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

Abstract

Hyalohyphomycosis are opportunistic fungal infections caused by fungi with colorless septate hyphae. *Fusarium* is a hyalohyphomycetes which can cause localized or disseminated infections depending on host immunity. Our patient had an infectious lesion over the coronary artery bypass grafting (CABG) scar which was not responding to antibacterial treatment. Further investigations revealed it to be localized cutaneous *Fusarium* infection. The patient was treated with fluconazole 3 mg/kg/day for 3 weeks and responded very well without any recurrence during the next 3 months follow-up. Thus, this case highlights the effectiveness of fluconazole in uncommon fungal infection.

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

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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*, *verticlloides* 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

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[Figure 3a and b]. However, special staining with Periodic acid-Schiff (PAS) and Grocott's methenamine silver (GMS) stain failed to show any fungal hyphae. Blood culture and tissue culture for bacteria and mycobacteria did not grow any organism. Tissue culture on Sabouraud's dextrose agar (SDA) without cyclohexidine at 25°C showed gray-white cottony colonies with brownish-yellow diffuse reverse pigmentation of the media on the 4th day [Figure 4a and b]. Lactophenol cotton blue (LCB) slide culture mount unveiled septate hyphae with sickle-shaped macroconidia and few microconidia in clusters, suggestive of *Fusarium* species [Figure 5].

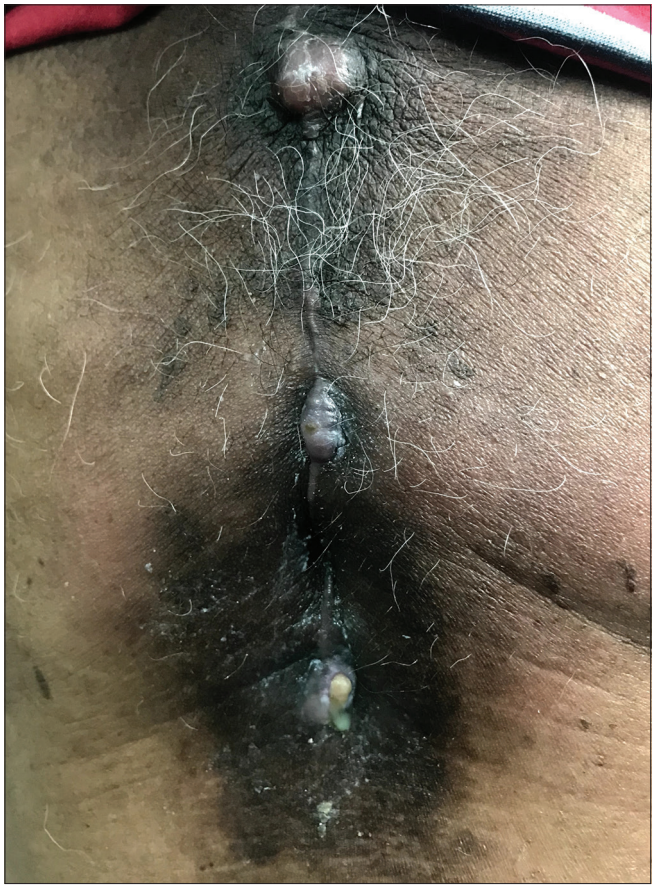

Figure 1: A nodule, an abscess and discharging sinus arranged linearly over CABG scar in midsternal line with surrounding hyperpigmentation

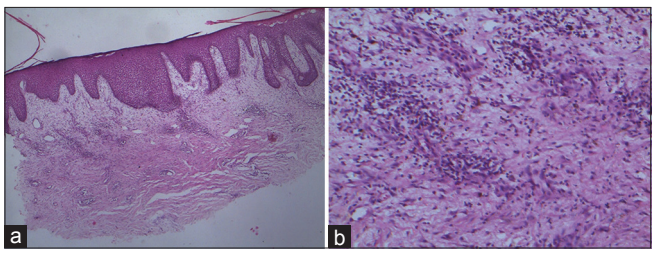

Figure 3: (a) Pesudoepitheliomatous hyperplasia of the epidermis (H and E stain, ×10). (b) Suppurative granulomatous infiltrate in dermis and leukocytoclastic fibrinoid necrosis of superficial capillaries (H and E stain, ×40)

