# *Acanthamoeba* Rhinosinusitis

*J. Matthew Dickson, MD, Peter J. Zetler, MD, Blair Walker, MD, and Amin R. Javer, MD*

*A*canthamoeba is a rare cause of infection in acquired immune deficiency syndrome (AIDS). First reported in 1986, the free-living protozoa continue to cause infection in the human immunodeficiency virus (HIV)-positive host.[1] The disease normally manifests cutaneously or neurologically, but it can present as rhinosinusitis. There are seven documented cases of *Acanthamoeba* rhinosinusitis in the world literature, only two of which have been treated successfully.[2–5] We present the eighth known case in a patient with end-stage AIDS. We also review the literature and discuss the pathogenesis, diagnosis, and potential treatment of this rare entity.

## Methods

A 31-year-old man with AIDS and a history of chronic rhinosinusitis presented to the emergency department at St. Paul's Hospital with a 1-week history of right-sided facial pain. The distribution of the pain was described as primarily retro-orbital. However, pain was also noted over the frontal and maxillary sinuses and over the temporal and occipital regions on the right side. He did not have any visual changes but did suffer from systemic symptoms of fever and chills. He had a 10-year history of chronic rhinosinusitis with one previous sinus surgery in 1994. The patient described chronic, purulent nasal discharge bilaterally with occasional blood-tinged mucus that had remained unchanged. There had been no response to outpatient treatment with intravenous ceftazidime and clindamycin.

He was diagnosed HIV positive in 1991 and had numerous AIDS-defining illnesses, including *Pneumocystis carinii* pneumonia, oral candidiasis, cytomegalovirus retinitis, systemic *Mycobacterium avium* complex infection, AIDS cholangiopathy, chronic neutropenia, recurrent pneumonia/sepsis, and chronic sinusitis. He had tried multiple antiretroviral regimens that he either did not tolerate or to which he became resistant. He had not been on any therapy since 1998. His CD4 count was measured at < 10 cells/µL since March 1998.

On physical examination, an ulcerative perforation measuring 1 cm in diameter was found on the anterior nasal septum (Figure 1). Rigid nasal endoscopy and pharyngoscopy revealed purulent discharge surrounding the middle turbinate stump on the right side. Cranial nerves were intact, and there was no nystagmus. No cutaneous lesions were seen. A high-resolution computed tomographic (CT) scan of the paranasal sinuses showed opacification of the right maxillary and ethmoid sinuses extending to the frontal and sphenoid sinuses. Intermittent dehiscence of the lamina papyracea was also visualized (Figure 2). The patient was taken to the operating room for urgent computer-assisted sinus surgery and debridement.

J. Matthew Dickson: *Division of Otolaryngology, St. Paul's Hospital, Vancouver, British Columbia, and Division of Pediatric Otolaryngology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; and* Peter J. Zetler *and* Blair Walker: *Division of Pathology, and* Amin R. Javer: *Division of Otolaryngology, St. Paul's Hospital, Vancouver, British Columbia.*
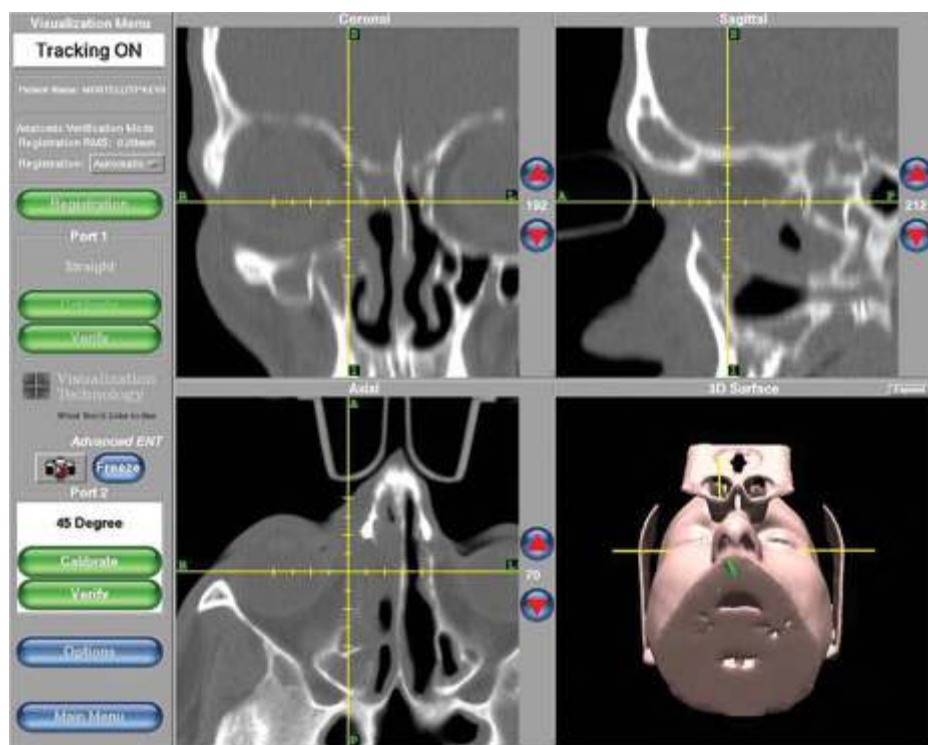
*Address reprint requests to:* Amin R. Javer, MD, *St. Paul's Sinus Centre, ENT Clinic, St. Paul's Hospital, 1081 Burrard Street, Vancouver, BC V6Z 1Y6; e-mail: sinussurgeon@shaw.ca.*

