnosis depends on demonstration of invasive fungal pathogens (mostly Aspergillus fumigatus) in tissue specimens.  

6. Therapy consists of adequate doses of Amphotericin B over a prolonged period of time.

7. Surgery is recommended for establishing the diagnosis and debridement of necrotic tissue.

References:


