

NOTES

Histoplasma capsulatum Sinusitis

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Sinusitis is commonly reported in patients with AIDS. In addition to the usual bacterial pathogens isolated from immunocompetent patients, sinusitis in patients with AIDS may be caused by a variety of unusual bacteria, viruses, fungi, parasites, and mycobacteria. *Histoplasma capsulatum* has not typically been associated with sinusitis in either group of patients. We report a case of sinusitis caused by *H. capsulatum* in a patient with AIDS.

Sinusitis is a common disease of adults and children (4). In both adults and children, the most common pathogens cultured from sinus aspirates of patients with sinusitis are *Streptococcus pneumoniae* and nontypeable *Haemophilus influenzae*. Viruses are the third most common cause in adults, while *Moraxella catarrhalis* is the third most common cause in children. While these organisms are frequently the cause of sinusitis in patients with AIDS, other organisms have also been implicated. These include *Pseudomonas aeruginosa*, fungi, viruses, parasites, and mycobacteria (4, 7). While the incidence of disseminated histoplasmosis is severalfold higher in patients with AIDS, sinusitis due to *Histoplasma capsulatum* is extremely rare in both immunocompetent and immunosuppressed patients. Our Medline database search revealed only one case of sinusitis caused by *Histoplasma*, which was secondary to direct extension to the sinuses from a palatal perforation caused by a palatal ulcer (3).

Case report. A 39-year-old African American male presented to our hospital with complaints of nasal congestion and postnasal drip of 2-month duration. These symptoms were accompanied by occasional "sinus headaches." He reported occasional fever, sometimes with chills, for the same duration. He had lost 35 pounds in 3 months. He also complained of a cough which produced greenish sputum for several days. However, no shortness of breath, chest pain, or hemoptysis was reported. He also noted a skin rash which had been present for three months.

His past medical history was significant, as he had had human immunodeficiency virus (HIV) infection for 8 years. He had had *Pneumocystis carinii* pneumonia (PCP) 5 years previously and gonorrhea 20 years previously. He had had oral candidiasis during the course of his HIV infection. He had a history of cocaine use but denied injection drug use or excessive alcohol intake. His medical regimen consisted of zidovudine, lamivudine, trimethoprim-sulfamethoxazole for PCP prophylaxis, and multivitamins. Physical examination revealed a temperature of 40°C, blood pressure of 76/54 mm Hg, and a pulse rate of 102/min. The respiratory rate was 16/min. A 2-cm right submandibular lymph node was palpable; it was non-

tender and fully mobile. Decreased air movement was noted in the lungs, and there was a grade II/VI systolic ejection murmur recorded with no radiation. The skin examination was significant for a macular papular rash on the face, arms, and trunk. Most of the rash had slightly raised edges. The patient's CD4⁺ T-lymphocyte count was 20/ μ l. A chest radiograph showed evidence of bilateral hilar lymphadenopathy and a diffuse reticulonodular infiltrate. There was a 1-cm pulmonary nodule in the superior segment of the right middle lobe. Sinus computerized tomography revealed complete opacification of the maxillary sinuses bilaterally and partial opacification of both frontal sinuses, consistent with acute sinusitis (Fig. 1). Sinus aspiration and skin biopsy were performed as part of the diagnostic workup. Microscopic examination with Gomori methanamine-silver staining showed organisms consistent with *Histoplasma* in both specimens (Fig. 2). The cultures of the sinus aspirate, skin biopsy, and sputum samples were positive for *H.*

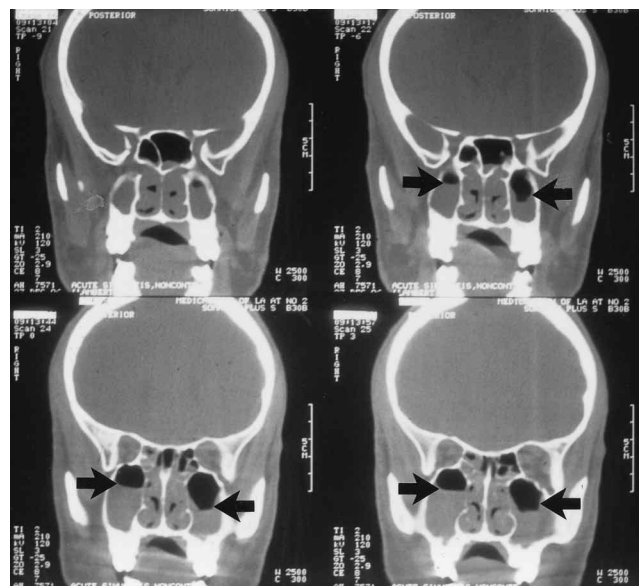


FIG. 1. A representative computerized tomography scan of the sinuses, showing complete opacification of both maxillary sinuses and partial opacification of the frontal sinuses (arrows).

