Invasive Aspergillosis of the maxilla – An unusual report.

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Abstract:
Aspergillosis is a fungal disease characterized by invasive and non-invasive forms. Non-invasive aspergillosis usually affects a normal host, appearing either as an allergic reaction or a cluster of fungal hyphae. With the advent of intensive chemotherapeutic regimens, AIDS epidemic, solid organ and bone marrow transplantation, the prevalence of invasive aspergillosis has increased dramatically in the past 20 years. In this paper we present a case of aspergillosis extensively involving the maxilla of a 60 year old male caused by aspergillus niger which is less likely involved in human infections which makes this case unusual and interesting to report.

Keywords: Aspergillosis, maxilla, Aspergillus Niger.

Key Messages: Aspergillosis is a fungal disease characterized by invasive and non-invasive forms. Non-invasive aspergillosis usually affects a normal host, appearing either as an allergic reaction or a cluster of fungal hyphae. In this paper we present a case of aspergillosis extensively involving the maxilla of a 60 year old male caused by aspergillus niger which is less likely involved in human infections which makes this case unusual.

Introduction:

Aspergillosis is a fungal disease characterized by invasive and non-invasive forms. The recent rise in mycotic infections is due to both improved diagnostic research and an increase of the conditions that favor fungal infections like immunosuppressive agents and immunocompromised conditions.[1]

Conditions that favour fungal infections are diabetes, long-term treatments (antibiotics and cortisones), radio- and chemotherapy, immunosuppressive treatments, and

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immunodeficient disease. The most frequent microorganism involved is Aspergillus fumigatus followed by aspergillus flavus.[2]

Aspergillus species are ubiquitous and exposure to this fungus is frequent, yet disease due to tissue invasion is uncommon in the immunocompetent host. However, in the immunocompromised patient, there is an increased incidence of invasive aspergillosis.[3]

Aspergillus infections comprise 54.4% of all mycotic infections in India.

It is an opportunistic infection affecting the maxillofacial region along with candidiasis followed by mucormycosis. Oral aspergillosis has a male preponderance with a range of 5-78 years.[4]

Aspergillosis of the paranasal sinuses has been classified into four types: allergic, non-invasive, invasive, and fulminant. Immunocompromised patients are at particular risk for fulminant invasive aspergillosis. The most frequent site of human aspergillus infection is the lung, followed by the liver, spleen, bone, meninges, and paranasal sinuses. In several reports, the coexistence of fungal infection and malignancy has been noted in the brain and thoracic cavity.[5]

Moreover, Tanaka et al.[6] reported the coexistence of aspergillosis and squamous cell carcinoma (SCC) in the maxillary sinus. That case was diagnosed using preoperative cytologic study of routine sinus washings.

Case History:

A 60 year old male reported to the dental OPD with a chief complaint of pain in the maxillary anterior region for the past 10 days. Pain was continuous in nature which is aggravated by taking food and relieved on taking medication. There was no history of extraction.

Patient was a known heavy smoker for the past 10 years; he was a known diabetic for the past 10 years and hypertensive. Extraoral examination was non- contributory and no lymph nodes were palpable.

Intraoral examination revealed a small swelling measuring 0.5 x 0.5cm in size with pus discharge in relation to 21. (Figure 1)

A diffuse swelling of the entire palate was seen which was extending onto the cervical aspects of the lingual side of the maxillary teeth. An ulcerated lesion measuring 1.5 x 1.5 cms was present in centre of the palate causing an oro-nasal communication. The palatal mucosa was edematous and swollen. The ulcer was covered with a white slough. (Figure 2)

On palpation the inspectory findings were confirmed, pus discharge was observed in relation to 21. The generalised palatal swelling was tender, soft and edematous. The slough covering the ulcer was scrapable. The entire maxillary segment was mobile and yielded to the pressure of the probing instrument.

Other intraoral findings included poor oral hygiene, generalised stains and calculus, generalised bleeding on probing and periodontal pockets.

Radiograph revealed radiolucency in the maxillary palatal region with erosion of the palatal bone. Computed tomography showed a hazy mass filling the left maxillary sinus. (Figure 3)

A provisional diagnosis of aspergillosis was made. Routine blood investigations were normal; the fasting and post prandial blood sugar levels were 175mg/dl and 380mg/dl respectively. The scrapings from the slough were subjected to antibiotic sensitivity and culture which showed aspergillus Niger grown on Sabaraud's dextrose agar. (Figure 4) Hyphae with a biseriate fruiting head were observed. (Figure 5)

An incisional biopsy was performed under local anaesthesia and the tissue subjected to histopathological examination which revealed necrotic bone along with RBC's. Long septate branching hyphae of aspergillus niger were seen. (Figure 6) A final diagnosis of apergillosis of the palate was established. Antifungal therapy was initiated with a loading dose of voriconazole 400mg IV followed by maintenance dose of oral voriconazole 400 mg q12h x 2 doses

A maxillectomy procedure was carried out. (Figure 7) An obturator was placed. Patient is under follow up and rehabilitation with a complete denture. (Figure 8)

His poor oral hygiene problem was taken care of and is under medication for diabetes and hypertension. The patient was under follow up for six months and was disease free, no sign of recurrence was seen.