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

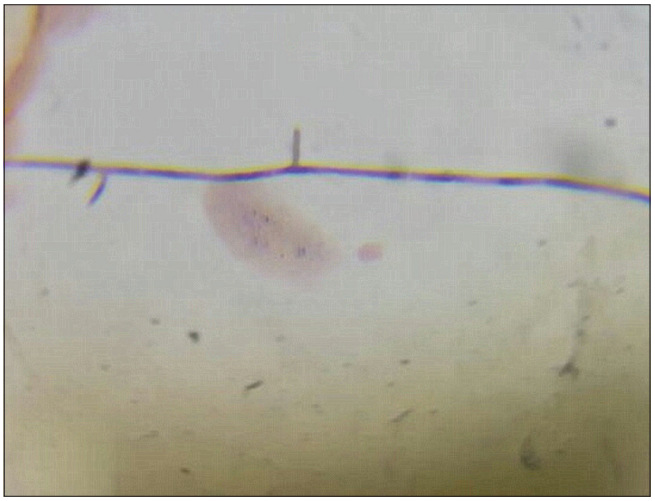

Figure 2: Acute angled septate hyphae (KOH mount, ×40)

Figure 4: Culture on SDA showing (a) gray white fluffy cottony colonies (b) obverse with brownish-yellow diffuse reverse pigmentation

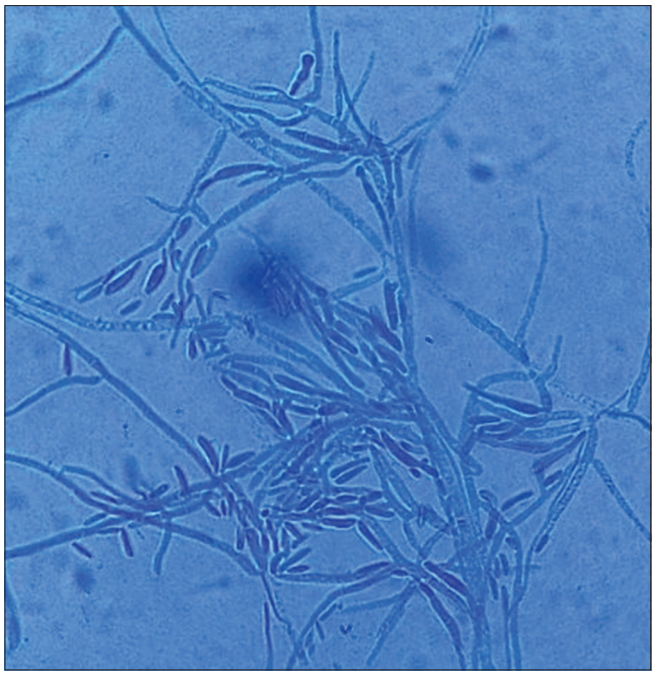

Figure 5: Slide culture smear showing hyaline septate hyphae with sickle shaped macroconidia and few microconidia in cluster (Lactophenol cotton blue stain, ×40)

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*, *Pseudallescheria*, and *Phialophora verrucosa*.[3] 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