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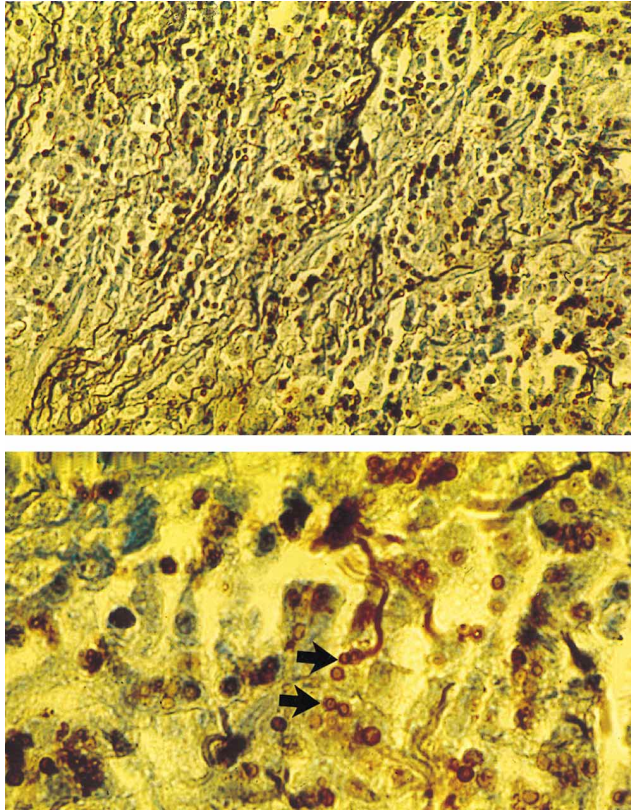


FIG. 2. Gomori methanamine-silver staining of the sinus aspirate showing multiple yeasts (arrows) compatible with *H. capsulatum*. Magnification: upper panel, $\times 27.2$; lower panel, $\times 68$.

capsulatum. In addition, histology of the skin biopsy specimen of the rash showed superficial and deep chronic granulomatous inflammation.

While awaiting the results of the above tests, the patient was started on itraconazole at 600 mg/day for the first three days followed by 400 mg/day. He responded well to this treatment, with resolution of fever, sinus, and pulmonary symptoms over a course of 2 to 3 weeks. He is currently on this regimen and is tolerating it well, without any evidence of relapse.

Recurrent sinusitis has been reported in 25 to 30% of patients infected with HIV (4). In these patients, such infection tends to be more severe, involves multiple sinuses, and responds less favorably to antibiotic therapy. Increasing immunosuppression, as evidenced by declining CD4⁺ T-lymphocyte counts, tends to be associated with an increasing frequency of infection and infection by otherwise uncommon organisms. Bacteria, fungi, viruses, parasites, and atypical mycobacteria have all been associated with sinusitis in these patients. *P. aeruginosa*, *Staphylococcus aureus*, *Aspergillus* spp., *Rhizopus* spp., *Cryptococcus neoformans*, cytomegalovirus, microsporidia, *Mycobacterium avium-M. intracellulare*, and *Mycobacterium kansasii* represent the atypical pathogens reported to cause sinusitis in patients with AIDS (4, 6, 7). Most cases of fungal sinusitis in patients with AIDS are caused by *Aspergillus* species, which account for up to 81% of such cases (1, 2, 7). *H.*

capsulatum is a very rare cause of sinusitis. A Medline database search revealed only one case of *H. capsulatum* sinusitis in a patient with AIDS (3), while no such case in an immunocompetent patient has been reported, to our knowledge. That patient had a palatal ulcer which eroded the palate and involved the sinuses by direct extension. Accordingly, the case we describe in this paper is the first case of *H. capsulatum* sinusitis without a contiguous source. We postulate that sinusitis occurred as a result of disseminated disease leading to seeding of the sinuses, possibly through the hematogenous route.

The diagnosis of fungal sinusitis in immunosuppressed patients, like those with AIDS, usually requires an invasive procedure (2, 7). Because morbidity and mortality are high in these patients, the etiologic agent should be promptly identified and treated (5). Cultures of sinus aspirates and histopathological examination of biopsy specimens with appropriate staining are cornerstones of the diagnostic algorithm. Evidence of dissemination should be sought with appropriate tests.

The optimal treatment of *H. capsulatum* sinusitis is not known, since reported studies have not involved enough patients to allow us to make recommendations. Patients with progressive disseminated histoplasmosis and those with AIDS should be treated with amphotericin B. The role of itraconazole in these cases is currently being investigated. Anecdotal reports suggest that itraconazole may be an attractive option in mild to moderate disease because of its oral administration, lower costs, and lower toxicity. Patients with AIDS and disseminated histoplasmosis should receive maintenance therapy with itraconazole after induction treatment with amphotericin B, a regimen which has been shown to be safe and effective in this setting (8). Based on the present case, we feel that treatment of primary *H. capsulatum* sinusitis may be undertaken with high-dose itraconazole if the patient is not severely ill and is able to tolerate the medicine. If the patient is unstable or critically ill, standard treatment with amphotericin B should be promptly initiated, followed by long-term maintenance therapy with itraconazole when the patient's condition permits. However, this is an isolated case, upon which generalizations should not be made; more studies are needed to determine the most appropriate treatment regimen for this disease.

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