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/mm³, and cytomegalovirus retinitis developed intermittent neutropenia while receiving treatment with iv ganciclovir that was administered via a rightsided, 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/mm³.

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/mm³.

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

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isolates from either patient. Patient 1 received itraconazole for 9 weeks and had complete resolution of the lesions by 4 weeks. Patient 2 received amphotericin B for 4 days as initial treatment after excision of the nodule during a skin punch biopsy procedure, followed by 4 weeks of itraconazole therapy. It is of interest that for patient 2, a new lesion (probably aspergillosis) appeared <1 week after discontinuing itraconazole therapy.

Previous reports concerning HIV-infected individuals have described a total of seven patients with primary cutaneous aspergillosis [1–5]. It is of interest that, to our knowledge, previous reports have not documented secondary cutaneous aspergillosis among HIV-infected patients. Itraconazole has been used to treat cutaneous aspergillosis in four HIV-related cases, including the two HIV-related adhesive tape/catheter cases we have described. Itraconazole was used successfully after surgical debridement of a chronic ulcer in a child with HIV. However, itraconazole therapy was not successful when used as first-line therapy for an HIV-related catheter infection that started as a primary infection and had already disseminated to the pulmonary tree by the time itraconazole therapy was started [4].

Among these nine cases of HIV-infected patients with primary cutaneous aspergillosis, use of adhesive-tape dressings was the most consistent risk factor associated with these infections. Although some of the nine patients had neutropenia, most did not, and we would thus conclude that neutropenia is not the most important risk factor in the development of cutaneous aspergillosis among HIV-infected patients. The range of clinical findings associated with these primary cutaneous aspergillosis lesions includes nodules, molluscum-like papules, plaques, and ulcers. An accurate diagnosis of cutaneous aspergillosis requires a skin biopsy of the lesion with histological evaluation (including silver staining). It appears reasonable to use itraconazole for treatment of patients for whom primary aspergillosis has localized at least several centimeters separate from a vascular exit site and for whom there is no evidence of extracutaneous aspergillosis. These patients should receive close monitoring and failure to respond should prompt a change in the therapeutic regimen to intravenous amphotericin B.

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