ASPERGILLUS OTOMASTOIDITIS IN ACQUIRED IMMUNODEFICIENCY SYNDROME

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ABSTRACT

The diagnosis and therapy of fungal infection in the paranasal sinuses of the immunocompromised host, including those with acquired immunodeficiency syndrome (AIDS), has been discussed in recent literature. However, only limited reports have been presented on otologic infection in AIDS patients. A review of 26 such patients with otologic disease included no cases of fungal otopathy. Our recent experience with two patients with Aspergillus otomastoiditis is presented. The extent of fungal infection in these cases was early-stage in one patient and late-stage in the other. The case histories, management, and outcomes are presented to provide insight into this previously unreported complication of AIDS.

Otomycess occur in immunocompetent and immunocompromised hosts. Nine percent of external otitides are due to fungal infection with the most common pathogens being *Candida* species and *Aspergillus niger*. Most of these infections are dealt with readily by surface cleaning and topical application of antifungal agents.

More extensive fungal infections can rarely occur in the immunocompetent host. Just as there have been unusual cases reported of normal hosts suffering from necrotizing external otitis of bacterial origin, so there have also been case reports of fungal origin in elderly immunocompetent patients with skull base osteomyelitis due to *Aspergillus fumigatus*. Immunosuppressed individuals are susceptible to all opportunistic infections including fungal infections of the ear and temporal bone. These reports, however, are much less frequent than those of paranasal sinus fungal infection. Pettrak et al published a case of necrotizing external otitis with skull base invasion due to *Aspergillus fumigatus* in a patient who was granulocytopenic secondary to acute myelogenous leukemia. Menachof et al presented a similar case. Schubert et al reported successfully treating a case of *Aspergillus fumigatus* otomastoiditis in a bone marrow transplantation patient.

Recently, there have been reports documenting the spectrum of head and neck manifestations of opportunistic infections in AIDS. There were no cases of fungal otomastoiditis included among these. Kohan et al reported otologic manifestations of AIDS in a series of 26 patients. These included otitis externa (16%), acute otitis media (16%), sensorineural hearing loss (19%), otitis media with effusion (14%), herpes zoster myringitis (5%), aural polyps with *Pneumocystis carinii* (5%), mastoiditis of unstated pathogen (5%), tympanic membrane perforation (5%), and cholesteatoma (2%). Williams reported a series of 10 pediatric AIDS patients with findings of serous otitis media, acute otitis media, and chronic otitis media with effusion.

We have had recent experience with *Aspergillus* otomastoiditis in two patients with AIDS. Each patient presented at a different stage of their disease; one late and one early. Case histories, management, and outcome are presented in an effort to provide insight into this previously unreported complication of AIDS.

Case 1

A 27-year-old woman with a history of right ear infections for several days was first seen by an otolaryngologist prior to cholecystectomy. The past medical history included colectomy with ileostomy for ulcerative colitis, following which she developed chronic non-A non-B hepatitis and became antibody positive for human immunodeficiency virus. Her initial complaint was right otalgia and otorrhea. Examination revealed thick, greenish-yellow fluid filling...
the right ear canal and underlying right anterior tympanic membrane perforations which, within a few days, coalesced to produce a single perforation of 25 percent of the tympanic membrane. The culture of the discharge grew *Staphylococcus aureus* and *Aspergillus fumigatus*. A CT scan of the temporal bone demonstrated thickened soft tissue in the middle ear and mastoid. A biopsy of the middle ear mucosa at the time of cholecystectomy showed chronic inflammation without invasive fungal elements. The patient's ear infection was treated with amphotericin B drops and Domeboro otic drops. She was admitted 3 weeks later for partial dehiscence of her cholecystectomy wound. Oral candidiasis was present and treated with Mycostatin. Nasal cutaneous herpetic-like lesions were present and treated with topical acyclovir. During the following weeks, there was continued otalgia and otorrhea, though examination revealed a smaller tympanic membrane perforation and clear drainage. Therapy was continued unchanged. Seven weeks after the first evaluation, she was readmitted for disequilibrium, nausea, and otalgia. The tympanic membrane had almost completely healed with greenish fluid behind it. This was re-opened with a myringotomy and a tympanostomy tube was inserted. A culture of the fluid grew *Aspergillus fumigatus*. The patient's symptoms improved with the drainage and meclizine. The patient at this time was neutropenic and the T4/T8 ratio (0.3) was depressed and becoming progressively worse. Nine weeks after initial evaluation, otalgia persisted and a CT scan was obtained. The findings were of extensive soft tissue density within the right mastoid region with no evidence of intracranial abscess (Fig. 1). The senior author first evaluated the patient at this time and recommended a mastoidectomy that, when performed, showed extensive bone destruction sparing only the bone of the tegmen.* The tissues submitted for microscopic examination revealed fungal hyphae present in necrotic granulation tissue (Fig. 2) and the culture confirmed the presence of *Aspergillus fumigatus*. Four days after the surgery, the patient developed a facial nerve paresis and, several days later, a partial dehiscence of her postauricular incision. Systemic amphotericin B therapy was started but, due to poor patient tolerance, it was discontinued and replaced with Itraconazole when it was established that the *Aspergillus* species isolated was sensitive to that drug. A postoperative MRI showed a striking degree of brain atrophy and no evidence of intracranial abscess. The patient's otalgia was improved and her course remained stable for 6 weeks. She then developed progressive lethargy and weakness. A lumbar puncture was performed and was unremarkable for evidence of infection. A repeat MRI showed inflammatory mastoid disease and thrombosis of the dural sinus with extension into the temporal lobe, cerebellum, and brainstem (Fig. 3).

