old age and underlying debilitating disorders.[1,2,5] In most of the reported cases, infection is seen in extremes of age[5,8]. In this report also the infected person was 73 years old. This bacterium is reported to exhibit low levels of single antimicrobial resistance.[4] Our isolate was sensitive to all the microbial agents routinely employed for treatment.

Cattle rearing is one of the major occupations in rural India. The transmission of S. Dublin infection is through raw milk and its products, a well known fact. Hence stringent steps should be taken to prevent the transmission of infection to humans by controlling the infection in animal reservoirs, prevention of contamination of foodstuffs and use of appropriate standards in food processing. Microbiologists should make an attempt to identify all the Salmonella isolates to serotype level. There is an urgent need for a regular monitoring system before the emerging zoonotic pathogen becomes a potential public health hazard.

References


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PRIMARY CUTANEOUS ASPERGILLOSIS DUE TO ASPERGILLUS NIGER IN AN IMMUNOCOMPETENT PATIENT

Primary cutaneous aspergillosis is a rare entity, usually caused by A. fumigatus and A. flavus. Here, we present such a case, manifested by ulceration due to A. niger, which remained undiagnosed for a prolonged period. The immunological status was intact, although the patient had associated severe fungal infection. Recurrence of the lesion occurred despite repeated anti-fungal therapies. Anti fungal testing was done based on the broth dilution (M-38A, NCCLS, USA) method. The culture isolate was found to be sensitive to fluconazole and amphoteracin B. Continuation of antifungal therapy improved the symptoms, reducing the size of the lesion.

Key words: Aspergillus niger, immunocompetent host, primary cutaneous aspergillosis

Introduction

Aspergillosis is an uncommon opportunistic fungal infection caused by a variety of species of which Aspergillus fumigatus, Aspergillus flavus and Aspergillus niger are the common ones.[1] It usually occurs as a complication of severe debilitating illnesses and is seen in patients suffering from malignancies, tuberculosis, silicosis and diabetes. It also occurs in patients who are receiving long-term corticosteroids, antibiotics or cytotoxic drugs and are in immunocompromised states with neutropenia. Cutaneous aspergillosis is a rare form of a locally invasive disease. It may be primary, involving the sites of skin injury following intravenous cannulation, trauma, occlusive dressing, burns or surgery. Secondary cutaneous lesions may result from widespread haematogenous seeding of the skin. In immunocompromised patients, primary cutaneous aspergillosis is most commonly caused by A. flavus and A. fumigatus.[2,3] However, this cutaneous lesion is rarely associated with Aspergillus niger. Here, we describe such an association in an immunocompetent host, and literature in this regard has been reviewed.
Case Report

A 33-year-old man presented with a large non-healing painful ulcer over an erythematous plaque on the upper arm, just below the shoulder, since the last 10 years. The ulcer had gradually increased in size to 20×20 cm (Fig. 1). It was characterized by a punched-out margin, indurated base and erythematous granulation tissue, with purulent discharge. The ulcer developed from an asymptomatic, painless nodule of about 4×5 cm in size. There was no history of trauma, invasive procedure, discharging sinus or grains at that site. An empirical diagnosis of cutaneous tuberculosis was made and he received anti-tubercular treatment for two years without much benefit. He then presented to our hospital where a punch biopsy from the ulcer edge revealed necrotizing granulomatous inflammation with septate fungal hyphae showing acute angle branching, suggestive of aspergillosis. He was treated with oral ketoconazole 200 mg twice daily along with oral drops of saturated solution of potassium iodide (SSKI, 45 drops thrice daily). He took the treatment regularly for six months. This led to near complete healing of the ulcer and about 50% reduction in the size of plaque. He then took treatment, albeit irregularly, for another two months, and there was near complete resolution of the ulcer and inflammation. The patient remained asymptomatic for the next one year except for the presence of a scar. Then, slowly an ulcerated plaque formed within the scar on the arm and a new ulcer appeared in the left groin. The recurrence was treated with a combination of itraconazole and potassium iodide for six months. The ulcer responded well to therapy, but once again recurred after he discontinued treatment. The sequence of nearly 80–90% resolution followed by a recrudescence occurred five more times despite various combination treatments including ketoconazole, potassium iodide and itraconazole. The patient revealed that he stopped treatment on his own after some improvement because he could not afford the medication. He never took the treatment for a complete duration, as advised.

