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The Deadly Fungus-A Case Series of Rhino-Facial Mucormycosis in Uncontrolled Diabetes

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Abstract

Mucormycosis is more common in conditions like uncontrolled diabetes Fungal infection invades body through inhalation of spores by nose /mouth or by skin laceration. Successful management of the deadly fatal infection requires early diagnosis of the disease and proper management for the aggressive disease. We hereby report a case of mucormycosis of the maxillary sinus in an uncontrolled diabetic patient. 47-year-old male complaints of facial pain, nasal block and headache . ENT examination revealed DNS to right with spur, left middle turbinate shows fungal debris with purulent discharge and middle meatus appears normal. Investigations revealed FBS 184 mg/dl and PBS 267 mg/dl . FESS surgery done and the specimen show Microscopically - mucormycosis. 52-year-old male chief complaints of headache , toothache and nasal block. ENT DNS to right, left middle turbinate hypertrophy with necrotic debris. FBS 289 mg/dl and PBS 380 mg/dl . FESS surgery done and the specimen was reported mucormycosis. A 48-year-old female chief complaints of bleeding nose, fever, nasal blockade and headache . ENT show DNS left with middle turbinate hypertrophy. FBS 214 mg/dl and PPBS 304 mg/dl .FESS surgery done, and the specimen was reported as mucormycosis. PAS stain show fungal hyphae. deadly fungal infection mucormycosis, Early detection and diagnosis of a such a dangerous invasive infection and proper management at the right time is essential for the overall survival and outcome for the patient.

Keywords: *Fungal Hyphae, Histopathology, Hypertrophy, Mucormycosis, Specimen.*

Introduction

Mucormycosis (phycomycosis, zygomycosis) is a deadly fungal infection belonging to the Mucorales order and the Mucoraceae family. Paultauf discovered fungal organism in 1885 [1]. It is the third most deadly angioinvasive fungal infection after candidiasis and aspergillosis [2]. It affects the immunocompromised individuals [3]. In the immunocompromised host, mucormycosis infection rapidly proliferate and fungal organisms invades to deeper tissues [4].

Mucormycosis is more common in conditions like uncontrolled diabetes (particularly in patients having ketoacidosis), malignancies such as lymphomas and leukemias, renal failure, organ transplant, long-term corticosteroid and immunosuppressive therapy, cirrhosis, burns, protein-energy malnutrition, and acquired immune deficiency syndrome (AIDS) [5]. Fungal infection invades body through inhalation of spores by nose or mouth or even through a skin laceration. The fungus extends to the paranasal sinuses , orbit, meninges, and brain by direct extension [6]. Successful management of the deadly fatal infection requires early diagnosis of the disease and proper management for the aggressive disease with prompt medical and surgical care to prevent the high morbidity and mortality with this disease process [7]. We hereby report a case of mucormycosis of the maxillary sinus in an uncontrolled diabetic patient.

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Case 1

A 47-year-old male patient came to the ENT department with chief complaints of facial pain for 15 days, nasal block in left side more than right side , and headache for 3 months. He also had right sided facial swelling for 4 months, history of frequent upper respiratory tract infections and history of reduced smell sensation. He is a known diabetic and hypertensive for 3 years under irregular medications. Patient had a history of seizures 8 months back. Family history of diabetes and hypertension is present in a first degree relative. On examination, the patient had mild pallor, clubbing and cervical lymphadenopathy. ENT examination revealed deviated nasal septum to right with spur, left middle turbinate shows fungal debris with purulent discharge and middle meatus appears normal. Investigations revealed fasting blood sugar level 184 mg/dl (normal 70–110 mg/dl) and post prandial sugar level 267 mg/dl (normal 70–140 mg/dl), complete blood count Hb% 7 g/dl, WBC 10,789 cells, differential leucocyte count neutrophils-65%, lymphocytes -28%, monocytes – 1%, eosinophils – 6%, basophils -0% and ESR-18mm/hr. CT PNS shows soft tissue mucosal thickening with bilateral frontal, maxillary, ethmoidal and sphenoid sinuses with complete left sided nasal blockage. Patient underwent FESS surgery, and the specimen was sent for histopathological examination. Grossly, we received a single grey brown to grey black soft tissue fragment measuring 1x0.5cmx0.2cm. Microscopy revealed fragments of fibrocollagenous tissue with large areas of necrosis, dense lymphoplasmacytic and neutrophilic infiltrate. Focal areas showed aseptate, broad fungal hyphae, morphologically resemblling mucormycosis(Fig no 1 and 2). Critical alert was issued to the operating surgeon and the patient was immediately started on intravenous antifungal medication. The patient's conditon improved consitently with the medication and he was discharged after complete recovery.

