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Aspergillus as a rare cause of non-healing traumatic breast wound

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Case Report: We report a case of *Aspergillus flavus*, identified within a non-healing ulcer in the breast of an immunocompromised host. The patient was a 63-year old lady with diabetes mellitus and severe rheumatoid arthritis requiring oral prednisolone therapy. She had developed a pressure ulcer on her right breast secondary to an upper extremity cast placed for conservative management of a humerus fracture. This pressure ulcer failed to improve despite multiple debridements, local wound care and antibiotic treatment. Tissue biopsy from the debridement specimen revealed fungal hyphae without evidence of malignancy. Formal fungal cultures confirmed this to be *Aspergillus flavus*. She was started on oral Itraconazole along with local wound care. She later succumbed to gram negative sepsis and Disseminated intravascular coagulation (DIC). Extensive literature search to identify causes of non-healing traumatic breast wounds revealed a few case reports only.
Conclusion: *Aspergillus* can present with extensive soft tissue or breast involvement in immune suppressed individuals and should be considered in patients with a non-healing breast wound with a high index of suspicion.

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Keywords: *Aspergillus*, Breast wound, Immune compromised, Non-healing

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INTRODUCTION

Invasive fungal infections in healthy individuals are very rare due to competency of immune system against such infections [1]. Opportunistic fungal infections in immunocompromised hosts have been reported and seem to be increasing over time merely due to increasing number of susceptible hosts, greater laboratory expertise in the detection and identification of fungi, use of new transplantation modalities and use of antimicrobial prophylactic practices. Among them, *Aspergillus* and *Candida* have a higher prevalence [2]. Immunocompromised patients are equally at risk of developing soft tissue fungal infections as they are at risk of acquiring other types of infections [3–6]. In breast, soft tissue fungal infections have been reported in

association with prosthetic breast implants [1, 7–9]. They are considered to colonize via airborne dissemination, contamination of implants during manufacture, hematogenous dissemination or nosocomial spread from the operating room environment or instruments during surgery [10, 11]. In most patients, the source was presumed to be airborne infection during a surgical procedure [10]. *Aspergillus* is an ubiquitous saprophytic fungus with more than 200 recognized species that may cause allergic bronchopulmonary aspergillosis, pulmonary aspergilloma, paranasal sinus infection, endocarditis, implant infections [10,12,13]. Few cases of aspergilloma of breast tissue have been reported in literature so far. We describe the case of *Aspergillus flavus* infecting breast tissue of an immune compromised host resulting in a non-healing wound.

CASE REPORT

A 63-year-old lady, known case of long standing diabetes mellitus with acceptable glycemic control and rheumatoid arthritis, on oral prednisolone therapy for five years, with normal white count, was admitted to our hospital with a non-healing fracture of the proximal shaft of right humerus. A road traffic accident two-months prior resulted in the upper extremity fracture that had been managed conservatively with a cast at an outside institution. This cast rested against her right breast and resulted in pressure necrosis. At the outside facility, she underwent two formal wound debridements for this necrotic breast wound resulting in a large ulcer. Without much improvement over a two-month period, frustrated, the patient transferred care to our institution that serves as a tertiary care referral center.

Examination at presentation showed a large ulcerated area in the lower half of the right breast with unhealthy edges. The base was heavily coated with necrotic tissue and fibrin. There were multiple dry scabs on the skin of the remaining breast (Figure 1). Neither purulent drainage nor cellulitis was seen. Examination did not identify a lump and the contralateral breast was normal. Mammogram and ultrasound of both breasts were negative for malignancy. Routine tissue culture did not grow any organism and histology showed dense acute and chronic inflammatory infiltrate with fat necrosis and microabscesses (Figure 2). Special stain PAS+D highlighted fungal hyphae (Figure 3). For the identification of fungal strain, a formal fungal culture of breast tissue revealed moderate septate hyphae on smear and heavy growth of *Aspergillus flavus* on culture.

The right humerus fracture was surgically managed with open reduction and internal fixation. Her breast wound was debrided down to healthy tissue. She was started on oral itraconazole 200 mg q 12 hourly along with local wound care and discharged home. 10-days after her discharge, she returned to the emergency Room with DIC secondary to *E. coli* septicemia from pyelonephritis.

Figure 1: Ulcerated wound with necrotic tissue over lower half of right breast.

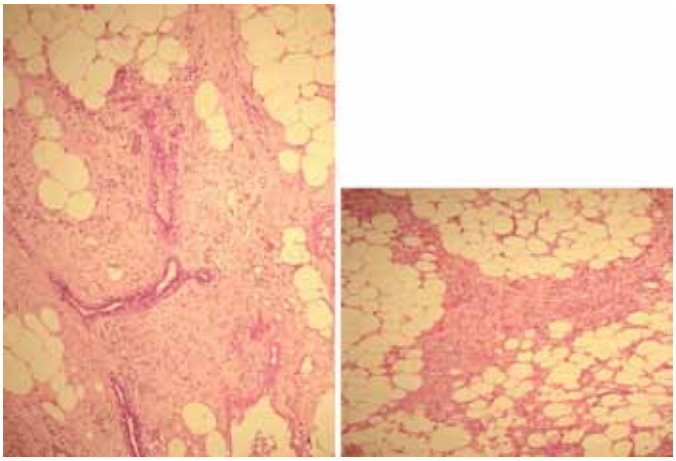

Figure 2: Breast tissue showing breast ducts and surrounding moderate degree of lymphocytic, plasma cell and eosinophilic infiltrate (H&E stain, x100).

