Parasitic Sinusitis and Otitis in Patients Infected with Human Immunodeficiency Virus: Report of Five Cases and Review

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We describe five cases of parasitic sinusitis and otitis in patients infected with human immunodeficiency virus (HIV) and review 14 reported cases. The pathogens identified in our group of patients included agents such as Microsporidium, Cryptosporidium, and Acanthamoeba species. The clinical features common to these patients included a long history of HIV seropositivity associated with advanced immunosuppression and multiple opportunistic infections as well as long-standing local symptoms refractory to multiple courses of antibacterial agents. Symptoms often included fever and chills in addition to local tenderness and discharge. Invasive diagnostic procedures were necessary to obtain the final diagnosis and to initiate appropriate therapy. Although most patients responded at least partially to specific therapy, relapses and recurrences were frequent in patients who did not receive long-term suppressive therapy. The general outcome for HIV-infected patients with parasitic sinusitis and otitis was poor; however, deaths were generally associated with other complications of the underlying HIV infection.

Optimal management of chronic HIV infection must include recognition of and therapy for opportunistic infectious complications, including otolaryngological infections. A variety of otolaryngological syndromes have been described in patients with AIDS. Although bacterial and fungal sinusitis and otitis in association with HIV infection has been reviewed [1], less has been written about parasitic sinusitis and otitis in patients with AIDS. Parasitic sinusitis and otitis, although still relatively unusual, is being reported with increasing frequency in patients with AIDS.

This report describes the clinical, radiographic, and laboratory features of parasitic sinusitis and otitis in patients with advanced HIV infection who were seen at our institution. The five patients described in this series were identified from records of HIV-infected patients seen at our Infectious Disease Clinic between January 1993 and December 1995. The Infectious Disease Clinic provides primary and/or consultative care for more than 500 HIV-infected patients in an urban setting. We also review the 14 cases of HIV-infected patients with sinusitis and otitis due to parasitic pathogens that were reported in the literature.

Case Reports

Case 1. A 37-year-old homosexual man with AIDS presented to our facility with a history of chronic intermittent sinusitis for 5–7 years; the infection was ultimately resistant to multiple courses of antibiotics. He had ongoing severe nasal congestion and loss of taste. Physical examination was remarkable for thickened and granular-appearing mucosa with polyoid tissue in the middle meatus and extending to the nasopharynx. He had not had any major opportunistic infections, although his CD4 cell count at presentation was 0/mm³. Sinus roentgenograms showed pansinusitis, which was confirmed by a CT scan of the head. The scan did not reveal any bony involvement.

The patient underwent endoscopic sinus surgery, which was remarkable for granular tissue in the sinus cavities. The results of routine bacterial cultures were negative. Electron microscopic examination of this sinus biopsy material revealed a large number of microorganisms that were consistent with the microsporidial species Encephalitozoon hellem. Examination of stool and urine for microsporidia was negative. The patient was treated with 400 mg of albendazole twice a day, and his sinus symptoms decreased moderately. He received suppressive therapy until his death, which occurred 8 months later.

Case 2. A 32-year-old male homosexual with AIDS, hairy leukoplakia, and a history of cytomegalovirus (CMV) pneumonia presented to the hospital because of fevers, chills, sinus congestion, and drainage. His CD4 cell count was 29/mm³. Sinus roentgenograms as well as a CT scan of the head showed pansinusitis without bony involvement. He underwent bilateral maxillary antrostomies, and electron microscopic examination of the sinus biopsy material showed microsporidia consistent with E. hellem (figure 1). The results of routine bacterial cultures were negative. Examination of stool and urine for routine microsporidia was negative. Therapy with albendazole (400 mg b.i.d.) was started. His sinus symptoms initially decreased after 1 month of treatment. He did not receive suppressive...
The patient underwent bilateral myringotomies, and the smear of the fluid from the middle ear showed numerous cryptosporidial oocysts (figure 2). He was treated with drainage and topical acetazole drops. The initial response to treatment was good, but when the tubes were removed, the patient experienced a recurrence of symptoms. The patient died 4 months later of complications of his underlying illness. To our knowledge, no other case of cryptosporidial sinusitis or otitis has ever been reported.

