Case Report

A rare coexistence of aspergillosis with actinomycosis

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Abstract

Aspergillosis is a common systemic mycosis which affects immunocompromised and immunocompetent hosts. *Aspergillus* spp. is wide spread in the environment in most countries, which renders an invasive form of disease. The presence conidial heads are pathognomic to aspergillosis in diagnosis. Actinomycosis is a subacute-to-chronic infection that causes sinus fistula, tract or abscess due to the invasion surrounding the soft tissue. Cervicofacial infection accounts for 50%–60% of all actinomycosis cases. The mandible and nasopharynx are the sites of predilection, but maxillary infection is rare. Aspergillosis and Actinomycosis each of them was reported in case, but mixed infection of both organisms is rare, only one case has been reported. This paper discussed about a case report of coexistence of aspergillosis with actinomycosis in 38-year-old male.

Keywords: Actinomycosis, aspergillosis, conidial head

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INTRODUCTION

Aspergillus is ubiquitous in nature and has a wide spectrum of pathogenicity in both humans and animals. In 1885, Schubert' described for the first time a case of aspergillosis of the nose and paranasal sinuses (PNS).[1] In recent years reported, cases of mycosis of the maxillary sinus have been on the increase. There are more than a hundred of species however the most common species causing infection in humans include *Aspergillus fumigatus*, *Aspergillus niger*, *Aspergillus flavus* and *Aspergillus clavatus*. The main portal of entry of this organism is via inhalation of spores; hence, infection usually starts from lungs and later on may involve other organs. The clinical manifestations of aspergillosis vary depending on the host immune status of the patient. Most often in immunocompetent individuals, macrophages and neutrophils destroy the inhaled fungus, but in immunocompromised patients, this does not happen due to neutropenia or neutrophil dysfunction.[2]

Actinomycosis is a rare chronic granulomatous suppurative disease caused by *Actinomyces* spp. The term *Actinomyces* (actis-ray and mykes-fungus) was given by Hartz based on the microscopic appearance of granules. Von Langenbeck was the one to describe the first case of actinomycosis in 1845 and attributed it to be a fungal infection because of their morphology.[3] However, they are now grouped under bacteria due to their cell wall composition, lack of nuclear membrane and lack of growth inhibition by antifungal agents. These organisms are considered as transitional form between bacteria and fungi. These anaerobic Gram-positive bacteria constitute a part of

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normal saprophytic component of oral flora, colon and vagina.[4] Underlying disease, break in the integrity of the mucous membranes and presence of devitalized tissue may provide medium to these organisms to invade deeper body structures and cause human illness. The most important species involved in clinical infection include *Actinomyces* israeli, *Actinomyces viscosus*, *Actinomyces Naeslundi* and *Actinomyces odontolyticus*. These bacteria may combine synergistically with companion bacteria such as *Staphylococcus* and *Streptococcus*. The companion bacteria appear to magnify the low pathogenic potential of actinomycetes. Infection can present as mass or abscess or as draining sinus tracts. Sometimes, hematogenous dissemination may occur to distant organs.[5] Here, we describe the simultaneous occurrence of invasive aspergillosis and actinomycosis of maxilla in a 38-year-old patient.

CASE REPORT

A 38-year-old male farmer consulted the hospital with the complaint of pus discharge from left upper back tooth region since 15 days. His past dental history revealed extraction of tooth in the same region due to mobility and pus discharge. Following extraction, the socket had not healed completely. The patient further gave a history of nasal regurgitation of food and fluids after 2 days of extraction. The vitals are normal. The patient is a known diabetic and is not under medication. On extraoral examination, there was gross facial asymmetry due to swelling on left side of the mid face region and was about 3 cm × 2 cm. On palpation, the swelling was firm and nontender. There was no local rise of temperature and no lymphadenopathy. Intraoral examination revealed the presence of oroantral fistula from maxillary left premolar till the third molar region extending buccally and palatally. The alveolar bone was exposed from 23 to 27. Infraorbital nerve paresthesia found positive, with the above findings, a provisional diagnosis of osteomyelitis with oroantral fistula secondary to extraction was made. The patient was advised for complete blood picture (CBP), computed tomography (CT) scan and random blood sugar (RBS). CBP revealed that leukocytosis and RBS were 290 mg/dl. The CT scan revealed moth-eaten appearance of the bone and radiopacity in maxillary sinus. There was sequestrum like appearance in the zygomaticomaxillary region. Due to above findings, osteomyelitis was confirmed and subjected for biopsy. The specimen obtained for histopathological examination consisted of gray-white, friable soft-tissue aggregate measuring 2 cm × 2 cm. Examination of H and E stained sections revealed mainly necrotic tissue. Amidst the necrotic material was seen branching septate hyphae of *Aspergillus* [Figure 1]. Apart from hyphal forms, many fruiting bodies of *Aspergillus* were also seen [Figure 2]. The conidial head (fruiting bodies) is composed of a vesicle, which is crowned by one layer of philalides (sterigmata), ending in chains of conidias at the extremity. A Grocott's methenamine silver stain was carried out, which highlighted the details of hyphae such as parallel walls, regular septa and dichotomous branching at 45° [Figures 3 and 4].

