Nonhealing Scalp Wound Infected With *Aspergillus niger* in an Elderly Patient

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Cutaneous aspergillosis is a rare infection most often seen in immunocompromised patients. We report a case of primary cutaneous aspergillosis infection in a nonhealing scalp wound of an immunocompetent elderly patient. The patient had a cutaneous malignancy of the scalp treated with surgical excision but complicated by poor wound healing. Fungal culture of the nonhealing wound revealed Aspergillus niger. *The nonhealing wound subsequently resolved with retapamulin ointment 1% and ketoconazole gel 2%.*

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Case Report

An 81-year-old man presented to the dermatology department for evaluation of a nonhealing wound on the vertex of the scalp. The patient was treated with Mohs micrographic surgery for a squamous cell carcinoma on the vertex of the scalp 4 years prior to presentation. The subsequent defect was left to heal via secondary intention. However, the wound failed to reepithelialize and when the patient returned several years later, a punch biopsy was performed to rule out cutaneous carcinoma. Pathology revealed acute and chronic inflammation with granulation tissue. There was no evidence of malignancy. Computerized axial tomography of the head was negative for soft tissue masses and bony metastases. The patient's medical history was remarkable for colon cancer following hemicolectomy and chemotherapy 4 years prior to presentation. The patient also had a history of multiple nonmelanoma skin cancers and a lentigo maligna on the left cheek.

At initial presentation to the dermatology department, physical examination revealed a 6×6-cm erythematous erosion with scattered pustules on the vertex of the scalp. The patient was afebrile and denied systemic symptoms. Bacterial and fungal cultures were obtained and the patient was instructed to apply wet dressings soaked with aluminum sulfate and calcium acetate solution twice daily for 2 days and retapamulin ointment 1% twice daily. At a 2-week follow-up examination, the patient noted slight improvement with persistence of pustules (Figure 1). Fungal culture grew *Aspergillus niger.* Therefore, 2 additional punch biopsies were performed and the tissue specimens were sent for histopathology and culture. Histopathology was negative for malignancy and fungi by periodic acid–Schiff stain, yet a smear from the lesion stained with chlorazol black E revealed branching hyphae. The patient was instructed to apply retapamulin ointment 1% in the morning and ketoconazole gel 2% in the evening to the scalp wound. At 1-month follow-up, marked improvement was noted (Figure 2). The patient continued to apply ketoconazole gel 2% with complete resolution.

Comment

Cutaneous aspergillosis may occur as a primary or secondary infection. Primary infection typically involves areas where trauma was experienced such as catheter sites, abrasions due to adhesive dressings or occlusion, burn wounds, and surgical wounds. Expectedly, burn victims, neonates, solid organ transplant recipients,

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and human immunodeficiency virus (HIV)–infected patients develop primary cutaneous aspergillosis following long-term local skin injury. Secondary cutaneous infections are caused by hematologic seeding of the skin or local extension of infected underlying structures. Bone marrow transplant patients more often develop secondary aspergillosis due to spread from infected structures such as the nasal cavity, sinuses, or embolic lesions. Cancer patients develop both primary and secondary aspergillosis. Cutaneous aspergillosis is rare in immunocompetent hosts but has occurred in cases of traumatic inoculation or exposure to high spore counts.[1-6] Risk factors for aspergillosis include immunodeficiency disorders, organ transplant, immunosuppressive medications, broad-spectrum antibiotics, chemotherapy, granulocytopenia, cirrhosis, diabetes mellitus, uremia, malignancy, tissue injury, neonatal status, and cytomegalovirus infection.[7]

Our patient had risk factors for a primary infection; he had a nonhealing wound following multiple surgical procedures, antibiotics, and adhesive dressings. He had been immunocompromised in the past, secondary to chemotherapy for colon cancer, but there was no evidence of decreased immunity at the time of presentation. Although they are rare, there are other cases of aspergillosis in immunocompetent hosts, including one following Mohs micrographic surgery.[8] A PubMed search of articles indexed for MEDLINE using the term *primary cutaneous aspergillosis* revealed 16 reported cases in immunocompetent hosts.[4,6,8-21]

Primary cutaneous aspergillosis and non–HIV-related secondary cutaneous aspergillosis often present as an erythematous nodule that may ulcerate and form a central black eschar.[1,22] Hemorrhagic bullae, erythema, and induration have been documented in infections due to local trauma.[23,24] Primary cutaneous aspergillosis usually is accompanied by fever.[25] In neonates, pustules and purulent discharge have been described.[26-29] The differential diagnosis for cutaneous aspergillosis includes ecthyma gangrenosum, cutaneous candidiasis, mucormycosis, vasculitis, pyoderma gangrenosum, and other fungal infections.[10]

The *Aspergillus* genus is ubiquitous in the environment; it is found in soil, water, and decomposing vegetation. In hospitals, the fungus has been cultured from air circulation systems, dust dislodged during construction, carpeting, potted plants, and foods such as black pepper and tea.[30-32] It is second only to *Candida albicans* as the most common cause of human opportunistic fungal infections.[26] Species determination has not been shown to guide therapy and the most likely species vary by patient population. For instance, *Aspergillus fumigatus* is the most commonly isolated species in HIV-related cutaneous aspergillosis. In cases of non–HIV-infected patients and non-burn patients, the following proportions of identified species have been reported: *Aspergillus flavus*, 44%; *A fumigatus*, 26%; *Aspergillus* species (undetermined), 10%; *Aspergillus terreus*, 6%; *A niger*, 6%; *Aspergillus glaucus*, 4%; *Aspergillus chevalieri*, 3%; and *Aspergillus ustus*, 1%.[1]