**Case 5.** A 37-year-old homosexual man with AIDS presented to our facility with a 3-month history of nasal discharge that was refractory to multiple courses of antimicrobial agents. He had ongoing severe nasal congestion with headaches and facial pain. Physical examination was remarkable for nasal passages that were impacted with hard brown crusts with pockets of purulence. The nasal septum and inferior turbinates were eroded. The patient also had nodules (1–2 cm in diameter) and papules that were disseminated on the lower extremities. His CD4 cell count was 178/mm³. A CT scan of the head showed mucosal thickening in the nasal vaults and osteomeatal complex.

The patient underwent endoscopic anterior ethmoidectomy and maxillary antrostomies as well as skin biopsies. Histological examination of nasal biopsy and skin biopsy specimens showed *Acanthamoeba* species in both locations (figure 3). The patient was treated with 5-fluorocytosine, and he had some response. This patient was not a swimmer and did not have a history of exposure to fresh water that would have predisposed him to *Acanthamoeba* species.

**Discussion**

We reviewed five cases of sinusitis and otitis in AIDS patients that were caused by *Microsporidium, Cryptosporidium,* and *Encephalitozoon* species.

**Figure 1.** Electron micrograph of microsporidial spores within a parasitophorous vacuole in the sinus mucosa. The sinus specimen was obtained from a 32-year-old male AIDS patient. Note the single row of polar tube filaments in the spore, which is consistent with an *Encephalitozoon* species (bar 1 mm; original magnification, ×12,500).

**Figure 2.** Cryptosporidial organisms (arrows) in a smear of fluid from the middle ear of a 42-year-old male AIDS patient. On modified Kinyoun stain, these organisms are clearly acid-fast (bar 5 mm; original magnification, ×1,200).
and *Acanthamoeba* species. Although other parasites such as *Toxoplasma gondii* cause respiratory illnesses in HIV-infected patients, we found no reported cases of sinusitis or otitis caused by these or other parasitic organisms.

Ten cases of microsporidial sinusitis in patients infected with HIV have been reported [2–7] (table 1). It is possible that one case was reported twice [4, 5]. Only two of the patients presented with symptoms limited to the sinus [3, 7]. Most of the patients presented with symptoms consistent with multi-organ microsporidial infection (e.g., fever, diarrhea, dysuria, bronchitis, nasal obstruction, and ocular discomfort). Accordingly, the parasite was found most frequently at various sites (stool, urine, sputum, sinus, and conjunctivae).

Two species, *E. hellem* and *Septata intestinalis*, were reported to be the cause of these infections with equal frequency. *S. intestinalis* has been reclassified as *Encephalitozoon intestinalis*. Different diagnostic methods were used in these reports, but the diagnosis was confirmed in each case by histologic examination or electron microscopy [4]. Every patient except one received albendazole therapy (400 mg b.i.d. orally) for 15 days to 1 month; this one patient received topical treatment with propamidine isethionate (0.1% 6 times daily) [3]. There was clear reduction in the sinus symptoms in all reported cases. Symptomatic relapses were frequent, even for patients who received suppressive therapy.

*Acanthamoeba* infection is a rare complication in immunocompetent or immunocompromised patients. This free-living amoeba typically involves the skin and CNS by disseminating from a primary focus in the lungs or respiratory tree [9]. It has been reported to occasionally cause skin nodules and ulcerations in patients with AIDS. To our knowledge, only four cases of *Acanthamoeba* infection involving the sinuses and skin without CNS involvement have been described in patients with AIDS [8–11].

Microsporidia are the most frequently recognized causes of parasitic sinusitis in patients with AIDS. However, awareness that parasitic agents can produce otolaryngological infections in HIV-infected patients may lead to increased recognition of cases and may potentially, through more-aggressive diagnostic procedures and earlier initiation of specific therapy, lead to a better understanding of the true prevalence of disease, its natural history, and outcome.

In our cases and in cases reported in the literature, parasitic otolaryngological infections occurred in patients who had advanced AIDS and who were severely immunocompromised, i.e., with CD4 cell counts <20/mm³. To our knowledge, none of the patients described in this report used nasal drugs. Most patients had symptomatic sinus or otic disease for prolonged periods before the pathogenic agent of the sinusitis or otitis was identified. The most prominent clinical symptoms were fever, headaches, nasal obstruction and/or rhinorrhea, otorrhea, local pain, and swelling. Most patients had involvement of multiple sinuses with occasional invasion of the surrounding tissues. It is impossible to say whether the parasitic pathogen was responsible for the entire duration of symptoms in these patients.