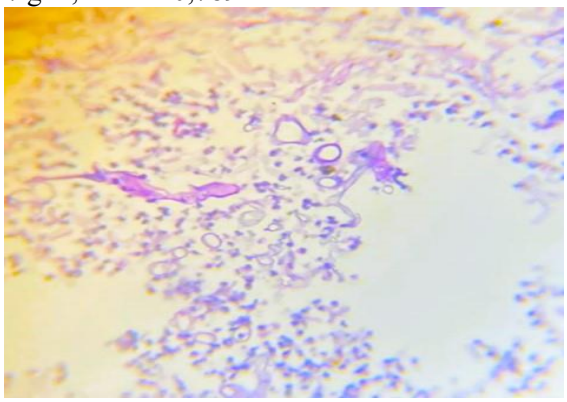

Figure 1: Aseptate Broad Fungal Hyphae – Mucormycosis

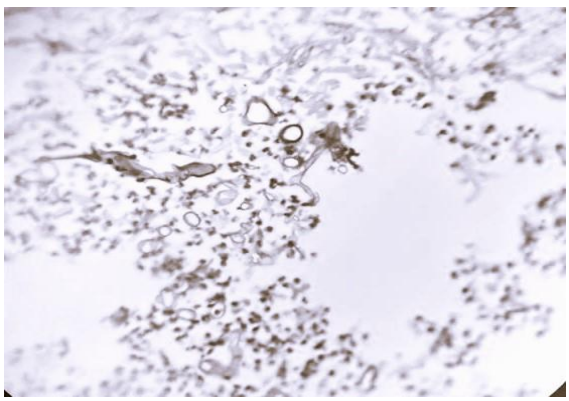

Figure 2. Silver Stain Highlighting Black Broad Fungal Hyphal - Mucormycosis

Case 2

A 52-year-old male patient came to the ENT department with chief complaints of headache on and off for 2 years, toothache for 4 months and nasal blockade for 3 months. Patient also has a history of reduced sensation of smell and fever for last 4 days. He is a known diabetic and hypertensive for the past 5 years under irregular medications. No relevant family history. On examination, he had cervical lymphadenopathy and mild pedal edema. ENT examination revealed deviated nasal septum to right, left middle turbinate hypertrophy with necrotic debris. Investigations revealed fasting blood sugar level 289 mg/dl (normal 70–110 mg/dl) and post prandial sugar level, 380 mg/dl (normal 70–140 mg/dl), complete blood count Hb 13 g/dl, WBC 11,214, differential count neutrophil- 80%, lymphocyte -8%, monocyte – 5%, eosinophil – 8%, basophil -0% and ESR-58mm/hr. CT PNS shows mucosal opacity of bilateral frontal, maxillary, ethmoidal and sphenoid sinuses with focal bony erosions and complete right nasal blockage. Patient underwent FESS surgery, and the specimen was sent for histopathological examination. Grossly, we received multiple grey, brown to grey black soft tissue fragments altogether measuring 2cc. Microscopy showed chronic inflammatory cell infiltrate, a tiny strip of respiratory epithelium and few islands of necrosis, bony spicules, blood clot and balls of fungal hyphae which were broad, irregular branching and aseptate along with areas of granulation tissue. Occasional multinucleated giant cells were also noted. PAS stain hilighted the presence of fungal organisms morphologically consistent with mucormycosis. It was reported as fungal sinusitis morphologically favouring mucormycosis (figures 3 and 4). After histopathology report, the patient was started on intravenous antifungal medication and analgesics. The patient's condition improved slowly and was later discharged from the hospital.