The H & E section also revealed actinomycotic colonies; they were seen as isolated masses of filamentous bacteria with a central area of necrosis and radiating filaments [Figure 5]. Eosinophilic club-shaped extensions were seen at the periphery of the filaments in most of the colonies. Multiple coccoid bacteria were also found throughout the colonies. Most colonies were surrounded by an inflammatory infiltrate composed of mainly polymorphonuclear leukocytes, lymphocytes and plasma cells. Grocott's methenamine silver stain was carried out, which showed masses of filaments extending in a radiating, spoke-like fashion or "sunburst radiation" [Figure 6]. Based on histopathology, final diagnosis of invasive aspergillosis and actinomycosis of maxilla was made, and the patient was appropriately managed.

DISCUSSION

Aspergillus is a hyalohyphomycete from the eurotiales order, first identified by the Italian biologist Pier Antonio Micheli in 1729, who named the fungus because of its similarity with aspergillum, an object used to sprinkle holy water.[6] It is the second most common opportunistic mycosis in patients after candidiasis. De Shazo *et al*. have classified aspergillosis of PNS into two broad groups: noninvasive and invasive aspergillosis. Noninvasive aspergillosis includes aspergilloma and allergic fungal sinusitis. Invasive aspergillosis spreads beyond the confines of the sinuses and consist of acute invasive aspergillosis (AIA), chronic invasive aspergillosis (CIA) and granulomatous invasive aspergillosis. AIA occurs as a result of invasion of the mucosa and blood vessels by fungal elements causing thrombosis, necrosis and eschar formation and is seen commonly in immunocompromised patients, because of cancer, therapeutic immunosuppression, poorly controlled diabetes mellitus, protein-calorie malnutrition or iron overload. Granulomatous invasive fungal sinusitis, granuloma composed of multinucleated giant cells, variable numbers of lymphocytes and plasma cells and center of granuloma may be composed of eosinophilic material surrounded by fungus, giant cells and palisading nuclei. CIA is also caused by invasion of mucosa and blood vessels by fungal elements; however, it has a more chronic course as compared with AIA. Tissue necrosis with

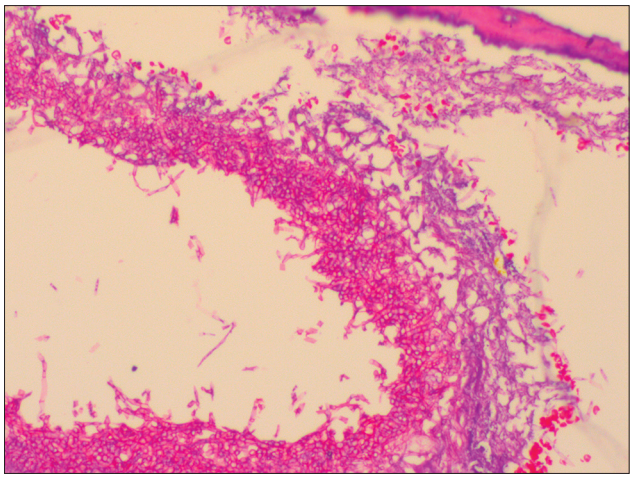

Figure 1: Necrotic material with branching septate hyphae of *Aspergillus* (H & E, ×10)

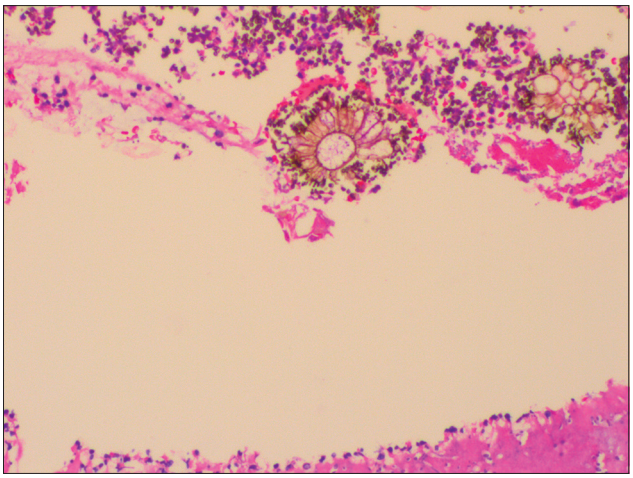

Figure 2: Conidial head (fruiting bodies) with a vesicle crowned by one layer of philalides (H & E, ×10)

