

Case report of chronic invasive fungal sinusitis in immunocompetent child treated with surgery and voriconazole

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Abstract: A case of invasive fungal sinusitis, in an apparently immunocompetent, nine year old child, successfully treated with a combination of surgery and Voriconazole, an antifungal agent, with good response. Voriconazole administration could form a new standard treatment for invasive fungal sinusitis.

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1. Introduction

Fungal sinusitis encompasses a wide variety of fungal infections that range from merely irritating to rapidly fatal.

Invasion of tissues adjacent to the sinuses occurs after the fungi establish local infection. The aggressiveness of tissue invasion may vary depending upon the underlying immune status of the host. Profoundly immunocompromised patients and those with poorly controlled diabetes can experience rapidly progressive disease over the course of a few hours, whereas the disease may be more indolent in patients with well-controlled diabetes or apparently normal immune function.

The spread of infection out of the sinuses is usually due to direct extension, but fungemia with metastatic spread can also occur.

Invasive fungal sinusitis is defined as fungal sinusitis with mucosal infiltration of mycotic organisms.¹ Both non-invasive and invasive fungal sinusitis is usually the result of *Aspergillus* species infection.²

They often endure the symptoms of chronic sinusitis for months before the development of a complication such as visual changes from orbital invasion or neurologic complaints due to brain involvement. The physical examination may reveal tenderness over the maxillary sinuses and erythema overlying the malar areas. Proptosis or fixation of the globe is seen with orbital involvement.

The gold standard for treatment has been wide surgical debridement, intravenous administration of antifungal agents such as amphotericin B, and correction of the underlying immunocompromised state.³ However, the prognosis remains poor, partly because the strong side effects of amphotericin B, which are sometimes critical and can, hinder long time administration. A large randomized open multicenter trial comparing amphotericin B and voriconazole for the treatment of invasive aspergillosis showed significant better outcome and fewer adverse events

with voriconazole group.⁴ However, no standard treatment option with the new antifungal agents has yet been established for chronic invasive fungal sinusitis.

I describe a case of chronic invasive fungal sinusitis in an apparently immunocompetent child who was treated with the combination of surgery and extended administration of voriconazole, resulting in good clinical outcome.

2. Case report

A 9 years old boy referred to our hospital, January 2008 complaining of protrusion of the left eye since 4 months, associated with headache but no visual disturbances. There was a history of recurrent upper respiratory tract infections, with nasal blockage and snoring since two years. Clinically ENT examination showed left nostril polypoidal mass with bilateral inferior turbinate hypertrophy with normal ears and throat examinations. Eye examination showed complete lid closure, visual acuity 6/6, normal papillary reaction, extraocular motility and color vision with nonaxial moderate proptosis of the left eye, normal fundal examination. His complete blood count showed normal eosinophil count with normal liver and kidney function tests and normal chest X-ray. CT Para nasal sinuses showed opacification and expansion of the left maxillary, ethmoid, and sphenoid sinuses causing mass effect of the left orbit, left medial rectus and optic nerve. (Fig.1). FESS (Functional Endoscopic Sinus Surgery) done and samples were sent for histopathology and microbiology studies.

Histological examination confirmed tissue invasion by narrow septate hyphae, consistent with *Aspergillus* species. Tissue culture reported as *Aspergillus Flavus*.

He was started on steroid and itraconazole. Steroid dose was tapered over 12 weeks and antifungal continued for 8 months. Follow up CT sinuses (Fig. 2), showed some improvement.

4 months later, he was seen in the clinic complaining of left nasal block, and CT sinuses showed progression of the sinuses' infiltrates (Fig. 3), so surgery was done again in February 2009, and histology showed moderate to severe active chronic inflammation but no fungal elements were seen. Culture was negative for fungus.

He was started on voriconazole 200 mg BID, and seen after 3 months with no complaint. CT sinuses (Fig.4) showed dramatic improvement of the left sinuses condition.

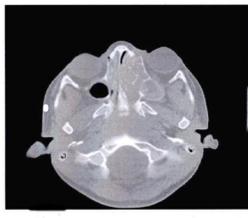


Figure 1: CT Para nasal sinuses showed opacification and expansion of the left maxillary, ethmoid, and sphenoid sinuses causing mass effect of the left orbit, left medial rectus and optic nerve.

