Rhinocerebral mucormycosis is a rapidly progressive and often fatal infection frequently seen in patients with uncontrolled diabetes mellitus and hematologic malignancies. The disease is difficult to diagnose because it often masquerades as bacterial sinusitis. The current report describes a 69-year-old white woman with diabetes mellitus who was prescribed high-dose prednisone therapy for chronic obstructive pulmonary disease. Two weeks after treatment initiation, she presented to the hospital with facial edema on the right side, mouth pain, and general weakness. No black eschars on the nasal mucosae or palates were present on admission. Although bacterial etiology was initially suspected, surgery and tissue samples revealed the presence of rhinocerebral mucormycosis. The patient died at 6 days postadmission despite aggressive medical and surgical intervention. The current report discusses the risk factors associated with rhinocerebral mucormycosis as well as the necessity of early diagnosis and treatment to improve patient outcomes.

J Am Osteopath Assoc. 2007;107:491-493

Rhinocerebral mucormycosis is a serious and life-threatening fungal infection of the sinuses and brain. Mucormycosis is caused by fungi of the Mucorales order, the largest and best studied order of Zygomycete fungi. Mucorales is identified by cultural and microscopic characteristics of broad, nonseptate hyphae. In rhinocerebral and pulmonary mucormycosis, sporangiospores colonize the paranasal sinuses, nasal cavities, and lungs, whereby they invade the neural tracts and blood vessels.1 Although this fungus has been reported to infect cardiac tissue as well as the gastrointestinal and genitourinary tracts, presentations most commonly occur in the sinuses and brain as well as the lungs.2,3

Mucormycosis is primarily seen in patients with chronic conditions, particularly uncontrolled diabetes mellitus and hematologic malignancies, because these patients are immunocompromised. Patients with extensive burn injuries, renal failure, prolonged corticosteroid use, and deferoxamine treatment have also been reported to have mucormycosis.4 However, because the disease often masquerades as bacterial sinusitis, it can be difficult to diagnose. The current report describes an incident of fatal, rapidly progressive rhinocerebral mucormycosis that occurred after a patient received a short course of corticosteroid therapy.

Report of Case
An elderly woman was admitted to the hospital for chronic obstructive pulmonary disease (COPD) exacerbation. The patient was prescribed 80 mg/d of oral prednisone. In the second week of treatment, daily dosage was reduced to 40 mg. She was discharged to a rehabilitation hospital 2 weeks after admission only to return to the hospital the following day.

On readmission, the patient’s blood pressure was 112/63 mm Hg; heart rate, 100 beats per minute; respiratory rate, 20 breaths per minute; and body temperature, 97.7°F. Physical examination revealed a 69-year-old white woman in good health and no apparent distress. She was well hydrated and nourished.

The patient’s past medical history was significant for COPD, diabetes mellitus, end-stage renal disease, hypercholesterolemia, and sick sinus syndrome. The patient had maintained glucose control the previous month (hemoglobin A1c [HbA1c], 7.0%) through regular insulin using a sliding scale regimen, pioglitazone hydrochloride, and glimepiride therapy. She was also prescribed aspirin for cardiac protection; clotrimazole for a recent thrush infection that had resolved more than a week before readmission; diltiazem hydrochloride for heart rate control; furosemide for edema; gabapentin for neuropathic pain; metoprolol succinate for hypertension; and simvastatin for hypercholesterolemia.

She presented with new onset facial edema, tenderness on the right side and on the maxillary sinuses on palpation, numbness, and facial paralysis on the right side associated with mouth pain, odynophagia, mild epistaxis, and cephalgia. She complained of fatigue, vertigo, dyspnea, nonproductive cough, and monocular diplopia in the right eye. The patient denied fever, chills, acute vision loss, hemoptysis, and abdominal pain.

The patient’s face was grossly edematous on the right side with a periorbital edema visible. The patient had no proptosis. Her right eyelids were both erythematous but not tender to palpation. Ecchymosis was also visible on the right
CASE REPORT

A noncontrast CT scan of the sinuses revealed bilateral maxillary sinus fluid levels consistent with acute maxillary sinusitis, an infundibular obstruction on the right, severe opacification of the right ethmoid sinus, and moderate opacification of the right frontal sinus (Figure 1). Right infraorbital facial swelling consistent with cellulitis was visible. Bony destruction was not seen.