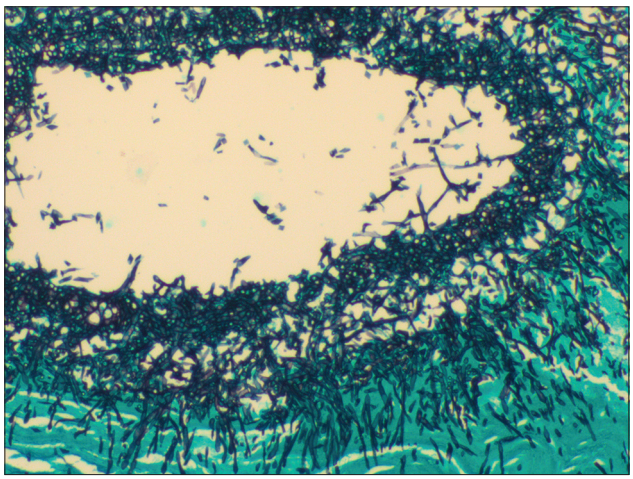

Figure 3: Grocott's methenamine silver stain highlighted the details of hyphae (×10)

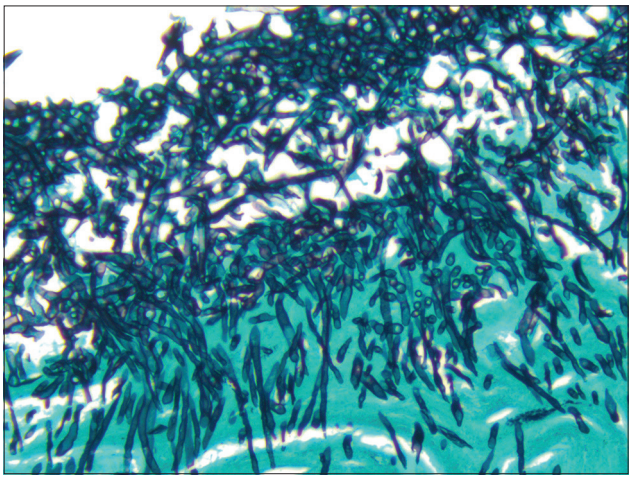

Figure 4: Hyphae showing parallel walls with regular septa and dichotomous branching at 45° (×40)

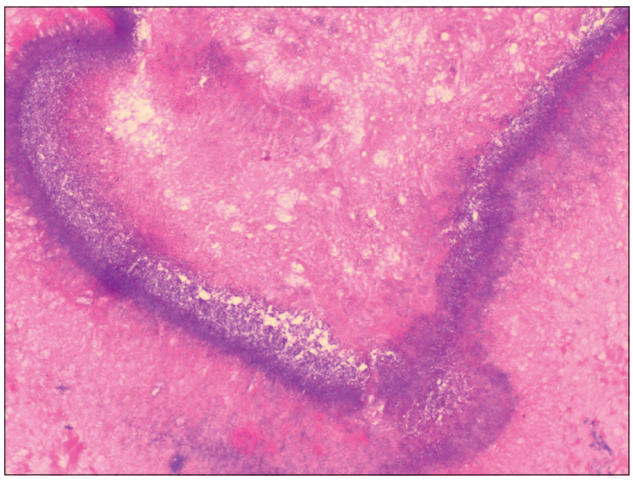

Figure 5: Central area of necrosis with surrounding radiating filaments (actinomycosis) (H & E × 4)

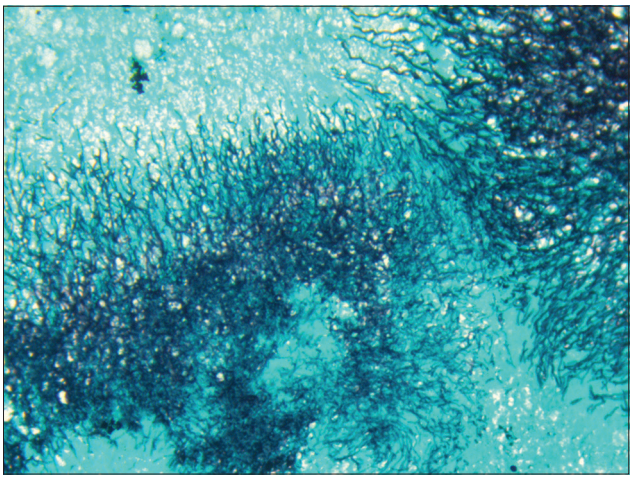

Figure 6: Grocott's methenamine silver stain showing masses of filaments extending in a radiating, spoke-like fashion or "sunburst radiation" (×10)

