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MUCORMYCOSIS – A CASE SERIES.

Abstract

Mucormycosis is a rare opportunistic fungal infection with a rapidly progressive and fulminant course with often fatal outcome. A less fulminant variety of this is the Rhino maxillary subtype which usually presents with palatal ulceration, facial swelling, turbinate necrosis and purulent sinusitis. We are reporting our experience of 4 such cases seen during the last 10 yrs. A strong suspicion, prompt diagnosis with pathological confirmation and aggressive surgical treatment gives a better outcome.

Introduction

Mucormycosis is an invasive fungal infection initiated in the nose and paranasal sinuses that frequently progresses to orbital and brain involvement. If recognized early, involvement is limited to the nasal cavity and paranasal sinuses. The purpose of this article is to report 4 cases of Rhino maxillary variety of mucormycosis, to emphasize the importance of early diagnosis, wide surgical debridement and systemic antifungal therapy in obtaining a favorable outcome.

Case report

Case 1

A 62 year old female reported to our department with complaints of pain and swelling in the left cheek for the past 1 month and ulcer in the palate for the past 15 days , gives history of dental

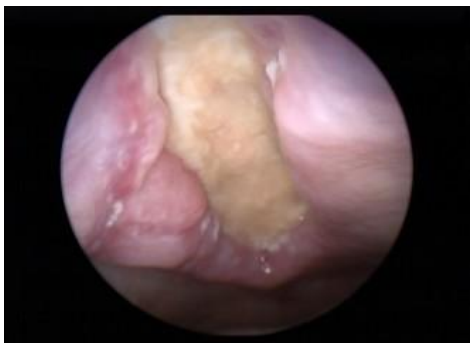
extraction done 1 month back., History of swelling around left eye. Patient was a known case of type 2 diabetes mellitus for 2 years and on irregular treatment.

On examination, a diffuse swelling noted in the middle third of face on left side, which was warm and tender. On oral examination, upper lateral incisors were missing. Granulations noted along the alveolar margin. Ulcerative lesion seen in the left half of hard palate of size 3x2 cm and covered with yellowish slough and everted borders. Oroantral fistula seen.

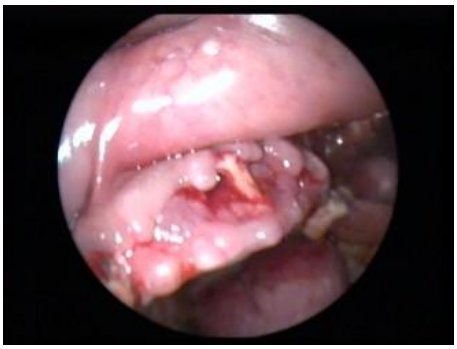
Diagnostic nasal endoscopy was done , pus seen in middle and inferior meatus. Granular mass seen in left nasal cavity and pushing the septum towards opposite side, partly eroding and destroying it. Considering the patient's medical history and a rapidly expanding ulcer involving palate and medial wall of maxilla , a provisional diagnosis of either osteomyelitis maxilla or mucormycosis was made.,even the possibility of malignant growth maxilla was considered .

Patient had the following investigations. Blood sugar – 136 mg/dl, FBS – 180 mg/dl, PPBS – 239 mg/dl, Blood urea – 20mg%, Creatinine – 0.6mgs%. Hemogram showed Hb – 10.4gms%, TC- 6800 cells/mm^3 (P – 57%, L – 39%, E – 4%). ESR was 35 and 70mm at ½ hr and 1 hr respectively

