Soft Tissue Infection with *Absidia corymbifera* in a Patient with Idiopathic Aplastic Anemia

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CASE REPORT

A nineteen-year-old man with aplastic anemia was referred to a tertiary referral hospital in February 2000. He initially presented to another hospital with a 1-week history of bleeding gums associated with tooth brushing. Panmyelopenia was detected on full blood count, and bone marrow examination confirmed bone marrow aplasia. Upon admission to this hospital, he was febrile and pale and had multiple bruises.

Broad-spectrum empirical antibacterial therapy with piperacillin-tazobactam and gentamicin was commenced. Because he remained pyrectile, vancomycin and subsequently fluconazole (400 mg daily) were added. On hospital day 4, an area of ecchymoses was noted on the dorsal aspect of the left forearm. The patient had no recollection of preceding trauma at the site of the lesion. The lesion became more extensive and necrotic over 2 days. Empirical therapy with liposomal amphotericin B (3 mg/kg of body weight) was commenced on hospital day 6 based on a clinical suspicion of mold infection, and fluconazole was discontinued at this point. The lesion was immediately and thoroughly debrided. Clinical and radiological assessment, including sinus and chest X-ray, revealed no evidence of disease at other sites. Further debridement was performed on hospital day 13, and on day 15, the wound was grafted with skin from the left inner thigh. On day 17, he was transferred to another hospital for HLA-matched bone marrow transplantation. Liposomal amphotericin B was continued until the bone marrow engraftment was confirmed and the forearm lesion was healed.

At no point in his clinical course was there clinical or radiological evidence of mucormycosis at any other site. The patient remains well more than 1 year post-bone marrow transplantation.

A piece of debrided tissue removed from the wound was submitted for microbiological and histopathological examination. The sliced tissue was inoculated onto a standard panel of agar plates for culture of tissue fragments (Columbia blood agar, cysteine lactose electrolyte-deficient agar [both for aerobic incubation at 37°C], Columbia chocolate agar [incubated in 5% carbon dioxide at 35°C], and Columbia blood agar [for anaerobic incubation]). In view of the clinical suspicion of fungal infection, the sliced tissue was also applied to Sabouraud’s dextrose agar (aerobic incubation at 30°C) and a small piece of tissue was transferred (using a sterile swab) into brain heart infusion (BHI) broth (aerobic incubation at 35°C). All culture media were prepared from dehydrated bases (Oxoid, Basingstoke, England).

No growth was observed on any of the solid media upon daily inspection for 5 days. After a 24-h incubation period, the BHI broth inoculated with the piece of tissue showed fine filamentous growth apparently originating from the tissue fragment. At 48 h, the filamentous material in the BHI broth had thickened considerably and was almost at the liquid surface of the broth. A portion of the filamentous growth was removed aseptically to inoculate a Sabouraud’s dextrose agar plate (aerobic incubation at 30°C). A subculture from the broth showed extensive filamentous growth with a white fluffy aerial mycelium at 24 h. Seventy-two hours postsubculture the Sabouraud dextrose agar plate was completely filled with an olive green-grey mycelium. Upon examination of a cellotape preparation stained with cotton blue lactophenol (Gurr), branching sporangiophores were evident, arising from stolons between rhizoids (Fig. 1). The sporangia were pear shaped and had prominent conical columellae. A funnel-shaped apophysis was evident beneath the sporangium. The isolate was capable of growth at 48°C. On the basis of the colonial and microscopic morphology and growth temperature characteristics, the isolate was identified as *Absidia corymbifera* (1).

