Cutaneous mucormycosis arising in the skin folds of immunocompromised patients: A case series

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INTRODUCTION

Mucormycosis is a fungal infection associated with high mortality in immunocompromised patients.[1] Early diagnosis results in improved patient outcomes; however, there is often a delay in confirming mucormycosis infections.[2] While rhino-orbital-cerebral mucormycosis is the most common clinical presentation, cutaneous mucormycosis is known to occur in susceptible populations and is characterized by painful lesions that can progress to tissue necrosis.[3] Skin trauma is a key predisposing factor for infection in prior reports of health care associated cutaneous mucormycosis in immunocompromised patients.[3,4] However, few reports exist of mucormycosis infections at locations not associated with trauma. Here we report 5 immunocompromised patients with a prolonged hospital course who developed cutaneous mucormycosis in intertriginous skin regions without clear predisposing trauma. These findings highlight the importance of routine skin examination and broadening the differential diagnosis of lesions in skin folds beyond common diagnoses such as candidiasis and cellulitis, especially in immunocompromised patients.

METHODS

A retrospective chart review of 5 patients with cutaneous mucormycosis within intertriginous anatomic regions from 2014 to 2021 was performed. These patients developed unresolving skin lesions for which dermatology was consulted for evaluation, diagnosis, and management. All patients underwent skin biopsy, histologic examination, and fungal culture to confirm mucormycosis infection. In all cases there were no prior documented skin traumas or wounds at the site of infection.

CASE SERIES

Case 1

A 63-year-old woman with diffuse large B-cell lymphoma was hospitalized for treatment with chimeric antigen receptor T-cell therapy. Her hospital course was complicated by cytokine release syndrome, posterior reversible encephalopathy syndrome, and pancytopenia requiring allogeneic stem cell transplantation. Her antifungal prophylaxis consisted of intravenous micafungin followed by oral posaconazole. The patient had been hospitalized for approximately 3 months prior to developing a painful and pruritic rash under her left breast (Fig 1, *A*). The rash was initially believed to be intertrigo and failed to improve with topical ketoconazole treatment for 5 days at which time dermatology was consulted. Skin biopsy, histologic examination with Periodic acid-Schiff stain, and fungal culture confirmed mucormycosis infection. The patient was subsequently treated with 5 mg/kg of

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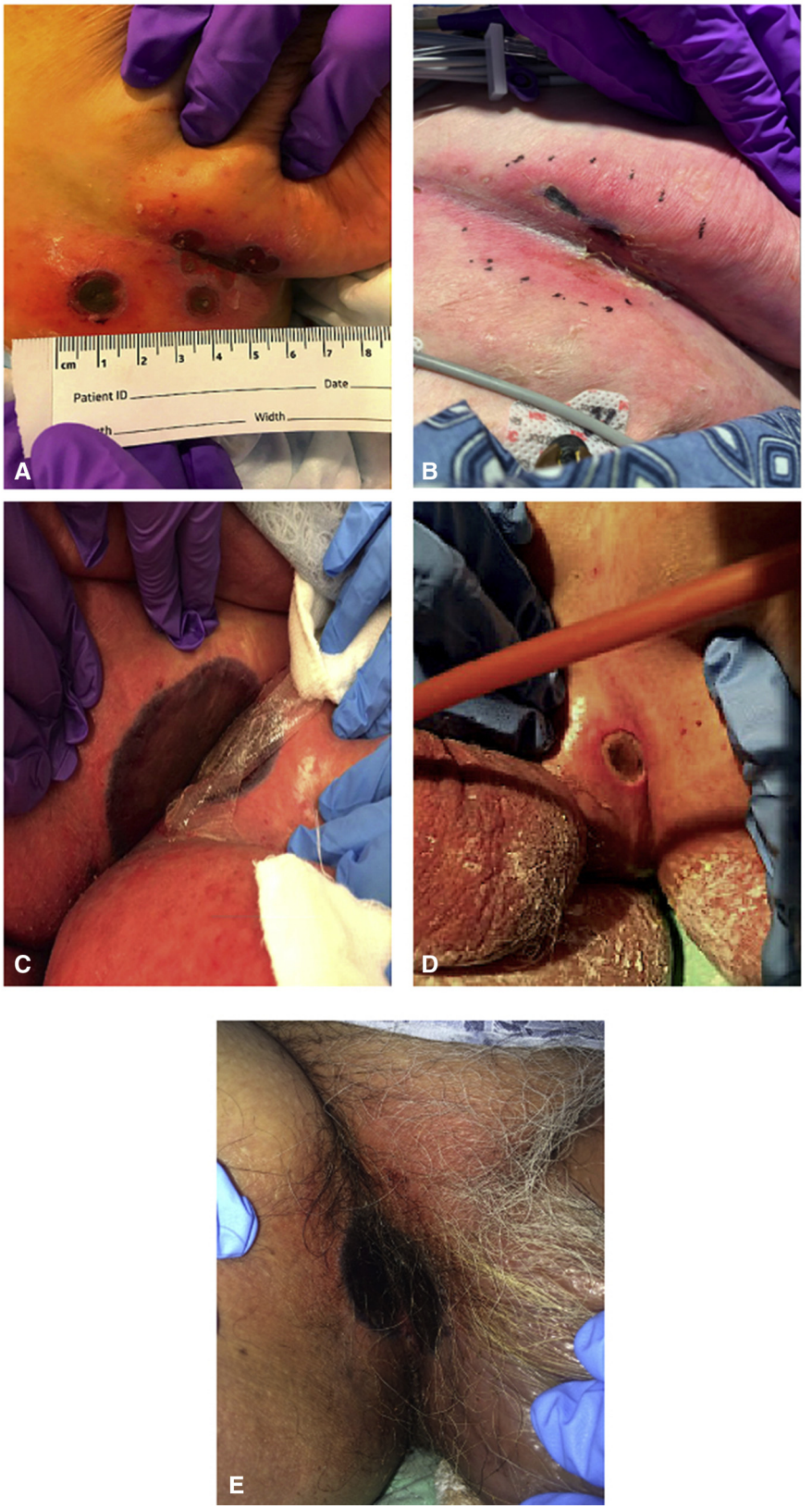