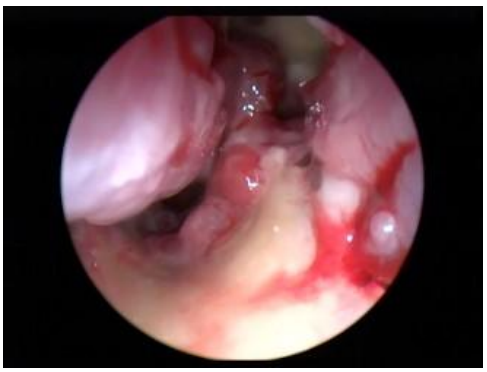
Ulcerative lesion in palate



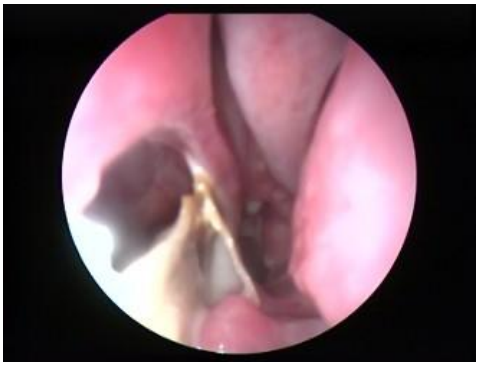
Granulation tissue alveolar margin



DNE picture showing granulations



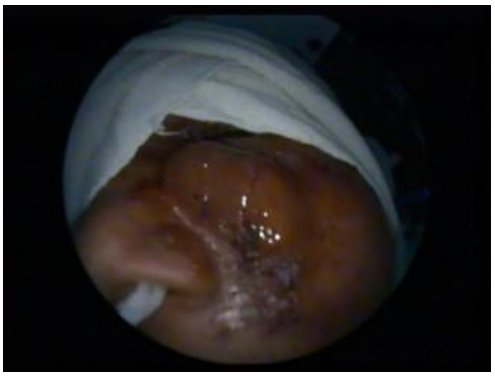
Septal perforation



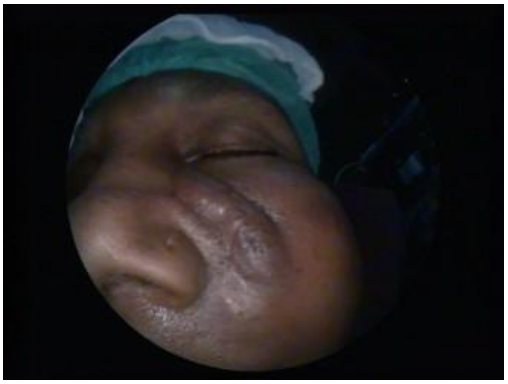
CT PNS showed diffuse radio- opacity of the left maxillary sinus and left nasal cavity with bony erosion ,palatal destruction with oroantral fistula. Patient was taken up for surgery and,wide Surgical debridement done including removal of part of the alveolar margin and medial wall of maxilla ., wide middle meatal antrostomy created. Necrotic material and granulation tissue removed from maxillary sinus.. Tthe materials were sent for histopathological examination, which was reported as mucormycosis (Path No.1016/09). Patient started to show improvement from next day. Subsequently after HPE results, patient started on antifungal treatment (Tab. Itraconazole 100mg bd for 1 month) and broad spectrum antibiotics (Inj. Ceftriaxone 1gm iv bd for 15 days and Inj. Gentamycin 80mg iv bd for 1 week). Patient's diabetes controlled with Insulin.

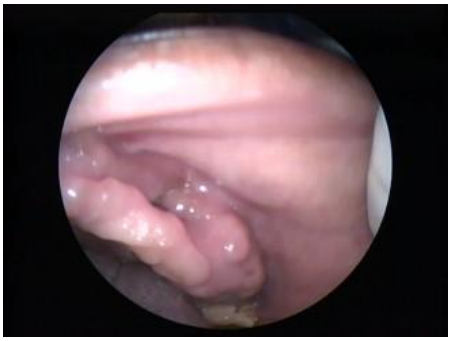
After 2 weeks post operatively, cheek swelling improved. Palatal lesion healing well. Normal lining of nasal mucosa started to appear. DNE done 3 weeks Post OP. Wound healing well, no granulations, antrostomy functioning well and oral antral fistula closed. Patient discharged and advised to control diabetes mellitus with Insulin treatment.Is disease free for past 2 yrs.