**Diagnostic procedures.** Aggressive diagnostic procedures were necessary for patients with nonbacterial infections to obtain tissue samples for culture and for histological and electron microscopic examination. Microsporidial infection may be diagnosed by a variety of techniques. Uvitex 2B is a fluorochrome stain that binds to chitin, a component of the microsporidial
Table 1. Summary of data on 10 HIV-infected patients with microsporidial sinusitis who were previously described in the literature (including three patients in the present report).

<table>
<thead>
<tr>
<th>Reference no.</th>
<th>Patient no.</th>
<th>Age (y)</th>
<th>CD4 cell count (/mm$^3$)</th>
<th>Symptoms at presentation</th>
<th>Sites of infection</th>
<th>Pathogen isolated</th>
<th>Treatment</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>[2] 1</td>
<td>1</td>
<td>28/NR</td>
<td>14</td>
<td>Fever, diarrhea, dysuria, cholangitis, sinusitis, conjunctivitis</td>
<td>Stool, urine, duodenum, nose, conjunctivae</td>
<td>Septata intestinalis</td>
<td>Albendazole</td>
<td>Improvement</td>
</tr>
<tr>
<td>[2] 2</td>
<td>2</td>
<td>36/NR</td>
<td>9</td>
<td>Fever, diarrhea, cholangitis, sinusitis, bronchitis</td>
<td>Stool, urine, duodenum, bronchoalveolar lavage</td>
<td>S. intestinalis</td>
<td>Albendazole</td>
<td>Improvement</td>
</tr>
<tr>
<td>[2] 3</td>
<td>3</td>
<td>41/NR</td>
<td>0</td>
<td>Fever, diarrhea, cholangitis, sinusitis, conjunctivitis, bronchitis</td>
<td>Stool, urine, duodenum, colon, nose, conjunctiva, sputum</td>
<td>S. intestinalis</td>
<td>Albendazole</td>
<td>Improvement</td>
</tr>
<tr>
<td>[3] 5</td>
<td>5</td>
<td>22/M</td>
<td>NR</td>
<td>Nasal obstruction, mild ocular discomfort, loss of visual acuity</td>
<td>Nasal polyps, conjunctivae</td>
<td>Encephalitozoon cuniculi</td>
<td>Propamidine isethionate</td>
<td>Improvement</td>
</tr>
<tr>
<td>[4] 6</td>
<td>6</td>
<td>NR/NR</td>
<td>NR</td>
<td>Diarrhea</td>
<td>Small bowel, urine, sinus, sputum</td>
<td>Encephalitozoon species</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>[4] 7</td>
<td>7</td>
<td>NR/NR</td>
<td>NR</td>
<td>Diarrhea</td>
<td>Small bowel, urine, sinus, sputum</td>
<td>Encephalitozoon species</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>[5] 8</td>
<td>8</td>
<td>NR/NR</td>
<td>NR</td>
<td>Diarrhea, nasal discharge</td>
<td>Small bowel, urine, sinus</td>
<td>Encephalitozoon species</td>
<td>Albendazole</td>
<td>Improvement</td>
</tr>
<tr>
<td>[6] 9</td>
<td>9</td>
<td>26/M</td>
<td>50</td>
<td>Fever, abdominal pain, dysuria, sinusitis, ocular pain</td>
<td>Small bowel, stool specimens, urine, nose, conjunctivae</td>
<td>Encephalitozoon hellem or S. intestinalis</td>
<td>Albendazole</td>
<td>Improvement</td>
</tr>
<tr>
<td>[7] 10</td>
<td>10</td>
<td>26/M</td>
<td>NR</td>
<td>Nasal discharge, conjunctivitis</td>
<td>Nasal polyps, cornea</td>
<td>Encephalitozoon species</td>
<td>Albendazole</td>
<td>Improvement</td>
</tr>
<tr>
<td>[PR] 1</td>
<td>37/M</td>
<td>0</td>
<td>50</td>
<td>Nasal discharge, loss of sensation of taste</td>
<td>Sinuses</td>
<td>Microsporidia</td>
<td>Albendazole</td>
<td>Marginal response</td>
</tr>
<tr>
<td>[PR] 2</td>
<td>32/M</td>
<td>29</td>
<td>Fever, chills, nasal discharge, headaches</td>
<td>Sinuses</td>
<td>Microsporidia</td>
<td>Albendazole</td>
<td>Improvement</td>
<td></td>
</tr>
<tr>
<td>[PR] 3</td>
<td>35/M</td>
<td>&lt;10</td>
<td>Fever, headache</td>
<td>Sinuses</td>
<td>Microsporidia</td>
<td>Albendazole</td>
<td>Improvement</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. NR = not reported; PR = present report.