Fig 1. Clinical presentation of intertriginous cutaneous mucormycosis. **A**, Erosions and eschars with indurated, erythematous bases and scalloped borders in the left inframammary area. **B**, Erythematous indurated plaque with central necrosis in the left inframammary area. **C**,

intravenous amphotericin B, dosed at 250 mg daily for a total dosage of 6.25 g over 25 days and surgical debridement. The patient tolerated amphotericin B treatment maintaining stable kidney function within normal reference range including serum creatinine, glomerular filtration rate, electrolyte levels, and liver function tests. She expired within 1 month due to refractory mucormycosis infection and concomitant *Mycoplasma pneumonia*.

Case 2

A 67-year-old woman with a history of breast cancer and interstitial lung disease was hospitalized for hypoxic respiratory failure, for which she had received a bilateral lung transplant but remained with persistent respiratory failure. Her antifungal prophylaxis consisted of oral voriconazole. The patient had been hospitalized for 5 months when she developed a rash under her left breast, which failed to improve with topical nystatin and intravenous antibiotic treatment for one week (Fig 1, *B*). Skin biopsy and fungal culture confirmed mucormycosis infection and the patient was treated with 5 mg/kg daily intravenous amphotericin B for a total of 5.2 g over 13 days and posaconazole and surgical debridement. The patient tolerated amphotericin B therapy with no major signs of nephrotoxicity or hepatotoxicity. She expired within 2 weeks due to refractory mucormycosis infection.

Case 3

A 72-year-old woman with a history of acute myelogenous leukemia status post chemotherapy with cytarabine and lenalidomide was hospitalized for allogenic peripheral blood stem cell transplantation. Her hospitalization was complicated by cytokine storm and vancomycin-resistant *Enterococcus* bacteremia. Her antifungal prophylaxis consisted of oral micafungin and fluconazole. The patient had been hospitalized for 3 weeks prior to developing a painful, purple lesion in her groin which failed to improve with skin fold drying and application of a commercial moisture-wicking antimicrobial fabric for 3 days (Fig 1, *C*). A skin biopsy of the groin and fungal culture confirmed mucormycosis infection. She was initiated on 5 mg/kg of daily intravenous amphotericin B and shortly expired 4 days later due to mucormycosis infection and sepsis from vancomycin-resistant *Enterococcus*.