PreOP picture of cheek swelling

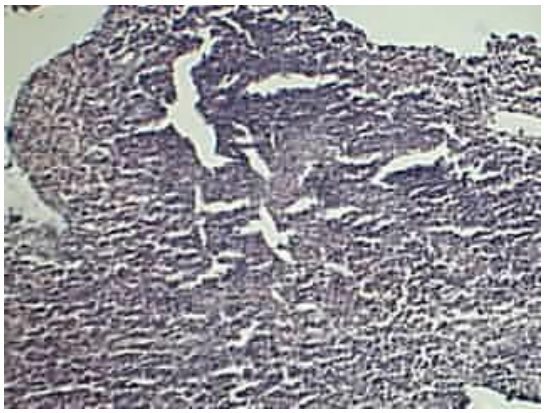


PostOP picture at 2 weeks





PostOP picture showing alveolar region

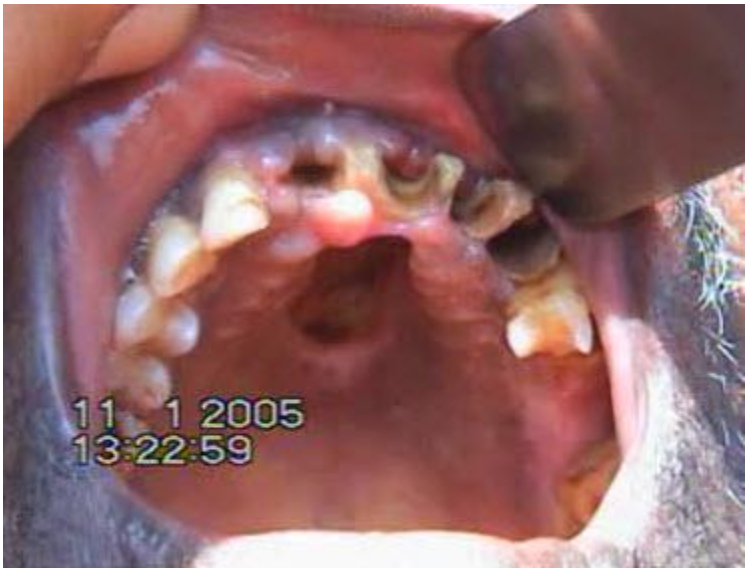


Histo Pathological picture

Case 2

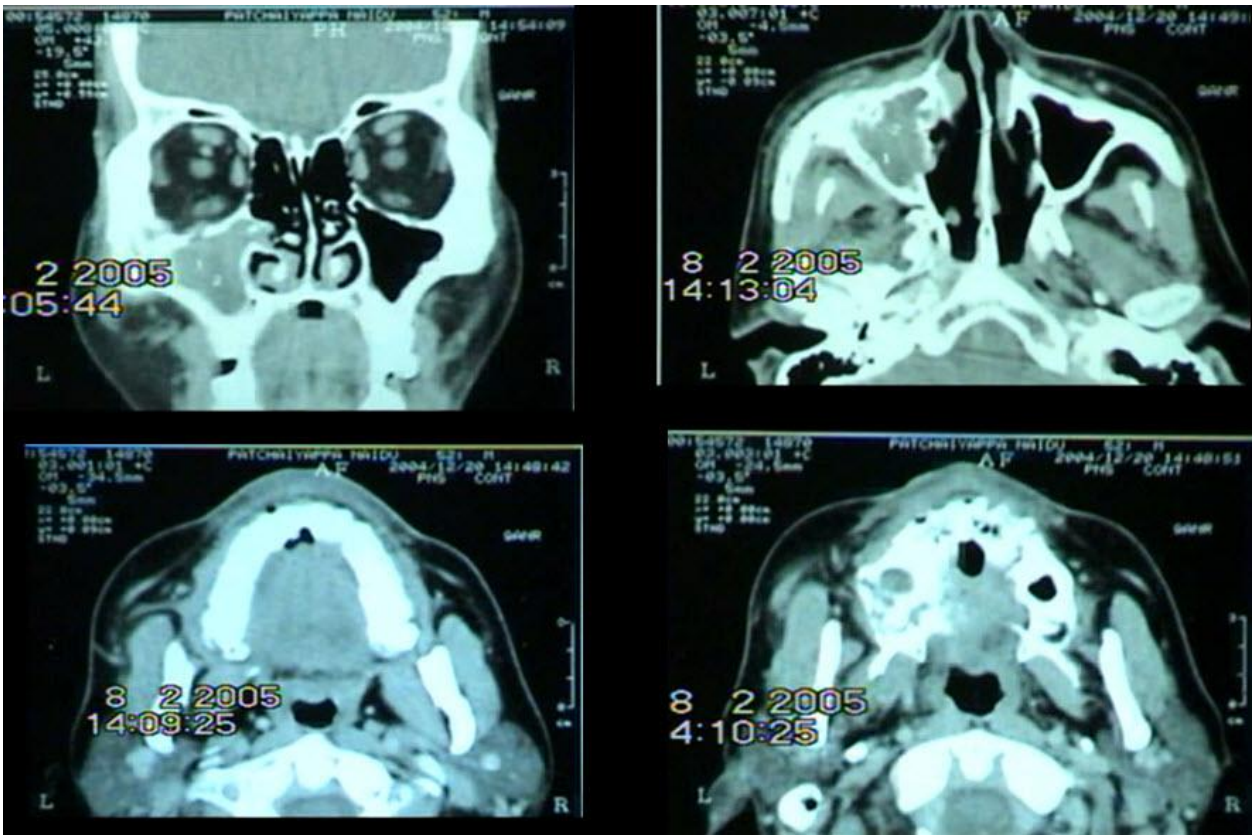
A 52 yr old male presented with midline palatal ulcer 1 month duration, gives H/O swelling in midline palate with history of needle aspiration done elsewhere. He is a known Diabetic on irregular treatment and hypertensive. Clinical examination revealed 5 x 3 cm oval shaped ulcer in the palate more on left side exposing the bone. Left side cheek swelling and Paraesthesia present.

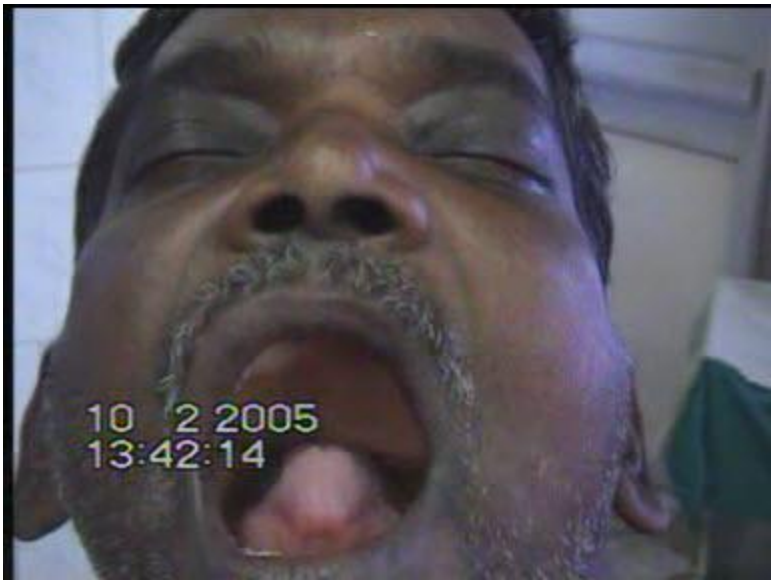
Investigations revealed blood sugar 220 mg/dl. CT revealed opaque left maxillary sinus with palatal erosion. Biopsy reported as granulation tissue with fungal elements. Proceeded with partial maxillectomy /surgical debridement. HPE proved Mucormycosis. Itraconazole was given for 3 wks and on adequate control of disease same was stopped. Wound healed well, pt was given an obturator and is disease free for past 6 yrs.