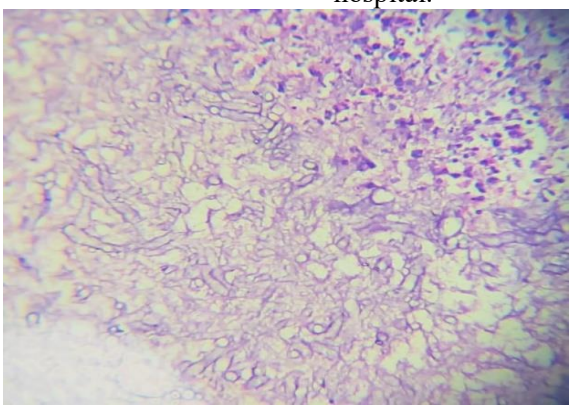

Figure 3: Fungal ball Composed of Broad Asepate Branching Hyphae - Mucormycosis

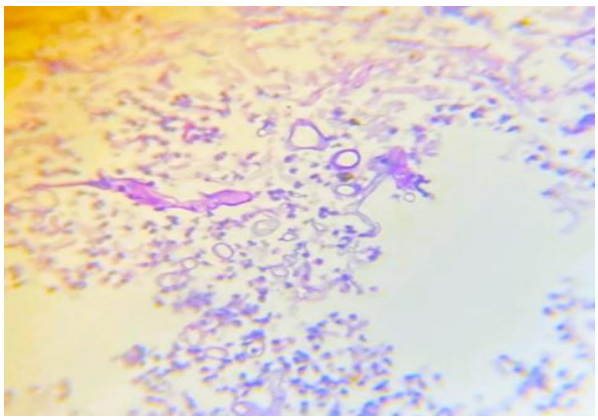

Figure 4: PAS Stain -Magenta Colored Fungal Hyphae of Mucormycosis

Case 3

A 48-year-old female patient came to the ENT department with chief complaints of bleeding from the nose on and off for 15 days, low grade fever for the last one-week, nasal blockade in left side more than right side and headache for 2 months. Left sided facial swelling for 1 month was also present. Patient does not have any history of diabetes or hypertension. Family history of diabetes present in mother. On examination, mild pallor and cervical lymphadenopathy present. ENT examination revealed left middle turbinate hypertrophy, congestion and necrotic debris. Investigations revealed fasting blood sugar level 214 mg/dl (normal 70–110 mg/dl) and post prandial sugar level 304 mg/dl (normal 70–140 mg/dl), complete blood count Hb 8.0%, WBC 9,646, differential count neutrophils 70%, lymphocytes 20%, monocytes 3%, eosinophils 7%, basophils -0% and ESR-50mm/hr. CT PNS – shows irregular mucosal opacities in left frontal and maxillary sinuses with left sided nasal blockage. Patient underwent FESS surgery, and the specimen was sent to histopathological examination. Grossly, we received multiple gray black soft tissue fragments altogether measuring 3cc. Microscopy revealed fragments of respiratory epithelium, large necrotic areas, mixed lymphoplasmacytic infiltrate and strands of fungal hyphae which were irregular, broad and aseptate resembling mucormycosis. PAS stain confirmed the presence of fungal hyphae(figures 5 and 6). After histopathology report the patient was started on intravenous antifungal drugs and the patient's condition improved.