Case 4

A 19-year-old man with recurrent acute lymphocytic leukemia status after bone marrow transplant was hospitalized for pneumomediastium and spontaneous bacterial peritonitis. His antifungal prophylaxis consisted of oral micafungin followed by fluconazole. The patient had been hospitalized for 1 month prior to developing a new left groin lesion (Fig 1, *D*), which failed to improve with nystatin powder for 3 days. A skin biopsy of the groin and fungal culture confirmed mucormycosis infection. The patient was initially treated with 5 mg/kg of daily intravenous amphotericin B for a total of 11.25 g over 25 days and maintained stable kidney and liver function tests throughout the treatment course. He also received oral posaconazole and underwent surgical debridement. The patient remained hospitalized for an additional 3 months for mucormycosis infection, pneumomediastium, and abdominal hemorrhage. He was discharged on isavuconazole, on which he remained for 1 year, which resolved his mucormycosis infection. The patient was alive at his recent 6-year follow up.

Case 5

A 32-year-old man with no past medical history was admitted to the neurologic intensive care unit for new onset refractory status epilepticus and concern for autoimmune encephalopathy. He was stabilized in a medically induced coma and his treatment course included methylprednisolone, cyclophosphamide, anakinra, and tocilizumab. The patient had been hospitalized and receiving immunosuppression treatment for 5 weeks when he developed new lesions on the groin and foot (Fig 1, *E*). Skin biopsy of both affected sites and fungal culture confirmed disseminated mucormycosis infection. He was initiated on 650 mg of daily intravenous amphotericin B for approximately 1 week for a total dose of 4.55 g and maintained stable kidney and liver function tests before expiring from disseminated mucormycosis. An autopsy confirmed disseminated mucormycosis infection and demonstrated immune mediated encephalitis as the etiology for his new onset refractory status epilepticus.

DISCUSSION

This report describes 5 immunocompromised patients with prolonged hospitalization who developed intertriginous cutaneous mucormycosis. All

Well-demarcated purple plaque with prominent border. **D**, Well-demarcated ulcer with a pink erythematous rim and brown fibrinous central debris on the left inguinal crease. **E**, Well-demarcated violaceous, indurated eschar of the right inguinal crease.

patients in the series were immunocompromised and included 3 patients with hematologic malignancy receiving chemotherapy, 1 solid organ transplant recipient, and 1 patient with a critical autoimmune condition. In addition, a sixth patient with similar clinical presentation who developed mucormycosis in the left axilla during prolonged hospitalization status after heart transplantation has previously been reported from our inpatient service.[5] The patients were susceptible to opportunistic infection from *Mucorales* fungi, which are commonly encountered in the environment, including on hospital linen.[4,6] Surgery, catheterization, and adhesive tape are potential forms of iatrogenic skin trauma that can promote inoculation.[4] All patients presented herein lacked documented trauma to their site of intertriginous mucormycosis infection. Intertrigo is common among bedridden patients; friction and moisture can lead to maceration disrupting the epidermal barrier and presumably serve as a portal of entry for *Mucorales* fungal spores. Common sites of intertrigo include the skin folds of the inguinal, axillary, and inframammary areas,[7] as seen in this cohort. Four patients were thought to have candidal intertrigo before their diagnosis of mucormycosis was made. Clues to cutaneous mucormycosis infection included ulceration, signs of inflammation, and induration.

All but 1 patient expired due to complications of mucormycosis infection. Delaying amphotericin B therapy and surgical intervention significantly increases mucormycosis-associated mortality, emphasizing the importance of early diagnosis.[2,8] Given its low incidence, the initial differential diagnosis for the skin findings did not include mucormycosis for all patients as initial treatments included oral fluconazole and topical nystatin before the correct diagnosis was confirmed via skin biopsy and fungal culture. *Mucorales* species are commonly resistant to most azoles, allylamines, and echinocandins. Inception or persistence of intertriginous lesions in the setting of typical antifungal prophylaxis agents should raise suspicion for mucormycosis, even without predisposing skin trauma as in this cohort.[9] Interestingly, voriconazole prophylaxis in immunocompromised patients has also been identified as a risk factor for mucormycosis infection.[10,11]

This series demonstrates that intertriginous skin lesions in immunocompromised patients should prompt concern for cutaneous mucormycosis. Measures to minimize moisture within skin folds such as application of drying powders or cloth can prevent the development of intertrigo. Further research is needed to determine effective strategies for prevention and management of cutaneous mucormycosis given the significant associated morbidity and mortality.

Conflicts of interest

None disclosed.

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