

## CUTANEOUS ZYGOMYCOSIS DUE TO *SAKSENAEA VASIFORMIS*: CASE REPORT AND LITERATURE REVIEW

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Zygomycosis is usually an acute fulminant infection of the immunocompromised patient, caused by fungi of the class Zygomycetes, order Mucorales.<sup>1</sup> The most frequently encountered agent of human zygomycosis is *Rhizopus arrhizus*, but many other agents have been reported to cause human infection.<sup>1,2</sup>

Different forms of zygomycosis have been recognized. These include rhinocerebral, pulmonary, abdominal-pelvic, cutaneous, disseminated and other miscellaneous forms.<sup>1</sup> *Saksenaea vasiformis* is the only known species of the genus *Saksenaea* which belongs to class Zygomycete.<sup>1</sup> It was first isolated and described by Saksena in 1953.<sup>3</sup> It is characterized by the production of flask-shaped sporangia, and has been isolated from soil in many countries.

The first human infection due to *S. vasiformis* was described by Ajello et al. in 1976.<sup>4,5</sup> Since then, 19 cases have been reported in the literature (Table 1). In this report, we describe a case of cutaneous zygomycosis caused by *S. vasiformis*, which to the best of the author's knowledge, is the first reported case from Saudi Arabia.

### Case Report

A 65-year-old Saudi male with no significant past medical history presented to the Infectious Diseases Clinic at King Khalid University Hospital in June 1994, complaining of painless nodules in the lateral aspect of the right forearm, which had persisted for about eight months. According to the patient, it started as a small nodule, gradually increasing in size to about 1-2 cm before rupturing and discharging a whitish purulent material. It eventually healed, but a new one appeared near the old site. This process had continued over the previous eight months. The patient had been seen in another hospital and given several courses of antibiotics, but he did not notice any change in his condition.

There was no history of trauma to the site, but the patient had had a palm tree thorn prick in the right hand,

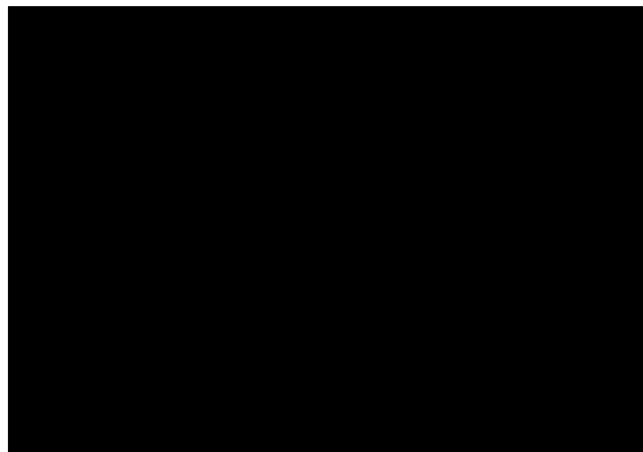


FIGURE 1. Multiple nodules at ulcer side of right forearm.

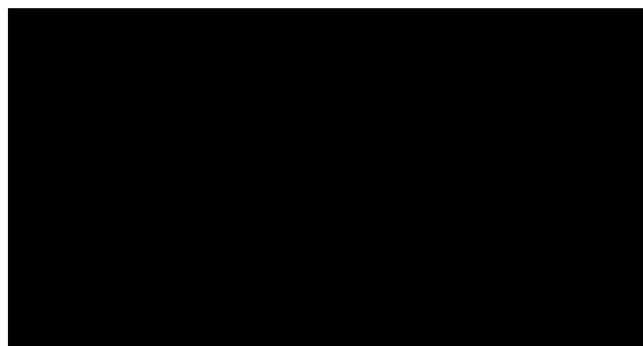


FIGURE 2. Flask-shaped sporangium and nonseptate hyphae characteristic of *S. vasiformis* grown on SDA lactophenol cotton blue mount.

about 5 cm distal to the site of the lesions, about two months prior to the development of these lesions. No history of diabetes mellitus, hypertension or use of steroids was given.

