Case Series of Opportunistic Deep Seated Fungal Infections in Surgical Practice in an Agrarian Society

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ABSTRACT

This article is to highlight the atypical presentations of fungal infections which may be encountered in surgical practice and to help surgeons to recognise these cases early and provide appropriate management. Three cases of skin and soft tissue fungal infections with atypical presentations have been discussed. All the patients are aged above 45 years and farmers by occupation with type 2 diabetes mellitus as a common co-morbidity. These cases showed aggressive progression of the disease and were started on anti-fungal agents along with serial aggressive debridement. Two patients deteriorated rapidly, as they succumbed to their illness. Fungal agents being commonly present in the environment, are likely to cause infection in immunocompromised states like diabetic patients, especially in those with a preceding history of trauma.

Keywords: immunocompromised state, anti-fungals, wound debridement.

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I. INTRODUCTION

Fungal organisms are commonly found in the environment. Fungal infections can occur either due to inhalation of fungal spores or through colonisation of skin by the organisms and often present as primary lung or skin infections [4]. Fungal infections of skin can occur frequently among immunocompromised individuals [3]. Patients on long term antibiotics, steroids, chemotherapy and Patients with HIV/AIDS, Diabetes Mellitus etc. are all at a higher risk of developing fungal infection [4].

Fungal infections can present as Superficial, Cutaneous, Sub – Cutaneous or Deep (Systemic) infections. In superficial mycosis the outermost layer of the skin is affected. Cutaneous mycosis involves deeper up to epidermis [5]. Subcutaneous mycosis can extend into dermis, subcutaneous layer, muscle, and fascia. Deep (Systemic) mycosis can be due to inhalation of fungal spores or can be due to opportunistic pathogens in immunodeficiency states [4]. Fungal skin infections can clinically manifest as Hypo/Hyper pigmentations of skin, rashes, Itching, induration, fever, and can progress to tissue infarction and necrosis. In severe cases sepsis can occur leading to mortality [5].

Subcutaneous mycosis is commonly encountered in surgical practice wherein the infection is usually preceded

by a penetrating/piercing trauma to skin leading to fungal invasion. These infections usually require surgical intervention in form of wound debridement [2].

In this series we describe fungal infections of various etiology with atypical presentations encountered at the Department of General Surgery, Saveetha Medical College and Hospital, Thandalam, Tamil Nadu, India for the benefit of practicing surgeons to achieve early recognition and adequate management of such rare cases.

II. CASE PRESENTATION

A. Case I

A 45 years old diabetic man on irregular medications presented with chief complaints of swelling and skin discoloration over left thigh region for a period of 10 days. He gave a history of thorn prick injury acquired at work fields 10 days prior to presentation. On local examination of the left thigh an induration of size 15×15 cm was seen with blackish discoloration of the skin around the region. A discharging sinus was seen over the centre of the lesion, with active pus discharge that was firm, non-fluctuant, warm, and tender showing in fig 1A. With a clinical diagnosis of necrotising fasciitis, wound was debrided under aseptic conditions. On Next day (post operative day 2) fungal moulds were noticed growing around the edges

showing in Fig 1b. Hence Patient was started on antifungal therapy (Injection Amphotericin B). Aggressive serial wound debridements were done daily. Tissue samples were collected and sent for fungal culture and biopsy. Fungal culture revealed *Apophysomyces elegans* as the etiological agent and Histopathology showed Mucormycosis.. Unfortunately, patient's general condition deteriorated rapidly leading to his demise.

(a)

(b)

Fig. 1, a, b. Initial presentation and post serial debridements with fungal moulds

B. Case II

A 75 years old diabetic man with renal dysfunction on irregular dialysis came with history of ulcer over the left little toe for two weeks. He had no recent history of trauma. He was admitted under nephrology department with complaints of breathlessness and abdominal distension. On local examination, ulcer of size 2x2 cm was seen over the dorsal aspect of the left little toe with foul smelling discharge and patchy gangrene. Distal pulses were present (Fig 2 a, 2 b). Emergency wound debridement was planned, and his left little toe was disarticulated. Samples were collected and sent for KOH (potassium hydroxide preparation) mount and fungal culture. KOH mount showed fungal hyphae. Hence Patient was started on Injection Amphotericin B. Fungal culture revealed *Rhizopus arrhizus*. Patient died on next day inspite of effective treatment.

(a)

(b)

Fig. 2, a,b. Initial presentation with fungal moulds

C. Case III

A 58-year old diabetic man on regular medication came with complains of right sided abdominal pain and swelling for the past 10 days. History of occasional low grade fever was also present. Patient denied recent history of trauma, accidental pricks, or injection at that site. Patient had undergone laparoscopic cholecystectomy 5yrs ago. Patient was a case of type 2 diabetic Mellitus on Tab Metformin 500 mg twice daily. Palpable firm mass of size 15x10 cm was seen occupying the right hypochondrium and right lumbar regions extending into the parietal wall. Pus was drained from the collection and initial fungal culture was negative. Five months later the patient presented again with

a swelling in the right lumbar region. The swelling was fluctuant and was 2 cm inferior to the right chest wall. Incision and drainage were done. Culture and sensitivity study revealed presence of fungal hyphae and revealed *Aspergillus nidulans* as the fungal agent. Patient was started on tablet Itraconazole for 2 months. Swelling decreased in size. Patient was on anti-fungal therapy and was asymptomatic.

III. DISCUSSION

Fungal infections in humans can be classified according to the tissues involved.