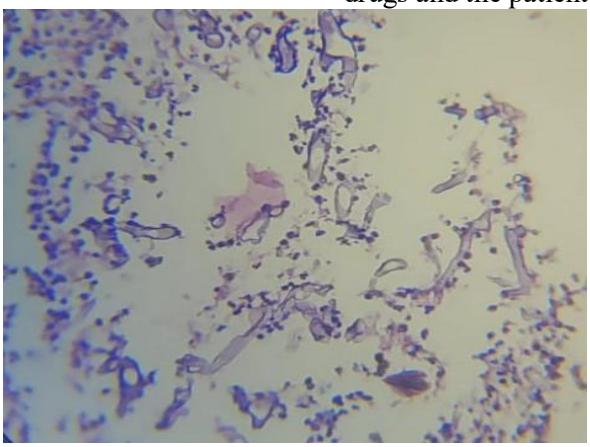

Figure 5. H&E Stain - Broad, Aseptate Branching Hyphae of Murcormycosis

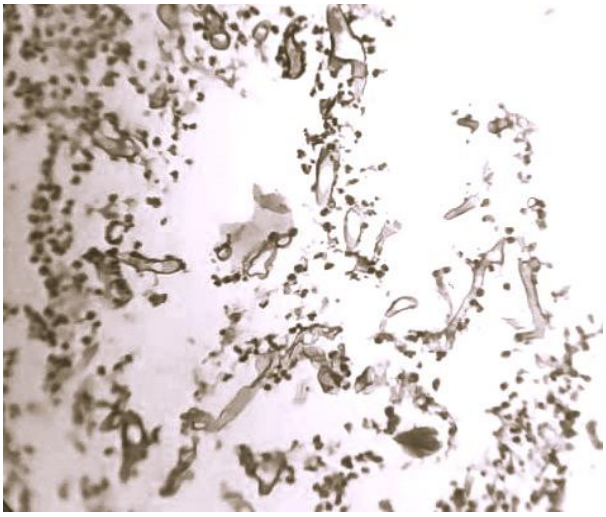

Figure 6: Silver Stain – Black Aseptate, Broad Irregular Branching Fungal Hyphae - Mucormycosis

Discussion

Fungal infection family has a vast variety of species of mucormycosis which includes Zygomycetes, and zygospores. Mucorales, a subtype of Zygomycetes, produces a striking pattern of clinical infection. The fungi are activated when they become pathogenic when the host resistance is low. In immunocompromised host, mucosal ulceration or tooth extraction aids entry of mucormysois in the maxillofacial region [8].

Asexual spores in mucormycosis cause airborne infection and settle in oral and nasal mucosa. In immunologically competent hosts, these spores will be limited by a phagocytic response and when there is decreased or failed host resistance, germination follows and hyphae develop. In immunocompromised individuals, neutrophils are ineffective in removing the fungal hyphae and the infection settles in the mocosa. The hyphae slowly begin to invade arteries, within the vessel walls and lumen causing thrombosis, ischemia, and infarction resulting in to dry gangrene of the affected tissue [9].

Nasal and Paranasal sinus fungal infections lead to palatal ulceration causing necrosis and appear black due to fungal pigmentation. Infections of the maxilla and mandible cause cavernous sinus thrombosis - a serious complication of maxillary infections [10].

Diabetes mellitus lowers the host immunological response. High blood glucose levels stimulate fungal proliferation and decrease the efficiency of chemotaxis and phagocytosis permitting organisms to thrive in acid-rich environment. In the diabetic ketoacidosis, mucormycosis caused by Rhizopus oryzae is very common. They produce the enzyme ketoreductase, which utilizes the patient's ketone bodies [8]. Diabetic ketoacidosis temporarily disrupts the ability of transferrin to bind iron leading to decrease in alteration causing elimination of host defense mechanism and permitting the growth of fungal organisms [11]. In the present case series, all the patients had a history of, uncontrolled diabetes mellitus.

The patients present with rhinomaxillary, pulmonary, cutaneous (superficial), gastrointestinal, disseminated, and miscellaneous forms [12]. Rhinomaxillary form is more common in uncontrolled diabetes [13]. These patirents clinically present with malaise, headache, facial pain, swelling and low-grade fever. The disease initially begins in the nasal mucosa or palate and extends to the paranasal sinuses and retro-orbital region [14]. Once fungal hyphae reach bloodstream, infection spreads to organs like cerebrum and lungs which can be fatal.

Clinical differential diagnosis includes squamous cell carcinoma, chronic granulomatous infection, tertiary syphilis, lethal granuloma, and deep fungal infections [15].

Radiographically, opacification of sinuses may be like in conjunction with patchy effacement of bony walls of sinuses [16]. CT with contrast or MRI shows erosion or destruction of bone and extent of disease [17].

Histopathologically, the lesion shows broad aseptate fungal hyphae with branching at right angles [18]. The histopathological differential diagnosis includes aspergillosis. The hyphae of Aspergillus species are septate, smaller in width and branch at acute angles [19].

Treatment of mucormycosis is a combination of surgical debridement of the infected area and systemic administration of amphotericin B for atleast 3 months [20]. Early diagnosis and intervention is pivotal to improve the patient’s condition and prevent life threatening complications [21]. In our case series, early diagnosis and treatment helped the patients recover and lead a disease-free life.

Conclusion

Mucormycosis is a deadly fungal infection that can occur in immunocompromised patients. In a patient with uncontrolled diabetes, even a small injury or minor procedure, can be

a floor of infection. Early detection and diagnosis of a such a dangerous invasive infection and proper management at the right time is essential for the overall suvival and outcome for the patient.

Acknowledgement and Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity.

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Nil.

Conflicts of Interest

There are no conflicts of interest.

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