Primary cutaneous infection by \textit{Aspergillus ustus} in a 62-year-old liver transplant recipient

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We report the first case of primary cutaneous aspergillosis caused by \textit{Aspergillus ustus}, a species that seldom infects human beings. The patient, a 62-year-old liver transplant recipient with end-stage hepatitis C-induced cirrhosis, was receiving the experimental immunosuppressive drug FK-506. Trauma to the skin of the right arm from tape and from an arm board holding intravenous and intraarterial catheters in place and to the left leg from an occlusive knee brace may have contributed to this unusual mycosis. The patient's cutaneous aspergillosis responded to a combination of intravenous amphotericin B and topical terbinafine cream. Although the patient died shortly thereafter from hepatic failure, there was no evidence of systemic aspergillosis. (J AM ACAD DERMATOL 1994;31:344-7.)

After \textit{Candida albicans}, \textit{Aspergillus} species are the second most common cause of opportunistic fungal infections in human beings.\textsuperscript{1-4} \textit{Aspergillus} is ubiquitous in the environment and is readily isolated from soil, plants, decaying vegetation, food, and water.\textsuperscript{3, 5, 6} When infections occur the usual portal of entry is the respiratory tract, where it causes necrotizing pneumonia, hemorrhagic pulmonary infarction, and allergic bronchopulmonary aspergillosis.\textsuperscript{1, 5, 7} Other anatomic sites that may be affected secondarily include the gastrointestinal tract, central nervous system, kidney, liver, heart, bone, eye, nails, and skin.\textsuperscript{2, 5, 7, 9} Cutaneous aspergillosis is uncommon and may occur as a result of hematogenous dissemination or by extension to skin from a contiguous anatomic site.\textsuperscript{2, 3, 7} Primary cutaneous aspergillosis is rare. It is most frequently caused by \textit{Aspergillus flavus},\textsuperscript{1, 3, 5, 10-13} although cases have been caused by \textit{Aspergillus fumigatus},\textsuperscript{2, 3, 12, 14} \textit{Aspergillus niger},\textsuperscript{12, 13, 15} \textit{Aspergillus terreus},\textsuperscript{13, 16, 17} and \textit{Aspergillus glaucus}.\textsuperscript{13}

Primary cutaneous aspergillosis is very rare in nonimmunocompromised hosts.\textsuperscript{1, 4, 13, 18} Most cases have been reported in immunocompromised patients with hematologic or lymphoreticular malignancies or in organ transplant patients receiving long-term therapy with cytotoxic or chemotherapeutic agents, systemic glucocorticosteroids, broad-spectrum antibiotics, or a combination of these agents.\textsuperscript{12, 13, 19-22} In this susceptible group of patients, additional risk factors for primary cutaneous aspergillosis include contaminated intravenous cannulas and Hickman catheters; trauma to skin from...
contaminated tape, gauze wraps, and arm boards; burns; and aerial dissemination of fungi during hospital reconstruction or renovation. 5, 18, 19, 21, 23-26

Aspergillus ustus ranks among the less pathogenic species of aspergillus, and rarely causes human infection. 26-28 It has caused endocarditis and disseminated infection in patients undergoing mitral valve replacement or coronary artery bypass surgery. It also rarely causes onychomycosis. 26, 28 We report the first case of primary cutaneous aspergillosis caused by A. ustus in a 62-year-old liver transplant recipient.

CASE REPORT

A markedly icteric, 62-year-old white man had diffuse cutaneous atrophy, widespread ecchymoses, and multiple crusted, indurated nodules and plaques on the right arm and left leg (Fig. 1).

After an accident in 1957, the patient received multiple blood transfusions, the presumptive cause of his hepatitis C–induced cirrhosis. After orthotopic liver transplantation in May 1992, he was treated with cyclosporin A (10 mg/kg/day) until acute transplant rejection occurred in November 1992. At that time treatment with FK-506 (2 to 8 mg/kg/day) was started.

A biopsy specimen from the right arm showed only at-
rophy, purpura, telangiectases, extravasated erythrocytes, and solar elastosis of the papillary dermis. A few days later extensive suppuration of the left leg developed. Treatment with hydrocortisone sodium succinate (Solu-Cortef) was initiated to suppress probable pyoderma gangrenosum. A second biopsy specimen of an exophytic lesion on the right arm revealed dermal neutrophils surrounded by aggregates of histiocytes, some of which were multinucleated. Pseudocarcinomatous hyperplasia and hyperkeratosis were noted.

KOH preparations of the tissue revealed numerous plump, bizarre-shaped hyphae (Fig. 2) and rare, dichotomously branching filaments characteristic of an *Aspergillus* species. Cultures identified the organism as *A. ustus*. A culture of purulent drainage from a lesion on the left leg also yielded *A. ustus*.

Chest x-rays and a bone scan showed no evidence of systemic mycosis; results of sputum cultures were also negative for fungi. The patient was treated with intravenous amphotericin B, 10 gm every other day for 2 weeks with a subsequent increase to 25 gm, and twice-daily applications of terbinafine cream. Within 3 days improvement was noted in the cutaneous lesions. Reepithelialization of the right arm occurred, and there was no further drainage from lesions on the left leg, although a few boggy, indurated areas persisted (Fig. 3). Despite continued improvement in the cutaneous lesions, the patient died of pulmonary insufficiency as a result of liver cirrhosis and renal failure.

**DISCUSSION**

We report the first case of primary cutaneous aspergillosis caused by *A. ustus*. In addition to hepatic failure and treatment with FK-506, our patient had other risk factors. An arm board secured by non-sterile paper tape was in place on the right forearm and arm before cutaneous lesions developed. Neither the arm board itself nor portions of the tape were used for culture of fungi. According to the nurses' notes, the tape abraded the patient's skin. During the final months of his life the patient wore a semirigid Zimmer brace to stabilize his left knee. This occluded and irritated the skin from the upper portion of the thigh to the lower part of the calf. Windows in the patient's room were removed and cleaned during his hospitalization, while major construction was under way. Approximately 6 weeks after our patient died, specimens from the two hospital rooms he had occupied were obtained for culture. Samples were taken from the windows, ledges, blinds, and air conditioning ducts. Cultures yielded *Aspergillus* species, including two colonies of *A. ustus*, and one colony each of *Penicillium*, *Alternaria*, and *Cladosporium*. This suggests that the patient's infection may have been nosocomial.

Initial signs of primary cutaneous aspergillosis may include erythematous to violaceous macules, papules, plaques, and nodules. Hemorrhagic bullae can occur, as can ulcerations with central necrosis or eschar formation. Pustular lesions rarely have been observed. Amphotericin B remains the treatment of choice for cutaneous aspergillosis in immunocompromised patients, although itraconazole and fluconazole may also be effective. There are anecdotal reports of suc-
cessful treatment with oral or topical nystatin, or both, but this approach is unproved. More than 200 species of *Aspergillus* have been isolated, but fewer than 10 cause disease in human beings, and only a few species cause primary cutaneous aspergillosis. It is uncertain whether we identified an atypically pathogenic strain of *A. ustus*, or whether the patient's severely immunocompromised state was sufficient to permit infection.

REFERENCES