On examination, the patient was well built and afebrile. There was no lymphadenopathy. There were multiple, firm, non-tender, red nodules on the ulnar surface of the right forearm, the largest of which was about 2 cm in size, with multiple small satellite nodules. Scars of old healed lesions were evident (Figure 1). Complete blood count, sedimentation rate, random blood sugar, urea, creatinine and liver enzymes were all normal. Skin-punch biopsy was taken for histopathological examination and fungal

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TABLE 1. Characteristics of patients with primary cutaneous zygomycosis due to *Saksanaea vasiformis*

Age (yrs) /sex	Predisposing factor	Type/site of infection	Treatment	Outcome
19/M <sup>5</sup>	Car accident; severe head trauma	Wound and orbital	Debridement + AmB	Cured
69/F <sup>6</sup>	Preleukemic syndrome; chemotherapy	Disseminated	None	Died
25/M <sup>7</sup>	Severe head injury; arterial line	Inflammation and extensive necrosis at the arterial line site	Removal of the catheter and debridement	Died due to other cause
14/M <sup>8</sup>	None	Multiple necrotic lesions on the legs, scalp and cheek	None	Died
26/F <sup>9</sup>	Intramuscular injection	Massive necrotizing infection of the right gluteal region	Debridement + AmB	Died
60/F <sup>10,16</sup>	Carcinoma of the bladder	Erythematous macule progressing to necrotic ulcer below right knee	Debridement + AmB, followed by amputation	Died due to other cause
17/M <sup>10,16</sup>	No data	No data	No data	No data
25/M <sup>10,16</sup>	Tattoo forearm	Ulcerated erythematous plaque	AmB	Cured
72/M <sup>11</sup>	Comatosed due to intracerebral hemorrhage	Irregular, necrotic ulcer on the scalp	Debridement + AmB and skin graft	Cured
24/M <sup>12</sup>	Severe crash injury of the right leg	Large soft tissue defect covered with filamentous fungus + osteomyelitis	Amputation when repeated debridement and AmB failed	Cured
34/F <sup>13</sup>	None	Swelling of the cheek	Debridement	Cured
55/F <sup>14</sup>	Compound fracture of the left leg	Inflamed, gangrenous wound with white fibers at the wound edges	Amputation when repeated debridement and AmB failed	Cured
71/M <sup>15</sup>	None	Right orbital cellulitis, sinusitis extension to the brain	AmB + repeated debridement	Died
29/M <sup>16</sup>	Crash injury of the left foot	Painful swelling of the left foot with discharging sinuses	Debridement, amputation of forefoot, skin graft +KI	Cured
25/M <sup>17</sup>	Severe burns	Yellowish, cheesy material on burn site, left forearm	Debridement + AmB	Cured
11/M <sup>18</sup>	Beta-thalassemia splenectomy fracture, both legs	Painful swelling, left calf	Debridement + AmB and skin graft	Cured
49/F <sup>19</sup>	Diabetes mellitus; arthropod bite	Violaceous nodule surrounded by erythema, right upper arm	Debridement, skin graft + AmB	Cured
79/M <sup>20</sup>	Major trauma, resection of gangrenous bowel	Multiple wound infection with gangrenous tissue	Serial debridement of the wounds; skin graft + antibiotic + AmB	Cured
70/M <sup>20</sup>	Diabetes mellitus; transvesical prostatectomy	Surgical wound infection with blackish discoloration at the margins	Debridement	Died
65/M (PR)	None (thorn prick?)	Painless, subcutaneous nodules, discharging cheesy material in right forearm	Cautery by traditional medicine practitioner	Cured

AmB=amphotericin B; KI=potassium iodide; PR=present report.

culture. After a few days, a mold consistent with zygomycete grew. Because of the possibility of contamination, a subcutaneous biopsy was done six weeks later, which confirmed the diagnosis of *Saksanaea vasiformis* subcutaneous infection.

While we were waiting to confirm the diagnosis, the patient went to a traditional medicine practitioner who performed cautery on the lesions. Two cauteries were performed by heated iron bar, one just proximal, and another just distal to the lesions. One month later, both the cautery marks and the nodules were completely healed, leaving only hyperpigmented areas and minimal scarring. The patient was followed up for two years with no evidence of relapse.