Table 2. Summary of data on four HIV-infected patients with Acanthamoeba species sinusitis who were previously described in the literature (including one patient in the present report).

<table>
<thead>
<tr>
<th>Reference no.</th>
<th>Age (y)</th>
<th>CD4 cell count (/mm$^3$)</th>
<th>Symptoms at presentation</th>
<th>Sites of infection</th>
<th>Pathogen isolated</th>
<th>Treatment</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>[8]</td>
<td>8/M</td>
<td>50</td>
<td>Nasal discharge, recurrent epistaxis, nasal crusting</td>
<td>Skin, bilateral ethmoid and maxillary sinuses</td>
<td>Acanthamoeba species</td>
<td>Ketoconazole</td>
<td>No</td>
</tr>
<tr>
<td>[9]</td>
<td>33/M</td>
<td>0</td>
<td>Fever, sinusitis</td>
<td>Skin, sinuses</td>
<td>Acanthamoeba species</td>
<td>Sulfadiazine, Ketoconazole</td>
<td>5 FC</td>
</tr>
<tr>
<td>[10]</td>
<td>29/M</td>
<td>NR</td>
<td>Sinus congestion, epistaxis, nasal crusting, frontal headache</td>
<td>Skin, bilateral ethmoid and maxillary sinuses</td>
<td>Acanthamoeba castellani</td>
<td>Rifampin, ketoconazole</td>
<td>No</td>
</tr>
<tr>
<td>[11]</td>
<td>34/M</td>
<td>NR</td>
<td>Sinus congestion, frontal and occipital headache</td>
<td>Skin, sinuses</td>
<td>Acanthamoeba species</td>
<td>Pentamidine + itraconazole</td>
<td>5 FC</td>
</tr>
<tr>
<td>[PR] 1</td>
<td>37/M</td>
<td>178</td>
<td>Sinus congestion, facial pain</td>
<td>Sinuses</td>
<td>Acanthamoeba species</td>
<td>5 FC</td>
<td></td>
</tr>
</tbody>
</table>

NOTE. 5 FC = 5-fluorocytosine; NR = not reported; PR = present report.
wall; although this stain is not specific for microsporidia, it will highlight the spores and sporoblasts in sinus debris, allowing identification of the organism. The modified trichrome stain may also be useful for identifying organisms [4].

Although the diagnosis of microsporidal infection may be made by examining sinus biopsy specimens by light microscopy, identification of microsporidal organisms to the species level is not possible with use of light microscopy. Electron microscopy permits differentiation of Enterocytozoon bieneusi from Encephalitozoon intestinalis and E. hellem but does not distinguish between the latter two organisms. This distinction must be based on immunohistochemical identification or genetic analysis [5, 12, 13]. The diagnosis of sinusitis or otitis caused by Cryptosporidium or Acanthamoeba species must be made histologically [9, 14].

Microsporidia. Microsporidia are small obligate intracellular spore-forming protozoan parasites. The phylum Microspora consists of ~80 genera and more than 700 species that may be differentiated by their morphological characteristics with use of electron microscopy [12]. They parasitize multiple species of vertebrates and invertebrates and may coexist as commensals with their animal hosts. In HIV-infected or other immunocompromised patients, infections with a variety of microsporidia are being recognized with increasing frequency. Single-organ involvement as well as systemic disseminated infections due to microsporidia have been reported [13].