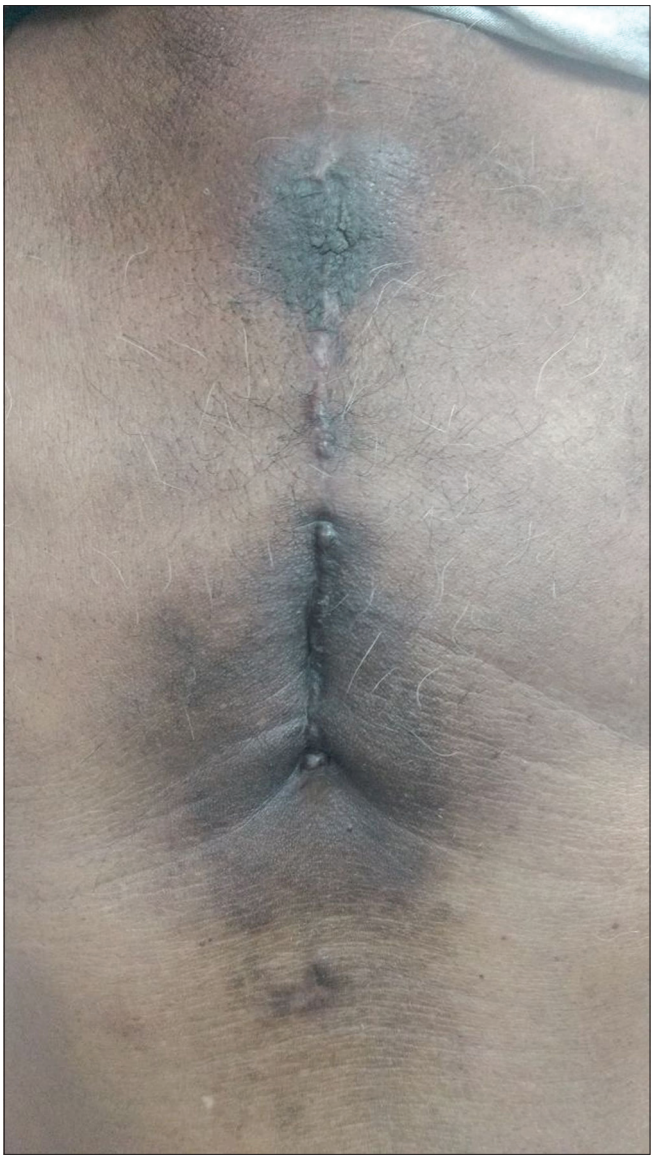

Figure 6: Resolution of lesions after 3 weeks

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

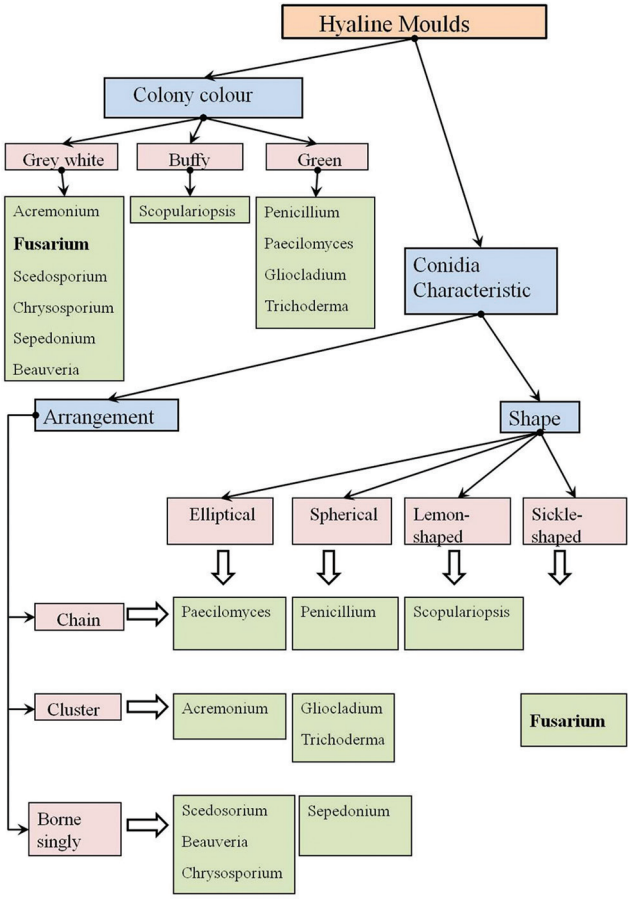

Figure 7: Culture and microscopy characteristic of different hyaline moulds

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.[6] In addition, elderly cardiac patients have high levels of low-density lipoproteins, which produce increased reactive oxygen species by polymorphonulcear 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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