Ptosis, Erythema, and Rapidly Decreasing Vision

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A previously healthy 63-year-old white man presents to the emergency department with a swollen right eye and complete ptosis. Three weeks prior, the patient was evaluated for sinusitis by a local otolaryngologist. Cultures were performed on sinonasal aspirates and empirical ciprofloxacin and oral prednisone were initiated. The patient’s symptoms, however, worsened. Cultures revealed *Enterobacter aerogenes*. On the morning of presentation, a complete ptosis of the right eye had developed (Figure, A). Vital signs were stable, but visual acuity was 20/200 in the right eye and 20/25 in the left. Examination was remarkable for limited ocular motility (Figure, B; Video at http://www.jama.com) and a right relative afferent pupillary defect (Figure, C). Within an hour, vision had deteriorated to light perception. Serum glucose level was measured at 690 mg/dL (38.3 mmol/L) without an anion gap, and hemoglobin A1c level was 8.9%. Maxillofacial computed tomography imaging revealed sinusitis and orbital stranding. The patient was transferred to our institution. On arrival he had lost light perception. An area of ocular adnexal tissue necrosis had developed.

What Would You Do Next?

A. Administer broad-spectrum antibiotics, culture necrotic tissue, obtain Gram stain, and await results as patient is transferred to the intensive care unit

B. Administer broad-spectrum antibiotics, obtain cultures, and request urgent infectious diseases and neurology consultation

C. Administer empirical liposomal amphotericin B, broad-spectrum antibiotics, and consult otolaryngology and ophthalmology services for urgent evaluation

D. Order immediate magnetic resonance imaging to reassess location and extent of lesion

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Diagnosis
Fungal sinusitis; mucormycosis orbital cellulitis

What to Do Next
C. Administer empirical liposomal amphotericin B, broad-spectrum antibiotics, and consult otorhinolaryngology and ophthalmology services for urgent evaluation.

The key clinical features include total internal and external ophthalmoplegia and necrotic ocular adnexal tissue in the context of sinusitis with laboratory data suggestive of uncontrolled diabetes. These findings are concerning for mucormycosis. If left untreated, the condition is often fatal. Therefore, empirical initiation of liposomal amphotericin B with broad-spectrum antibiotics is appropriate. Otorhinolaryngology and ophthalmology services should be promptly consulted to evaluate the eyes, orbits, and sinuses.

Discussion
A computed tomography scan revealed invasive sinusitis. The patient developed a total internal and external ophthalmoplegia and necrotic ocular adnexal tissue. The assumption at this point must be that the patient has a fungal orbital cellulitis. Fungal orbital cellulitis will not respond to antibiotic therapy and has a tendency to occur in immunocompromised patients. It is aggressive and potentially fatal. It is unnecessary to extract tissue prior to initiation of antifungal therapy because this could be performed afterward without a deleterious effect on the diagnosis.

Mucormycosis is a rare, serious fungal infection also known as zygomycosis and phycymycosis. It is caused by a variety of phycomycete fungi, including Rhizopus, Apophysomyces, Cunninghamamella, Absidia, and Rhizomucor. Microscopy reveals characteristic broad, nonseptated hyphae that branch at 90°. Their growth is limited by iron availability, and all processes that alter physiological iron stores either increase or decrease the risk of this disease. For example, diabetic ketoacidosis, by affecting iron-binding proteins, increases free iron and thus increases risk of fungal infection. Disease is ultimately caused by direct invasion of the fungus into the vasculature, causing thrombosis and end-organ pathology.

A delay in diagnosis of this disease is potentially fatal. A careful history and focused review of systems, especially noting a history of diabetes and sinus disease, is essential. Physical examination may reveal evidence of orbital cellulitis as well as necrotic tissue in the nose, ocular adnexal tissue, or the hard palate. A noncontrast maxillofacial computed tomography scan is sufficient for evaluation of the sinuses and orbit. In an acute setting, cultures have a limited role because there are many naso-opharyngeal organisms that could confuse the diagnostic picture. Therefore, actual tissue biopsy is the criterion standard. Some argue against the presumptive use of antifungals prior to acquisition of tissue, but most agree that treatment is most important if highly suspected; and a plan for tissue acquisition could still be planned and performed without altering the diagnostic yield. Treatment often involves liposomal amphotericin B and immediate and extensive surgical debridement. Mortality rates overall are nearly 50%; rates for patients with AIDS and those with disseminated Mucor are nearly 100%. An expedited and thorough evaluation should always be performed in patients with orbital cellulitis and highly suspected to have fungal sinusitis. Antifungal therapy should be started as soon as there is sufficient clinical evidence of invasive fungal sinusitis.

Patient Outcome
The patient was taken to the operating room for emergent endoscopy and debridement by otorhinolaryngology, and after viable tissue was found in the posterior aspect of the septum, it was decided that exenteration with wide resection of tissue would be potentially lifesaving. Culture from nasal biopsy specimens revealed fungal elements and grew Rhizopus. Pathological review from the right side of the nose revealed invasive zygomycosis involving the mucosa, blood vessels, fibrous tissue, and bone, with associated extensive soft tissue and bone necrosis. Pathological review of the eye revealed invasive zygomycosis of the subdural space around the optic nerve and extensive fungal invasion of the iris. The leptomeninges and the optic nerve proper were not involved.

Following surgery, the patient was transferred to the surgical intensive care unit. After stabilization, he was ultimately transferred to the floor. The endocrinology service initiated diabetic management, and the infectious diseases team managed antifungal therapy. The interventional radiology service inserted a gastrostomy tube to maximize nutrition.

No other systemic complications arose. He was hospitalized for 17 days before discharge to a rehabilitation center. As of this report, the patient is 8 months into his recovery and has undergone facial reconstruction with a left anterolateral thigh free flap.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported. Funding/Support: The Department of Otorhinolaryngology at the University of North Carolina Hospitals is a recipient of an unrestricted grant from Research to Prevent Blindness Inc, New York, New York. Role of the Sponsor: Research to Prevent Blindness Inc had no role in the preparation, review, or approval of the manuscript or the decision to submit the manuscript for publication. Online-Only Material: The Video is available at http://www.jama.com.

Additional Contributions: We would like to acknowledge significant contributions to this patient’s care from Brian Thorpe, MD (Otolaryngology), Eric Halverson, MD (Plastic Surgery), Cindy Wu, MD (Plastic Surgery), Lori Scang, MD, PhD (Pathology), Spencer Rusin, MD (Pathology), and Anne Lachiewicz, MD (Infectious Disease). We also thank the patient for providing permission to share his information.

REFERENCES

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