Although reports in the literature suggest that microsporidal infections of the sinuses in HIV-infected patients frequently represent disseminated disease, the three cases in this report demonstrate sinus involvement without evidence of dissemination of the organisms. Of the three species of microsporidia that infect patients with HIV, E. bieneusi infection is limited to epithelial cells of the small bowel and of the biliary tract and presumably involves sinus or tracheobronchial mucosa by direct inoculation; in contrast, Encephalitozoon and Septata species may disseminate after infecting macrophages [12, 13].

Albendazole, a drug that blocks the division of microsporidia by interfering with microtubule formation through its action on tubulin, is probably the most promising potential therapeutic agent for microsporidal infection [6, 12]. The clinical usefulness of atovaquone for the treatment of microsporidal sinus disease remains to be defined. It is of interest that infections with Encephalitozoon or Septata species seem to be more responsive to albendazole (therapy results in clear clinical improvement and clearance of the organisms) than are Enterocytozoon species [2].

Cryptosporidia. Cryptosporidium species is another protozoan parasite that is able to infect and reproduce in epithelial cells lining the digestive or respiratory tracts of most vertebrates. Cryptosporidial infections of the gastrointestinal tract are frequently reported in patients with AIDS. Cryptosporidial infections of the respiratory tract are less common in these patients [14]. To our knowledge, no case of cryptosporidial sinusitis or otitis has been reported in a patient with AIDS. Cryptosporidial infection occurs after person-to-person, animal-to-person, and environmental transmission and has been reported in individuals of all ages, with or without immunosuppressive underlying illness. No cases of disseminated cryptosporidial infection have been reported, as cryptosporidia are not invasive organisms. Disease in the respiratory tract is due to inhalation of the organisms and may represent colonization by aspirated organisms or true infection [14].

A variety of agents have been tested as therapy for cryptosporidial infection but have met with little success. Paromomycin, a poorly absorbed antibiotic, may result in symptomatic improvement and eradication of parasites when used to treat intestinal disease [15]. The clinical usefulness of nitzoxanide for cryptosporidial infection remains to be defined. The symptoms in the case of cryptosporidial otitis reported herein were reasonably resolved with long-term drainage through myringotomy.

Acanthamoeba. Acanthamoeba species are ubiquitous free-living amoeba that inhabit soil and water. Both cell-mediated and humoral immunity may play a role in containing acanthamoeba infection in the healthy human host. In immunodeficient patients, however, Acanthamoeba species can cause skin lesions, sinus infection, and granulomatous encephalitis [8, 9]. We describe the clinicopathological features of one case of sinusitis due to Acanthamoeba species. Acanthamoeba species have been isolated from human stool specimens, ear discharge specimens, and corneal specimens as well as from the nasal, pharyngeal, and bronchial secretions of healthy and sick individuals. Although Acanthamoeba species are known to cause granulomatous encephalitis with concomitant skin and sinus infection in immunocompromised hosts, infections of the skin and sinuses without CNS involvement seem to be recognized with increasing frequency in AIDS patients [9].

Little is known about the treatment of acanthamoeba infection. In general, the diamidine derivatives (propamidine, pentamidine, dibromopentamidine) have the greatest activity against this particular amoeba. Other drugs active against Acanthamoeba species in vitro include ketoconazole, miconazole, paromomycin, neomycin, 5-fluorocytosine, and, to a lesser extent, amphoterin B. Clinical isolates of Acanthamoeba may be tested for drug susceptibilities [16].

Conclusion

Nonbacterial sinusitis and otitis progress frequently in patients with AIDS. This is not surprising considering that these susceptible patient populations are severely immunocompromised and considering the difficulty of eradicating these pathogens in immunocompetent hosts. Although no controlled studies exist, suppressive therapy seems to be indicated for parasitic otorlaryngological infections in patients with AIDS. The increasing recognition of parasitic agents as otorlaryngological pathogens in patients with AIDS may be related to the increased intensity of diagnostic evaluations. Aggressive
surgical diagnostic procedures are indicated for patients with chronic otolaryngological complaints that are unresponsive to empirical therapy. Without suppressive therapy, progression of disease is common. At this time, the outcome is poor for HIV-infected patients with otolaryngological infections due to these nonbacterial pathogens, although it is not clear if this is due to the refractory nature of the infections or to the advanced state of disease in the patients in whom these infections occur.

References