Short Report

Multiple Skin Abscesses Caused by *Rhizopus* sp. Infection after *Candida albicans* Infection in an Immunocompromised Patient

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ABSTRACT

A 66-year-old woman with diabetes who was treated with prednisolone (15 mg/day) for autoimmune hepatitis developed multiple erythematous nodules with retention of purulent fluid on her lower right limb. *Candida albicans* was cultured from the nodules. She was started on oral fluconazole, and the lesions subsided. However, multiple dark-red abscesses and indurations newly appeared on the left crus. Histopathological examination showed numerous branched hyphae, and tissue culture yielded a *Rhizopus microsporus*-related fungus. She was treated with liposomal amphotericin B combined with drainage and debridement. However, she died because of poor control of the infection and hepatic disorder.

Key words: abscess, hepatic disorder, immunocompromised host, *Rhizopus microsporus*

Introduction

Immunosuppression due to long-term steroid treatment often results in opportunistic fungal infections in cutaneous and subcutaneous tissues. Although the prevention and treatment of candidiasis and aspergillosis have improved, breakthrough mucormycosis is increasingly reported. This study describes a patient with autoimmune hepatitis who developed multiple abscesses in both lower limbs during treatment with prednisolone and was found to be infected with *Candida albicans* and a *Rhizopus microsporus*-related fungus.

Case report

A 66-year-old woman with diabetes, being treated with 15 mg/day prednisolone for autoimmune hepatitis, developed painful redness and swelling on her right lower limb several months before initial presentation. Upon admission, multiple erythematous sites with fluid were observed on her right crus, along with several 1 to 2 cm bright-red nodules on her right limb, especially from the thigh to the knee joint periphery (Fig. 1). Her white blood cell (WBC) count was 22,200/µl and her C-reactive protein (CRP) concentration was 4.3 mg/dl. Liver and myogenic enzymes were almost normal, and her hemoglobin A1c concentration was 8.9%. Because her β-D-glucan concentration on day 8 was high (1,320 pg/ml), whole-body computed tomography was performed. No infectious lesions were detected elsewhere.

An abscess from the crus and tissue samples from her right femoral nodule were cultured on sheep blood agar, Drigalski medium, and CHROMagar Candida medium at 35°C for 48 h. Lustrous white colonies developed on sheep blood agar, whereas green colonies emerged on the CHROMagar Candida medium. These colonies were identified as *C. albicans*. Biopsy of the thigh induration (Fig. 2) revealed abscesses in
Fig. 1. Photographs of the lower right limb of our patient at first admission, showing many 1 to 2 cm bright red nodules. 
(a) Photograph of the right thigh, showing multiple hard erythemic sites, especially from the thigh to the knee joint periphery. 
(b) Photograph of the right crus, showing erythemic sites with fluid.

Fig. 2. Pathological characterization of femoral swelling in the patient on day 1 of first admission.
(a) H&E staining, showing an abscess in all layers of the dermis. 
(b) Grocott staining, showing yeast-like fungi, stained black, in the abscess. 
(c) Periodic acid-Schiff staining, showing yeast-like fungi, stained red, in the abscess.
the dermis and subcutis, and Periodic acid-Schiff and Grocott staining showed the presence of yeast-like fungi.

She was started on 100 mg/day oral fluconazole, which improved her general health and skin ulcers, allowing her transfer back to the referring hospital on day 15. Eighteen days after transfer, however, fresh erythema developed on her left lower limb. Within 2 days, the erythema worsened dramatically, accompanied by severe pain, and an incision was made. Her systemic condition also deteriorated, and she was readmitted to our department 26 days after her previous transfer.

Examination showed that the right crus ulcer had decreased in size, and epithelialization had progressed; but multiple dark-red abscesses and indurations had appeared on her left crus (Fig. 3). Liver enzyme concentrations had increased, especially the concentrations of alkaline phosphatase (1,192 IU/l) and γ-glutamyl transpeptidase (540 IU/l). Her CRP concentration was 7.6 mg/dl, her blood sugar concentration was 466 mg/dl, and her β-D-glucan concentration was 2,380 pg/ml, but she was negative for Candida antigen.

Pus samples from the abscess on the lower left crus were cultured and rapidly growing fungal colonies were observed. Slide cultures of one fungal strain (KMU 9525) revealed wide hyphae without bulkheads, sporangia, or circular sporangia. Rhizopus species were suspected because of the presence of opposite rhizoids (Fig. 4). Nucleotide sequences of the internal transcribed spacer regions of the ribosomal RNA (rDNA) gene and the D1-D2 region of the large subunit of rDNA showed that the strain was consistent with R. microsporus. Examination of debrided tissue showed that most of the adipose tissue was necrotic, accompanied by numerous branched hyphae (Fig. 5a). Fungal invasion was observed in blood vessel walls (Fig. 5b).

The abscess was treated by discharging abundant pus and debridement, as appropriate, resulting in a gradual decrease in inflammation. After the diagnosis of Rhizopus mucormycosis, the patient was treated with 200 mg/day liposomal amphotericin B. On day 10, her lower left limb was debrided under general anesthesia.

Although her condition improved temporarily, blood tests showed a gradual increase in liver enzymes and a gradual deterioration of her biliary tree system. Beginning on day 32, disseminated intravascular coagulation, abdominal distension, wound aggravation, and dyspnea were observed. The patient died on day 43.

**Discussion**

Treatments administered to this patient would likely have been effective against skin candidiasis alone, but were insufficient in treating secondary mucormycosis, and thus her overall condition worsened. The failure to promptly treat mucormycosis could have been due to the inability of blood tests alone to screen for this condition. Findings in this patient confirmed that secondary infections such as mucormycosis are likely to develop. Therefore, efforts must be made to detect infections from skin examinations and to better understand the pathogenesis of mucormycosis.

Subcutaneous candidiasis is rare and classified as a consequence of visceral or primary deep cutaneous
Secondary candidiasis results from candidemia, causing skin lesions that are sudden-onset, painless pustules on erythemas in any area of the body. These lesions develop from small pustules into 2 to 3 cm nodular lesions, with their centers undergoing necrosis. In contrast, primary candidiasis causes isolated nodules or abscesses.

Approximately 19% of patients with mucormycosis develop this condition in the skin, and 39% of patients with sinus mucormycosis show rapid development of facial skin necrosis. The lesions may progress rapidly into reddish purple, indurated plaques, followed by necrosis and eschar formation with pain due to angioinvasion by the organisms.

Our patient initially presented with small nodules in the right lower limb, followed by larger indurations in the left lower limb. Although abscesses in patients with candidiasis are bright red in color, abscesses in patients with mucormycosis...
cosis are dark red in color, likely because blood flow is impaired by mucor angioinvasion. Monitoring of color may therefore be useful for the early detection of fungal infections. Few reports to date have described patients with both skin-related candidiasis and mucormycosis. Greater understanding of the pathogenesis of mucormycosis requires monitoring of larger numbers of patients, detailed assessments of skin eruptions, and more accurate differentiation of mucormycosis from skin eruptions.

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Conflicts of interest

None.

References