Picture showing palatal ulcer and necrotic alveolar margin

CT Picture of case 2

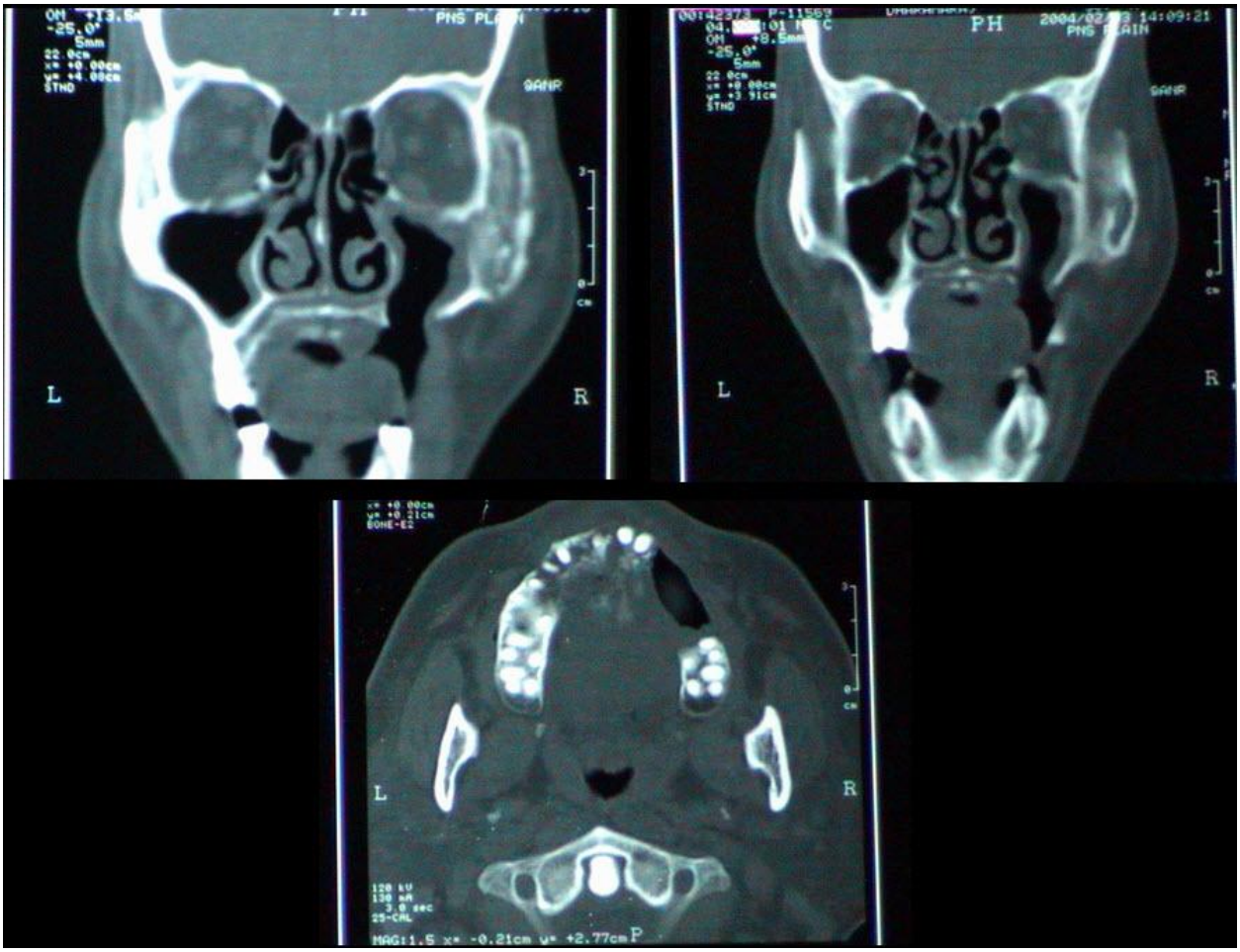




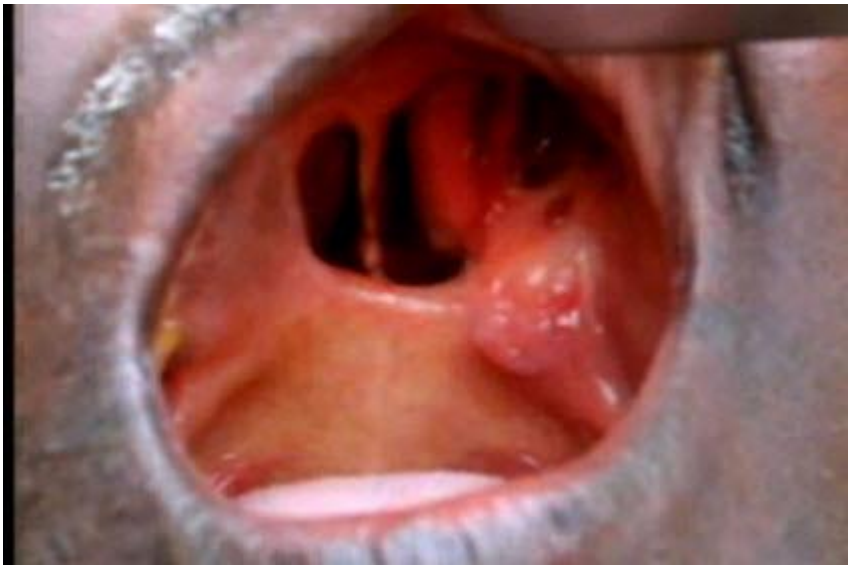
Post op picture with obturator

Case 3

A 50 yr old male presented with swelling and numbness over the rt cheek and upper lip for 6 months, mucopurulent discharge over the alveolar margin for 5 months. Gives H/O dental extraction of 3 tooth, and says he developed this problem following it. On clinical examination,mucopurulent discharge noted in floor of rt nasal cavity, X ray PNS showed bilateral maxillary sinusitis, CT revealed oroantral fistula on rt side. Biopsy reported as sub acute sinusitis with osteomyelitis with evidence of mucormycosis. Control of diabetes initiated and wide surgical debridement with sequestrectomy of devitalized floor of maxilla done.HPE confirmed mucormycosis. Pt was given obturator on dental opinion and is disease free .



