
MYCOLOGY

First Case of Subcutaneous Zygomycosis Caused by *Saksenaea vasiformis* in India

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The first case of subcutaneous zygomycotic infection caused by *Saksenaea vasiformis* in a rice mill worker from India is described. The infection, confined to the man's left foot, showed multiple draining sinuses, inflammation, and intermittent low-grade fever following a crushing injury when a log fell on his foot. Histopathologic examination of two biopsy specimens, taken at 3-wk intervals, revealed the presence of broad, sparsely septate, branched, hyaline hyphae characteristic of a zygomycete. When they were grown on a nutritionally deficient medium, two cultures isolated from the biopsied tissues formed numerous, vase-shaped sporangia typical of *S. vasiformis*. Necrosis of the affected area led to amputation of the fore part of the foot. A split thickness graft was well accepted, and treatment with potassium iodide, following the graft, cured the infection.

INTRODUCTION

The pathogen *Saksenaea vasiformis* was first isolated and described, as a new genus and species, from forest soils collected in India by Saksena in 1953 (Saksena, 1953). Since that time, this zygomycete, characterized by the production of vase-shaped sporangia, has been isolated from soils from Honduras (Goos, 1963), Israel (Joffe and Borut, 1966), Panama (Farrow, 1954), and the United States (Hodges, 1962). The first human infection due to *S. vasiformis* was described by Ajello et al. in the United States (Ajello et al. 1976). Since then, 11 additional cases of cutaneous zygomycosis have been described in the literature from Australia, Colombia, Iraq, Israel, and the United States (Table 1). We are aware of two other cases from the United States (included in Table 1) of zygomycotic infections caused by *S. vasiformis* that are not yet described in the literature. Despite the discovery of this fungus in Indian soil, *S. vasiformis* had never been encountered as an etiologic agent of zygomycosis in India. For this reason, we describe the first case of localized cutaneous zygomycotic infection caused by *S. vasiformis* in a man from south India.

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TABLE 1. Human *Saksenaea vasiformis* Infections

Country	Case no.	Age/sex	Areas affected	Portal of entry	Immune status	Therapy	Outcome	Reference
U.S.A.	1	19/M	Facial and orbital muscles, brain	Cutaneous (auto accident)	Competent	Surgery, antibiotics, AMB	Recovered	Ajello et al., 1976 Dean et al., 1977
	2	69/F	Breast tissue, lung, mediastinum, blood	Cutaneous	Compromised (granulocytic leukemia)	Antibiotics	Fatal	Torell et al., 1981
	3	25/M	Blistering, necrotic lesion on wrist	Cutaneous (auto accident) I.V. catheter	Competent	Cortico steroids	Fatal due to other causes	Oberle and Penn, 1983
	4	24/M	Tibial fracture, osteomyelitis	Cutaneous (severe crush injury)	Competent	Antibiotics, AMB, amputation	Recovered	Pierce et al., 1987
	5*	71/M	Pansinusitis, sphenoid, ethmoid, maxillary sinusitis rhino-cranial	Sinuses	Competent	Debridement AMB, antibiotics	Fatal	Kaufman et al. (personal communication)
Australia	6*	36/M	Lesions on nose, left eye, neck collar bone	Cutaneous (burn patient)	Competent	Antibiotics	Fatal	Greer (personal communication)
	7	25/M	Ulcerated, erythematous plaque on tattooed forearm	Cutaneous	Competent	Antibiotics, AMB	Recovered	Ellis and Kominsky, 1985
	8	60/F	Erythematous macule progressing to necrotic ulcer below right knee	Cutaneous	Compromised (carcinoma of bladder)	Debridement AMB, amputation	Fatal due to other causes	Ellis and Kominsky, 1985

9	17/M	No data	No data	No data	No data	Ellis and Kominsky, 1985
10	3M/F	Abscess on left cheek	Cutaneous	Competent	Surgery	Pritchard et al., 1986
11	26/F	Right gluteal, sacro lumbal area, right flank skin lesions	Cutaneous	Competent	Antibiotics, AMB, surgery	Patino et al., 1984
12	14/M	Necrotic skin arterial occlusion, bronchopneumonia	Cutaneous	Competent	Antibiotics	Hay et al., 1983
13	72/M	Fronto-parietal lesion on the scalp	Cutaneous	Competent	AMB, skin graft	Koren et al., 1986
14	29/M	Blistering necrotic lesion on left foot	Cutaneous	Competent	Antibiotics, KI amputation	Present case

Note: Antibiotics = antibacterial antibiotics.
AMB, amphotericin B.

