

Rhino-Orbito-Cerebral Mucormycosis: Neglected Mycoses in Childhood Malignancies

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Abstract

Background: Rhino-orbito-cerebral mucormycosis is an invasive fungal infection affecting mainly the immune-compromised population. Untreated, it is a fatal disorder.

Case details: An 8 year old Ethiopian boy under care for Pancytopenia due to aplastic anemia developed bilateral maxillary swelling while on treatment for febrile neutropenia. He had bilateral nasal discharge mixed with blood, stuffiness, high grade fever and a soft palate ulcer. Diagnosis was made clinically and using paranasal sinus imaging.

Conclusion: Early diagnosis of Rhino-orbito-cerebral mucormycosis in patients at risk can prevent disfigurement, bacterial super-infection, invasion to contiguous structures and death.

Keywords: Rhino-orbito-cerebral; Mucormycosis; Zygomycosis; Child; Ethiopia

Background

Mucormycosis is a disfiguring rapidly evolving opportunistic fungal infection with high mortality rates. The etiologies are *Mucorales* fungi of which *Rhizopus* and *Rhizomucor* are frequent pathogens [1]. Immuno-suppression, uncontrolled Diabetes Mellitus, trauma, burns and use of iron-binding medications like Deferoxamine are predisposing factors. The fungi are usually found in decaying vegetation and animal excreta [2]. Individuals get infected following inhalation of spores, superficial trauma, ingestion of spores or nosocomial use of a contaminated tape [3]. Phagocytic defects play an important role in the pathogenesis. Mortality rates exceed 60% [4].

There are five major groups of patients, of which Rhino-orbito-cerebral mucormycosis is the commonest syndrome, accounting for half of all diagnoses. The others include Pulmonary, Disseminated, and Cutaneous and Gastro-intestinal mucormycoses. It is very rarely reported worldwide [4,5].

The literature on the illness among African children is scanty. In a rare report, Mugambi et al. described an HIV infected infant aged 3 months and another child aged 3 years (on chemotherapy for Burkitt's lymphoma) with disseminated mucormycosis complicated by necrotizing fasciitis from South Africa [6].

The nose and maxillary sinuses are frequently affected sites. Rhino-orbito-cerebral mucormycosis progresses with invasion of the base of skull through blood vessels. This is mainly due to the secretion of toxins or proteases destroying endothelial cells in mucosal membranes [3]. An 8 year old Ethiopian boy is hereby reported after developing bilateral maxillary swelling while on treatment for febrile neutropenia and an underlying pancytopenia due to aplastic anemia.

Case Presentation

An 8 year old boy from Addis Ababa presented with high grade fever and gum bleeding of 3 days to the Pediatric department of Tikur Anbessa Specialized hospital, Addis Ababa, Ethiopia. He had been on follow-up at the Pediatric hematology/oncology clinic for the past year for pancytopenia due to aplastic anemia. On physical examination, vital signs showed a temperature of 39°C, with a respiratory rate of 44/minute, a pulse rate of 105/minute and a blood pressure of 100/65 mmHg. He had paper white conjunctivae with diffuse petechiae.

His lab studies revealed severe anemia (Hemoglobin 2.1 mg/dl), severe thrombocytopenia (Platelets of 2000/mm³), a white blood cell count of 990/mm³ and an absolute neutrophil count of 70/mm³. His past records showed a highly diluted marrow upon bone marrow aspirate examination with peripheral smear lacking blast cells. His urine culture grew *Enterococcus faecalis* while his blood culture was negative.

The boy was admitted and received different regimens of parenteral antibiotics, oral Fluconazole and Acyclovir over 3 weeks. He remained persistently febrile with very low absolute neutrophil number (less than 50/mm³). At the start of his 4th week of admission, he developed bilateral maxillary swelling (Figure 1A) accompanied by bilateral serous nasal discharge mixed with blood and stuffiness. The swelling was tender over the nasal bridge as well as over his maxillary sinuses. There was also peri-orbital swelling.

The para nasal sinus CT scan showed a right maxillary sinus mucosal thickening and opacified ethmoid and right frontal sinus. Opacification of the left otomastoid air space and septal destruction was also seen.

He subsequently developed darkness and superficial necrosis of the overlying skin extending to the cheeks and the tip of the nose (Figure 1B). Within days a necrotic ulcer also appeared over his soft palate.



Figure 1: Initial and subsequent pictures of the child's presentation.

Despite the initiation of parenteral liposomal Amphotericin B therapy, the child succumbed to the infection after 4 days of treatment.

Discussion

Though rarely reported, Mucormycosis is the third most important invasive mycoses following Candidiasis and Aspergillosis. It is also termed as Zygomycosis. Incidence shows no geographic predilection [3]. The most important risk factors are Diabetes Mellitus, Leukemia, Lymphoma, transplant recipients and Deferoxamine therapy [7,8]. Pathologic features include invasion of blood vessels, thrombosis complicating with necrosis and formation of black eschars and gangrenous masses [9].

Rhino-orbito-cerebral mucormycosis is the commonest form of illness. Its symptoms include facial pain, nasal discharge and stuffiness, orbital pain, fever with neurologic sequelae as infection advances. Examination can reveal peri-orbital or maxillary swelling, and impaired vision with red eyes [9]. The nasal discharge can be bloody and nasal mucosa appears necrotic. Infection can be indolent or aggressive. Extension into the oral cavity via palates is common in nasal disease due to angioinvasion or direct pressure. Intracranial extension can also occur [10].

Differential diagnoses for Rhino-orbito-cerebral mucormycosis include Aspergillosis, acute and chronic sinusitis, allergic fungal sinusitis, nasal or sinus malignancy, cavernous sinus thrombosis and orbital tumors [11].

For a definite diagnosis, examination of necrotic tissue with Grocott-Gomori methenamine silver stain is effective in visualizing fungi. Broad, thin-walled, branching aseptate hyphae with angioinvasion and tissue necrosis are indicative of mucormycosis. Fungal culture is another tool and utilizes sabouraud agar [12]. Thickening of the sinus mucosa is frequently reported on CT scanning of patients [13]. Isointense and hypointense lesions are observed within nasal cavity, maxillary sinuses, ethmoid cells and orbit upon MRI evaluation [14]. We couldn't do the former at our hospital but imaging was possible and findings correspond to typical descriptions.

Our patient was a severely neutropenic patient and he was diagnosed after noting his presentation (maxillary and peri-orbital swelling, facial pain, ulcerative lesion over the nasal bridge extending sideways bilaterally, nasal discharge mixed with blood and subsequent soft palate necrosis) and performing CT scans. Histologic examination could not be done at our hospital. Management of Rhino-orbito-cerebral mucormycosis consists of early surgery and antifungal agents, preferably parenteral Amphotericin B. While Posaconazole is reported to be as an alternative, other anti-fungals like Caspofungin and Voriconazole have limited use in treating mucormycosis [15].

In conclusion, invasive mycoses should be given early attention to prevent high mortality. This is particularly true among immune-suppressed children and especially with Rhino-orbito-cerebral mucormycosis. Diagnostic and therapeutic services for invasive mycoses should also be addressed in developing countries like ours.

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