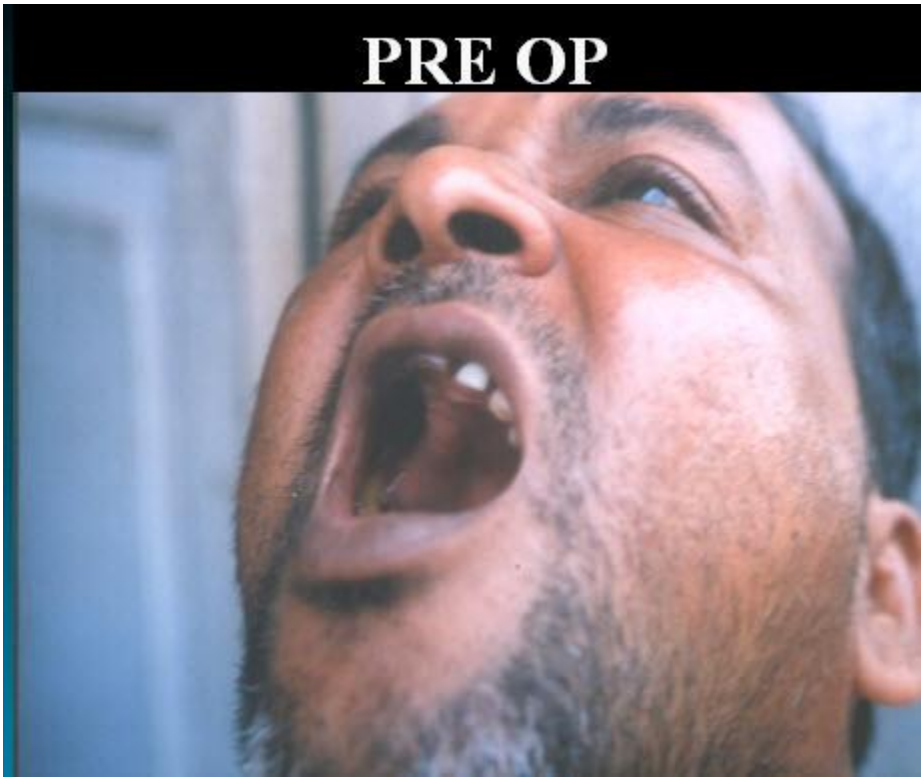
CT picture showing oroantral fistula



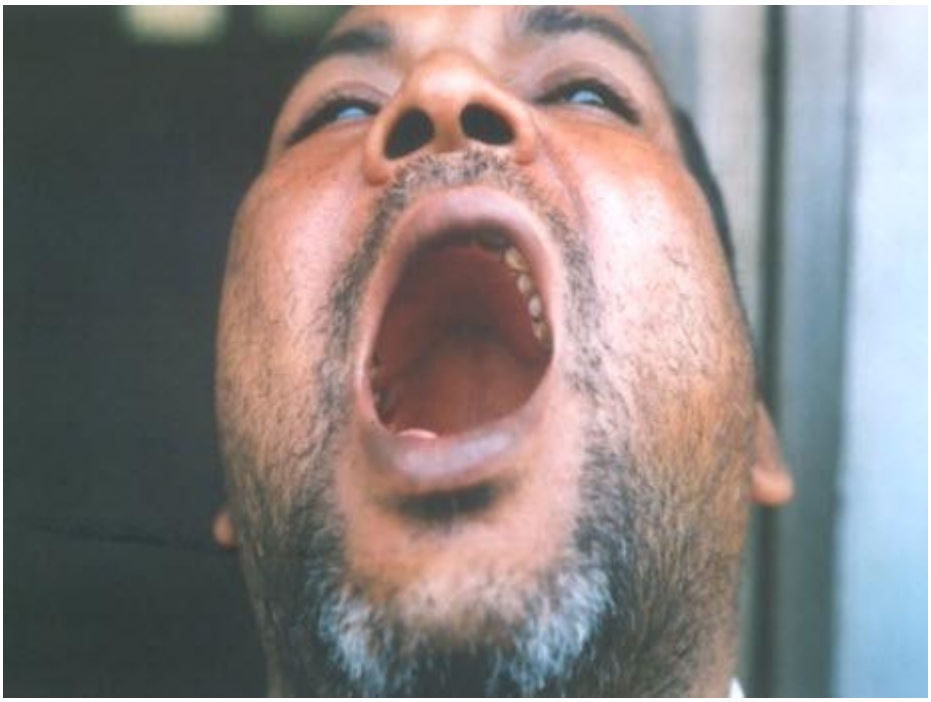
Defect after clearing the disease post op after 1 wk

