Mycobacterium avium-intracellulare Sinusitis

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Mycobacterium avium-intracellulare (MAI) sinusitis is rarely diagnosed. There are only nine previous cases documented in the literature,[1–9] most of which are in patients with acquired immune deficiency syndrome (AIDS). Awareness of MAI sinusitis may prove valuable to the practicing otolaryngologist, and an elevated index of suspicion is necessary in all immunocompromised patients with sinusitis, especially those refractory to medical management. Unless specific investigations for MAI are ordered, the diagnosis may be missed and complications may result.[2,5] We present the first case report of MAI sinusitis in a diabetic or organ transplant patient and the first in a non–HIV-infected immunocompromised adult. We also present a discussion of MAI and a literature review of MAI sinusitis.

Case Report

A 40-year-old male with type 1 diabetes, on immunosuppressive treatment 10 years post–renal transplantation, presented in August 2005 with a 6-week history of left-sided nasal obstruction, left-sided facial pain, hyposmia, and a mild left-sided headache.

He had no previous history of sinus disease or nasal trauma. His past medical history included the diagnosis of type 1 diabetes at the age of 7 years and a cadaveric renal transplant in 1994 at the age of 29 years while on hemodialysis for chronic renal failure. Other complications of his diabetes included retinopathy, a toe amputation owing to gangrene, and hypertension from his nephropathy. The patient was on multiple medications, including immunosuppressives (cyclosporine, prednisone, and mycophenolate mofetil) and insulin. The patient was human immunodeficiency virus (HIV) negative, and no other infectious diseases were identified.

His physical examination was remarkable for what was described as a papillomatous-like growth in his left nasal cavity, presenting on the septum and lateral nasal wall. The growth was biopsied, and the tissue sample was directly stained with auramine-O (fluorochrome technique) and showed 4+ acid-fast bacilli (AFB). The sample was subsequently smeared, after cultures grew, using the Kinyoun acid-fast stain and showed nontuberculous AFB; it was then probed for MAI. This isolate grew on both the Liquid–bioMérieux BacT/ALERT (bioMérieux Industry, France) (bioMérieux Incorporated, Durham, NC) and solid culture Lowenstein-Jensen media specific for mycobacteria. DNA probes (Gen-Probe AccuProbe system; Gen-Probe Incorporated, San Diego, CA) confirmed the diagnosis of MAI. The patient was subsequently referred to Infectious Diseases in September 2005, where he was followed monthly and started on a triple-antibiotic regimen consisting of rifampin 300 mg once daily, azithromycin 625 mg once daily, and ethambutol 800 mg once daily.

His symptoms persisted with no improvement despite treatment with the standard triple-antibiotic regimen for 5 months. As a result, the patient was referred to the St. Paul's Hospital Sinus Centre. His physical examination was unremarkable except for a narrow left nasal cavity that was almost obstructed with the papillomatous-like growth. No pus, polyps, or other abnormalities were seen. A computed tomographic (CT) scan revealed complete opacification of his left frontal sinus, almost complete opacification of his left sphenoid sinus, mild-moderate right and left maxillary sinus mucosal thickening, and a left-sided nasal spur (Figure 1).

Owing to his persistent symptoms of sinusitis refractory to medical management, image-guided functional endoscopic sinus surgery (FESS) was carried out together

