Cutaneous scedosporiosis in an 83-year-old man with chronic hepatitis C

Dear Editors,

An 83-year-old man, who worked as a bone collector in a cemetery, had medical history of chronic hepatitis C. He was admitted to our hospital due to a persistent itchy sensation over his right upper limb after being struck by the branch of a pine tree. On physical examination, there were multiple painful irregular-shaped ulcerations on erythematous plaques with yellowish discharge over the right forearm (Figure 1A). Laboratory investigations revealed a white blood cell count of 7.3 x 10^9/L, hemoglobin 142 g/L, platelet count 109 x 10^9/L, C-reactive protein 21.2 mg/L, and alanine aminotransferase 2.76 g/L. Serum chemistry, such as prothrombin time, serum albumin level, and serum bilirubin level, urinalysis, and serologic evaluations of thyroid and renal functions were all within the normal ranges. Serologic tests for rapid plasma reagin and human immunodeficiency virus were negative. Abdominal sonography showed no obvious evidence of liver cirrhosis but right renal cysts. Pathology of skin biopsy revealed skin tissue with a granulomatous inflammation in the dermis, and clusters of pigmented spores and hyphae in multinucleated giant cells and microabscess formation (Figure 2A and B). Cultures of the wounds over the right arm and right forearm on separate days yielded Scedosporium apiospermum (Figure 1C and D). Slide culture stained with toluidine blue revealed numerous single-celled, ovoid conidia, rounded above with truncate bases. Conidia were borne singly or in small groups on elongate, simple, or branched conidiophores or laterally on hyphae. There were no seeding cleistothecia (ascocarps). The final diagnosis was cutaneous scedosporiosis.

Amphotericin B 50mg daily was prescribed. However, acute renal failure with oliguria developed 4 days after treatment. Antifungal agent was shifted to voriconazole 400 mg daily (8 mg/kg). One week later, his skin lesions improved, leaving only slight erosion over the right arm (Figure 1B). Due to symptoms of gastrointestinal upset that developed, the dosage of voriconazole was decreased to 200 mg daily and continued for another week. Then, icteric sclera developed. His family refused further antifungal treatment owing to his age, persistent dyspepsia, and the potential liver toxicity of the medication. However, recurrence of erosions and ulcerations were noted over the right arm days later. Voriconazole 200 mg daily (4 mg/kg) was reinitiated. Due to the deterioration of hepatic function, voriconazole was then decreased to 75 mg daily. Even under the adjusted dosage of voriconazole use, his skin condition gradually improved, leaving only scaling. During hospitalization, he developed a catheter-related blood stream infection with vancomycin-resistant Enterococcus and Enterobacter faecalis. Finally, the patient died from septic shock even under systemic antibiotics and a total of 11 weeks of voriconazole treatment.

Scedosporium apiospermum is a saprophytic fungus with a global distribution, such as soil and stagnant water, agricultural land, thorny shrubs, and in temperate climates. Scedosporium infections are uncommon, even in immunocompromised individuals. Caia et al. reported that overall incidence of Scedosporiosis was about 0.08% in a 20-year retrospective survey of 8633 patients with newly diagnosed acute leukemia in Italy. From 1995 to 2014, there were only two reported cases of Scedosporium apiospermum infection in Taiwan; one with mycetoma and the other with non-mycetoma at presentation. However, increased frequency and high mortality rates of invasive Scedosporium spp. infections were noted in immunocompromised hosts. In an Australian surveillance study of Scedosporiosis, skin/subcutaneous tissue accounted for 14.5% of the primary sites of infection. The most common skin manifestations are multiple subcutaneous nodules in a sporotrichoid distribution after injuries. Other rare skin manifestations are non-mycetoma-like cutaneous and subcutaneous infections, which present as necrotic ulcer encased by a circumferential area of extensive skin sloughing, violaceous discoloration, and erythema. A similarity in clinical presentation was noted between our patient and that of the previously reported case mentioned above.

Scedosporium apiospermum has been reported to have very high levels of antifungal resistance, most notoriously to amphotericin B. Voriconazole is a compound with low minimal inhibitory concentration values. Micafungin and posaconazole are reported to have moderate activity against the majority strains of Scedosporium. A combination of two antifungal agents with different mechanisms or antifungal treatment used in combination with surgical intervention may be warranted for intractable cases. The synergistic interaction between azoles and terbinafine blocks different steps of the fungal ergosterol biosynthesis pathway. In a case report, surgical debridement and intraleisional injection of voriconazole (a concentration of 3 mg/mL, once weekly for 2 weeks) were used to treat successfully a patient with a hepatic contraindication for voriconazole.

Our patient had impaired liver function and underlying chronic hepatitic C status so azole could only be used sparingly. Extensive surgical debridement might not be appropriate for patients with advanced age. Intraleisional injection of voriconazole may be considered in such patients. In summary, this is the first formally reported case of non-mycetomatous S. apiospermum infection in an immunocompetent patient in Taiwan, who received oral voriconazole but eventually died of a hospital-acquired infection.

Conflicts of interest: The authors declare that they have no financial or nonfinancial conflicts of interest related to the subject matter or materials discussed in this article.
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