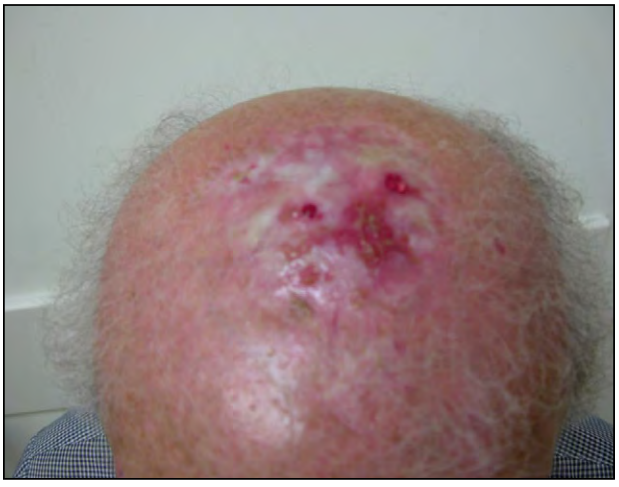

Figure 1. Scalp lesion 2 weeks after treatment with wet dressings soaked with aluminum sulfate and calcium acetate solution and retapamulin ointment 1%.

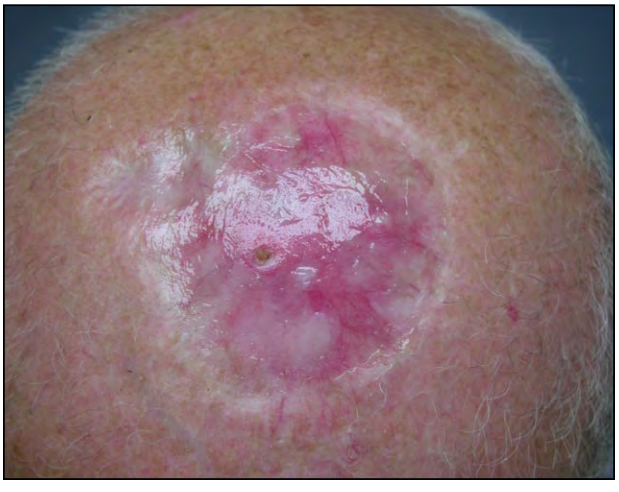

Figure 2. Scalp lesion at 1-month follow-up. The patient applied retapamulin ointment 1% in the morning and ketoconazole gel 2% in the evening.

A presumptive diagnosis of cutaneous aspergillosis can be made from a positive potassium hydroxide preparation of lesional skin or exudate. The hyphae of *Aspergillus* are 3 to 4 mm in diameter and septate.[33] In invasive aspergillosis, the hyphae branch at regular acute angles. However, chronic granulomatous lesions do not always exhibit this characteristic branching

pattern.[34] Additionally, acute angle branching is not specific to *Aspergillus*; other potentially pathologic filamentous molds such as *Pseudallescheria boydii* and *Fusarium* species may exhibit acute angle branching.[1] Thus biopsy for histopathology and tissue culture is the gold standard for diagnosis. The fungal culture specimen should be obtained from the center of the lesion and extend into the subcutaneous fat, as the organism has a predilection for blood vessels in the dermis and subcutaneous tissue.

Tissue specimens can be stained with calcofluor, a whitening agent. Fungal structures will fluoresce when exposed to UV light. The specimens also should be plated on media specific for yeast, mold, and dermatophytes, and allowed to grow for 6 weeks. Isolates can be identified by morphology, color, and sporulation.[1] Pathology specimens stained with hematoxylin and eosin inconsistently demonstrate *Aspergillus* hyphae; therefore, Gomori methenamine-silver, which stains hyphal cell walls black, and periodic acid–Schiff stains are more reliable for identifying fungal elements.[35] In immunocompromised patients, serum galactomannan and 1,3-β-D-glucan (major components of the *Aspergillus* cell wall) have been used to aid the diagnosis of invasive aspergillosis.[36]

Secondary cutaneous aspergillosis can be seen in 5% to 10% of patients with invasive aspergillosis.[37] Therefore, patients should be evaluated for systemic involvement. Of primary importance is the assessment of risk factors such as immune status, invasive lines, and skin wounds. If pulmonary signs and symptoms are present, computed tomography of the chest should be ordered; if abnormalities are detected, a bronchoscopy is indicated.

Aspergillosis can be treated with 3 classes of antifungals: polyenes, azoles, and echinocandins. Our patient responded well to treatment with topical ketoconazole, which is an azole. However, intravenous therapy with amphotericin B and oral itraconazole are common first-line agents, though resistance has been reported.[38] A review by van Burik et al[1] suggested oral itraconazole as first-line therapy for localized primary cutaneous aspergillosis at least a few centimeters from a catheter site; with signs of clinical failure, therapy should be switched to intravenous amphotericin B. Additionally, intravenous amphotericin B with or without surgery was recommended as first-line therapy for patients with catheter site involvement, tunnel infections, secondary infections, or extensive primary disease.[1] In a case of primary cutaneous aspergillosis in an immunocompetent patient, clinical improvement was observed within 2 weeks and resolution was noted in 3 months following treatment with oral terbinafine 250 mg once daily for 35 days and local neomycin solution 0.5%.[6] For invasive aspergillosis, improved survival rates have been reported following treatment with voriconazole when compared with intravenous amphotericin B.[39,40] For severe infections with necrotic tissue, surgical debridement and amputation are therapeutic options.

Our patient's infection resolved with consistent application of a topical antifungal agent, demonstrating that systemic therapies may not be necessary to treat localized cutaneous aspergillosis. The case also serves as a reminder to keep aspergillosis in the differential, even in immunocompetent hosts.

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