BRIEF REPORTS

Primary Cutaneous Aspergillosis in Human Immunodeficiency Virus–Infected Patients: Two Cases and Review

Primary cutaneous aspergillosis is an unusual infection in HIV-infected patients. To our knowledge, only seven cases of primary cutaneous aspergillosis have been reported [1–5]. We describe two additional cases of primary cutaneous aspergillosis in patients with AIDS.

A 57-year-old HIV-positive male was admitted to Hacettepe University Hospital (Ankara, Turkey) on 4 October 1996. On 25 December, amphotericin B deoxycholate therapy was instituted, 1 mg/(kg · d), for treatment of fungemia due to fluconazole-resistant *Candida albicans*. On 15 January 1997, multiple erythematous papules were noted on the dorsal penis and scrotum, as well as two ulcerated plaques (one beneath the adhesive tape around the condom catheter and the other at the urethral meatus). Direct microscopic examination of scrapings obtained from the base of the ulcers revealed branching hyphae, and cultures yielded *Aspergillus fumigatus*. Povidone-iodine was applied topically to the lesions (local care), and his therapy was changed to that with liposomal amphotericin B (AmBisome; Nexstar, San Dimas, CA) administered at a dosage of 3 mg/(kg · d). The general status of the patient gradually deteriorated and he died on 1 February 1997 of multiorgan failure caused by *Escherichia coli* sepsis. The lesions had not changed. No autopsy was performed.

See editorial response by Walsh on pages 453–7.

A 38-year-old HIV-positive male was admitted to the hospital on 3 February 1997. Physical examination revealed an erythematous papule on the right forearm measuring 1.0 cm in diameter, at the insertion site of a peripheral intravenous cannula that had been placed during his previous hospitalization in December 1996. The lesion was completely excised, and histopathologic examination of the specimen demonstrated fungal hyphae consistent with *Aspergillus* species. Culture of the specimen yielded *A. fumigatus*. Povidone-iodine was applied topically to the excisional area (local care), and the patient was discharged from the hospital on 24 March 1997. There was no recurrence of aspergillosis as of his last follow-up on 1 September 1997.

Primary cutaneous infection due to *Aspergillus* species has been reported mainly for patients with leukemia or lymphoma who were undergoing intensive cytotoxic chemotherapy, or who were recipients of organ transplants and receiving immunosuppressive agents. However, very little is known about this infection in HIV-infected patients. A computer-based search of the English-language literature, between 1977 and 1997, identified seven AIDS patients with primary cutaneous aspergillosis [1–5]. Because one of the cases was diagnosed postmortem no clinical information could be obtained [1].

Several features are common among these patients. First, only one patient was neutropenic when these lesions developed; however, all had CD4+ lymphocyte counts of $<200/mm^3$, suggesting an advanced HIV infection and, hence, profound immunosuppression. Second, the probable source of infection appears to be the adhesive tape or catheter exit site in all cases, except for one patient who developed cutaneous aspergillosis after trauma. Third, there appears to be an indolent clinical course for this infection. The lesions resolved for all patients with or without any systemic antifungal treatment. However, dissemination may still occur despite resolution of lesions (table 1, patients 1 and 3).

There is no uniform approach for treatment of primary cutaneous aspergillosis in HIV-infected patients. Five of the eight cases reported received a systemic antifungal agent that was effective against *Aspergillus* species. Of the three untreated patients, two (patients 2 and 8) had no evidence of recurrence or dissemination (table 1), whereas pulmonary involvement was evident in the third patient (patient 1) at autopsy (table 1). On the other hand, systemic antifungal therapy is not always successful (table 1, patients 3 and 7). It is of interest that our first case developed cutaneous aspergillosis while receiving amphotericin B therapy, after a cumulative dose of 20 mg/kg. His therapy was switched to that with AmBisome, 3 mg/(kg · d), with no change in the lesions during the 2 weeks before his death.

In conclusion, primary cutaneous infection due to *Aspergillus* species is rare among HIV-infected patients, but it should be considered in the differential diagnosis of skin lesions that develop beneath adhesive tape or at catheter exit sites. Although the lesions are usually indolent, the infection can disseminate and result in death. Catheter removal is an important component of therapy when the source of infection is the catheter site. Because the available data are limited, the optimal therapeutic approach has yet to be determined.

Reprints or correspondence: Dr. Ömrüm Uzun, Hacettepe University School of Medicine, Department of Medicine, Section of Infectious Diseases, Ankara, 06100, Turkey.

