

Progressive left-sided facial swelling and proptosis

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CASE PRESENTATION

A previously healthy 87-year-old African-American man presented to an urgent care facility with left nasal congestion. He reported a two-week history of nosebleeds, low-grade fever, night sweats and general malaise. He was treated with intravenous ceftriaxone and prescribed oral levofloxacin for suspected acute bacterial sinusitis. Due to worsening symptoms, left eye swelling and continued bloody nasal discharge, he went to a local emergency department and was admitted to the hospital and treated with intravenous ampicillin plus sulbactam for community-acquired acute bacterial rhinosinusitis; however, despite empirical therapy, his facial swelling progressed to involve the peri-orbital region. He developed left facial numbness, proptosis and decreased vision in the left eye (Figure 1).

On examination, he was afebrile and his heart rate was 82 beats/min, respiratory rate was 23 breaths/min and blood pressure was 130/86 mmHg. The patient was alert and cooperative. He had a small amount of bloody nasal discharge and left-sided facial swelling with tenderness noted in the maxillary area. Additional findings included left eye swelling without erythema that limited eye opening and examination. There was no pharyngeal erythema or oral lesions. He had no cervical adenopathy or organomegaly. There were no cutaneous or musculoskeletal findings. His respiratory, cardiovascular, abdominal and neurological examination were unremarkable. He had a white blood cell count of $170 \times 10^9/L$ with 60% neutrophils, 8% bands, 16% monocytes, 14% metamyelocytes and 2% lymphocytes. He was anemic and thrombocytopenic; his hemoglobin level was 74 g/L and platelet count was $13 \times 10^9/L$. His prothrombin time was 17.9 s, partial thromboplastin time 34.5 s and international normalized ratio was 1.44. His plasma chemistry, including liver function tests and blood glucose measurements, were normal. Magnetic resonance imaging of the brain with contrast demonstrated the presence of extensive left-sided sinusitis involving the frontal, sphenoid, ethmoid and maxillary sinuses, with intraorbital extension of infection to the left medial superior orbit.

As part of management, debridement and left inferior turbinate biopsy was performed by ear, nose and throat surgery.

Based on the patient's history, physical examination and clinical findings, what is the most likely diagnosis?

DIAGNOSIS

The patient was diagnosed with rhino-orbital-cerebral mucormycosis with acute myeloid leukemia. Left inferior turbinate biopsy revealed scattered ribbon-like fungal microorganisms demonstrating 90° branching without septae in a background of necrosis consistent with mucormycosis (Figure 2). Peripheral blood flow cytometry was consistent with acute myeloid leukemia.



Figure 1) Left facial and periorbital swelling

DISCUSSION

Fungal rhinosinusitis encompasses a wide variety of fungal infections that range from merely irritating to a rapidly progressive and often fatal course. Fungal colonization of the upper and lower airways is a common occurrence because fungal spores are constantly inhaled into the sinuses and lungs (1).

Mucormycosis is an opportunistic infection caused by fungi of the order Mucorales, and has angioinvasive and proliferative pathology in the susceptible host. Mucorales are ubiquitous in nature, and can be found on decaying vegetation and in the soil. The incidence of mucormycosis in adult leukemia patients is approximately 2% (1), and patients with hematological malignancies, especially those who develop graft-versus-host disease due to hematopoietic cell transplant, are highly susceptible (2). Typically, mucormycosis occurs in patients with diabetes mellitus (especially those who present with ketoacidosis), patients on glucocorticoid therapy, transplant recipients, patients with iron overload receiving deferoxamine therapy and AIDS patients (3). The most common clinical presentation of mucormycosis is rhino-orbital-cerebral infection, which is presumed to start with inhalation of spores into the paranasal sinuses of a susceptible host (4). Mucormycosis is characterized by infarction and necrosis of host tissues resulting from invasion of the vasculature by the spores. Infection usually presents as nasal congestion, sinusitis with fever, purulent nasal discharge and headaches. It then spreads to contiguous structures, such as the palate, orbit and brain, and usually progresses rapidly. Signs of orbital involvement include periorbital edema, proptosis, blindness and ophthalmoplegia (5). The nares and oral cavity should be carefully examined for necrotic areas. The diagnosis of rhino-orbital-cerebral mucormycosis is based on the identification of organisms in tissue by histopathology with culture confirmation; thus, early nasal endoscopic evaluation by an otolaryngologist is critical. Mortality rates in patients with hematological malignancies and mucormycosis

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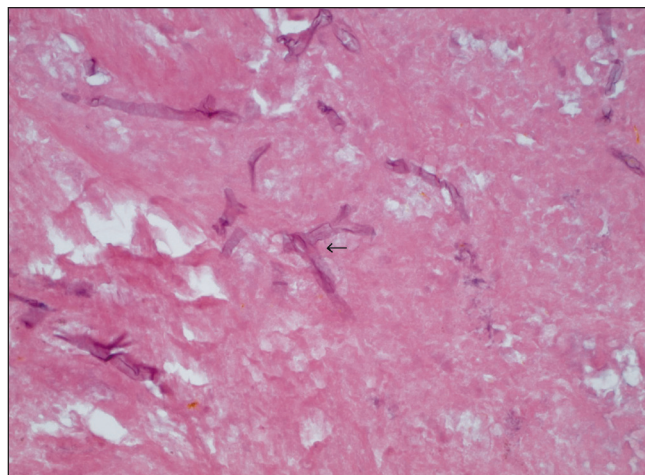


Figure 2) Scattered ribbon-like aseptate fungal hyphae demonstrating 90° branching in a background of necrosis

have been reported to be as high as 80% (6,7). Surgical intervention and debridement along with antifungal therapy using intravenous amphotericin B is the gold standard for eradicating the infection (8,9). Posaconazole can be used as a step-down therapy in patients who have responded to liposomal amphotericin B. In addition, treatment of predisposing factors, such as hyperglycemia, metabolic acidosis and neutropenia, is essential. In patients with rhino-orbital-cerebral infections, the most significant factors associated with death were delayed diagnosis, central nervous system involvement, leukemia, renal disease

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and treatment with deferoxamine. Our patient opted for palliative measures (9,10).

Common and selected differential diagnosis includes:

- Acute bacterial rhinosinusitis. Acute bacterial rhinosinusitis occurs most commonly as a complication of viral infection such as the common cold or allergic rhinitis. Symptoms typically improve with supportive measures and antibiotic treatment.
- Basal cell carcinoma. This is a common malignancy typically observed in Caucasians; it appears on the surface of the skin, and is rarely invasive.
- Chronic and compulsive intranasal use of cocaine. This condition causes progressive damage of the mucosa and perichondrium, leading to ischemic necrosis of septal cartilage and perforation of the nasal septum.
- Leukemoid reaction or hyperleukocytosis. In patients with hyperleukocytosis, white blood cell count is $>100 \times 10^9/L$ and life-threatening pulmonary and central nervous system disease results due to vascular occlusion of the leukocytes.

CONCLUSION

Mucormycosis should be suspected in high-risk patients, especially those who have diabetes mellitus with ketoacidosis, and immunocompromised hosts who present with sinusitis and necrotic tissue in the nose or palate. Timely endoscopic evaluation of the sinuses should be performed to identify tissue destruction and to obtain specimens for histopathology. The diagnosis of mucormycosis depends on identification of organisms and culture confirmation. Treatment of mucormycosis involves a combination of surgical debridement of the involved tissues and antifungal therapy. Despite diagnosis and aggressive combined surgical and medical therapy, the prognosis for recovery from mucormycosis is universally poor.