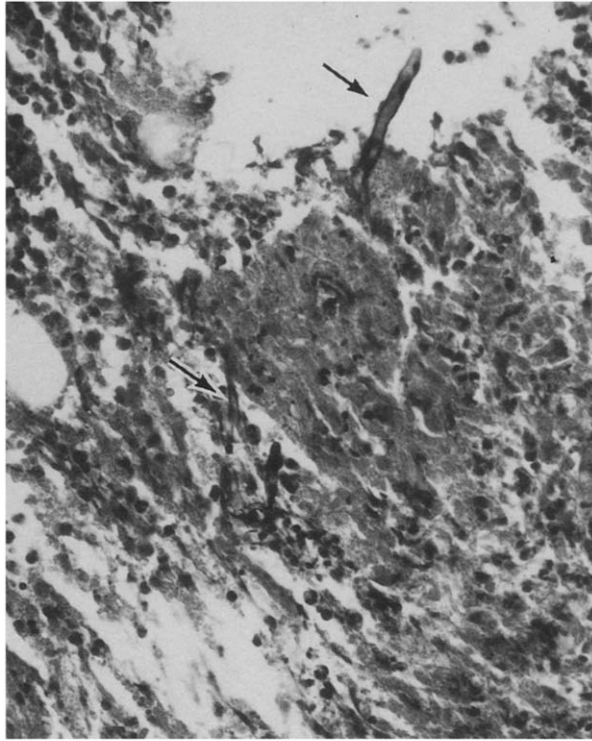


FIGURE 1. Cutaneous zygomycosis caused by *Saksenaia vasiformis*. Hyphal fragments (arrows) are embedded in an area of suppurative necrosis. The overlying epidermis was ulcerated. $\times 340$; hematoxylin and eosin stain (H & E).

CASE REPORT

A 29-year-old man, a rice mill worker, was first seen in September 1986 with complaints of painful swelling of the left foot with multiple discharging sinuses and intermittent low-grade fever, with a duration of 18 mo. His complaints began following a crushing injury when a log fell on his left foot. The abrasion over the dorsum of the foot healed slowly, but the foot gradually became swollen, and bullae appeared, which then broke down and discharged pus. The local physician diagnosed the infection as a mycetoma, and the patient was initially treated with dapsone. Because a tuberculoid granuloma was diagnosed elsewhere, he was then treated with streptomycin and isoniazid for 6 mo.

On admission to the Christian Medical College Hospital in September 1986, general systemic examination revealed no other abnormalities except the left foot, which was swollen up to the ankle and was "woody hard." The advancing margin of the swelling was delineated, as an erythematous swollen border extending to the insole medially and to the ankle proximally. The skin was hyperpigmented and showed multiple areas of oozing and superficial ulcerations covered with yellowish exudate and brownish adherent crust. Regional lymph nodes were enlarged, discrete, and tender. Roentgenographic examination showed no bone involvement.

The initial biopsy report suggested zygomycosis. Therapy with 1 g, once daily, of oral potassium iodide (KI) was started. Within 3 hr of administering the first dose of KI, the patient complained of an intense pain in the foot; and within 24 hr, the erythematous border of the foot became very red and swollen. The pain could not

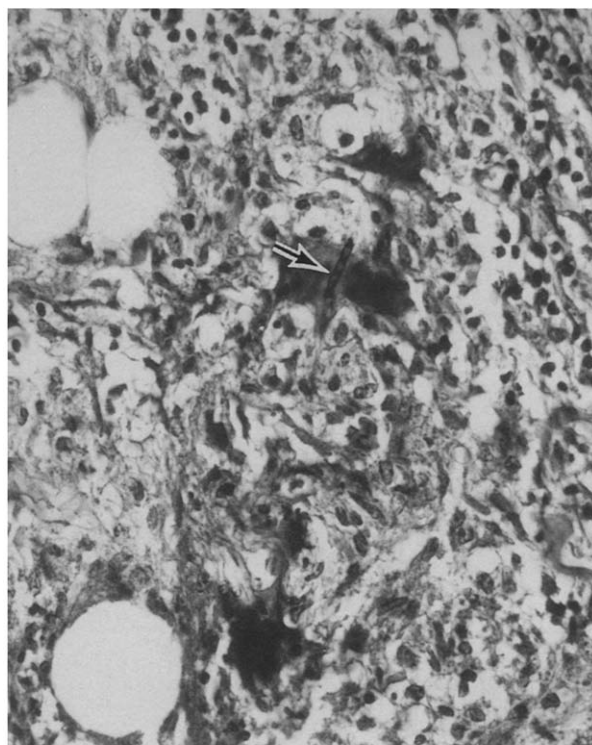


FIGURE 2. Hyphal fragments of *S. vasiformis* (arrow) within the cytoplasm of a multinucleate giant cell. $\times 340$; Gomori's methenamine silver (GMS) with H & E counterstain.

be controlled with routine analgesics. Continuation of the treatment with KI for 3 more days resulted in intensification of the pain. The swelling and cutaneous erythema increased over the involved region and several contiguous areas. On the fourth day, the patient became febrile. At this time, because some form of Jarisch-Herxheimer reaction to KI was suspected, the treatment was stopped. To control the severe inflammation, prednisolone and broad-spectrum antibiotics were administered. The pain and erythema soon subsided. Four days later, when KI treatment was resumed, the patient again experienced severe pain. The ulcers were more necrotic, and debridement of the ulcers was carried out under general anesthesia. Examination of the excised tissue reconfirmed that the infection was due to a zygomycete.