The patient refused further therapy and died at home 6 months after initial evaluation of her aural symptoms.

**Comment**

This case exemplifies an indolent course of invasive *Aspergillus* otomastoiditis in an AIDS patient. The physicians initially caring for the patient felt that the fungal isolates from the ear cultures represented colonization, and not true infection. However, the patient's symptoms were progressive and, in the setting of an immunocompromised host, should have been considered significant and have led to more ag-
gressive documentation of persistent and/or progressive otomastoiditis disease by earlier follow-up with CT or MRI. Once failure of response to therapy was documented clinically and/or radiologically, mastoidectomy was indicated to obtain tissue for histology and culture and to debride the infected mastoid. Additional therapy following mastoidectomy was not well tolerated and the T4/T8 ratio in this patient became ominous, suggesting that no additional therapy (i.e., drainage and/or ligation of the sigmoid sinus) would have altered the patient’s course.

Case 2

A 27-year-old male with AIDS diagnosed 3.5 years previously and on zidovudine therapy presented with fever, headache, rhinorrhea, left-sided otalgia, tinnitus, and hearing loss. Examination demonstrated an erythematous left ear canal with moist debris. The tympanic membrane was intact, but with decreased mobility and with an opaque, thickened appearance compared to the normal right side. An audiogram revealed a mild left conductive hearing loss. A sinus x-ray series was normal. Lymphocyte parameters on initial evaluation revealed a favorable T4/T8 ratio of 0.9.

A phenol-tipped probe was applied to the left tympanic membrane and tympanocentesis performed. No fluid was obtained. Culture showed only scant *Aspergillus fumigatus*, coagulase positive *Staphylococcus* and diphtheroids. Initial follow-up examination 48 hours after tympanocentesis showed a small tympanic membrane perforation, but larger than expected. Follow-up 1 week later showed white fungal balls and green discharge in the ear canal and middle ear and an enlarging perforation. Cultures again grew *Aspergillus fumigatus* and stains and cultures were negative for bacteria. Clotrimazole topical drops were started at this time for the infection. The patient was followed for the next 2 weeks with frequent topical cleansing and Cortisporin otic drops were added. Though the otorrhea diminished, the patient complained of intermittent fevers, left dull aching otalgia, and mild positional disequilibrium. A temporal bone CT scan was obtained and showed soft tissue filling the mastoid and petrous air cells without signs of bony destruction (Fig. 4). Ciprofloxacin 750 mg b.i.d. was added to the therapy and administered for 2 weeks. All of the patient’s symptoms except hearing loss resolved. A follow-up audiogram demonstrated some slight progression of the conductive loss consistent with the increased size of the perforation and a small 4000-Hz depression of bone conduction. A repeat culture from the ear produced no growth of any organism. A follow-up CT scan obtained 2 months after therapy was initiated showed complete resolution of the previously noted changes (Fig. 5). Follow-up at 12 months after initial examination...
Figure 5. Case 2. CT scan of temporal bone with complete resolution of the soft tissue that previously filled the mastoid and petrous air cells.

revealed a stable, dry total perforation and normal CT scan of the temporal bone.