Potassium hydroxide (KOH) direct smear from the skin-punch biopsy was negative for fungal elements, but the direct smear examination in KOH and smears stained by hematoxylin and eosin (H&E) of the subcutaneous tissue biopsy revealed the presence of broad non-septate hyphae consistent with zygomycete. Histopathological

examination revealed small focal areas of necrosis, with collection of neutrophils, surrounded by lymphocytes, plasma cells, and foreign body giant cells.

Culture on Sabouraud-dextrose agar (SDA) grew a zygomycete mold after a few days, but it did not sporulate. The fungus was subcultured to fresh SDA, cornmeal agar, and potato dextrose agar. Plates were incubated at 26 °C. After about 30 days, the fungus produced the classical flask-shaped sporangia, which are characteristic of *S. vasiformis* (Figure 2).

## Discussion

Zygomycosis (mucormycosis) is usually an acute fulminant infection of the immunocompromised host.<sup>1</sup> Cutaneous infections account for 16% of all forms of zygomycosis, with an associated mortality of 16%, compared to 67% for rhinocerebral, 83% for pulmonary and 100% for disseminated infection. The most common causative organism is *Rhizopus* spp., although others like

*Mucor* and *Absidia* are also frequently seen, whereas *Saksenaia vasiformis* and *Apophysomyces elegans* are rare pathogens. Cutaneous zygomycosis is less likely to be associated with severe systemic illness compared to other forms, while local predisposing factors like burn, trauma, surgery, needle sticks and others play a major role.<sup>2</sup> The most common sites involved by cutaneous zygomycosis are the lower and upper extremities, followed by the head and neck, and then the abdomen.<sup>2</sup>

In spite of the worldwide distribution of *S. vasiformis* in soil, the number of human infections caused by this zygomycete remain relatively small. This may be due to the fact that many zygomycotic infections are diagnosed only by histopathology. *S. vasiformis* does not usually sporulate on routine mycological media when it is isolated from these infections, therefore, it usually passes without identification.<sup>16</sup> The characteristics of the 19 reported cases of *S. vasiformis* infections and our case are summarized in Table 1.

Most of the reported infections caused by *S. vasiformis* are subcutaneous, with only two being disseminated<sup>6,8</sup> and one rhinocerebral infection.<sup>15</sup> The subcutaneous infections can be mild and chronic, as in our patient, or severe and aggressive.<sup>9</sup> Local predisposing factors are common. Fourteen cases had a known local predisposing factor, which can be mild, as in thornprick or injection, or severe, as in major trauma. Systemic illnesses which might predispose patients to zygomycosis were present in only five (25%) patients. There were two patients with diabetes mellitus, one with  $\beta$ -thalassemia with splenectomy, one preleukemic who received chemotherapy, and one with carcinoma of the bladder.

*S. vasiformis* usually grows easily on routine mycological media, but it fails to sporulate on those media. It usually produces sporangia when it is grown on nutrition-deficient media, such as inoculation of agar blocks containing hyphal growth on sterile distilled water with sterilized yeast extract solution added to it,<sup>22</sup> Czapek's agar,<sup>7,8</sup> or 1%-1.5% agar in saline.<sup>17,19</sup> In most reported cases, sporulation was successfully induced using the sterile distilled water method, although it may fail occasionally,<sup>19</sup> and on rare occasions, sporulation may occur on routine media, such as SDA<sup>6</sup> and cornmeal agar.<sup>12</sup>

In our case, the organism produced abundant sporangia when it was subcultured on SDA, cornmeal agar and potato-dextrose agar and incubated at 26°C. Another unique feature of our case was the chronicity of the infection. All the reported cases have acute infections, with the lesions appearing and progressing within a few days or weeks. The infection in this case healed completely after cautery without debridement or antifungal therapy. Most of the reported cases required occasional debridement with amphotericin B, but no spontaneous resolution of the infection was reported, therefore, we think that this case was most likely cured by cautery rather than through

spontaneous resolution. The mechanism of this mode of therapy is not clear.

In conclusion, *S. vasiformis* is increasingly being recognized as a cause of subcutaneous zygomycosis. The pattern of infection is variable, from mild chronic infection to severe, acute fatal infection. When this infection is suspected, the organism should be cultured on nutrient-deficient media, in order to induce sporulation, although it can rarely sporulate on routine mycological media. Aggressive debridement and amphotericin B remain the treatment of choice for such infection.

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