Histological examination of hematoxylin- and eosin-stained sections of the wound biopsy showed florid pseudopodithiomatous hyperplasia in continuity with proliferating granulation tissue containing a small number of lymphocytes and neutrophils. An organizing thrombus within the vessels was present in the deep dermis, and fungal hyphae were observed within the vessel lumen, in the vessel wall, and in adjacent connective tissue. Gomori methenamine silver (Fig. 2)- and periodic acid-Schiff-stained sections confirmed the presence of nonseptate hyphae with branching at wide angles and the crinkled cello-

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Mucormycosis is an infection with fungi of the class Zygo-
mycetes and the order Mucorales. The organisms most com-
monly implicated belong to the genus Rhizopus (about 90% of
all cases) (6). Infection primarily affects the immunocompro-
mised patient, the poorly controlled diabetic, and patients with
iron-overload states and extensive burns. The use of broad-
spectrum antibiotics has also been associated with an increased
risk of mucormycosis (6). Mucormycosis has been reported
occasionally in immunocompetent individuals, usually follow-
ning trauma (5, 6, 7, 8). Zygomycetes characteristically invade
blood vessels, leading to thrombosis and infarction, with sub-
sequent tissue necrosis and eschar formation. The resultant
necrotic tissue favors further growth of the fungus and limits
penetration of systemic antifungal agents. Because of the mor-
tality associated with mucormycosis, immediate aggressive
treatment is required, including control of the underlying dis-
 ease process, surgical intervention, and administration of am-
photericin B. Surgical debridement is intended to remove ne-
crotic tissue and obtain an uninfected bleeding margin. The
favorable outcome in this patient may be related to the local-
ized nature of the process at diagnosis and to the immediate
surgical intervention together with the antifungal therapy.

A. corymbifera is the only species of the genus Absidia rec-
ognized as a human pathogen. It accounts for perhaps 2 to 3% of
culture-confirmed cases of zygomycete infection (6). The
organisms are ubiquitous. Infection occurs as a result of the
inhalation of spores or the direct inoculation of spores into
tissue. Rhinocerebral, cutaneous, pulmonary, and disseminated
forms of mucormycosis with this species have been de-
scribed (3, 4, 5, 6, 7, 8).

A. corymbifera grows readily upon subculture to routine my-
cology media, growing more rapidly at 37°C than at 25°C, and
it is capable of growth at temperatures up to 48 to 52°C, which
distinguishes it from the other Absidia species (2). A. cory-
mbifera produces a woolly colony which can fill a petri dish in
24 h. Initially, the colony is white, but it changes to grey-brown
to olive green on the surface with no color on the reverse. The
microscopic features are the presence of branching sporangi-
ophores arising from stolons between rhizoids, conical columel-
lae, and funnel-shaped apophyses (1, 6).

The laboratory aspects of this case support previous recom-
mendations for the inoculation of the tissue into a rich organic
liquid medium in addition to the inoculation of solid mycolog-
ic medium in cases where there is a clinical suspicion of
mucormycosis. The use of BHI broth is recommended in Clin-
ical Microbiology Procedures Handbook (2); however, the value
of these processes is not well recognized in practice. A recent
comprehensive review of zygomycetes in human disease rec-
ommends the use of a number of approaches to enhance the
likelihood of isolation of zygomycetes but does not refer to
inoculation of BHI broth (6). Placing unprocessed tissue in
BHI broth minimizes the damage to zygomycetes. This ap-
proach is convenient because BHI broth is widely available and
inexpensive and because the technical time involved in pro-
cessing the specimen is minimal. Environmental contamina-
tion must always be considered when isolation of a common
environmental organism is achieved only from a broth culture.
Routine checks of uninoculated BHI broth confirmed that it was sterile, and the clinical significance of this isolate is supported by consistent clinical and histopathological findings.

Although the primary isolation of *A. corymbifera* only from BHI broth in this case may be attributed to a number of factors, it is likely that placing unprocessed tissue into a broth medium may facilitate the culture of zygomycete fungi because of minimal disruption of the hyphae and because the broth may provide osmotic support for damaged hyphae, thereby facilitating recovery. Other rich organic liquid media may be equally useful. Comparative prospective studies of solid versus broth media, of multiple medium types, and of differing incubation temperatures for the primary isolation of zygomycetes would be of great interest but are difficult to perform, as the condition is relatively uncommon.

This case illustrates the potential for a favorable outcome in localized cutaneous mucormycosis associated with *A. corymbifera* if managed immediately and aggressively and supports recommendations for inoculation of tissue specimens into BHI broth when mucormycosis is suspected.

**REFERENCES**


**FIG. 2.** Gomori methenamine silver-stained tissue section showing extensive infiltration with fungal hyphae. Magnification, ×250.