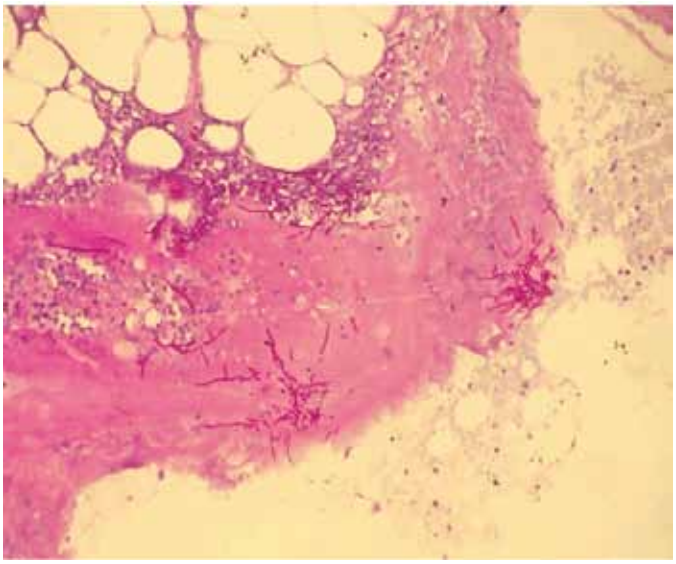

Figure 3: Breast tissue showing necrosis with collections of septate, branching fungal hyphae highlighted by PAS+D special stain (H&E stain, x400).

She was admitted to the intensive care unit and given supportive therapy along with culture specific antibiotics. Despite local wound care at home and itraconazole, her breast wound failed to improve and was once again covered with fibrinous exudate and necrotic tissue. Due to elevated bilirubin and deranged renal function, itraconazole was switched to oral voriconazole. Due to her overall status, further debridement of breast wound was deferred. Her septicemia resulted in multi system organ failure and due to their inability to pay in a self-pay system, the patient elected to leave against medical advice and passed away shortly after.

DISCUSSION

Fungal infections of the breast are very rare [1, 3]. They are usually present in relation to breast malignancy and implants in otherwise immunocompetent individuals [1, 3, 7]. Patients who are severely immunocompromised can present with fungal infections involving virtually any organ of the body such as lungs, skin, gastrointestinal tract, etc. with the breast being a very rare site of involvement [3, 8, 10]. Until 2013, only 13 cases of fungal infection of breasts were reported in literature [8]. These were reported in patients with diabetes mellitus [4], postoperative status for breast carcinoma [4], acute myeloid leukemia [5], transplantation [6] and breast implants [1, 7]. Few cases of fungal infection of breasts and chest wall are also reported in immunocompetent individuals and also in male breasts [8, 9].

Aspergillus is an opportunistic mold, the virulence of which depends on the biological features of the fungus and the immune status of the host [3]. There are more than 200 recognized *Aspergillus* species. Among them, *A. fumigatus* is the most common form, followed by *A. flavus* and *A. terreus* [3, 10, 12]. *A. fumigatus* and *A. flavus* are also the most common cause of cutaneous manifestation of locally invasive aspergillosis [8]. The production of conidia characterizes the infectious life cycle of *Aspergillus* [3, 8]. These conidia are easily dispersed into the air and when they reach a permissive environment such as the lung of an immunosuppressed host, they germinate and become hyphae, which is the invasive form of *Aspergillus*. The hyphal growth invades the blood vessels, resulting in hemorrhagic necrosis, infarction, and potential dissemination to any other organ in susceptible patients [3, 8, 14]. It most commonly affects the lungs and paranasal sinuses, less frequently, the brain, skin, gastrointestinal tract, heart, or kidney may show extra-pulmonary manifestations [3–5]. Over 90% of patients who develop aspergillosis have at least one of the following factors: cytotoxic chemotherapy, corticosteroid therapy, solid organ or bone marrow transplantation, AIDS or prolonged neutropenia [15].

Our case of culture proven *Aspergillus flavus* was seen in an immunocompromised host with diabetes mellitus and long-term steroid therapy without neutropenia. An additional factor promoting initial colonization may have been indiscriminate use of multiple antibiotics over a two-month period for a conservatively managed humerus fracture. It is postulated that *Aspergillus* may have inoculated the breast wound from the cast that initiated the ulcer from pressure necrosis or possibly during surgical debridements at outside facilities.

The purpose of presenting this case is to highlight fungal infections as one of the rare causes of a non-healing breast wound, other being mycobacteria [16]. The surgeon should have a high index of suspicion for diagnosis [15]. Fungal infections should be suspected in a non-healing breast wound especially in the absence of malignancy, with appropriate wound therapy and negative routine cultures. Smears, tissue cultures, histopathology and special stains for fungi and mycobacterium should be ordered to establish the diagnosis. To the best of our knowledge, this is the only reported case of aspergillosis in a non-healing breast wound from Pakistan.

Recommended treatment for aspergillosis of the breast comprises voriconazole, itraconazole and amphotericin b. Dose adjustment may be necessary with certain inhaled steroids. Surgical excision of partial or entire breast may be necessary as blood vessel involvement can lead to extensive soft tissue necrosis rendering the breast non-salvageable [17,18].

CONCLUSION

Aspergillus can present with extensive soft tissue or breast involvement in immune suppressed individuals and should be considered in patients with a non-healing wound. High index of suspicion is necessary to send appropriate cultures. Infected patients should receive early, aggressive combined medical and surgical therapy.

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Sana Zeeshan – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Syed Faisal Mahmood – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published

Abida K. Sattar – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published

Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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