Four days after readmission, the patient’s face became ecchymotic with bullous formation over the right cheek and cyanosis on the tip of her nose. Necrotic skin was apparent on her right upper gingiva and nasal septal mucosa. Progressive weakness of cranial nerve VII was also noted. The appearance of necrotic tissue and blood cultures negative for aerobic and anaerobic bacteria suggested invasive fungal sinusitis. The patient was given 430 mg of amphotericin B lipid complex every 24 hours. As a result of the patient’s worsening condition, and less than 24 hours after amphotericin B administration, she was quickly weaned from prednisone therapy and prepared for surgery.

The surgeons first obtained a biopsy from the gingival mucosa and nasal skin, but no Mucorales species was found. A right resection of the cheek, nose skin, and soft tissue; inferior and middle turbinectomy; partial septectomy; and infraorbital and hemipalatectomy were performed, sparing the patient’s right eye. Amphotericin B was used to flush the debrided areas.

The gross specimens showed tissue infarction and necrosis. Numerous fungal elements were present in the tissues and in multiple vascular spaces. Figure 2 shows the characteristic broad nonseptate hyphae branching at right angles as well as spore formation. The patient was diagnosed as having rhinocerebral mucormycosis.

One day postsurgery, the patient went into respiratory distress and became hypotensive. Despite aggressive therapy, her status worsened and multiorgan failure occurred. She died on the second postsurgical day, which was 6 days after hospital readmission.

Discussion

Patients with rhinocerebral mucormycosis commonly present with black eschars on the nasal mucosa or palate. In the current case, the patient’s diagnosis of this troubling disease was delayed 4 days as a result of the absence of such characteristic symptoms. In addition, the elevated white blood cell count and facial cellulitis suggested a bacterial etiology. However, the CT scan showed right sinus opacification without evidence of bony erosion, which indicated either bacterial or fungal sinusitis. Rhinocerebral mucormycosis was suspected only when necrotic tissue appeared over the patient’s right cheek and the tip of her nose. This diagnosis was later confirmed by histology.

The case of rhinocerebral mucormycosis described in this report demonstrates the disease’s rapidly progressive nature. Based on the patient’s previous HbA1c levels, the patient had
Acknowledgment

I thank the pathology technicians at Plaza Medical Center in Fort Worth, Tex, for taking pictures of the bacteria stains.

References


controlled diabetes mellitus before administration of prednisone. Her resulting elevated glucose levels (>300 mg/dL) after corticosteroid therapy may have contributed to the spread of the fungal infection because fungi receive nourishment from sugars. The patient’s other risk factors for mucormycosis included end-stage renal disease with extremely low creatinine clearance as well as gapled metabolic acidosis, which was indicated by the anion gap and low pH values on arterial blood gasses.

Until the advent of amphotericin B in the 1950s, mucormycosis was a universally fatal fungal infection. One case series by Ericsson and colleagues reported that the survival rate is approximately 80% when medical and surgical interventions are both administered. A small retrospective analysis by Strausser and colleagues reported that the survival rate is closer to 48%. The predictors of a decreased survival rate appear to be associated with renal disease, leukemia, hemiparesis or hemiplegia, bilateral sinus involvement, and deferoxamine therapy. In a study by Alleyne and colleagues, the most important predictor of survival was the underlying disease. Early diagnosis and intervention with amphotericin B lipid complex and surgery directly correlated with patient survival.

Although it is a rare disease, rhinocerebral mucormycosis should be included in the differential for facial pain, edema, paresthesia, and paralysis in patients with risk factors. Earlier recognition of the condition, medical attention specific to the patient’s needs (eg, aggressive insulin control, withdrawal of prednisone, initiation of dialysis, and earlier administration of amphotericin B), and surgical debridement may improve patient outcome.

Figure 2. Gomori methenamine silver stains reveal presence of bacteria in a 69-year-old woman with rhinocerebral mucormycosis. The stains reveal (A) broad nonseptate hyphae with right-angle branching and (B) a mucormycosis spore.