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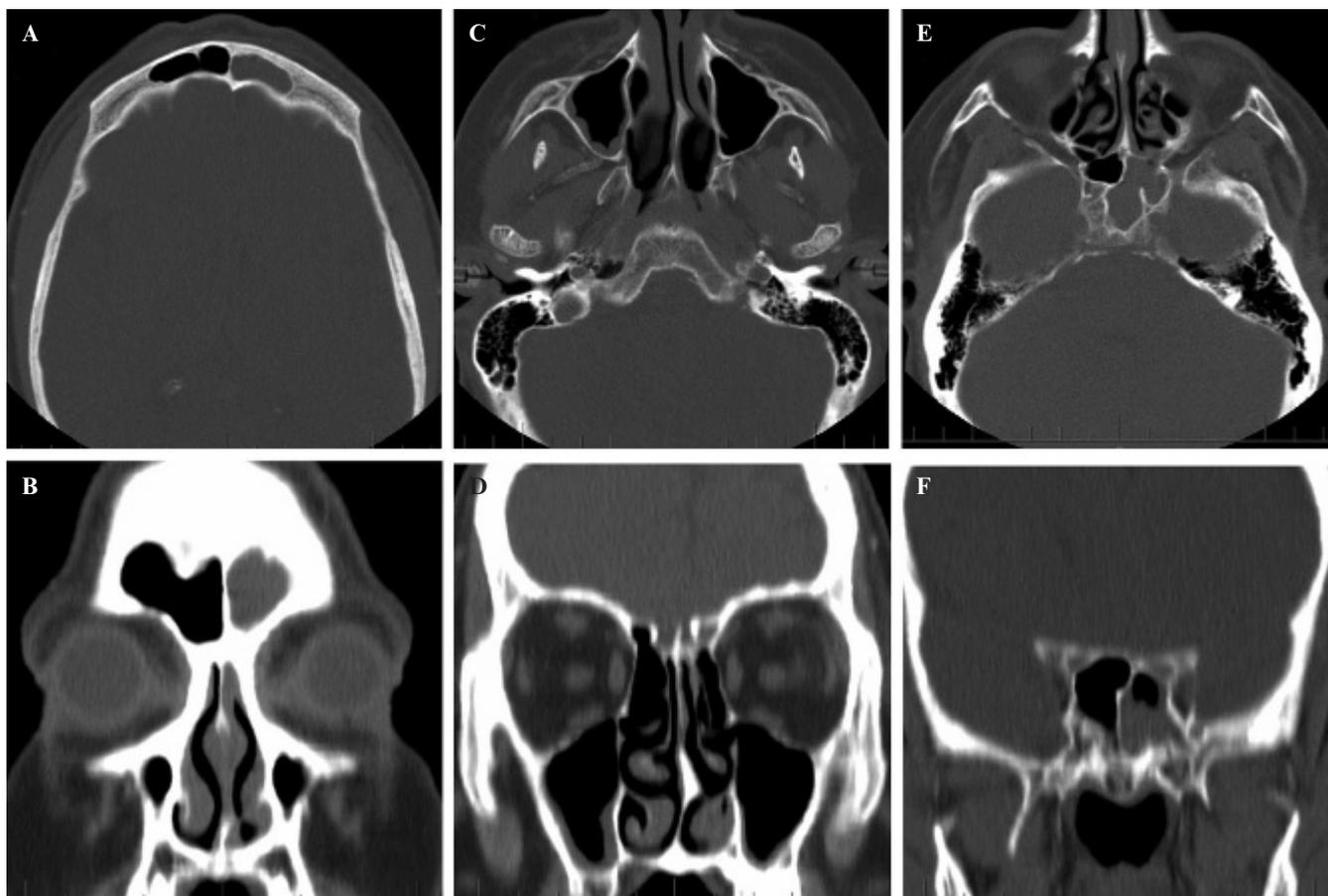
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Figure 1. Preoperative computed tomographic scans showing complete opacification of the left frontal sinus (A, B), mucosal thickening of the maxillary sinuses (C, D), and significant opacification of the left sphenoid sinus (E, F).

with a nasal septal reconstruction. The left agger nasi cap was removed, and the frontal sinus was widely opened. The mucous membrane within the frontal sinus was thickened and fragile. Copious saline and antibiotic steroid solution lavage was carried out intraoperatively for the accessed sinuses. His triple-antibiotic therapy was continued postoperatively.

The patient showed an immediate improvement of his symptoms postoperatively. At 6 weeks postoperatively, he had no signs or symptoms of sinusitis. His sense of smell improved, and his nasal obstruction, headache, and facial pain were alleviated. On endoscopic examination, his nasal cavity and ethmoid, maxillary, and frontal sinuses appeared clear bilaterally, with no signs of infection. The patient's sinuses appeared well healed from his surgery. His triple-antibiotic therapy was discontinued at that point. Four months after surgery, a CT scan showed resolution of the left sphenoid opacification (Figure 2). At the 1-year follow-up, he continued to have no signs or symptoms of sinusitis, with healthy and clean-appearing sinuses on endoscopic nasal examination.