During the course of illness, he was found to have concomitant paucibacillary leprosy (pure neuritic type,

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**Figure 1:** Shows punched-out ulcer on the upper arm, just below the shoulder

**Figure 2:** Haematoxylin and eosin stain of the tissue biopsy showing (arrow) thin septate hyphae 40X (A) giant cells with dense lymphocytic infiltrate in the upper and lower dermis 40X (B)

**Figure 3:** KOH mount showing thin septate hyphae with acute angle branching 40X
which does not present with primary skin lesions) and received treatment with pauci-bacillary multi-drug therapy (PB-MDT) for six months. He developed extensive tinea corporis, which cleared after therapy with griseofulvin 250 mg once daily orally and ketoconazole 200 mg twice daily, for one year. There were no other associated medical illnesses and his general health remained good during the entire period of follow-up. The patient was found to be HIV negative with CD4 count 965 cells/ml.

Repeated attempts to isolate the causative organisms by fungal culture during his previous hospital admissions had been unsuccessful. During the current hospital stay, a punch biopsy sample was taken from the ulcer edge as a base for histopathological and microbiological examinations. Haematoxylin and eosin staining of the tissue showed several acute angle branching septate hyphae and giant cells with dense lymphocytic infiltrate in the upper and lower dermis (Fig. 2A, 2B). A direct KOH mount revealed the presence of thin hyaline septate hyphae with acute angle branching (Fig. 3). The Gram stain showed the absence of bacteria and the Ziehl Neelsen stain was negative for acid fast bacilli. The biopsy material was inoculated in sabouraud dextrose agar (SDA) with and without cycloheximide in duplicate and incubated at 37°C and 25°C, respectively. After 72 hours, all tubes were seen with cottony white mycelium growth, which was soon covered with abundant black spores. No bacterial growth was detected in the culture. Microscopic characterization of the fungal isolate was carried out by preparing a lactophenol cotton blue mount from the growth. They mostly consisted of erect conidiophores. The conidiophores terminated in a vesicle covered with phialides (biseriate). The secondary phialide bore chains of globose conidia that were dark and covered the entire surface. The conidial head was large, black and radiate. The fungal isolate was confirmed to be Aspergillus niger by the above-mentioned features. We also performed antifungal susceptibility testing for fluconazole and amphotericin B using the broth dilution method (M-38A, NCCLS, USA). The isolate was sensitive to both the drugs and showed inhibition of growth for amphotericin B and fluconazole at the lowest minimum inhibitory concentration (MIC).

During the current admission, the patient was treated with ketoconazole 200 mg twice daily. After receiving the fungal culture report, intravenous amphotericin B was instituted, initially 0.5 mg / kg / day, and then increased to 0.75 mg / kg / day. However, he was unable to tolerate the drug, hence, oral ketoconazole was continued. There was significant improvement in pain and discharge, and about two-third reduction in the size of the ulcer after four weeks of treatment. The patient was advised to take treatment regularly and report for follow-up.

Discussion

Aspergillus species is the most ubiquitous fungi seen in soil, water and decaying vegetations. It affects the lungs, central nervous system, naso-orbital area, skin and sometimes, it may be disseminated. Cutaneous aspergillosis is mostly caused by A. flavus, A. fumigatus, and rarely, by A. niger. Clinically, the lesion is characterized by macules, papules, plaques or haemorrhagic bullae, which may progress into necrotic ulcers that are covered with a heavy black eschar. The condition usually occurs in association with immunocompromised patients.[4] Our patient was not having a compromised immune status. However, cutaneous aspergillosis is not uncommon in immunocompetent patients.[5,6] Burik et al. found 6% of lesions caused by A. niger in patients not infected with HIV.[7] Prompt recognition and appropriate treatment is necessary to prevent adverse outcomes.