Clinical Infectious Diseases 1998; 27:641–3

1058–4838/98/2703–0033$03.00

Sevtap Arikan, Ömrüm Uzun, Yeşim Çetinkaya, Sesin Kocagöz, Murat Akova, and Serhat Ünal

Department of Microbiology and Clinical Microbiology, and Section of Infectious Diseases, Department of Medicine, Hacettepe University School of Medicine, Ankara, Turkey

Table 1. Clinical characteristics of eight HIV-infected patients with primary cutaneous aspergillosis due to *Aspergillus* species.

Patient no.	Patient's age (y)/sex [reference]	Associated diseases	Skin lesions		Organism	CD4+ lymphocyte count (/mm^3)	Neutrophil count (/mm^3)	Probable source of infection	Treatment	Outcome
			Site	Morphology						
1	27/M [2]	Kaposi's sarcoma, cerebral lymphoma, CMV retinitis, MAC infection	Chest, exit site of a Hickman catheter	Several umbilicated papules	*Aspergillus fumigatus*	14	1,800–6,700	Adhesive tape	Local care	Lesions abated, patient died of CMV ventriculitis and encephalitis, pulmonary nodule found at autopsy
2	43/M [2]	Cerebral toxoplasmosis, CMV retinitis, MAC infection	Chest, exit site of a Groshong catheter	Two papules	NA	NA	NA	Adhesive tape	Local care and fluconazole, 200 mg/d	Lesions abated, patient died of MAC infection, no autopsy
3	26/F [3]	Acute lymphoblastic leukemia	Chest, exit site of a Groshong catheter	Indurated erythema without skin necrosis	*A. fumigatus*	145	3,140	Catheter exit site	Catheter removal, itraconazole (200 mg/d) for 1 mo, then amphotericin B (1 mg/[kg · d])	Lesion abated, patient died of pulmonary aspergillosis, no autopsy
4	37/M [4]	Gastrointestinal tract cryptosporidiosis	Chest, exit site of a subclavian catheter	Verrucous plaque	*A. fumigatus*	67	NA	Catheter exit site	Catheter removal, amphotericin B	Lesion abated, patient died, no autopsy
5	14/M [5]	None	Right calf	Chronic, nonhealing postraumatic ulcer	*Aspergillus glaucus*	143	1,591	Trauma	Amphotericin B, switched to itraconazole	Cured
6	10/F [5]	None	Chest, exit site of a subclavian catheter	Tender skin nodule	*A. fumigatus*	2	196	Catheter exit site	Debridement and skin graft, amphotericin B	Cured
7	57/M [PR]	Aspiration pneumonia, *Escherichia coli* bacteremia, *Candida albicans* fungemia	Penis and scrotum	Ulcerated plaque and several papules	*A. fumigatus*	145	1,260	Adhesive tape	Local care, AmBisome, 3 mg/(kg · d)	Lesions unchanged, patient died of sepsis, no autopsy
8	38/M [PR]	Intraabdominal infection, CMV colitis	Forearm, insertion site of iv cannula	Solitary papule	*A. fumigatus*	51	1,700	Catheter exit site	Local excision and wound care	Cured, no recurrence in 6 months

NOTE. CMV = cytomegalovirus; MAC = *Mycobacterium avium* complex; NA = not available; PR = present report.

References

1. Hui AN, Koss MN, Meyer PR. Necropsy findings in acquired immunodeficiency syndrome: a comparison of premortem diagnosis with postmortem findings. Hum Pathol **1984**;15:670–6.
2. Hunt SJ, Nagi C, Gross KG, Wong DS, Matthews WC. Primary cutaneous aspergillosis near central venous catheters in patients with the acquired immunodeficiency syndrome. Arch Dermatol **1992**;128:1229–32.
3. Girmenia C, Gastaldi R, Martino P. Catheter-related cutaneous aspergillosis complicated by fungemia and fatal pulmonary infection in an HIV-positive patient with acute lymphocytic leukemia. Eur J Clin Microbiol Infect Dis **1995**;14:524–6.
4. Romero LS, Hunt SJ. Hickman catheter-associated primary cutaneous aspergillosis in a patient with the acquired-immunodeficiency syndrome. Int J Dermatol **1995**;34:551–3.
5. Shetty D, Giri N, Gonzalez E, Pizzo PA, Walsh TJ. Invasive aspergillosis in human immunodeficiency virus-infected children. Pediatr Infect Dis J **1997**;16:216–21.