Case 4

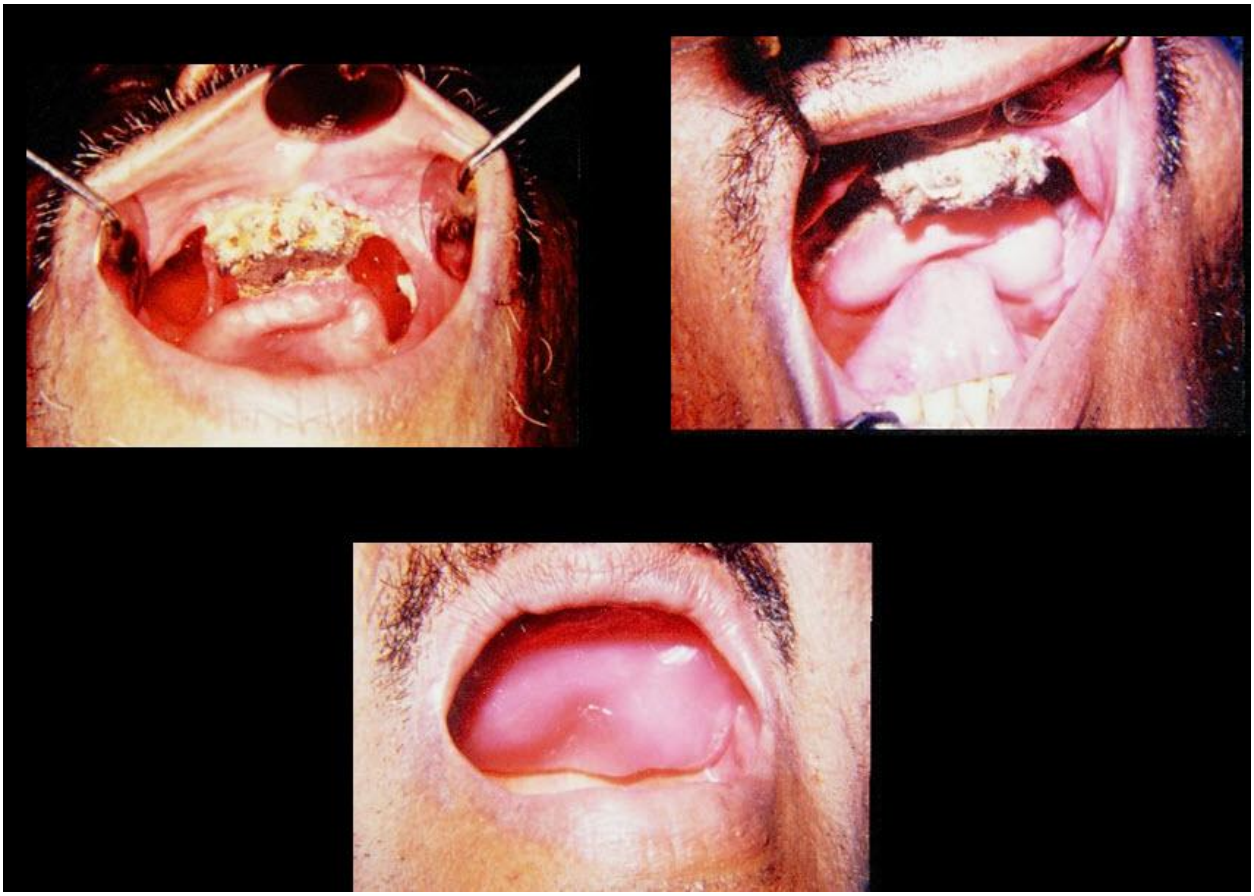
A 53 yr old male presented with ulcer in the palate for 1 yr. He had uncontrolled Diabetes.,gives H/O dental extraction. Clinical examination revealed a large ulcerated lesion over the rt alveolar margin extending to the palate .CT revealed oroantral fistula.Surgical debridement done,almost the entire floor of rt maxilla was unhealthy and was removed as a sequestrum.HPE of the specimen confirmed mucormycosis. This patient was better during the post op period,,was having problems with the interim obturator and was being attended by the dental department., was lost to our follow up . It was later known that this patient expired due to diabetes related renal complications.