little inflammatory infiltrates, dense hyphal accumulation resembling mycetoma may be present, fungi breach the mucosal barriers to invade blood vessels and cause tissue necrosis and is mostly seen in immunocompromised

patients with diabetes mellitus.[7] In our case, as the patient is farmer, it is most likely that he inhaled the fungal spores from his environment and further his immunocompromised state (diabetes mellitus) contributed to invasiveness (CIA). In head and neck, the lesions are more likely to occur in the nasal cavity, PNS, palate and tongue. These lesions are clinically manifested as a painful ulcer surrounded by necrotic tissue. Sometimes, the necrosis may result in perforation of the palate. The fungus has a tendency to invade adjacent arterial walls, which may lead to hematogenous spread. Rarely a periodontal presentation may be noted usually in immunocompromised patients as in our case. On histopathological examination, aspergillosis shows septate hyphae which are uniform, narrow, tubular and dichotomous branching at 45°. The presence of conidial heads, commonly found in areas with high oxygen tension, such as PNS, bronchi and lungs or in lesions with a high with fungal burden is pathognomic of the diagnosis of aspergillosis.[8] Description of conidial heads and fruiting bodies is scant in medical literature; there are only eight cases reported with conidial heads and hyphae.[9] When the conidia is not present, then other diagnostic methods such as culture and antigen detection should be done, if not pitfalls can happen in the diagnosis of aspergillosis, based only on the histopathology.

Actinomycosis is a relatively infrequent saprophytic infection caused by Gram-positive, nonspore forming bacilli *Actinomyces*. Actinomycosis is classified by Cope in 1938 into: cervicofacial, thoracic, abdominal and pelvic. Cervicofacial is the first identified and most common actinomycosis. The most frequently affected cervicofacial sites are the salivary glands and mandible.[10] Actinomycosis in the maxilla accounts for only 0.5%–9% of all head and neck cases. The pathogenesis of actinomycosis is not exactly known; however, caries and trauma seems to be precipitating factors. Extracted socket, periodontal socket and nonvital tooth may act as a portal of entry for these bacteria. It usually occurs in adults although cases are reported in children.[11] The most common clinical presentation is soft tissue abscess and draining cervical fistulae. Sometimes it involves the bone resulting in osteomyelitis. Actinomycosis is termed as "masquerader" in head and neck because of its uncommon presentations. The diagnosis of actinomycosis is often difficult as it mimics several infectious, noninfectious pathologies and even malignant neoplasms.[12] Hence, it is more important for the dental surgeon to understand and rule out actinomycosis; otherwise, it will result in misdiagnosis as in our case. In the present case, the lesion presented as periodontal abscesses with pus discharge.[13] The exact pathogenesis is unknown here; however, the presence of poor oral hygiene and periodontitis might have facilitated the penetration and pathogenicity of the microorganisms. As these organisms are opportunistic, in periodontitis, they can become pathogenic. Suzuki and Delisle reported a case that pulmonary actinomycosis which occurred as a result of aspiration of *Actinomyces* organism originated from dental plaque, dental calculus and diseased periodontium. In our case, extraction may have also aggravated the infection. Histologically, *Actinomyces* shows granulomatous inflammatory response with central abscess formation. The central part contains colonies of organisms and along its periphery, there are macrophages and granulation tissue. The bacterial colony in the central part has characteristic morphology. The organisms have tiny basophilic heads called conidiophores toward the center and slender eosinophilic hyphae radiating outward toward the periphery. Because of this arrangement, the cluster is known as the ray fungus. Long-term high dose penicillin is required for treatment. In addition, drainage of abscesses, debridement and surgical excision of sinus tract is recommended to enhance penetration of antibiotics. Here, we report an extremely rare case of simultaneous occurrence of invasive aspergillosis and actinomycosis of maxilla. Only two similar cases have been reported in the literature: 54-year-old female patient involving the maxillary sinus and 32-year-old female patient involving the sphenoid sinus.[14]

CONCLUSION

Because of its rarity, there is a chance of missing its diagnosis and proper treatment leading to substantial morbidity and mortality. Maltreated patients are at risk of developing life-threatening complications. Maxillary invasive aspergillosis and actinomycosis are relatively rare oral infectious diseases, and their occurrence simultaneously is even rarer.

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Conflicts of interest
There are no conflicts of interest.

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