Discussion

MAI is an atypical or nontuberculous mycobacterium. There is some controversy in the literature regarding the nomenclature, but in the clinical and health care realm, it is generally accepted that MAI is synonymous with *Mycobacterium avium* complex (MAC), and both terms represent an infection by either *Mycobacterium intracellulare* or *Mycobacterium avium*.[5,10–12]

The present case report is the first to document MAI sinusitis in a diabetic or organ transplant patient and the first in a non–HIV-infected immunocompromised adult. A previous literature review exists on nontuberculous mycobacterium sinusitis.[7] Table 1 is an updated review of all previous cases of MAI sinusitis published in the English-language literature.[1–7] There are two other cases
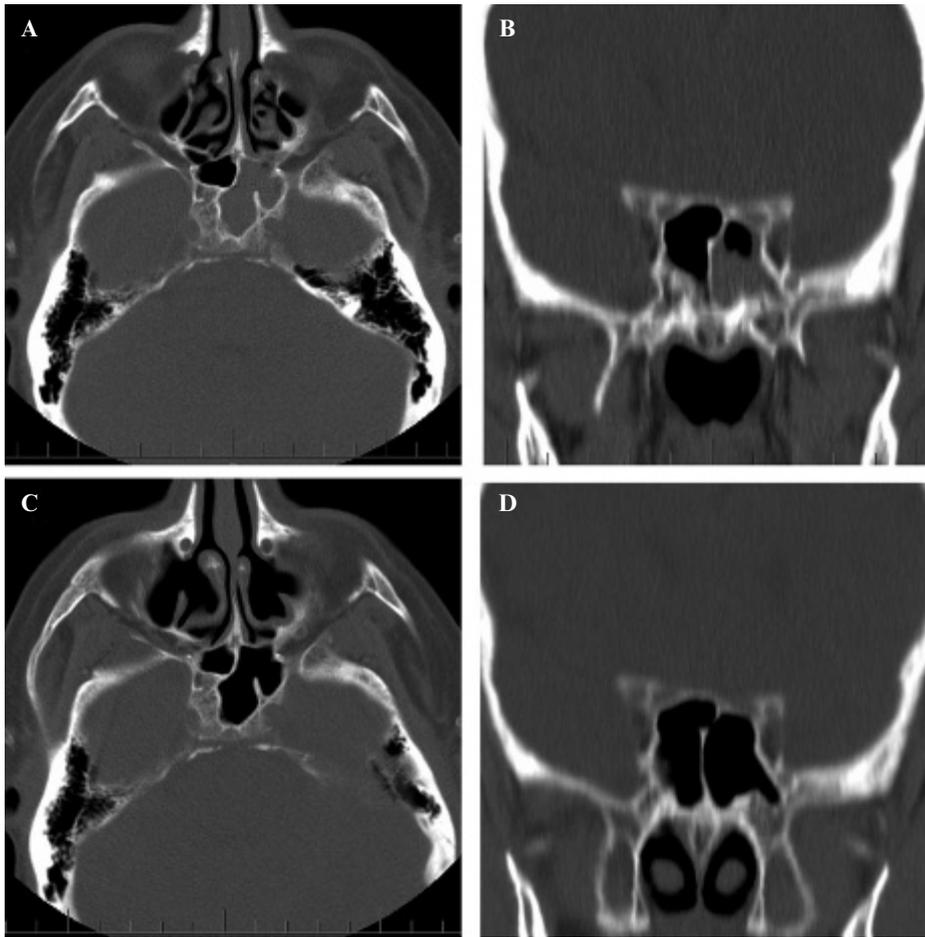
Figure 2. Preoperative computed tomographic (CT) scans showing significant opacification of the left sphenoid sinus (A, B) versus postoperative CT scans showing complete resolution of the opacification (C, D).

published in the international non–English-language literature, both in AIDS patients.[8,9] Other cases of non-MAI nontuberculous mycobacterial sinusitis have been reported involving *Mycobacterium chelonae*,[13,14] *Mycobacterium kansasii*,[2,15,16] and *Mycobacterium chelonae-abscessus* complex.[7]

MAI is omnipresent in the environment (soil, water, animals, dust, and dairy products).[4,5,11,12,17–19] Unlike *Mycobacterium tuberculosis*, human-to-human transmission is rare.[4,5,11,12] Inhalation, ingestion, and direct inoculation are thought to be the primary methods for MAI colonization of the respiratory and gastrointestinal tracts.[4,5,11,12] It is possible that the proximal location of the nasal cavity and paranasal sinuses in the aerodigestive tract in relation to the environment enables MAI to colonize these areas more easily.