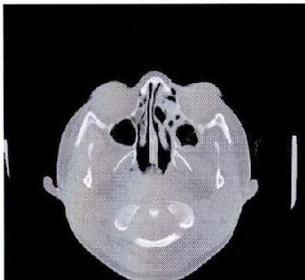


Figure 2: CT scan of the para nasal sinuses 4 months on itraconazole showed interval improvement.

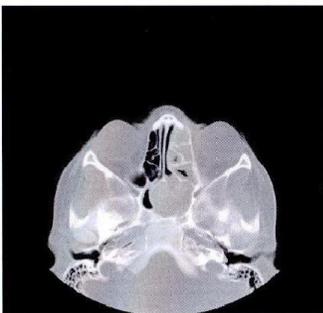


Figure 3 CT scan of the para nasal sinuses 8 months on itraconazole showed interval progression.

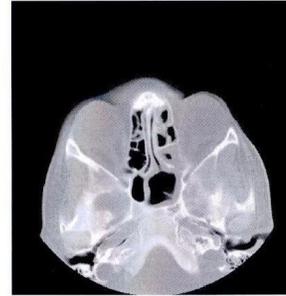


Figure 4 CT scan of the para nasal sinuses 3 months on voriconazole showed interval improvement.

3. Discussion

The diagnosis of invasive fungal sinusitis is dependent upon histopathologic demonstration of fungal invasion by biopsy of involved areas. Imaging modalities such as CT scanning can be suggestive but are not sufficiently sensitive or specific to confirm a diagnosis.

Evaluation of patients with suspected fungal sinusitis should include early nasal endoscopy with biopsies of affected tissues. Cultures of the biopsy specimen are usually positive. Isolation of the infecting fungus is necessary to guide therapy.⁵

Intravenous amphotericin B deoxycholate (0.7 to 1 mg/kg per day) or a lipid formulation of amphotericin B (5 mg/kg per day) has been used as initial therapy of invasive fungal sinusitis.

Voriconazole is a broad-spectrum triazole that is active in vitro against various yeasts and molds, including aspergillus species.⁶

Voriconazole can be used as alternative to amphotericin B preparations for empirical antifungal therapy in patients with neutropenia and persistent fever.⁷ Therefore, voriconazole has been recommended in international guidelines as the primary therapy for acute invasive aspergillosis.⁸

However, invasive fungal sinusitis is rare compared to pulmonary invasive aspergillosis, so any evidence-based treatment is difficult to recommend. Only a few case reports have described the clinical course of invasive fungal sinusitis treated with new antifungal agents.⁹⁻¹¹

A 12-year-old girl with diabetes mellitus who had invasive fungal ethmoiditis with *Rhizopus* species extending to the orbit and frontal lobe successfully treated for 15 months with posaconazole.¹¹

Recently three adult cases with invasive fungal sinusitis treated with surgery and voriconazole were published.¹²

Our case of chronic invasive fungal sinusitis was successfully treated with surgery and voriconazole administration after he failed itraconazole treatment,

which was the only available antifungal in our institute. The patient was apparently immunocompetent.

Neuroimaging and Endoscopic examination showed that the unresected lesions continued to diminish during voriconazole administration (Fig. 4).

The duration of voriconazole administration for chronic invasive fungal sinusitis is controversial, and reports vary widely depending on the severity of the disease and institution from 3 months to more than 15 months.¹²

The biopsy specimen taken at the second surgery was free of fungal hyphae. The discontinuation of voriconazole is an open question. We have continued administration considering the risk of recurrence and the safety of voriconazole to the patient.

He had some visual complaints in forms of red eyes with burning sensations responded well when the dose was decreased to once daily.

Neuroimaging studies such as CT and MR imaging with contrast medium are reliable modalities to monitor the clinical course.

Conclusion

Voriconazole is a new antifungal agent effective against invasive aspergillosis. The case of chronic invasive fungal sinusitis was treated successfully with surgical removal and oral voriconazole administration. The patient had excellent clinical outcome. Voriconazole use for invasive fungal sinusitis may create the opportunity to change the conventional treatment approaches based on Amphotericin B.

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