Cutaneous Zygomycosis Caused by Saksenaea vasiformis in a Diabetic Patient

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A 49-year-old woman with diabetes mellitus rapidly developed necrotizing cellulitis with fat necrosis and vasculitis after minor trauma to the right arm. Zygomycosis was diagnosed histologically. The lesion responded to aggressive debridement, amphotericin B, and normalization of blood glucose. Cultures yielded structures characteristic of Saksenaea vasiformis only after transfer to saline agar.

Genera of the order Mucorales are justly feared as causes of rhinocerebral zygomycosis, but they have also been isolated from other organs including skin, where they may cause progressive and potentially fatal disease. Risk factors associated with primary cutaneous zygomycosis include burns and other skin trauma, immunosuppressive therapy, acidosis, and diabetes (5). Although the most common isolates are Rhizopus spp., Saksenaea vasiformis has been isolated from the tissues of 16 patients with cutaneous zygomycosis (2, 4, 9). S. vasiformis was first isolated from Indian soil (7), and most infections have been associated with soil contamination of traumatized skin in immunocompetent individuals. None of the reported patients were diabetic. We describe a patient with cutaneous zygomycosis caused by S. vasiformis in the setting of uncontrolled diabetes.

A 49-year-old woman with hypothyroidism, a 10-year history of insulin-dependent diabetes mellitus, and asthma that did not require corticosteroids was admitted to a local hospital on 13 June 1993 with a right upper arm lesion of 4 days’ duration. Progressive erythema and tenderness that followed a possible arthropod bite to the dorsal upper arm failed to respond to cephalaxin prescribed on 11 June. There were 1 cm of violaceous discoloration and 5 cm of erythema over the triceps area at admission. Blood glucose was 479 mg/dl, and serum bicarbonate was 23 mEq/liter. She was treated with ceftriaxone, but the lesion extended and ticarcillin-clavulanate was added on 15 June. By 17 June, a draining ulcer had developed and a portion of tissue (16 by 11 cm) with a 7.5-cm ulceration was surgically debrided. Hyphae were observed in the KOH preparation, and histologic examination revealed acute suppurative cellulitis with extensive ulceration and superficial and deep mycosis suggestive of a zygomycete. Although hyphae were not observed in tissue debrided on 21 June, they were found again in specimens obtained on 23 June. Three fungal cultures were sterile after 4 weeks of culture, but the fourth yielded a rapidly growing zygomycete without sporangia.

On 23 June, the patient was transferred to University of California, San Diego Medical Center. Glycosylated hemoglobin was 11.3% (reference range, 3.8 to 6.3%). Treatment with cefazolin, ceftazidime, and amphotericin B was begun. On 25 June, necrosis of wound edges was apparent. Histologic preparations of debrided tissue revealed broad, nonseptate, ribbon-like hyphae in areas of fat necrosis. Mild to severe transmural vasculitis with destruction of vessel walls was evident. Hyphae were not detected within vessel walls, although fibrin thrombi were seen within several small vessels.

The wound was examined in the operating room and pulse lavage was performed at 24- to 48-h intervals subsequently. No signs of progressive infection were observed. Cefazolin and ceftazidime treatments were discontinued and primaxin/cilastatin treatment was begun on 27 June. Although the hospital course was complicated by persistent nausea and vomiting necessitating hyperalimentation and intravenous insulin to control fluctuations in blood glucose, the wound slowly developed a base of granulation tissue. Hyphal elements were not found in tissue debrided on 2 July. Primaxin/cilastatin treatment was discontinued on 11 July. On 12 July, amphotericin B treatment was discontinued after a cumulative dose of 1,096 mg. A split thickness graft was applied to the wound on 22 July, and the patient was discharged to home 1 week later.

Three sets of blood cultures drawn at admission were sterile after 12 days of incubation. Bacteriologic cultures of tissue debrided on 26 June were sterile, but minced tissue processed in a Stomacher (Tekmar, Cincinnati, Ohio) and cultured on Sabouraud agar at room temperature produced abundant nonseptate, aerial, hyaline hyphae by 9 days of culture. No sporangia were found. In an attempt to promote sporulation, we transferred blocks of potato dextrose agar with hyphal growth to petri plates containing distilled water and yeast extract according to the procedure of Kaufman et al. (3). Plates were incubated at room temperature under ambient lighting, but sporulation was not observed. A small amount of mycelium was then transferred to a plate of 1.5% agar in saline (6). After 8 weeks of incubation, distinctive vasiform sporangia were identified (Fig. 1).

As described above, surgical debridement of an arm lesion in a 49-year-old diabetic woman revealed evidence of cutaneous zygomycosis and fungal cultures yielded S. vasiformis. The infection was controlled with surgical debridement, amphotericin B, and normalization of blood glucose. Although disease due to S. vasiformis is strongly associated with soil contamination of traumatic wounds, this patient suffered minimal trauma and soil contamination of the wound was not recognized. Hyperglycemia may have contributed to establishment and progression of disease, as recognized previously in patients with cutaneous zygomycosis caused by other members of the order Mucorales. Envenomation by an unidentified arthropod could have contributed to vasculitis and tissue infarction. On
the other hand, invasive hyphae were found in most areas of tissue pathology, and thrombosis, infarction, and necrosis are common manifestations of cutaneous zygomycosis.

Microbiologic identification of agents of zygomycosis is obtained in less than 50% of histologically diagnosed infections (8). Culture may not be requested if the diagnosis is not suspected, and microbiologically diagnostic structures may not be detected in histologic specimens. Certain methods of processing, such as use of a tissue grinder, may damage the coenocytic mycelium. Isolates may be discarded as contaminants, fail to grow on subculture, or fail to sporulate. Only two of five tissue specimens from this patient yielded a zygomycete, and sporangia were not detected in either primary culture. Sporulation was not observed until 8 weeks after the initial subculture onto saline agar, but sporangia were identified within 10 days after repeated subcultures. Although the use of saline agar to induce sporulation has not been reported previously, the technique is similar to that of Ellis and Ajello (1), wherein hyphal growth is transferred to plates of 1% agar in distilled water. Subcultures of this particular isolate of S. vasiformis consistently sporulated earlier and produced more abundant sporangia on saline agar than they did on 1% agar in distilled water. As multiple methods of inducing sporulation of S. vasiformis have met with variable degrees of success, when a zygomycete is isolated from tissue in a patient with histologically documented disease, persistent attempts to induce sporulation are appropriate.

REFERENCES