Standard cultures often do not grow mycobacteria.[5] Mycobacteria-specific cultures should be obtained from the sinuses for definitive diagnosis[5,17,20]—AFB stains and histopathology alone are much less sensitive and specific than mycobacteria-specific cultures.[4] With sufficient cultures, molecular testing techniques such as DNA probing can diagnose MAI within hours.[5,17,20]

MAI infections in immunocompromised individuals are not uncommon,[12] and its treatment in this population can be challenging. MAI is an opportunistic organism that is relatively more pathogenic than other environmental mycobacteria and very resistant to first-line antimycobacterial medications.[21] Treatment with multiple antibiotic agents allows rapid clearance of MAI from the bloodstream and decreases the danger of drug resistance.[17,20] Long-term antibiotic therapy with a macrolide (azithromycin or clarithromycin), in combination with companion drugs (ethambutol and rifampin), is an accepted protocol in the literature.[5,17,20] Nonetheless, surgical treatment of nontuberculous infections is often considered essential, as was the case in the present report.[4,22–24]

MAI has a predilection to disseminate in the immunocompromised host[4,12]—especially if left untreated. MAI infection is well documented as a recognized danger of renal transplant surgery.[12] It is the most common cause of disseminated bacterial infection in AIDS patients.[5] Of the

Table 1. Previous Cases of *Mycobacterium avium-intracellulare* Sinusitis

Year	Study	Sinus	Age (yr)	Sex	Presentation	Risk Factors	Definitive Management	Outcome
1992	Zurlo et al[1]	NR	NR	NR	Disseminated MAI	AIDS	NR	NR
1994	Naguib et al[2]*	Frontal	33	M	Persistent acute frontal headaches and unilateral facial edema secondary to frontal sinus osteomyelitis and subgaleal abscess	AIDS	Incision and drainage of subgaleal abscess and antimycobacterial agents	Initial remission then relapse, death secondary to disseminated MAI 9 mo later
1995	Sussman[3]	Bilateral maxillary	Child, age NR	F	Fever of unknown origin and history of chronic rhinosinusitis	AIDS	Drainage of maxillary and ethmoid sinuses; failed antibiotics and antimycobacteria-specific agents	Death secondary to disseminated MAI 6 mo after presentation
1997	Weiss et al[4]	Frontal, maxillary, and ethmoid	13	F	Periorbital cellulitis and subperiosteal abscess (without osteomyelitis) secondary to frontoethmoid sinusitis	None	Endoscopic sinus surgery and external frontal sinus trephination with postoperative antimycobacterial agents	Resolved at 5 mo postoperatively
1997	Ferguson et al[5]	Pansinus disease	38	M	Acute pansinusitis and history of disseminated MAI	AIDS	Revision endoscopic sinus surgery with postoperative triple antimycobacterial agents	Death secondary to AIDS and disseminated MAI infection 2 mo postoperatively
2002	Mra et al[6]	Bilateral sphenoid	56	F	Orbital cellulitis with cranial nerve involvement and cavernous sinus thrombosis	None	Operative sphenoid sinus drainage; postoperative antibacterials, antimycobacteria-specific agents, and warfarin	Gradual partial recovery of eye at 1 yr postoperatively
2007	Brown et al[7]	Bilateral maxillary, ethmoid, and sphenoid	8	M	Recurrent rhinosinusitis with polyposis and headaches	CF	Endoscopic sinus surgery with postoperative antibiotics	Clinically well at 1 mo postoperatively

AIDS = acquired immune deficiency syndrome; CF = cystic fibrosis; MAI = *Mycobacterium avium-intracellulare*; NR = not reported.
*MAI and *Mycobacterium kansasii* coinfection.

many known diseases that MAI can cause in immuno-compromised hosts, standard medical textbooks seldom mention MAI sinusitis.[3,12] MAI infection in the sinuses can serve as a nidus for disseminated disease.[2–5,11] MAI disseminates via the heterogeneous route and has a predilection to spread to many sites, including the bone marrow, spleen, and liver.[2–5,11]

Conclusion

The present case report is the first to document MAI sinusitis in a non–HIV-infected immunocompromised adult. It is also the first case report of MAI sinusitis documented in a diabetic or organ transplant patient. Nontuberculous mycobacterial sinusitis should be considered in all immunocompromised patients presenting with signs and symptoms of sinusitis, especially those refractory to standard medical treatment.[2,5] Routine cultures do not grow mycobacteria; thus, mycobacteria-specific cultures should be obtained from the sinuses in combination with molecular techniques such as DNA probing.[5,17,20] AFB stains and histopathology alone are much less sensitive and specific.[5,17,20] MAI infection of the sinuses can serve as a nidus for disseminated disease. A delay in diagnosis can result in high mortality owing to an increased likelihood of dissemination to vital organs in untreated immunocompromised patients. Meticulous FESS in conjunction with antimycobacterial triple medical therapy appears to be an effective and safe treatment option.

