



Invasive Aspergillosis treated with Voriconazole and Surgical Debridement: Case report

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Abstract

Background: Paranasal sinus Aspergillosis is a fungal infection caused by *Aspergillus* species. This is a case of invasive Aspergillosis treated with Voriconazole and surgical debridement.

Case presentation: A twenty-four-year-old male presented with left cheek swelling, headache, left-sided nasal obstruction, thick nasal discharge, and fever for 20 days. The swelling was extending from the upper lip to the left infraorbital region pushing the lateral nasal wall medially involving the nasal floor and extending to the palate. He had left infraorbital edema with normal left eye movement and normal vision. The patient was admitted to the hospital; all investigations were normal apart from high TWBCs. He was treated with antibiotics and steroids without improvement. The diagnosis of Aspergillosis was confirmed by radiology, histopathology, and mycology. The patient started Itraconazole before surgical exploration, which was carried out under general anesthesia, postoperatively the patient developed gross facial edema with facial skin necrosis, left eye chemosis, blurring of vision, and proptosis. Itraconazole was discontinued because his liver function deteriorated and Amphotericin B injections were started; his condition started to improve, but again his liver function deteriorated, and the treatment was interrupted. His left eye became completely blind with thick eye discharge; surgical removal was done. The patient received oral Voriconazole (with no side effect) combined with surgical debridement and regular follow-up for 6 months without clinical or radiological evidence of recurrence.

Conclusions: Fungal rhino sinusitis can start as non-invasive fungal granuloma which becomes invasive with an orbital extension that responds very well to Voriconazole and surgical debridement. Early diagnosis and proper treatment decrease morbidity and mortality. Voriconazole is a recommended drug for the treatment of invasive Aspergillosis with good effects and minimal side effects.

Keywords: Invasive Aspergillosis, Voriconazole, surgical debridement, paranasal sinuses

Abbreviations: TWBCs: Total white blood cells; CT: Computed tomography; MRI: Magnetic resonance imaging

Introduction

Fungal rhino sinusitis includes a wide variety of fungal infections that affect the nose and paranasal sinuses. Fungal colonization of the upper and lower airways occurs by inhalation of fungal

spores into the sinuses and lungs. However, colonization is distinct from infection and most colonized patients do not develop a fungal infection. (Fungal rhino sinusitis) is the appropriate term to describe fungal infection of the paranasal sinuses because nasal

involvement is common in most cases [1]. An additional disorder, which involves hypersensitivity to colonizing fungi, is called allergic fungal rhino sinusitis. Invasive Aspergillosis is a major cause of death in immunocompromised patients [2].

Case Report

A twenty-four-year-old male presented with left cheek swelling, headache, left side nasal obstruction, thick nasal discharge, and fever for 20 days. On examination the patient was generally ill, febrile local examination showed a firm mass extending from the upper lip to the left infraorbital region and pushing the lateral nasal wall medially involving the nasal floor and extending to the palate. He had left infraorbital edema with normal left eye movement and normal vision. The patient was admitted to the hospital; all his investigations were normal apart from high TWBCs (14.800). He received antibiotics and steroids without improvement. CT revealed a soft tissue mass involving the left nasal cavity and palate with the opacity of the left maxillary and ethmoid sinuses, there was no bone destruction and no orbital or intracranial extension. Biopsy was performed under local anesthesia through sub-labial incision, histopathology result was *Aspergillus granuloma*, and mycology study isolated *Aspergillus flavus*. After the diagnosis of fungal sinusitis. Medical treatment was started with Itraconazole before surgical exploration; which was done under general anesthesia through a combined sub-labial approach and nasal endoscopy; there was a firm mass occupying the left maxillary and left ethmoid sinuses, left nasal cavity, and extending to the palate. Debulking of the mass was done. Postoperatively the patient developed gross facial edema, left eye chemosis, blurring of vision, and proptosis with facial skin necrosis bilaterally. Itraconazole was discontinued because his liver function deteriorated and Amphotericin B injections were started; his condition started to improve, but again his liver function deteriorated, and the treatment was interrupted. His left eye became blind with thick discharge; the eye was removed surgically. Medical treatment with oral Voriconazole was started (with no side effects) combined with surgical debridement and removal of dead tissues. The patient became asymptomatic with no clinical or radiological evidence of recurrence. After 6 months follow up, he was referred for facial reconstruction.