Treatment of cutaneous aspergillosis included a combination of surgical debridement and multi-drug antifungal chemotherapy.[9] In view of extensive tissue involvement, debridement was not done in this case, as it would have led to a larger defect. Itraconazole was used as the first line of therapy in localized lesions.[7] Ajith et al. reported a case of cutaneous aspergillosis which showed complete clearance of the lesion with oral itraconazole treatment.[9] It had to be changed to intravenous amphotericin B if the lesion worsened or if there was other evidence of clinical failure. The recurrence of the lesion in our patient was probably due to poor compliance with the antifungal agents he was administered, namely, KI, ketoconazole and itraconazole. Drug resistance was unlikely because there was a clinical response whenever he restarted regular treatment. In addition, the isolate was sensitive to fluconazole by drug susceptibility testing. To conclude, we report a case of primary cutaneous aspergillosis due to Aspergillus niger in an immunocompetent host that recurred owing to irregular treatment.

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Due to cefazolin. There is no other report of such red grain botryomycosis in world literature.

**Key words:** Botryomycosis, red grain, Staphylococcus aureus

**Introduction**

Botryomycosis is characterized by chronic, purulent and granulomatous lesions of the dermis, and subdermal tissue and viscera. Similar to eumycetoma and actinomycetoma, it is characterized by tumefaction, sinus tract formation and discharge of sulphur granules. *Staphylococcus aureus* and *Staphylococcus epidermidis* are the most common agents, but other species like *Pseudomonas aeruginosa*, *Escherichia coli*, *Proteus*, *Bacteroides* and some other bacteria are fairly common.[1]

Hands, pinna, feet and head are common sites of botryomycosis, although any part of the body skin may be involved. Folds of skin in obese persons, skin under pendulous breasts are other vulnerable areas.[1]

Botryomycosis can be cutaneous or visceral. Visceral botryomycosis may be a primary or a secondary infection due to dissemination. Pulmonary botryomycosis is the most common entity in visceral involvement.[1-3] Intraoral granulomatous pyogenic botryomycosis has also been reported.[4]

Surgery, abrasions and lacerations in road accidents, piercing of pinna are documented etiological factors that may lead to the development of botryomycosis. Chronic cutaneous irritation and lichenified lesions of the scalp often predispose to botryomycosis. Diabetes, alcoholism, poor hygiene, cystic fibrosis and general debility are the known predisposing factors. Botryomycosis is often associated with children. In most cases infection remains localized, although occasionally it spreads to other organs like the liver, kidney, lungs, heart and prostate, and lymph nodes may occur.[1] It is increasingly being reported from AIDS cases.[3]

Cellular response in general is similar to actinomycetoma and eumycetoma. The grain is surrounded by acute suppurative response. Neutrophils in various stages of degeneration, in large numbers, are seen surrounding the grain. Lymphocytes, eosinophils, plasma cells, histiocytes, few foreign body giant cells and fibroblasts surround the central suppuration; Surrounding this is the fibrosis and granulation response, with capillary formation.[1]

**Case Report**

A 35-year-old male labourer presented with swelling, redness and multiple sinuses, with foul smelling discharge containing red granules. He gave a history of trauma on the foot, with an iron rod, eight months back. In a few days, he noticed a small nodule, on the back of right foot. Gradually the swelling increased in size, and formed a discharging sinus. In the following months many more nodules and sinuses appeared around this lesion.

On examination, it was observed that the entire back of the right foot was severely swollen with intense erythema, with numerous elevated, well-demarcated, small and large nodular lesions and many discharging sinuses were present (Fig 1). Sinus openings were inflamed and mostly blocked with dried pus and sulphur granules. The foot appeared...