Acknowledgement

References

1. Zurlo JJ, Feuerstein IM, Lebovics R, et al. Sinusitis in HIV-1 infection. Am J Med 1992;93:157–62.
2. Naguib MT, Byers JM, Slater LN. Paranasal sinus infection due to atypical mycobacteria in two patients with AIDS. Clin Infect Dis 1994;19:789–91.
3. Sussman SJ. Sinusitis caused by Mycobacterium avium-intracellulare in a patient with human immunodeficiency virus. Pediatr Infect Dis J 1995;14:726–7.
4. Weiss RL, Zahtz GD, Isenberg H. Nontuberculous mycobacterial infection of the frontal sinus in a child. Otolaryngol Head Neck Surg 1997;116:110–2.
5. Ferguson BJ, Kapadia SB, Carrau RL. Mycobacterium avium complex infection of the paranasal sinuses. Otolaryngol Head Neck Surg 1997;117(6):S160–2.
6. Mra Z, Roach J, Brook A. Infectious and neoplastic disease of the sphenoid. Rhinology 2002;40:34–40.
7. Brown SM, DeCelie-Germana JK, Shikowitz MJ, et al. Nontuberculous mycobacterial sinusitis in children with cystic fibrosis. Int J Pediatr Otorhinolaryngol Extra 2007;2:9–13.
8. Cibrian F, Quiles I, Anaut P, et al. Sinusitis caused by Mycobacterium avium-M. intracellulare in a patient with HIV infection. Enferm Infecc Microbiol Clin 1996;14:401–2.
9. Tsi L, Galvez A, Broto J, et al. Sinusitis in HIV infection. Acta Otorrinolaringol Esp 1994;45:301–2.
10. Turenne CY, Wallace R, Behr MA. Mycobacterium avium in the postgenomic era. Clin Microbiol Rev 2007;20:205–29.
11. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med 2007;175:367–416.
12. Grange JM. Mycobacteria and human disease. 2nd ed. London: Arnold; 1996.
13. Spring PM, Miller RH. Initial report of primary sinusitis caused by an atypical pathogen (Mycobacterium chelonae) in an immunocompetent adult. Ear Nose Throat J 1999;78:358–9, 362–4.
14. Eron LJ, Huckins C, Park CH, et al. Mycobacterium chelonei infects the maxillary sinus. Va Med 1981;108:335–8.
15. Li CX, Szuba MJ, Schuman P, et al. Mycobacterium kansasii sinusitis in a patient with AIDS. Clin Infect Dis 1994;19:792–3.
16. Upadhyay S, Marks SC, Arden RL, et al. Bacteriology of sinusitis in human immunodeficiency virus-positive patients: implications for management. Laryngoscope 1995;105:1058–60.
17. Wagner D, Young LS. Nontuberculous mycobacterial infections: a clinical review. Infection 2004;32:257–70.
18. Falkinham JO. Nontuberculous mycobacteria in the environment. Clin Chest Med 2002;23:529–51.
19. Horsburgh CR. Epidemiology of Mycobacterium avium complex. In: Korvick JA, Benson CA, editors. Mycobacterium avium–complex infection: progress in research and treatment, Lung biology in health and disease. Vol 87. New York: Marcel Dekker; 1996. p. 1–22.
20. Katoch VM. Infections due to non-tuberculous mycobacteria (NTM). Indian J Med Res 2004;120:290–304.
21. Horsburgh CR. Mycobacterium avium complex infection in the acquired immunodeficiency syndrome. N Engl J Med 1991;324:1332–8.
22. Wolinsky E. Nontuberculous mycobacteria and associated diseases. Am Rev Respir Dis 1979;119:107–59.
23. Olsen NR. Nontubercutous mycobacterial infections of the face and neck, practical considerations. Laryngoscope 1981;91:1714–26.
24. Schaad UB, Votteter TR, McCracken GH, et al. Management of atypical mycobacterial lymphadenitis in childhood: a review based on 380 cases. J Pediatr 1979;95:356–60.