Discussion:

The Priest botanist Michelli first described aspergillosis in 1729. Morrel Mackenzie in 1893 published the first report of aspergillosis of the maxillary sinus.[7] Invasive aspergillosis has been recognized as an opportunistic infection occurring most commonly in immunocompromised individuals and patients with debilitating illness.[8] Due to its

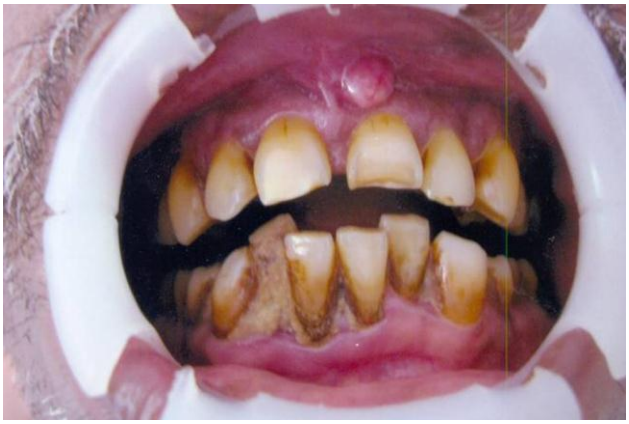

Figure 1: Small swelling measuring 0.5 x 0.5cm in size with pus discharge in relation to 21.

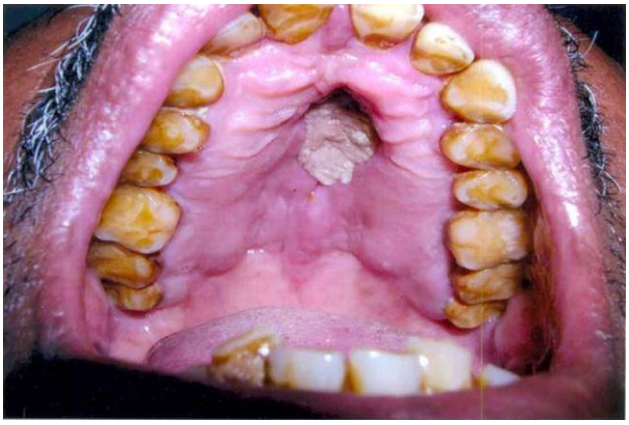

Figure 2: An ulcerated lesion in centre of the palate covered with a white slough with boggy edematous enlargement of the entire palatal mucosa.

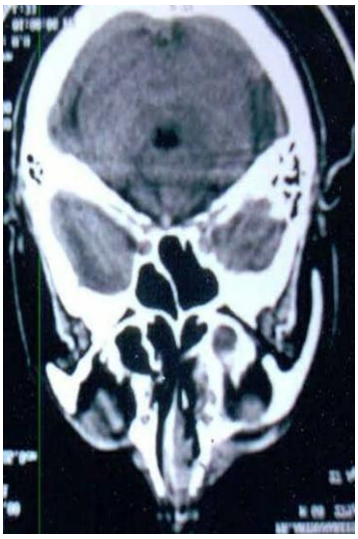

Figure 3: Computed tomography showing erosion of palatal bone and a hazy mass filling the left maxillary sinus.

Figure 4: Aspergillus Niger grown on Sabaraud's dextrose agar.

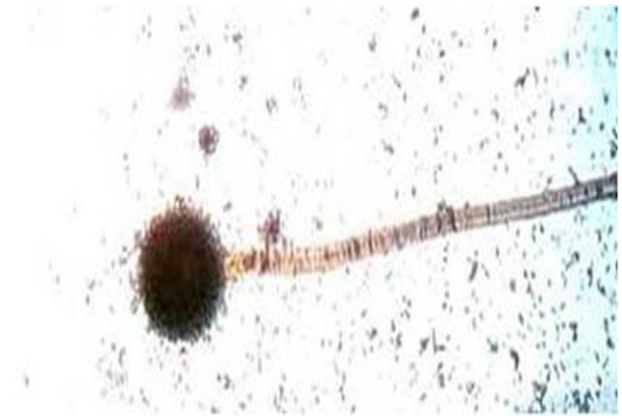

Figure 5: Hyphae with a biseriate fruiting head.

