Invasive Aspergillosis of the Temporal Bone: An Unusual Manifestation of Acquired Immunodeficiency Syndrome

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(Editorial comment: Invasive mycotic infection of the inner ear is rare and is almost invariably associated with an immune disorder. Radical mastoidectomy and high-dose amphotericin B apparently eradicated the disease in this patient with acquired immunodeficiency syndrome.)

Invasive fungal infections have become increasingly common and represent a situation in which ubiquitous fungal species become aggressive opportunistic pathogens in immunocompromised hosts. Invasive aspergillosis is most frequently encountered in patients with lymphoproliferative disorders. Additional risk factors include prolonged courses of antibiotics, cytotoxic chemotherapy, steroids, neoplasia, organ transplantation, and disorders of cell-mediated and humoral immunity. Manifestation of invasive aspergillosis in the head and neck are infrequent and generally limited to the paranasal sinuses. Involvement of the inner ear is rare, and to the authors' knowledge, this represents the first report of invasive aspergillosis confined to the temporal bone presenting with acute facial paralysis and sensorineural hearing loss.

CASE REPORT

The patient was a 49-year-old bisexual white man with a history of acquired immunodeficiency syndrome (AIDS) referred to the otolaryngology service with a 2-week history of left facial paralysis. He had developed left purulent otorrhea 6 months previously and had been treated with numerous courses of oral antibiotics at an outlying clinic with intermittent improvement. Before the onset of the acute facial paralysis, he had noted otalgia and increased ototympanous discharge, possibly representing fungal superinfection of chronic bacterial otitis media. The past medical history was significant for a positive antibody test to the human immunodeficiency virus (HIV) 31 months and clinical manifestation of AIDS 13 months before presentation. He had confirmed cutaneous Kaposi's sarcoma that was treated with low-dose chemotherapy, alternating vincristine and vinblastine, on a weekly basis for the 5 months before presentation. Chemotherapy was complicated by prolonged leukocytopenia with a low absolute neutrophil count. Medications at the time of admission included zidovudine (AZT), acyclovir, terfenadine, and ciprofloxacin.

On examination, he was a thin male with multiple areas of Kaposi's sarcoma involving his face, trunk, and extremities. Examination of his head and neck showed a left peripheral facial paralysis. Higuer stimulation of the facial nerve required 6 mA on the left compared with 2 mA on the right. The left tympanic membrane had two perforations in the pars tensa. The pars flaccida was pale and the middle ear filled with debris. The remainder of the examination was unremarkable.

Pertinent laboratory data include a white blood cell count (WBC) of $1.8 \times 10^9/L$ with 0.30 neutrophils, 0.12 bands, 0.35 lymphocytes, 0.25 monocytes, 0.08 eosinophils, and 0.02 basophils. The absolute neutrophil count was 0.54 $\times 10^9/L$. The anti-HBs and the anti-HBc were positive whereas the HBsAg and the anti-HAV IgM were negative. No evidence of erosion of the scutum was evident. A tuberculin skin test (PTD) and a candidal antigen control were both negative.

Audiogram demonstrated a profound mixed hearing loss on the left with a normal hearing level on the right. The patient was initially treated with Timentin (SmithKline Beecham Pharmaceuticals, Philadelphia, PA) 3.2 g intravenously every 4 hours. A thin-cut computed tomography (CT) scan of the temporal bones was obtained that showed soft tissue filling the middle ear (Figs. 1A,B). There was opacification of the mastoid air cells with fluid density. Focal areas of erosion anterior to the tegmen involving the facial nerve at its genu and the scutum were noted.

Microscopic examination of the left ear on the third day of hospitalization showed a significant change, with the perforation of the pars tensa now being almost complete. There was extensive necro-
Fig 1. (A) Axial CT section shows soft tissue in the middle ear and mastoid air cells. There is bony erosion in the vicinity of the geniculate ganglion (arrow). (B) Serial coronal CT sections show soft tissue in the middle ear and mastoid with dehiscence of the tegmen (arrow). Thickening of the skin of the external auditory canal is present.

sis of the mucosa of the mesotympanum. The tympanic membrane and mucosa of the middle ear were noted to be completely insensate. A biopsy was performed, and histological examination of the frozen sections showed an invasive mycotic infection. The patient was taken to the operating room where he underwent a radical mastoidectomy. The mucosa of the mastoid air cells was thickened, consistent with chronic otitis media. There was a defect in the anterior tegmen with exposed dura, which was repaired with a temporalis muscular flap. Permanent histological sections of the material were consistent with invasive aspergillosis (Figs. 2A,B). Cultures of the material grew Aspergillus fumigatus. Postoperatively, the patient was begun on intravenous amphotericin B (1 to 2 g) at 0.5 to 0.6 mg/kg/week.

