Disseminated Fusariosis in a Bone Marrow Transplant Patient

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ABSTRACT

The authors present a case report involving an immunocompromised patient with fusariosis, an often fatal fungal infection in this group of patients. This mycosis needs to be recognized and treated in the initial phases, although this does not guarantee improvement. (*J Clin Aesthet Dermatol.* 2012;5(12):40–42.)

Fusariosis is the second major cause of fungal infection after Aspergillosis in immunocompromised patients.[1] The fungus of genus Fusarium is present in the environment as a soil, water, and plants saprobe and may occasionally cause infections in humans. The clinical forms of the disease are related to the mode of contamination and the host's immune status and may present as a superficial, locally invasive or disseminated infection.[2] The invasive form of the disease occurs almost only in immunocompromised patients.[3] Therefore, special attention has been given to this micro-organism lately, since the disease in these patients very frequently has a fatal outcome despite the treatment.

CASE REPORT

A 62-year-old man diagnosed with acute myeloid leukemia since 2007 was admitted due to a relapse of the disease and pancytopenia. His condition progressed with febrile neutropenia and severe sepsis. Broad-spectrum antibiotic treatment was started with good response. He was then submitted to allogeneic bone marrow transplant during hospitalization and experienced new peaks of fever. His computed tomography chest scan revealed bilateral pulmonary nodules suggestive of Aspergillosis, and treatment with oral voriconazole was initiated. Erythematous nodules appeared seven days after the transplant and six days after voriconazole was initiated. Some of the erythematous nodules had a purplish central area and appeared on the face, abdomen, and lower and upper limbs (Figures 1, 2, 3). A biopsy was performed on a skin lesion and sent for histopathological and microbiological study. Amphotericin B was administered due to the suspicion of fusariosis. The routine histopathological staining revealed mild inflammatory infiltrate and thrombosis. The special periodic acid-Schiff (PAS, Figure 4) and Grocott (Figure 5) staining techniques demonstrated the presence of fungal tubular forms with acute angle branches within the vessels and interstitium. The histopathological diagnosis of hyaline-hyphomycosis was made. Septate hyaline hyphae and blastosconidia were seen in the direct mycological exam. *Fusarium sp.* (Figure 6) grew in a culture for fungus. The patient had partial improvement of skin lesions, but the pulmonary condition worsened, leading to death due to respiratory failure.

DISCUSSION

Fusarium sp. has been gaining importance recently because it is an emerging pathogen in immunocompromised patients.[1,2] Several species were isolated; those that are most commonly involved in human disease are *Fusarium solani*, *Fusarium oxysporum*, and *Fusarium moniliforme*.[2] The main route of infection is through inhalation of conidia, but can also occur through the skin, where there is a tearing of the skin barrier, and possibly through the mucous

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membranes.[2] *Fusarium sp.* causes a wide spectrum of infection in humans.

The superficial forms, most commonly onychomycosis and keratitis, usually occur in immunocompetent patients often by inoculation of the fungus in the area of infection and have good prognosis. Patients with intense and prolonged neutropenia and/or severe immunodeficiency in T cells, as those with hematological malignancies, bone marrow or solid organ transplant, on chemotherapy, or severely burned, are at high risk of developing an invasive form of infection and dissemination. The other forms can also be observed in immunocompromised patients and should be treated quickly due to the risk of progression to invasive and disseminated forms.[2,4]

In disseminated fusariosis, the skin is affected in more than 70 percent of cases[1,5]; however, multiple organs may be affected, such as the lungs and facial sinuses.[3] The skin lesions may correspond to the area of primary infection or metastatic infection manifestation in disseminated cases.[2] In these cases, lesions tend to be pleomorphic,[4] occurring as multiple erythematous papules or nodules that sometimes have central necrosis and surrounding erythematous halo. These plaques or nodules form target lesions located anywhere on the body, predominantly in the extremities, that rapidly evolve in a few days.[2] Thus, the skin may be an important site for the diagnosis of fusariosis, as shown in the case presented here.

The histopathological examination shows septated hyaline hyphae with typical branching at an acute or 90-degree angle that may invade blood vessels, forming clots and tissue necrosis very similar to *Aspergillus sp.* The confirmation of diagnosis requires the isolation of *Fusarium sp.* through culture. The colonies are cotton wool with variable color, and culture microscopy shows septate hyaline hyphae macroconidia in "banana" shape.[6] The identification of the *Fusarium sp.* is difficult and therefore requires molecular methods.