- Superficial mycosis
 - Surface mycosis
 - Cutaneous mycosis
- Deep mycosis
 - Subcutaneous mycosis
- Systemic mycosis
- Opportunistic mycosis

Systemic mycosis is caused by fungi. They are present as saprophytes in soil and on plant material. The fungus is known to disseminate to Central nervous system, bone, and other internal organs from the lungs. Thermally dimorphic fungi more often are the reason for systemic mycosis. Systemic mycosis include blastomycosis, histoplasmosis, coccidioides-mycosis and paracoccidioidomycosis. We have observed in our study that opportunistic mycosis occurs in patients who are immunocompromised such as diabetes, cancer, steroids or broad spectrum antibiotics. Two of three cases in this case study had type 2 diabetes mellitus, an immunocompromised state. One patient had renal disease and was on regular dialysis, making him more vulnerable for opportunistic infections. We have observed in this study that opportunistic mycosis are caused mostly by fungi that are normal commensal flora such as *Mucor*, *Penicillium* species and *Aspergillus* species [1].

In systemic Zygomycosis there appears to be no predilection of sex or race, since it is primarily and "opportunistic" infection, which is linked with an impaired immune mechanism, caused by debilitating conditions. Most commonly the patient suffers from severe uncontrolled diabetes, from malignant tumours, leukaemia, malnutrition, prolonged steroid therapy, persistent neutropenia, desferoxamine therapy, haematological malignancies, illicit use of intravenous drugs, autoimmune disorders, and the breach of cutaneous or mucous membrane barrier due to trauma, burns and surgical wounds [2]. Mucormycosis in debilitated patients is acute and fulminant infection.

Cutaneous mucormycosis is usually caused by the traumatic implantation of fungal elements through the skin especially in patients with extensive burns, diabetes or steroid induced hyperglycemia. This leads to a chronic indolent ulcer. It may resolve spontaneously or extend into subcutaneous tissue and become rapidly progressive. Very rarely the moulds can be seen growing on the edge of the wound. They more often present as abscesses, discharging sinuses and ulcers with superadded bacterial infection [3]. This array of clinical presentation misguides the surgeon/consultant into treating them as bacterial infections. Hence,

it becomes of paramount importance to thoroughly investigate the wound smears and stains further. Tissue sections should be stained with haematoxylin and eosin (HandE), Gomorimethenamine silver (GMS) and periodic acid-Schiff (PAS) stains. Sabouraud dextrose agar (SDA) containing antibacterial antibiotics is used as a primary isolation medium [4].

Mucormycosis is rare in healthy individuals unless trauma has provided a portal of entry for the fungus. Case I in our study of a 45-year old man had a history of thorn prick injury, following which he developed swelling and discolouration over his left thigh.

Sputum and needle biopsy from pulmonary lesions, bronchoalveolar lavage fluid, nasal discharges, scrapings, and aspirates from sinuses in patients with rhinocerebral lesions, skin scrapings from cutaneous lesions and biopsy tissue from patients with gastrointestinal and disseminated disease. Mucorales have coenocytic hyphae that will often be damaged and become nonviable during the biopsy procedure. Therefore, a positive direct microscopy, especially from a sterile site, should be considered significant. Direct microscopy examination can be done after mounting the specimen with 20% potassium hydroxide and gently heating the slide to clear the tissue.

Fungal infections require multidisciplinary management involving correction of underlying risk factors, antifungal therapy and aggressive debridements. Early identification and prompt treatment are essential as it is life-saving. Antifungal therapy involves starting IV antifungals like Amphotericin – B preferably the liposomal form of it. Amphotericin-B has given encouraging results in systemic and opportunistic fungal infections. The calculated dose (1 mg per kg body weight) is dissolved in 5 per cent glucose solution (1 mg per 10 ml) and administered intravenously for about 6 hours daily. Amphotericin B is currently the drug of choice for the treatment of systemic infections caused by *Aspergillus* and *Candida* spp. We have used it for treating cases I and II in our study. However, the high incidence of toxicity associated with amphotericin B has limited its use in many patients. The drug is highly nephrotoxic and caution to be taken is using it in patients with known renal disease. Other newer and more efficient IV antifungals like Fluconazole, Posaconazole, voriconazole, Caspofungin can be added as well. Isavuconazole has been recently FDA approved to treat invasive mucormycosis.

Given their increasing frequency and unacceptably high morbidity and mortality rates, prevention of invasive fungal infections has become of vital importance. Even with prompt identification and appropriate treatment we had unfortunately lost 2 of our patients from this case study. Vaccination of high-risk groups is a particularly promising strategy to prevent invasive fungal infections. To date, few vaccines have reached the clinical trial stage. However, the importance of mycosis to public health around the world indicates that efforts should be given to the discovery of new molecules and compounds that can be used in the prophylaxis and treatment of these diseases [5]. Early and prompt identification of the disease is of paramount importance, as delay in treatment can cause rapid progression of disease and high mortality. The challenges

are numerous, but the efforts offer hope for controlling these diseases that tend to increase in incidence over time. Apart from antifungals, extensive wound debridement surgery along with proper local care is a mainstay treatment to limit progression.

IV. CONCLUSION

Aggressive fungal soft tissue infections are rare entities in surgical practice. They are difficult to diagnose and require immediate surgical intervention along with administration of appropriate anti-fungal agents. Delay in doing so results in extremely high mortality rates. Fungal agents are commonly presented in the environment. Fungal infections are more likely to occur in immunocompromised states like that of a diabetic patient, and in patients with preceding history of trauma, cutaneous infections are more likely. Henceforth, it is important for the practicing surgeons to be aware of the atypical presentations of fungal infections especially with a history of trauma in all immunocompromised patients with cutaneous and subcutaneous lesions.

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