The packing was removed from the mastoid cavity on the 10th postoperative day, at which time viable mucosa was noted. There was no improvement in facial nerve function as determined by electrical stimulation. A CT scan performed on the 12th postoperative day showed a clear mastoid defect without evidence of further fungal disease of the temporal bone or intracranial extension. Amphotericin B therapy was complicated by fever, mild renal insufficiency, bone marrow suppression, altered mental status, and electrolyte abnormalities. The patient refused to have a lumbar puncture (LP) performed. His altered mental status...
Fig 2. (A) Microscopic photograph shows branched, septate hyphae of Aspergillus fumigatus infiltrating the middle ear tissue (hematoxylin and eosin, original magnification x 600). (B) Microphotography showing the presence of numerous Aspergillus hyphae in the mastoid bone material (Gomori's silver methenamine stain, original magnification x 400).
improved with correction of his electrolyte abnormalities. He received a total of 420 mg of amphotericin B before he refused further treatment as an inpatient, and arrangements were made for Broviac catheter placement and continued therapy as an outpatient.

Three days after discharge, the patient came to the emergency room after sustaining a fall while walking. Examination was significant for a nasal fracture. He was alert and oriented, and with the exception of his facial paralysis, he was neurologically intact. Skull series were negative. He refused CT scan and LP as well as reduction of his nasal fracture, and signed himself out of the hospital. According to his family, he experienced increased confusion and ataxia over the following 5 days. He subsequently became unresponsive and was taken to an outside hospital. He developed respiratory distress in the emergency room and died.

An autopsy was performed that showed no evidence of persistent fungal infection of the temporal bone or CNS extension. Death was attributed to severe cachexia and diffuse Kaposi's sarcoma.

**DISCUSSION**

Invasive mycotic infections of the inner ear are rare and are invariably associated with altered immunocompetence. Invasive inner ear involvement is typically secondary to either a direct spread from adjacent structures, including the middle ear, meninges, or nasopharynx, or by hematogenous dissemination. *Mucor* sp, *Cryptococcus* sp, and *Candida* sp have been the fungi implicated in sporadic case reports. However, involvement of the acoustic nerve by *Aspergillus* has been documented in several cases of *Aspergillus* meningoencephalitis. Otomycosis due to *Aspergillus* sp is more frequently associated with external otitis. Necrotizing external otitis due to *Aspergillus fumigatus* has been previously reported in two individuals, one of which developed delayed facial paralysis. Both responded to surgical debridement followed by intravenous antifungal therapy.

Invasive *Aspergillus* mastoiditis resulting from a tympanogenic source is a rare entity but is being found with increased frequency in immunocompromised individuals. The clinical presentation is one of otorrhea, which is not responsive to medical management, and hearing loss. Facial nerve involvement occurred in each of the three reported cases, and intracranial complications developed in the two individuals with AIDS. Facial nerve involvement in patients with chronic ear disease, especially in those who are immunocompromised, should raise the suspicion of invasive aspergillus mastoiditis.

Invasive aspergillosis is most commonly observed in patients with lymphoproliferative disorders, but it may occur in a variety of diseases characterized by defective humoral or cell-mediated immunity. The most frequent site of involvement in the head and neck are the paranasal sinuses. Risk factors include prolonged use of antibiotics, corticosteroids, organ transplantation, chemotherapy, and prolonged granulocytopenia. Prolonged granulocytopenia has been identified as the major risk factor for the development of invasive aspergillosis in patients with malignancies. Invasive aspergillosis is an infrequent manifestation of AIDS, having an incidence of 1.6% in Blaser and Cohn's series. The lung is the most frequently involved organ, being found in up to 91% of the cases. Hematogenous dissemination is common, with the central nervous system being the most frequently involved extrapulmonary organ, observed in 30% to 40% of cases in an autopsy series.

The patient in this report had multiple risk factors, including numerous courses of antibiotics and chemotherapy and prolonged granulocytopenia. The role that chemotherapy and prolonged antibiotic use played in his susceptibility to invasive mycosis is uncertain due to the additional variables of his underlying immunodeficiency, malnutrition, chronic hepatitis, and Kaposi's sarcoma. The cause of the primary infection appears to have been tympanogenic, as no other source was identified during the autopsy. Thickening of the skin of the external auditory canal noted on CT scan is believed to be due to secondary involvement by the infectious process. To our knowledge, this represents the first report of invasive aspergillosis limited to the temporal bone presenting with acute facial paralysis and sensorineural hearing loss.

Successful treatment depends on early recognition, which requires a high index of suspicion in susceptible individuals, including those infected with HIV. Treatment consists of improving the immunologic status when possible. Aggressive surgical debridement is cru-
cial. Systemic antifungal therapy should be instituted once the diagnosis has been confirmed.

REFERENCES