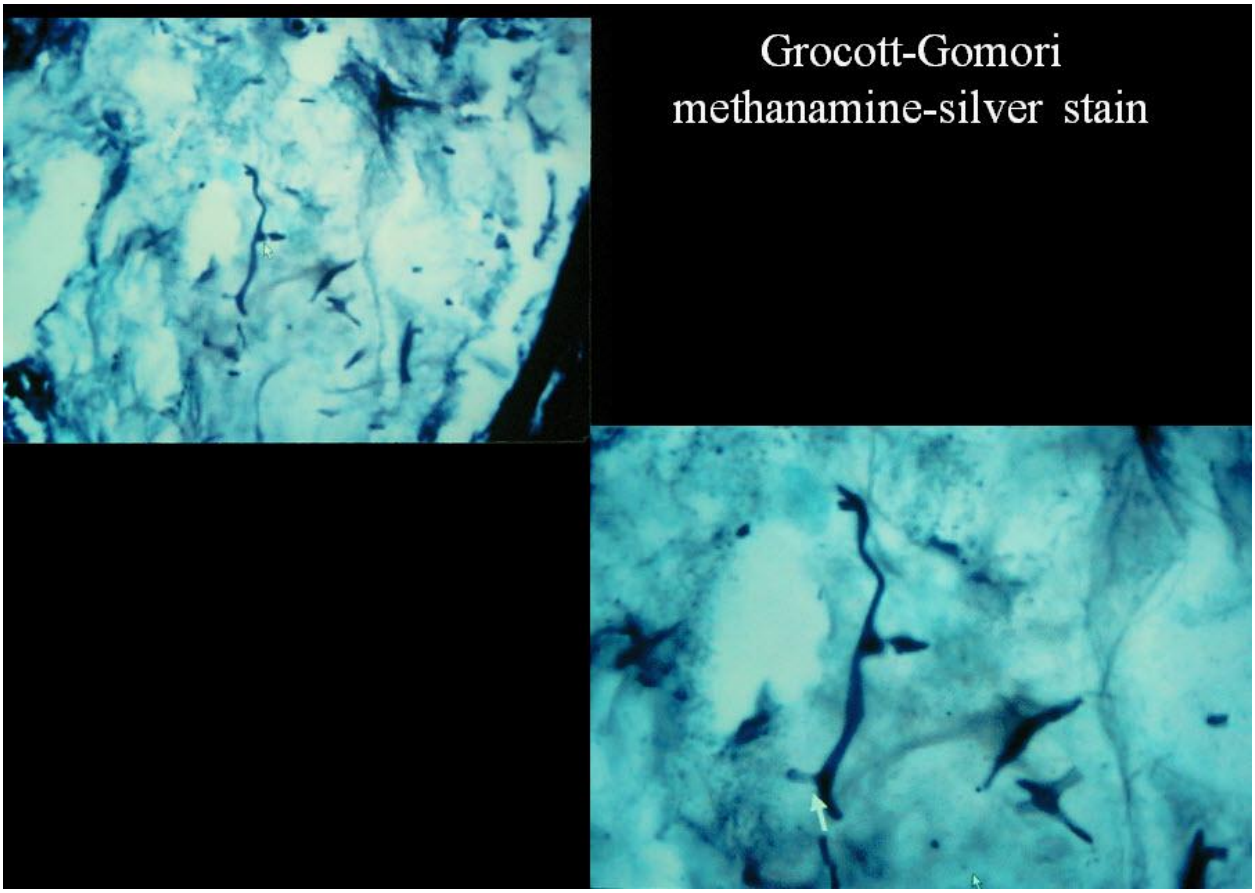


Picture showing palatine defect



patientt with obturator

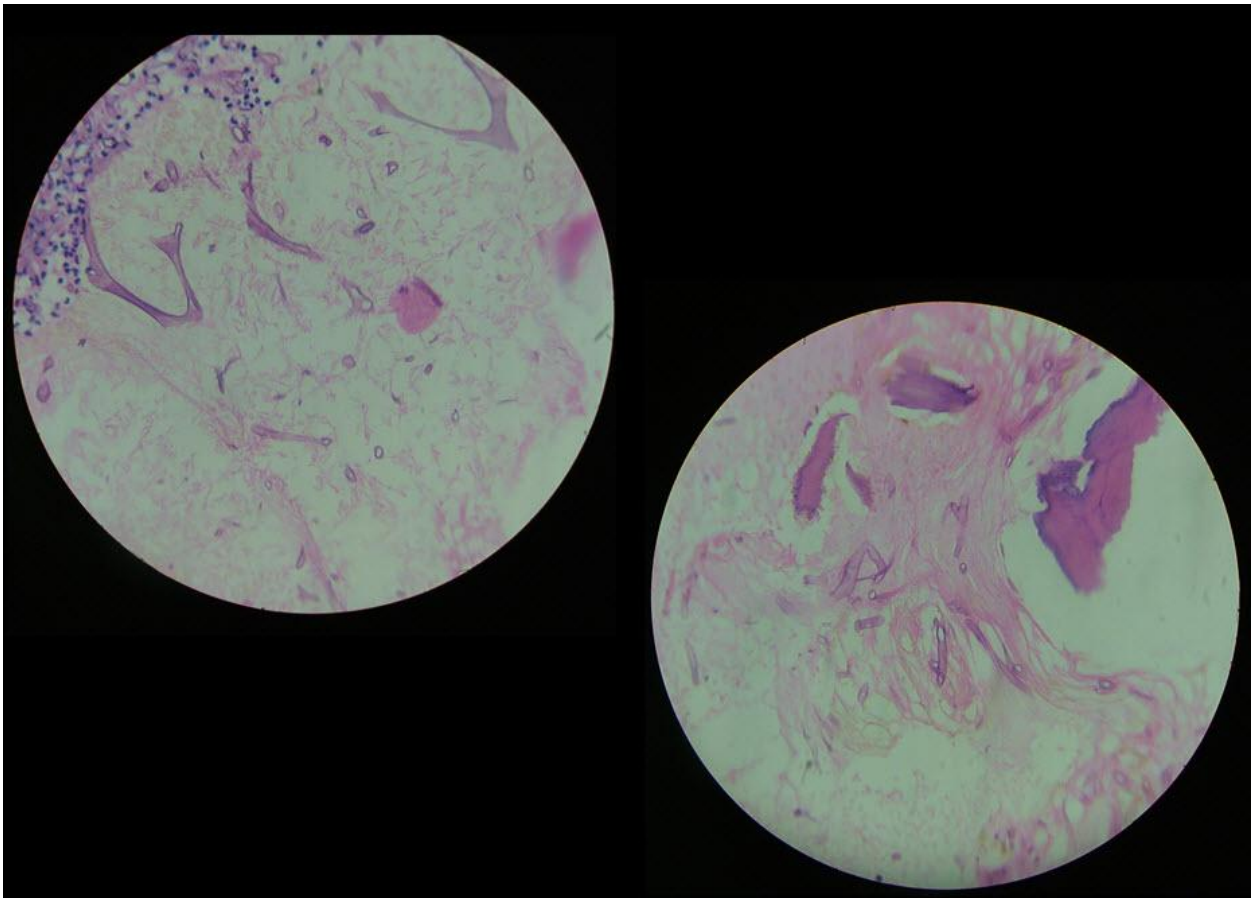




Discussion

Mucor mycosis is a rapidly progressive opportunistic infection caused by an organism of the family mucoraceae order mucorales class zygomycetes. These fungi are ubiquitous found in soil, bread molds, decaying fruits and vegetables, usually are harmless and become pathogenic in man under certain conditions like immunosuppression, diabetic acidosis, antibiotic, steroids and cytotoxic therapy, with other predisposing factors like malignancy, burns, malnutrition, renal failure and blood dyscrasias. The affinity for Diabetic patients is related to the fact that Rhizopus organisms thrive in an environment rich in glucose and an acid PH, because they have an active ketone reductase system, decreased phagocytic activity of polymorhonuclear leucocytes may also be a factor[1].