**Figure 1.** Ulcerative septal perforation viewed from the right nare.

**Figure 2.** High-resolution computed tomographic images showing intermittent dehiscence of the lamina papyracea.

Previous antral windows, ethmoidectomies, and middle turbinectomies were noted during the surgery. There was fungal debris around the right periorbita and white necrotic tissue along the lamina papyracea. There was also opacification of the right maxillary and ethmoid sinuses. Complete debridement of the right nasal cavity with completion anterior and posterior ethmoidectomy, maxillary antrostomy, and removal of the lamina papyracea was performed. All tissue appeared necrotic, and numerous biopsies and cultures were taken bilaterally. The sinuses were irrigated with amphotericin B solution intraoperatively.

*Aspergillus niger* and *Penicillium* species were isolated in cultures performed from the maxillary and ethmoid sinuses bilaterally. Histopathology testing of tissue biopsies indicated involvement by *Acanthamoeba*. The right maxillary sinus was lined with inflamed mucosa with extensive ulcerative necrosis extending to the underlying bone. Acanthamoebal cysts were noted in the tissue and appeared to be angioinvasive (Figure 3 and Figure 4). Septal biopsies were also indicative of ulcerated and necrotic mucosa with occasional *Acanthamoeba*. The left frontal recess tissue was consistent with chronically inflamed mucosa.

Medical treatment prior to the identification of *Acanthamoeba* was directed at a suspected bacterial and invasive fungal sinusitis. The patient was originally treated with imipenem, vancomycin, ciprofloxacin, and amphotericin B. After *Acanthamoeba* was isolated, the patient was started on intravenous pentamidine 240 mg daily, intravenous liposomal amphotericin B 300 mg daily, and oral 5-flucytosine 1500 mg every 8 hours. Amphotericin B nasal flushes were also administered. After 2 weeks of treatment, the flucytosine dose was increased and intraconazole was added.
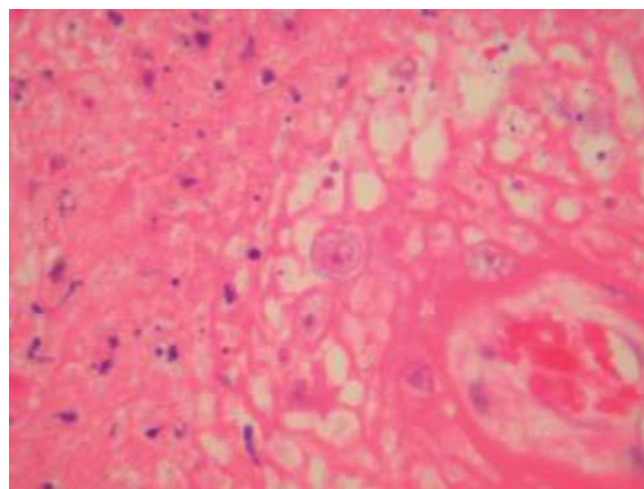


**Figure 3.** Necrotic debris with cysts of *Acanthamoeba* focally invading small vessels (hematoxylin-eosin stain; ×168 original magnification).
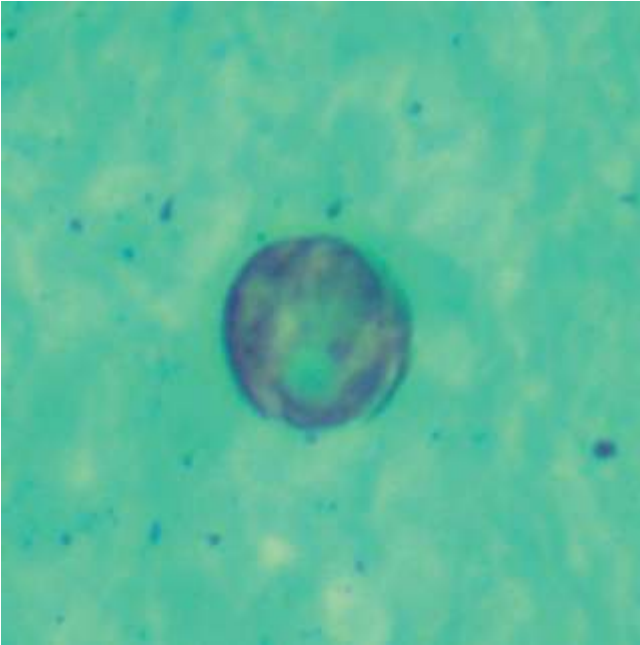
**Figure 4.** Characteristic acanthamoebal cysts (13–20 μm) showing a clear nucleus with a central dense karyosome (Grocott-Gomori methenamine-silver nitrate strain; ×625 original magnification).