Discussion

Fungal infection of the nose and paranasal sinuses should be recognized early to avoid morbidity and mortality and suspected in any case of chronic rhino sinusitis not responding to antibiotics, based on radiological features even in immunocompetent patients [3-5]. Our patient was an immunocompetent young male who presented with unilateral facial swelling which was not responding to antibiotics. The common clinical presentation of fungal rhino sinusitis includes headaches, nasal congestion, fever, and facial pain. Invasive Aspergillosis can extend to the orbit or intracranial along the skull base or larger vessels. In cases of orbital involvement, the patient complains of blurred vision, loss of vision, chemosis, and proptosis [2]. In this case the condition was started as unilateral

facial swelling which later extended to the other side of the face causing facial skin necrosis and orbital extension.

Both CT and MRI can help to establish the diagnosis of invasive fungal sinusitis, opacity of the sinuses with or without bone destruction may be demonstrated, while bone destruction and extra sinus extension are the classical CT findings, these are usually found late. The most common early signs are massive unilateral nasal cavity and soft tissue edema [6]. The early CT of the patient showed edematous soft tissue mass involving the left nasal cavity and palate with the opacity of the left maxillary and ethmoid sinuses, there was no bone destruction and no orbital or intracranial extension. A biopsy is necessary to establish the diagnosis. The histology should be specific about whether there is mucosal involvement (invasive) or the mucosa is intact (noninvasive) [7]. Three histological variants of the lesion were distinguished as proliferative, exudative-necrotizing, and mixed form [8]. The histopathology of this patient was that of the mixed form with both granulomatous pseudotuberculosis and the exudative necrotic foci. Worldwide, *A. fumigatus* is the most common species of fungal rhino sinusitis followed by *A. flavus* [9]. In Sudan both paranasal sinus and pulmonary Aspergillosis were caused by *A. flavus* [8,10-12] which was the causative fungus in the studied case.

Fungal rhino sinusitis is classified into an invasive and non-invasive types according to the degree of mucosal invasion and bone destruction. The non-invasive are allergic sinusitis and aspergilloma which leads to sinus mucosa destruction and bone atrophy, while the invasive type can be either (chronic or indolent) or (acute fulminant) with a rapid course causing destruction of the nose, sinuses, and extending to the orbit and brain within a few days [9]. The most recent classification has been put by Rowe-Jones in 1994; [13] who reported three main types of Aspergilloses:

- a. Noninvasive
- b. Invasive
- c. Destructive noninvasive which is further classified into:
- d. Aspergilloma.
- e. Fungal ball.
- f. Mycetoma (usually affecting one sinus) or *Aspergillus sinusitis* (involving more than one sinus).

The condition of this patient can be classified as destructive noninvasive fungal granuloma which was becoming aggressive to involve the surrounding structures and extended to the orbit. Management of invasive Aspergillosis is still controversial and depends on the nature of the disease, host immunity, and degree of tissue invasion. The Infectious Disease Society [IDSA] released updated guidelines for the treatment of invasive Aspergillosis in 2008 Voriconazole [broad-spectrum triazole] has become the drug of choice for invasive Aspergillosis [7]. Voriconazole is recommended for the treatment of invasive Aspergillosis due to its better tolerance, increased efficacy, improved survival, and less toxicity

with fewer drug interactions [4,14,15]. The recommended dose of Voriconazole is 6 mg/kg IV every 12 hours on day one followed by 4 mg/kg twice daily then 200 mg orally twice daily. The common side effects of the drug are visual disturbances, skin reactions, and hepatotoxicity. All side effects were transient and resolved when the drug was discontinued [16]. Our patient was given oral Voriconazole with a good response without any side effects. Early diagnosis, proper antifungal, and surgical debridement is the key to successful treatment of invasive Aspergillosis [4].

Declaration Section

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Ethical consideration: Verbal Informed consent was received from the patient.

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