Upper airway mucormycosis was first described in 1885 by Paltauf, who coined the term Mycoris mucorina, which subsequently became Mucormycosis[(2)(7)]. Mucormycosis can infect the lungs, central Nervous System, Gastro intestinal tract and skin (burns patients) but is known best for its rhinocerebral presentation, which is usually initiated with sinonasal involvement and may progress to the orbit and the brain[2]. Rhinocerebral form is further



Showing cellophane tubule appearance,aseptate hyphae

subdivided into two subtypes : a highly fatal rhinoorbitocerebral form which is invasive and may involve the ophthalmic and internal carotid arteries and a less fatal rhinomaxillary form which involves the sphenopalatine and greater palatine arteries, resulting in thrombosis of the turbinate and necrosis of the palate[3]. All our four cases belong to this group.

Everyone is exposed to and inhales spores of the mucorales; the nasal ciliary clearance system,however transports these spores out of the nasal cavity, down the pharynx, to be cleared out by the gastrointestinal tract. Spores inhaled into the lungs are cleared by phagocytes. In the susceptible individual, the infection usually begins along the middle or inferior turbinate[2]. Depending on the degree of immunocompromise the disease process can be indolent or fulminant. Once the spores have entered the tissues, the organism becomes angioinvasive and has a predilection for the internal elastic lamina of the arteries. This invasion causes thrombosis, with secondary ischemic infarction and haemorragic necrosis. The organism thrives in the necrotic tissue and spreads by direct extension along injured blood vesssels[1].

MEDICALLY IMPORTANT MEMBERS OF THE CLASS ZYGOMYCETES[2]

Class	Order	Family	Genus	Species
Zygomycetes	Mucorales	Mucoraceae	Absidia*	
			Mucor*	
			Rhizomucor*	
			Rhizopus*	
				oryzae(or Arrhizus)
		Cunninghamellaceae	Cunninghamella*	bertholetiae
		Mortierellaceae	Mortierella*	wolfii
		Saksenaeacea	Saksenaea*	
		Syncephalastraceae	Syncephalastrum elegans*	
		Apophysomyceae		
		Thamnidiaceae	Cokeromyces	
	Entomophthorales			
		Ancylistaceae	Delacroixia	
			Basidiobolus	

*Reported to have caused rhinocerebral mucormycosis.

Involvement of the oral cavity usually appears as palatal ulceration or necrosis and later as perforation of the palate as a result of infection in the nasal cavity or paranasal sinuses. Patients often exhibit facial cellulitis and anaesthesia, nasal discharge,necrotic turbinates, fever, headache and lethargy[3]. These findings were noted in our patients.

Early and late cavernuous-carotid fistulas and mycotic aneurysms of the carotid have been reported. Patients should therefore be followed for sometime after the initial response to therapy[1].

Differential diagnosis of the lesion should include Squamous cell carcinoma, Chronic granulomatous infection like tuberculosis, tertiary syphilis, midline lethal granuloma and other deep fungal infections.

Radiographic analysis by routine radiographs may reveal clouding of multiple sinuses, mucosal thickening and bone erosion. CT better defines soft tissue invasion and necrosis, early bone erosion and cavernous sinus thrombosis.All our parients exhibited these findings with bone erosion and oroantral fistula. MR imaging, with or without gadolinium,is the best way of evaluating changes in major vessels, including carotid artery thrombosis and cavernous sinus thrombosis, and any intracranial extension.

Once patient presents with above said findings, tissue diagnosis should be established with a biopsy to look for non septate hyphae representing fungal invasion. The best demonstration of the tissue invasive, nonseptate hyphae (cellophane tubules) is with silver methanamine stain[1].

As the disease progresses with alarming rapidity, early diagnosis, prompt and aggressive therapy is essential[4]. Successful treatment of mucormycosis consists of aggressive repeated surgical debridement of necrotic tissue, systemic antifungal therapy and immediate control of underlying systemic diseases. Correction of acidosis and hyperglycemia contributes to better survival rates. The fungus thrives in devitalized and necrotic tissue hence rigorous debridement is indicated[1]. Areas of ischemic tissue should also be removed because vascular thrombosis prevents chemotherapeutic agents from reaching the diseased tissues.

In acute fulminant fungal sinusitis with invasion of blood vessels, amphotericin B has been considered the drug of choice(at a dose of 1 – 1.5 mg/kg per day).There is now growing consensus that the newer lipid based formulations of the drug,in particular high doses of liposomal amphotericin B (10-15 mg/kg per day),should be adminmistered and be continued until the patient recovers[5].Renal parameters have to be continually monitored.Other agents like Itrocanozole, Voriconazole and Posaconazole have been reportedly tried with varying results., however, the optimum dosage and duration of treatment have not been defined[5]. Itraconazole (100 mg bd) results in remineralization of the eroded skull base[5] and is also said to prevent recurrence.The role of topical amphotericin B has not been studied systematically,but because of the small risk associated with administration it is often employed.(50 mg vial of intravenous amphotericin B and 10 ml of sterile water, in a dosage of 4 ml in each nostril 2 to 6 times daily). This can also be nebulized into the nose with a Rhinoflow device[2].

Hyperbaric oxygen therapy is theoretically attractive because it reverses the ischemic acidotic conditions that perpetuate fungal growth. Hyperbaric oxygen treatments are usually given at two atmospheres for 1 hour on a daily basis for upto 30 treatments. This may limit deformity by decreasing the required area of debridement[6].

Conclusion

Early diagnosis is important in the success of treatment. A patient presenting with nasal and palatal lesions, facial swelling or cellulits with history of dental extraction and being a known diabetic should immediately rise a suspicion of this dreadfull condition. Active surgical treatment with removal of all dead and necrotic tissue, control of diabetes and systemic antifungal therapy gives good results,reducing the mortality and morbidity due to mucormycosis.

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