Visual loss due to paranasal sinus invasive aspergillosis in a diabetic patient

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Aspergillus species are commonly found in the soil and decaying organic matter. The spores can be typically inhaled or ingested, yet disease due to tissue invasion is rarely seen in the immunocompetent host. In the immunocompromised patient, there has been an increased incidence of invasive aspergillosis in the last 20 years. Invasive aspergillosis of the maxillary sinus with orbital and cranial spread can be lethal, therefore, necessitates early diagnosis and prompt treatment. The predilection of Aspergillus for infiltration of blood vessels can result in serious ocular complications which can lead to loss of vision. We present the case of an uncontrolled diabetic patient with invasive maxillary sinus aspergillosis and extension to the orbital contents. Our purpose was to emphasize the need of early recognition and prompt initiation of combined antifungal treatment and surgical intervention with the intent to preserve the involved vital structures.

Keywords: Aspergillosis, diabetes, orbital apex syndrome

INTRODUCTION

Aspergillus species are commonly found in the soil and decaying organic matter. The spores can be typically inhaled or ingested, yet disease due to tissue invasion is rarely seen in the immunocompetent host. In the immunocompromised patient, there has been an increased incidence of invasive aspergillosis in the last 20 years. Manifestations of invasive aspergillosis in the head and neck area are infrequent and usually involve the paranasal sinuses. This recent rise in the recognition of fungal paranasal infections is attributed to both modern diagnostic modalities, mainly the use of computed tomography (CT) and a significant increase of the predisposing conditions to these infections.

Invasive aspergillosis of the maxillary sinus with orbital and cranial spread can be lethal, therefore, necessitates early diagnosis and prompt treatment. Long-term administration of antibiotics and corticosteroids, diabetes mellitus, radiotherapy, chemotherapy, immunosuppressive medications, and lymphoproliferative disorders represent factors that favor the occurrence and spread of this opportunistic infection.

Dissemination of Aspergillus in the debilitated patient may involve various sites such as the lung, brain, kidney, myocardium, liver, spleen, and the eyes. The predilection of Aspergillus for infiltration of blood vessels can result in serious ocular complications which can lead to loss of vision. We present the case of an uncontrolled diabetic patient with invasive maxillary sinus aspergillosis and extension to the orbital contents. Our purpose was to emphasize the need of early recognition and prompt initiation of combined antifungal treatment and surgical intervention with the intent to preserve the involved vital structures.

CASE REPORT

A 37-year-old man presented in the Emergency Department with a persistent left-sided facial swelling, constant headache, ptosis and paresis of all branches of left facial nerve [Figure 1]. Clinical examination revealed a palatal ulceration covered by a pseudomembrane [Figure 2] and visual acuity of 9/10 of the left eye. A neurologist’s assessment was sought and confirmed the peripheral type of the facial nerve palsy. The patient was pyrexial, and the initial blood examinations showed a white cell count of...
11,000/mm$^3$, and blood sugar level of 495 mg/dl. The hemoglobin A1c was 9.7% consequently, a diagnosis of uncontrolled diabetes was reached. Broad spectrum antibiotic treatment and normal saline IV infusion with insulin and potassium supplements were initiated in an attempt to control the infection and his uncontrolled diabetic status.

A CT revealed a soft tissue mass of enhanced density in the left maxillary sinus extending to the ipsilateral ethmoid, sphenoid sinuses, and adjacent tissues. The orbit was also involved [Figure 3]. The sinus pathology and palatal ulceration did not appear to be connected in the CT. In addition, no obvious perforation of the palate was seen in the scan. The patient
subsequently underwent a diagnostic Caldwell-Luc procedure with conservative debridement of the soft tissue mass and an incisional biopsy of the palatal lesion.

On the third postoperative day, the patient developed acute visual loss of the left eye. His left visual acuity deteriorated to hand movement, with a left relative afferent pupillary defect, ptosis, chemosis of the conjunctiva and ophthalmoplegia. A detailed ophthalmoscopic examination revealed thrombosis of the left retinal vasculature and infarction of the inner retinal layers. The ophthalmologist’s report was consistent with retinal ischemic necrosis and exudative detachment from an infectious agent.

Histopathologic examination of the maxillary sinus mass disclosed the presence of septate hyphae of the filamentous fungus [Figure 4]. The result of the incisional biopsy of the palate was negative for malignancy. Culture and sensitivity test for common pathogens was not indicative, however, further nonculture tests were positive for galactomannan antigen, and whole blood real-time polymerase chain reaction was positive for Aspergillus species. Subsequent cultures of the sinus material grew Aspergillus section Fumigati. The patient’s medical therapy was subsequently altered to IV liposomal amphotericin B and broad spectrum antibiotics to cover any possible bacterial super-infection.

A further CT of the head revealed extension of the infectious infiltrate adjacent to the left orbital apex, however, there was no evidence of intracranial extension. The microbiology department was consulted, and voriconazole was initiated as the treatment of choice. The patient underwent an extended, more aggressive surgical debridement of the left maxillary sinus to treat invasive aspergillosis. Due to adverse reactions to voriconazole, the antifungal treatment was adjusted, and posaconazole was administered.

Gradual and steady improvement of the patient’s condition was noted in the following 12 months with good response to the antifungal therapy and resolution of his ophthalmoplegia, facial nerve palsy and palatal ulceration [Figure 5]. A CT scan revealed a maxillary sinus clear of disease [Figure 6], however, the patient’s visual acuity of the left eye was recorded as light perception after 3 years.