The patient was treated with dry dressings and underwent debridement again after 18 days. In spite of repeated dressings, the area distal to the metatarsals did not respond to treatment. Hence, a transmetatarsal amputation was performed. One month after surgery, treatment with KI was reinstituted. The dosage was gradually increased up to 10 g once a day. Repeat biopsy from the amputated end of the foot after 6 wk of treatment with KI showed no evidence of fungal infection. A split-thickness skin graft was applied 2 mo after surgery. At the time of discharge, the graft was accepted well, and treatment with KI was continued at 4 g per day. The patient was advised to return for follow-up.

Two biopsy specimens were received at an interval of 3 wk. The first specimen consisted of skin and subcutaneous tissue containing part of a sinus tract. The second specimen was a disarticulated toe, where the dorsal surface near the nail showed an elevated ulcer. Direct examinations in KOH mounts of the necrotic tissue received after debridement showed broad, hyaline, branched, sparsely septate hyphae with

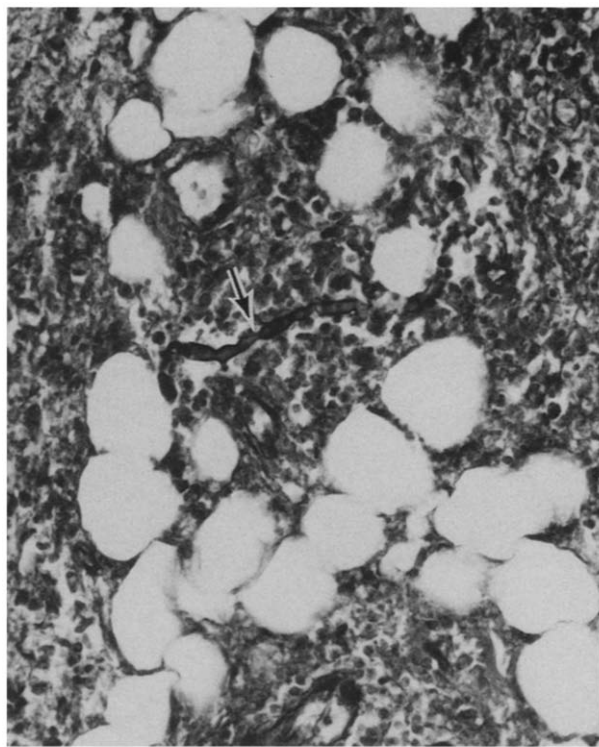


FIGURE 3. *S. vasiformis* in subcutaneous tissue. A broad, branched hypha (arrow) with irregular contours and infrequent septations is surrounded by mixed inflammatory cells. $\times 340$; GMS and H & E.

intercalary swollen cells. Similar examination of the tissue from the amputated foot showed similar zygomycetous hyphae.

Two histologic slides from the first biopsied tissue and two subcultures of a white, floccose, nonsporulating, zygomycetous fungus isolated from the two biopsies were sent to the Division of Mycotic Diseases, Centers for Disease Control (CDC), Atlanta, Georgia, for specific identification.

Histopathologic Findings

Histopathologic examination of the skin, soft tissue, and bone showed ulceration of the epidermis and focal areas of hemorrhage and suppurative necrosis involving the dermis (Fig. 1). The deep dermis, subcutaneous tissue, and periosteum contained multiple discrete granulomas composed of epithelioid histiocytes and numerous multinucleate giant cells of both the foreign body and Langhans' types (Fig. 2). Some granulomas also showed central necrosis. Hyphal fragments that were hyaline, hematoxylinophilic, and poorly stained with the periodic acid Schiff's and Gomori's methenamine silver procedures were located in foci of suppurative necrosis (Fig. 1), in the necrotic centers of granulomas, and within the cytoplasm of multinucleate giant cells (Fig. 2). The pleomorphic hyphae were broad (5–20 μm in diameter), infrequently septate, and haphazardly branched. They had thin walls and irregular contours (Fig. 3). These morphologic features were characteristic of a zygomycete. Hyphal angioinvasion was evident in the dermis and subcutaneous tissue, and some