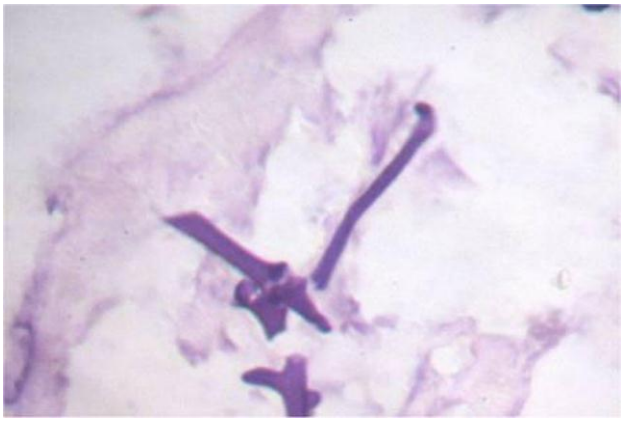

Figure 6: H & E STAIN 40X VIEW Long septate branching hyphae of aspergillus niger.

ubiquitous nature, aspergillosis has been reported as occurring in both healthy and compromised individuals. According to its interaction with the host's defense mechanisms, aspergillosis may take one of the following forms: noninvasive, including the saprophytic and allergic forms affecting

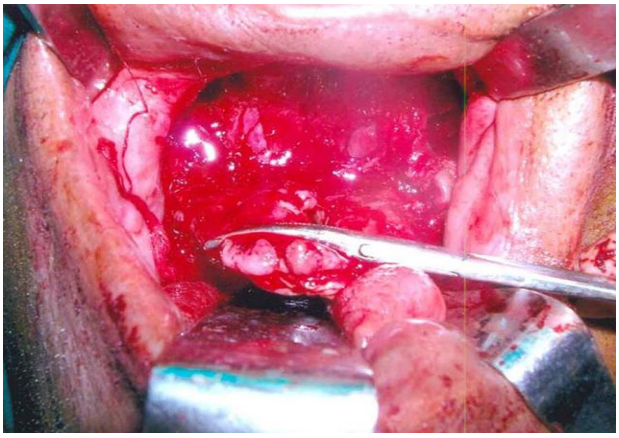

Figure 7: Maxillectomy procedure

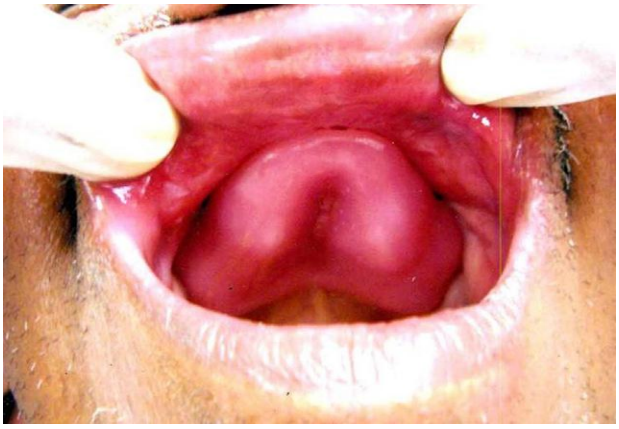

Figure 8: An obturator placed to cover the defect

immunocompetent hosts with low morbidity and mortality, and invasive, in which there is an extension of the fungus into viable tissues, resulting in severe necrosis.

The latter form is more likely to occur in immunocompromised, it has higher morbidity and mortality, and its frequency is second to candidiasis among invasive mucoses in patients with leukemia and lymphoma.[9] The etiopathogenesis of aspergillosis of the maxilla has been debated, and there have been 3 theories: odontogenic, aerogenic, and mixed origin theory. The odontogenic school of thought maintains that the pathogenesis is based on an initial colonization of the maxillary sinus by means of iatrogenic oral-antral communication. This theory holds that the zinc oxide which can be found in endodontic sealers paralyzes the epithelial cilia or causes edema and hyperemia of the soft tissues, affecting the Schneiderian (sinus membrane) epithelium function. This favors the accumulation of fungal waste and impairs elimination of the spores.[10] No restorations were present in our patient

The aerogenic theory suggests that aspergillus growth is due to inhalation of high quantities of spores over extended periods. It is also called semi-invasive form of fungal sinusitis.[11]

The third theory is based on the ubiquitous nature of the aspergillus spores. They can be inhaled at any moment and are normally present as saprophytes in the maxillary sinus. Aspergillus growth can be due to poorly ventilated sinus, a pre-existing sinusitis, or foreign bodies in the sinus. For the ostium to be ventilated and drained, it must be unobstructed. If the ostium is blocked, the mucociliar clearance system is negatively influenced and aspergillus growth is favored.[11]

Aspergillosis of the maxillary sinus secondary to overfilling of a root canal has been reported[12] no root canal fillings were observed in our case. Certain conditions may change the normal ecosystem to allow fungal proliferation. The most common of these favorable conditions are prolonged antibiotic and corticosteroid treatments, nasal obstructions that aid blockage of the ostium and anaerobic conditions, and endosinal penetrations at the time of a dental procedure or a dental extraction. These findings were absent in our patient.