Itraconazole Therapy for Primary Cutaneous Aspergillosis in Patients with AIDS

Cutaneous aspergillosis occurs infrequently among HIV-infected patients; previous reports describe a total of seven patients with primary cutaneous aspergillosis [1–5]. Thus far, however, the risk factors, expected outcome, and therapeutic approach have not been defined for HIV-infected patients with primary cutaneous aspergillosis. We describe two cases of primary cutaneous aspergillosis in patients with AIDS who were treated with itraconazole, and we present our approach to the diagnosis and management of cutaneous aspergillosis.

A patient with Centers for Disease Control and Prevention (CDC) class C3 AIDS, a CD4 cell count of 15/mm^3, and cytomegalovirus retinitis developed intermittent neutropenia while receiving treatment with iv ganciclovir that was administered via a right-sided, antecubital, peripherally inserted central catheter (PICC). Because of the patient's preference (unrelated to any skin lesions), the PICC line was removed after 5 weeks of therapy and a subclavian intravenous Groshong catheter was placed. Three weeks after starting ganciclovir therapy, the patient noted two small papules under an adhesive dressing near the PICC-line insertion site. These lesions gradually enlarged and became tender during the following 4 weeks, finally prompting him to seek medical attention. The patient had received granulocyte colony-stimulating factor, 300 μg subcutaneously as needed, to maintain a neutrophil count of $>$500/mm^3.

See editorial response by Walsh on pages 453–7.

Physical examination identified two firm, tender, and mildly erythematous right forearm nodules, that measured 0.6 cm and 0.8 cm in diameter, located distal to the prior PICC insertion site (figure 1). The remainder of his physical examination did not reveal any abnormalities, and a chest radiograph was normal. Histopathologic evaluation of a skin biopsy specimen showed abundant, branching septate hyphae consistent with *Aspergillus* species (figure 1), and cultures later yielded *Aspergillus fumigatus.* The patient received itraconazole, 200 mg po b.i.d. for 9 weeks. The lesions had resolved completely at follow-up 4 weeks after starting the course of itraconazole; the patient died 2 years later without recurrent aspergillosis.

A patient with CDC class C3 AIDS, a CD4 cell count of zero, and cytomegalovirus retinitis developed intermittent neutropenia during treatment with iv ganciclovir. The ganciclovir maintenance had been administered via a right-sided, antecubital PICC line for 16 weeks before the line was obstructed by clots and then removed. At a clinic visit 2 weeks after catheter removal, the patient was evaluated for the complaint of dyspnea and a nonproductive cough. At that time he also reported a painful nodule in the antecubital fossa of the right forearm, near the insertion site of the PICC line. He had first noted the lesion under an adhesive dressing 4 to 5 weeks before, and the lesion had not changed significantly in size. Granulocyte colony-stimulating factor, 300 μg, was administered subcutaneously as needed to maintain a neutrophil count of $>$500/mm^3.

Physical examination identified a well-circumscribed, firm, tender, erythematous, 0.5-cm right forearm nodule located distal to the prior PICC insertion site. A chest radiograph showed evidence of chronic right middle lobe infiltrate and volume loss. Histopathologic evaluation revealed abundant, branching septate hyphae consistent with *Aspergillus* species and cultures later yielded *A. fumigatus.* A punch biopsy was performed which excised the right arm nodule. On the basis of the biopsy results, treatment was initiated with amphotericin B and continued for 4 days until CT scans of the chest and sinuses showed no evidence of disease. The patient refused to undergo bronchoscopy. Therapy was changed to that with itraconazole, 200 mg po b.i.d., but after 4 weeks of therapy, the patient discontinued most oral medications including itraconazole. One week later he had a recurrence of tenderness and swelling immediately proximal to the region of the previous nodule, and he restarted itraconazole. The patient died of progressive wasting syndrome 3 weeks later; an autopsy was not performed.

We have described two HIV-infected patients who were treated with itraconazole for primary cutaneous aspergillosis, both of whom had advanced AIDS and intermittent episodes of neutropenia that preceded the diagnosis of primary cutaneous aspergillosis. In addition, both developed nodular cutaneous aspergillosis lesions under an adhesive dressing near the exit site for an intravenous catheter, and neither had evidence of disseminated aspergillosis. Fungal drug susceptibility testing was not performed on the

Financial support: J.-A.H.V.B. was supported by the Clinician Scientist Award (K08 AI-01411) from the National Institutes of Health.

Reprints or correspondence: Dr. Jo-Anne van Burik, 1100 Fairview Avenue North D3-100, P.O. Box 19024, Seattle, Washington 98109-1024.

Clinical Infectious Diseases 1998;27:643–4

1058–4838/98/2703–0034$03.00