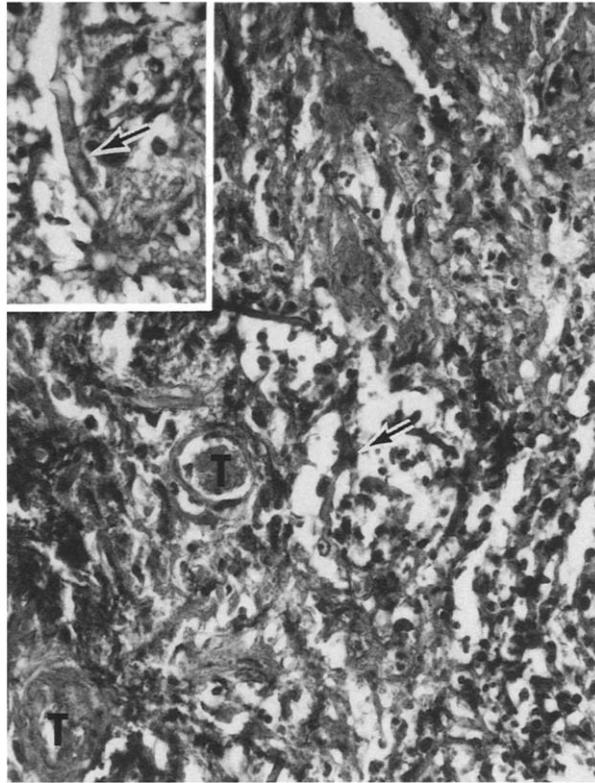


FIGURE 4. Hyphal angioinvasion by *S. vasiformis* (arrows). Dermal blood vessels contain thrombi (T) one of which appears to be occluded. $\times 215$; H & E. Inset: Detail of hypha (arrow) contiguous to a large subcutaneous blood vessel. $\times 340$; H & E.

of the blood vessels were occluded by mycotic thrombi (Fig. 4). The surrounding stroma consisted of granulation tissue infiltrated with neutrophils, lymphocytes, and plasma cells. Eosinophils were not conspicuous.

The histologic features in this case were typical of a severe, localized, cutaneous infection caused by a zygomycete in the order Mucorales. The hyphae were not bordered by Splendore-Hoeppli material, and the host reaction was not like that encountered in subcutaneous zygomycosis (caused by *Basidiobolus haptosporus* and *Conidiobolus coronatus*) (Chandler et al., 1980). No histologic evidence was found of a coexisting infection.

Mycologic Findings

When they were grown on Sabouraud dextrose agar (Difco), the two isolates failed to sporulate. Growth consisted of only broad, hyaline mycelium. Accordingly, the isolates were subcultured on corn meal sucrose yeast extract agar (Ellis and Ajello, 1982) and incubated at 25°C for 7 days. After 7 days of incubation, 3mm³ agar blocks permeated with hyphae, and the accompanying aerial growth were cut from the agar plates and placed in Petri plates containing 20 ml of sterile distilled water and 0.2 ml of 10% yeast extract solution. The yeast extract (10%) in distilled water had been filter sterilized. The plates were incubated in the dark at 37°C and observed periodically. After 10 days, the fungus was growing as a thin film over the surface of water.



FIGURE 5. Typical vase-shaped sporangia of *S. vasiformis* (B-4455) produced in distilled water with 10% yeast extract at 37°C after 7 days. $\times 875$.

Microscopic examination of the growth film revealed vase-shaped sporangia characteristic of *Saksenaea vasiformis* (Fig. 5). The two Indian isolates have been deposited in the Division of Mycotic Diseases' culture collection under accession numbers CDC B-4455 and CDC B-4456.

DISCUSSION

In spite of the worldwide distribution of *S. vasiformis* in soil, the number of human infections caused by this zygomycete remains relatively small. Only 12 cases of cutaneous zygomycosis due to *S. vasiformis* have been described in the literature. The paucity of reports may be due to the fact that *S. vasiformis*, when it is isolated in culture, does not sporulate on routine mycological media and is mistaken for and discarded as a contaminant.

In the 12 published case reports, the portal of entry of *S. vasiformis* was through traumatized skin. In only one case (Kaufman et al., personal communication), the fungus gained entry through the nasal sinuses rather than through traumatized skin. The fact that *S. vasiformis* can occur in a hospital environment (Oberle and Penn, 1983) and rapidly attack the vascular system of either immunocompromised or immunocompetent patients makes it vital that a rapid and specific diagnosis be achieved so that appropriate treatment can be initiated. Since its clinical features mimicked a mycetoma, the case described here was initially misdiagnosed. Amphotericin B therapy was not considered because of the localized nature of the lesion. The administration of potassium iodide precipitated the Harisch-Herxheimer reaction. The intense pain and acute inflammation necessitated administration of steroids. The necrosis, caused by secondary pyogenic infection, led to amputation of the infected fore part of the foot.

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