The clinical manifestations of aspergillosis vary, depending on the host immune status and presence or absence of tissue damage. In an immunocompetent host the disease may appear as an allergy. Sometimes a low grade fungal infection becomes established in the maxillary sinus called an aspergilloma. In immunocompromised patients the portal of entry has been suggested by researchers to be the gingival sulcus or the marginal gingiva. Painful gingival ulcerations are initially noted and peripherally the mucosa and soft tissue develops diffuse swelling with a grey or violaceous hue.[13] Our patient had gingival manifestation in the anterior maxillary gingiva along with involvement of the entire palatal mucosa and had a positive history of diabetes since 10 years with poor oral hygiene.

The pathologic features of oral aspergillosis have been studied by Myoken et al[14] in an effort to correlate study, they distinguished between early, advanced, and late stages of oral aspergillosis. In the early stage, isolated areas of violaceous marginal gingiva consisted of degenerated epithelium and connective tissue were seen. These findings correlated with our case.

Aspergillus fumigatus is one of the most common aspergillus species to cause disease in

immuno-compromised individuals. Aspergillus flavus is the second most common agent of aspergillosis.[15]

Aspergillus niger can cause opportunistic infections it is less likely to cause human disease than some other aspergillus species, but, if large amounts of spores are inhaled, a serious lung disease, aspergillosis can occur. Aspergillosis is, in particular, frequent among horticultural workers that inhale peat dust, which can be rich in aspergillus spores.[15] Our patient was a farmer by occupation.

Lab diagnosis includes demonstration of the fungus in culture, commonly used culture medium is Sabaraud's dextrose agar. Tissue biopsies can also be used to demonstrate the fungus. Among the staining procedures routine hematoxylin and eosin or PAS can be done with silver stains also giving good detail of the fungal organisms.

Hyphae are septate and hyaline. Conidial heads are radiate initially, splitting into columns at maturity. The species is biseriate (vesicles produces sterile cells known as metulae that support the conidiogenous phialides). Conidiophores are long (400-3000 µm), smooth, hyaline, becoming darker at the apex and terminating in a globose vesicle (30-75 µm in diameter). Metulae and phialides cover the entire vesicle. Conidia are brown to black, very rough, globose, and measure 4-5 µm in diameter.[16] The colonies we found in our case on sabaraud's dextrose agar had similar features.

The presence of a deep necrotic palatal ulceration may be attributed to various causes including traumatic, infectious, granulomatous, neoplastic, and others. Infectious possibilities include bacterial, fungal, parasitic, or spirochete related, which may present as palatal-perforating ulcerations. Specific infections may include fungal mucormycosis, tuberculosis, or syphilis. Granulomatous infections may include Wegner granulomatosis, or leprosy. Neoplastic sources include squamous cell carcinoma or lymphoma. These above mentioned pathologies should be considered in the differential diagnosis.

Invasive aspergillosis is a disease typically related with prolonged neutropenia or the use of corticosteroids. However, the increased use of new therapeutic modalities such as biologic agents that act by blocking specific immune pathways have put more patients at risk for invasive aspergillosis. Most cases of aspergillosis in patients taking monoclonal antibodies have been associated with the use of tumor necrosis factor (TNF)-alpha blockers. No such drug history was present in our patient.[17]

Although it is not understood how aspergillosis could induce carcinoma formation, the chronic inflammation caused by prolonged fungal infection might be carcinogenic. Moreover, it is well known that chronic inflammatory cells can facilitate the initial steps in carcinogenesis.[18]

The overall case fatality rate of 58% to 67% demonstrates that invasive aspergillosis of any type remains a highly lethal opportunistic infection despite the availability of newer antifungal therapies and improved management of underlying diseases.[19]

Possible complications include cavernous sinus thrombosis, perforation of the palate, involvement of the orbit and cranial extension and gross facial disfigurement.

With respect to the treatment of aspergillosis, it is necessary to remove surgically the sinus fungal masses and ensure the establishment of adequate sinus drainage with appropriate antifungal therapy, the underlying predisposing conditions should also be addressed.

We have presented a case of invasive aspergillosis which affected the maxilla of a 60 year old male extensively caused by aspergillus niger which is unusual. It was treated by aggressive surgery and antifungal therapy, no recurrence has been observed yet.

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