Comment

The absence of documented tissue invasion by *Aspergillus* and this patient’s course are most consistent with a noninvasive *Aspergillus* otomastoiditis. This patient had more favorable prognostic features than Case 1 in that he was not as lymphocytopenic and had a more favorable T4/T8 ratio. The cause for the progressively enlarging tympanic membrane perforation is not clear as it was not felt that the extent of phenol application could account for it. In addition, the salutary effect of the broad spectrum antibiotic, ciprofloxacin, raises the question of whether the *Aspergillus* cultured was merely colonizing and not a true pathogen. If this patient had not rapidly responded to the therapies applied, mastoidectomy would have been recommended to debride the area and to determine whether invasive *Aspergillus* was present and whether systemic antifungal therapy was necessary.

DISCUSSION

In paranasal sinus disease it is postulated that *Aspergillus* spore inhalation into the sinus cavity is ordinarily well-tolerated, but that in either an anaerobic environment (i.e., underlying bacterial sinusitis) or in cases with previous prolonged antibiotic treatment, the immunocompetent host may develop a noninvasive form of the disease in which the fungal elements do not actually invade the mucosa or deeper lying structures but colonize the surface.12-14 However, in the immunoincompetent patient (i.e., cancer, chemotherapy, AIDS), where there is a coincident leukopenia, resistance of the tissue to invasion is impaired. This poses an increased risk for local fungal invasion with vascular extension that may result in regional or distant spread. Although there is no reason to believe that a similar sequence of events does not take place with *Aspergillus* otomastoiditis, based on its relative infrequency, there must be differences in predisposing local factors between otologic and paranasal involvement.

The possible routes by which *Aspergillus* obtains access to the ear may be more variable than with paranasal sinus disease. Access via an initial external otitis extending as a necrotizing external otitis, though rare, is reported.23 Loss of tympanic membrane integrity would provide access to the middle ear for external pathogens. Tympanic membrane perforation may occur spontaneously, as in Case 1. Additionally, as in Case 2, it is possible that a fungal external otitis may extend through an iatrogenic portal to the middle ear and mastoid or may occur in a setting of chronic otitis media. In AIDS patients who often demonstrate lymphoid hyperplasia including the adenoids, there may be eustachian tube obstruction with secondary serous otitis or acute otitis media. If anaerobic conditions precede fungal spore presentation to the middle ear of a susceptible host, an environment that fosters *Aspergillus* infection is present. It is not clear whether the earlier form of *Aspergillus* otomastoiditis in Case 2 would have progressed to that of Case 1, but it is suspected that this would have occurred, because a prolonged noninvasive infection may convert to an invasive form.15 It is possible that the effect of ciprofloxacin in Case 2 was to eradicate any underlying bacterial infection and to decrease the anaerobic conditions in the middle ear and mastoid that may have favored fungal growth.

It is well documented that successful treatment of invasive fungal infection consists of early diagnosis, surgical debridement of infected tissues, and intravenous antifungal therapy.1617 Of prime importance is a high index of suspicion when an immunocompromised patient presents with otomycoses. Prompt institution of therapy consisting of cleansing and application of antifungal agents is important. If initial therapy does not result in resolution and symptoms continue or progress, this may indicate that extension into underlying tissues has occurred. At this time a CT or MRI scan is necessary to fully evaluate deeper-lying structures and the extent of the disease. Consequently, if invasion is suspected, surgical debridement and intravenous antifungal therapy (amphotericin B) is indicated. Additionally, if there is a therapeutic drug-induced immune suppression, consideration should be given to reducing the immunosuppressed state, allowing a more vigorous immune response to be generated. In patients with immunosuppression that is drug induced, this can, at times, be accomplished more readily than with
AIDS patients. However, there are varying degrees of immunocompetence in patients with AIDS as noted in Cases 1 and 2 reported here. The state of immunocompetence as reflected by such measures as the T4/T8 ratio or the absolute T4 cell count may be used as a guide as to when to apply the therapies that are available.

**SUMMARY**

Two patients with AIDS and *Aspergillus* otomastoiditis, a previously unreported head and neck complication of AIDS, are presented.

The increased risk of oomycoses progressing to otomastoiditis in the immunocompromised hosts mandates that these patients be treated with a high degree of suspicion at evaluation. This will lead to the early recognition and institution of appropriate medical therapy and surgical intervention.

**REFERENCES**