**DISCUSSION**

Aspergillosis is a fungal infection of opportunistic character that may present with various features depending on the strength of a specific pathogenic species and the status of the host’s immune response. In the head and neck, the involvement of the sinuses and the orbit is not uncommon, in the immunocompromised patient, and often presents in association with fever, cellulitis, ptosis, proptosis, and visual disturbance. Oral lesions are encountered more rarely and may arise as primary infections of the mucosa or after dental procedures. Dissemination of the disease from the lungs or extension from the maxillary sinus to the oral mucosa may also occur. The characteristic appearance of the oral lesions in invasive aspergillosis is that of grey ulcerated, necrotic areas which can be attributed to thrombotic vascular infarction and destruction of the tissue directly. The most commonly reported sites are the palate and posterior tongue.[3]

The invasive form of aspergillosis has been associated with symptoms of pain and edema caused by tissue invasion and can be misdiagnosed as malignancy. Aspergillosis which involves the paranasal sinuses can extend to the orbit and the cranial vault along the skull base and the large vessels. In this occasion, patients, usually, present with ophthalmoplegia, proptosis, facial swelling, hypoesthesia of the upper branches of the trigeminal nerve, and loss of vision. Therefore, the possibility of opportunistic infections by fungi must be included in the differential diagnosis in all immunocompromised patients as they may prove to be both vision and life-threatening.

Computed tomography can accurately demonstrate the extent of Aspergillus infection to the paranasal sinuses, facial, orbit, and intracranial contents. Abnormal enhancement of nerve sheath with enhancing soft tissue which infiltrated the optic and facial nerves, respectively, has been well described in the literature.[4,6] In our case, the patient was not able to wrinkle his forehead and presented with a typical peripheral paralysis of the ipsilateral facial nerve. This was verified by the Neurologist who confirmed the diagnosis and expressed the opinion that the left facial nerve was involved and paralyzed by direct fungal invasion. This diagnosis is further supported by the fact that as soon as the infection was controlled, with surgery and medication, the function of the nerve showed immediate signs of improvement.

Invasive aspergillosis is characterized by a rapidly progressive, gangrenous process caused by fungal vascular invasion which results in thrombosis of the involved vessels and necrosis of tissue.[6] Hematogenous spread of the fungus to the brain, orbit, and adjacent structures can be attributed to Aspergillus angioinvasive potential which may lead to tissue necrosis beyond the area of direct extension. Dissemination to the eye can occur following hyphal penetration of blood vessels. When the retinal vasculature is acutely occluded, an infarction of the inner retinal layers occurs as a result of interruption of perfusion. The ophthalmoscopic examination in the present case confirmed this etiopathogenesis which is well-reported in the literature.[9]

Signs and symptoms of invasive aspergillosis can be rather subtle, therefore, reaching an early diagnosis in the immunocompromised patient may be challenging. Differential diagnosis includes benign and malignant neoplasms of the antrum, mucormycosis, lymphoma, syphilis, tuberculosis, sarcoidosis, Wegener’s granulomatosis, and allergic fungal sinusitis.

Histopathologic examination is considered to be the most reliable test to diagnose aspergillosis, however, this may delay the initiation of treatment as it can be a slow process.[10] While blood cultures can frequently give false results as an outcome of contamination, there has been the development of nonculture-based diagnostic methods, such as serodiagnosis and polymerase chain reaction. In addition, the detection of galactomannan, a component of cell wall of Aspergillus species, can be a rather useful marker for early diagnosis. In patients at high risk for invasive aspergillosis, positive results for Aspergillus by polymerase chain reaction of blood samples are highly suggestive of the disease and contribute...
to the diagnosis. The positive predictive and negative predictive values of these methods have been reported to be as high as 83.8% and 98.1%, respectively.\[10\]

The combination of aggressive surgical debridement and systemic antifungal therapy is considered to be the standard management for invasive aspergillosis of the paranasal sinuses. Effective surgical treatment requires adequate exposure to remove all necrotic, devascularized tissue with the ultimate purpose to permit the antifungal agent to reach the involved site. Although endoscopic techniques have the advantage of maintaining the sinus anatomy, they can limit the access and suboptimize the results of debridement. In the cases that extensive invasive disease needs to be treated, open approaches allow sufficient control of the surgical field and permit the removal of sinus, orbital, and facial infected tissue. In the presenting case, we selected to control the infection with a radical antrostomy and removal of the entire necrotic maxillary sinus mucosa with purpose to allow drainage into the inferior meatus. The second more aggressive procedure which included debridement of the affected bone was attempted with good results when the infection recurred.

Antifungal agents with proven activity against Aspergillus such as amphotericin b, itraconazole, voriconazole, micafungin, and posaconazole can be used to restrain the expansion of the infection. The patient was initially treated with liposomal amphotericin b which was changed to voriconazole after his clinical and radiological deterioration. Despite the fact that voriconazole has shown good tolerability in immunocompromised patients adverse reactions to the medication necessitated the cation of medical treatment to posaconazole. This alteration combined with a further extensive surgical debridement resulted in stemming the infection and allowed the gradual improvement of the patient’s condition.

Invasive aspergillosis of the paranasal sinuses in the immunosuppressed host may follow an insidious course, far more destructive than in an otherwise immunocompetent patient. Although the anatomic confines of the antrum can be breached early in the infection, the signs and symptoms of the patient may be subtle and misleading. Specific species of Aspergillus have the potential of vascular invasion and thrombosis and may affect tissue that is found beyond the front line of the infection. Prompt recognition with the use of modern imaging modalities and identification of the fungus is of paramount importance in early diagnosis. Complete surgical removal of the necrotic tissue with a view to preserve the vital structures and immediate initiation of effective antifungal therapy constitutes the cornerstone of treatment.

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