The disseminated infection by *Fusarium sp.* has a bad prognosis.[7] The treatment in such cases should be initiated as soon as possible in suspected cases of invasive infection due to the severity and high mortality rate associated with this condition. The frequent resistance of these micro-organisms to various antifungal drugs, the weakened immune system of patients, and the small number of studies available make treatment more difficult. In addition to local measures, such as lesion debridement, intravenous antifungal drugs are used and, in some cases, immunotherapy with granulocyte colony-stimulating factor and others.[2] Deoxycholate and liposomal amphotericin B are considered first-line drugs; however, failure rates reaching 70 percent have been reported.[1,2]

Voriconazole has been used as a promising option for the treatment of disseminated fusariosis. There are reports on its use as monotherapy[8] and in combination with amphotericin B[7,9,10] in cases where there was no response to monotherapy with these same agents, but further studies are necessary. On the other hand, it is well established that the improvement of neutropenia may contribute to a better

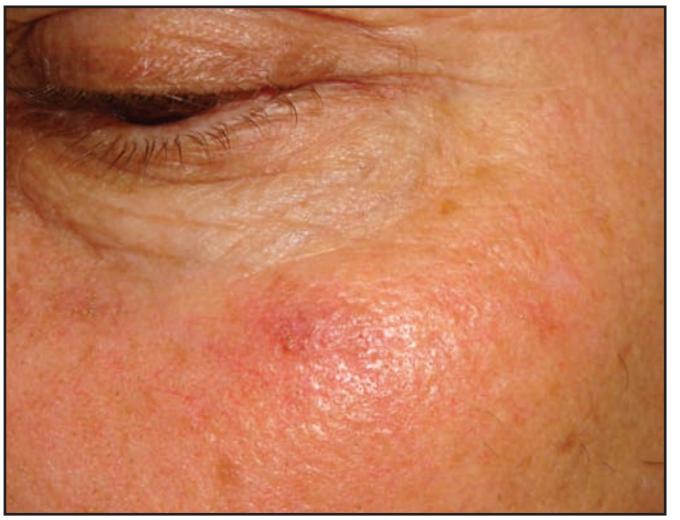

Figure 1. Erythematous nodules on the face

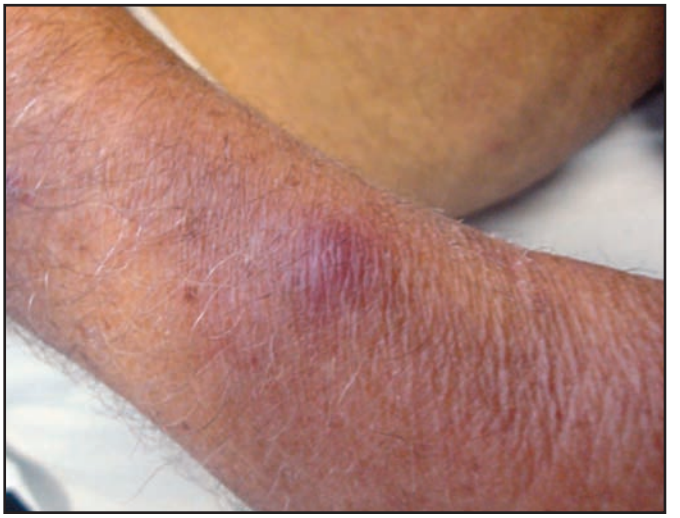

Figure 2. Erythematous nodules on the right forearm

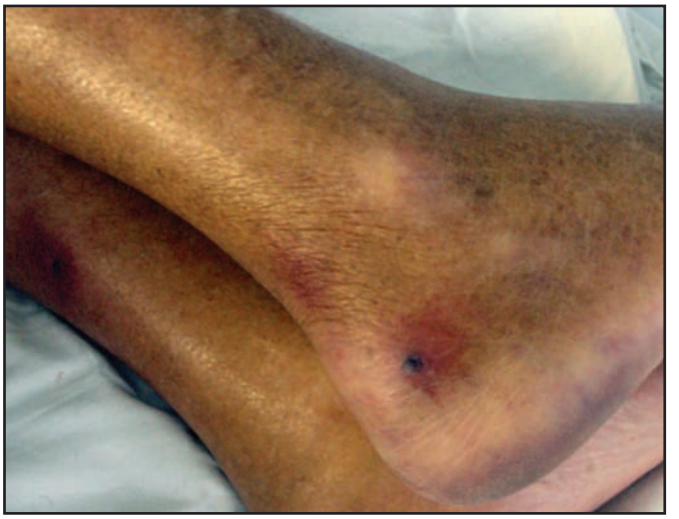

Figure 3. Erythematous lesion on the right ankle

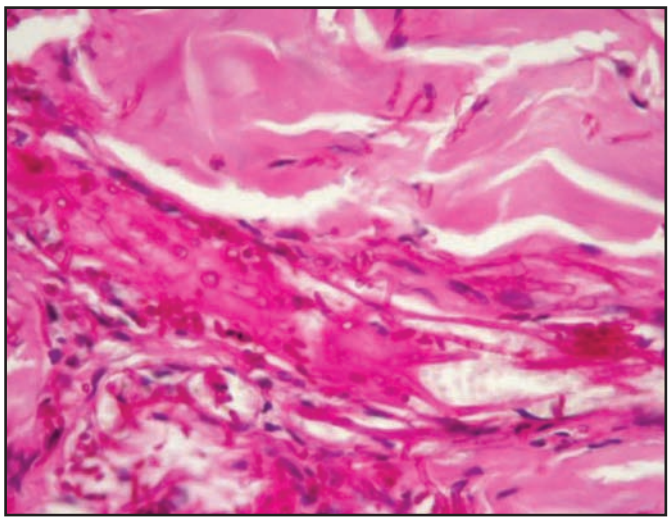

Figure 4. Presence of hyphae in the vessel and the interstitium (PAS 400x)

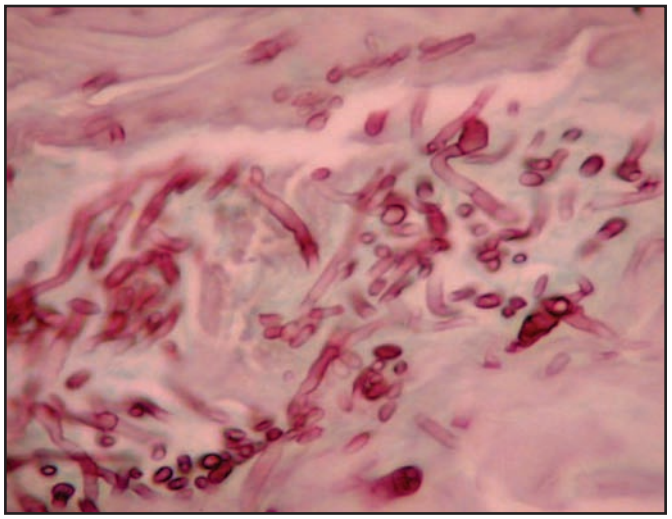

Figure 5. Hyphae branching in acute angle (Grocott 400x)

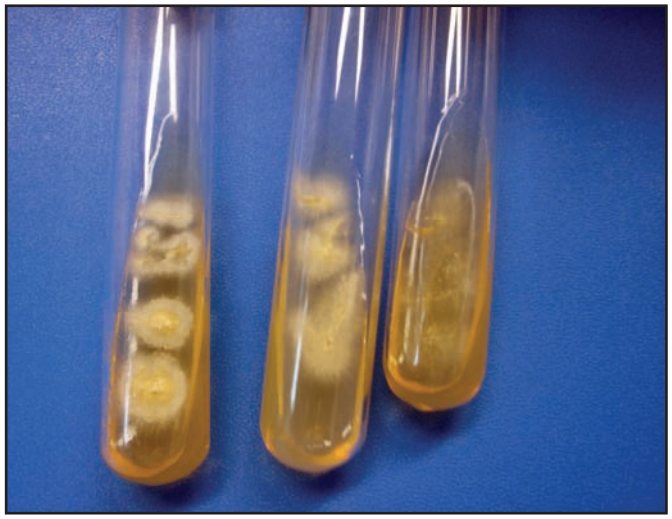

Figure 6. Cultures with *Fusarium sp.* growth (agar yeast extract, agar Sabouraud-dextrose 2%, and agar niger, respectively)

response to the treatment,1 although it does not guarantee the cure.

With the current increase of immunocompromised patients with neutropenia due to the disease itself or to iatrogenic injury by chemotherapy treatments and transplant, it is imperative that dermatologists are aware of the possibility of fusariosis diagnosis.

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