CT performed on the twenty-first day after admission indicated the progression of disease into the frontal and sphenoid sinus mucosa, although meningeal spread could not be determined. The patient developed abdominal distension and pneumonia, and his renal and hepatic function deteriorated despite maximal medical management. He continued to suffer from right-sided facial pain until he died 22 days after admission. An autopsy was not performed.

## Discussion

The susceptibility of HIV-infected individuals to sinusitis has been attributed to acquired atopy, decreased muco-ciliary clearance, and low CD4 counts.[2] These factors lead to infection with both common bacterial pathogens and less common opportunistic pathogens, such as fungi, cytomegalovirus, cryptosporidia, *Legionella*, and protozoa.

*Acanthamoeba* are free-living protozoa commonly found in the environment. They have been isolated from soil, dust, water (natural, treated, sea, bottled), sewage, air conditioning units, hospitals, dental treatment units, contact lenses, and the respiratory tract of healthy individuals.[1] The organisms gain access to the body through the respiratory mucosa or skin but can dissemi-nate to involve the central nervous system and cause death. Manifestations of the disease include granulomatous amebic encephalitis, amebic keratitis, otitis, and cutaneous

lesions.[1] Rhinosinusitis is one manifestation of *Acanthamoeba* infection that has been seen only in immunocompromised individuals, particularly those with HIV disease. The signs and symptoms of *Acanthamoeba* rhinosinusitis are nasal obstruction, crusting, and epis-taxis.[4] There may be necrosis of bone and cartilage in the nasal cavity bordered by heaped, erythematous mucosa.[6]

*Acanthamoeba* exists in two forms, an actively dividing trophozoite and a dormant cyst. The size of the trophozoite ranges from 25 to 40 μm and is distinguished by the presence of acanthopodia or spiny surface projections.[1] Under adverse environmental conditions, formation of the wrinkled, double-walled cyst occurs. The cysts, measuring 13 to 20 μm, remain viable for over 20 years, with some decline in virulence.[1] Laboratory confirmation is aided by wet preparations, electron microscopy, indirect immunofluorescence, and a variety of stains, including calcofluor white, which stains the cyst wall green.[1,3] The gold standard of diagnosis, however, is by culture. *Acanthamoeba* can be grown on non-nutrient agar housing a lawn of *Escherichia coli*.[1,4]

The role of the immune response in acanthamoebal infection is not well understood and may involve both innate and acquired immunity. With a high prevalence and a low infection rate, the organisms may cause transient infections in apparently healthy individuals with little clinical significance. Chappell postulated that these infec-tions may contribute to undiagnosed rhinosinusitis or pulmonary disease.[1]

Rhinosinusitis owing to *Acanthamoeba* is a rare entity. Only two of seven reported cases have survived, and no effective treatment has been identified. Treatment has consisted of surgical debridement followed by long-term systemic therapy. In the two successfully treated cases, ongoing office debridement was continued for up to 1 month.[3,4] Systemic therapy with pentamidine, amphoter-icin B, and flucytosine was administered for 4 to 6 weeks.[3,4] A number of other medications, including antibiotics such as metronidazole, levofloxacin, rifampin, and itraconazole, have also been used.[2–4] Successfully treated patients continued oral therapy for up to 6 months with trimethoprim-sulfamethoxazole and intraconazole.[3]

Our experience is difficult to compare with those documented in the literature. Our patient had end-stage AIDS without antiretroviral therapy and had compro-mised hepatic and renal function, which limited ther-apeutic options. Our case was further complicated by a history of respiratory infection owing to methicillin-resistant *Staphylococcus aureus* and infection owing to *Penicillium* and *A. niger*; hence, the clinical significance of

*Acanthamoeba* in such a polymicrobial infection is uncertain.

Although *Acanthamoeba* infection in HIV-positive individuals can manifest as cutaneous lesions, otitis, rhinosinusitis, or central nervous system symptoms, the diagnosis is often overlooked. For example, in the absence of pathologic confirmation, cerebral disease may be attributed incorrectly to toxoplasmosis, vasculitis, or squamous cell carcinoma without the diagnosis of *Acanthamoeba* infection being entertained and excluded.[1] In the sinuses, *Acanthamoeba* can be incorrectly identified as macrophages or fungi.[1,3] Therefore, it is important to consider the diagnosis in HIV/AIDS patients with chronic sinusitis that is unresponsive to conservative or first-line treatment.

## Conclusion

*Acanthamoeba* is a free-living organism found commonly in the environment that rarely causes infection. It has been reported only seven times involving the nose and paranasal sinuses. All cases have been patients with HIV, and only two have survived. The diagnosis of *Acanthamoeba* rhinosinusitis is difficult as it can mimic other disease processes and resemble macrophages. No efficacious treatment protocol has been established so far. Therapy has consisted of a number of medical and surgical interventions. We have presented the pathogenesis, diagnosis, and potential treatments for *Acanthamoeba* rhinosinusitis in an attempt to shed light on this rare, opportunistic pathogen.

## Acknowledgement

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