Localized Cutaneous Hyalohyphomycosis by *Fusarium* spp. Over a Postsurgical Scar: Response to Fluconazole

**Introduction**

Opportunistic infections are caused by pathogens which have tendency to infect host when there is breach in host immunity. *Fusarium* is a ubiquitous saprophytic fungi found in soil. *Fusarium* species including *solani*, *oxysporum*, *verticloides* and *moniliforme* are rare opportunistic mycotic pathogens causing hyalohyphomycosis.[1] In immunocompromised patients, they cause disseminated infections known as fusariosis. However, occasionally even immunocompetent individuals get infected leading to localized skin infections. Our patient had *Fusarium* infection confined to postoperative scar and responded very well to systemic antifungal therapy.

**Case History**

A 75-year-old male presented with discharging sinuses over the coronary artery bypass grafting (CABG) scar for 4 months. Six months back, he underwent CABG surgery with *in-situ* thoracic drain which he removed himself and started dressing on his own. This resulted in the formation of an irregular scar. After 4 weeks, nodules developed along the scar and turned into abscess and sinuses. There was no history of fever, coryza, or cough with expectoration. He was treated with multiple antibacterial drugs without any improvement.

On cutaneous examination, a soft, nontender nodule, an abscess, and a nonfoul smelling discharging sinus arranged linearly at the site of operative scar in midsternal line was observed which was surrounded by diffuse hyperpigmentation [Figure 1]. General and systemic examination were within normal limits.

On investigation, patient had anaemia (hemoglobin, 8.9 g/dl) and raised erythrocyte sedimentation rate (120 mm/h). Other hematological and biochemical investigations were normal, except high triglyceride, cholesterol, and low-density lipoprotein level. Radiological investigations, X-ray chest, abdominopelvic ultrasonography, and computed tomography of the chest were within normal limits. Gram stain and 20% Ziehl–Neelsen stain of pus smear did not show any organisms, whereas 10% potassium hydroxide (KOH) mount revealed acute angled septate hyphae [Figure 2]. Hence, patient was put on fluconazole 3 mg/kg/day therapy. Simultaneously, multiple biopsies from the lesions were performed. Hematoxylin and eosin staining showed pseudoepitheliomatous hyperplasia with suppurative granulomatous infiltrate in the dermis and leukocytoclastic fibrinoid necrosis of superficial capillaries.

**Keywords:** Coronary artery bypass grafting surgery scar, fluconazole, *Fusarium*, hyalohyphomycosis

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Lesions subsided after 3 weeks of fluconazole therapy [Figure 6], without any recurrence during the next 3 months follow-up period.

Discussion

Phaeohyphomycetes and Hyalohyphomycetes are groups of saprophytic fungi known to cause opportunistic infections. Phaeohyphomycetes or dematiaceous fungi have dark-yellow brown septate hyphae whereas Hyalohyphomycetes have colorless hyaline septate fungal hyphae [2]. Hyalohyphomycetes include a variety of species such as *Penicillium*, *Paecilomyces*, *Scopulariopsis*, *Acremonium*, *Fusarium*, *Gliocladium*, *Trichoderma*, *Scedosporium*, *Chrysosporium*, *Sepedonium*, and *Fusarium* species [Figure 5].
**Beauveria.** These are divided according to characteristic colony color, shape, and arrangement of conidia, as shown in Figure 7.[2]

In this case, 10% KOH mount of crush tissue smear showed acute angled septate hyphae, suggestive of fungal species such as *Aspergillus*, *Fusarium*, *Trichophyton*, *Scedosporium*, *Penicillium*, and *Phialophora verrucosa*. Gray-white cottony colonies on SDA and sickle-shaped macroconidia on LCB staining of slide culture confirmed it to be hyalohyphomycosis caused by *Fusarium* species in this case. Culture from tissue remains the gold standard for diagnosis of *Fusarium*, however, more sensitive polymerase chain reaction (PCR) assay and serological tests were not done in this case. *Fusarium* species on gram stain shows gram negative septate hyphae, gram positive microconidium, and macroconidium, however, in this case gram stain was normal. Blood culture was negative which suggested that there was no sustained release of fungal spores into the bloodstream via angioinvasion and adventitious sporulation.

Adventitious sporulation is the presence of fertile cells known as phialides and conidia that arise from each phialide-like reproductive structures within infected tissue.[4] Wolf in 1955 described this phenomenon, and in 1973 Kidd and Wolf described dimorphism incorrectly in a patient with mycotic keratitis.[4]

*Fusarium* species enter through airways or breach in skin due to burns, trauma, and intravenous catheters, and cause localized, focally invasive, or disseminated infections depending on host immunity.[1] Patients with decreased immunity due to neutropenia, corticosteroid therapy, hematologic malignancies, and hematopoietic stem cell transplant (HSCT) recipients are the major risk factors for disseminated fusarium infection.[5] Portal of entry in disseminated fusariosis is respiratory tract, gastrointestinal tract, and cutaneous sites.[6] In disseminated fusariosis, cutaneous lesions can be seen in approximately 85% of patients evolving from painful disseminated erythematous to violaceous, purpuric necrotic, or centrally ulcerated papules or nodules along with myalgia, fever, and respiratory system involvement.[7] Localized skin infection present after skin breakdown as necrotic lesions, cellulitis, abscesses, chronic ulcers, and paronychia secondary to underlying onychomycosis in immunocompetent patients.[1] *Fusarium* species are known to cause septic arthritis, endophthalmitis, osteomyelitis, cystitis and brain abscess, sinusitis, keratitis, onychomycosis, and intertrigo.[6] Index
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The case had only localized cutaneous lesions most probably caused by thoracic drain, which would have served as port of entry of infection. Cutaneous lesions may be observed in early stage of the disease, which gives early clue to diagnosis, and dissemination can be prevented.[5]

In addition, elderly cardiac patients have high levels of low-density lipoproteins, which produce increased reactive oxygen species by polymorphonuclear leukocytes that impairs phagocytosis making them prone to mycotic infections.[7]

Immunocompromised patients generally carry bad prognosis and may have fatal outcome. Voriconazole and lipid-based amphotericin B is generally used as first line antifungal therapy.[8] Posaconazole is used as salvage therapy.[9] Granulocyte monocyte colony stimulating factor (GM-CSF) has been tried in neutropenic patients as adjuvant treatment in disseminated fusariosis.[10] Immunocompetent patients with localized Fusarium infection have treatment options of surgical debridement and antifungal therapy with fluconazole, voriconazole, and posaconazole.

In the index case, the lesions subsided after 3 weeks of fluconazole therapy. Although a previous study observed higher minimum inhibitory concentration values for fluconazole in Fusarium species infection with no in-vitro activity,[11] in vivo response in the index case was seen. Greater efficacy of fluconazole in vivo can be due to high absorption of drug, lower percentage of serum protein binding, prolonged half-life, and high skin concentration compared to plasma concentration.[12]

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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