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Cutaneous infection by *Alternaria infectoria* in a renal transplant patient

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Abstract: Skin lesions are common in renal transplant recipients (RTR) and the clinical distinction of malignancy versus infection may be difficult in this patient population, with the need for further histological and biological investigations. We report here on a 73-year-old male RTR who presented with *Alternaria infectoria* phaeohyphomycosis of 1 year's duration. Mycological cultures were negative, and the diagnosis was performed by real-time polymerase chain reaction assay and direct sequencing. The extension of the lesion under itraconazole treatment required its surgical excision. *Alternaria* are ubiquitous plant-inhabiting saprobes, which are increasingly associated with opportunistic phaeohyphomycosis in immunocompromised individuals.

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Skin lesions are common in renal transplant recipients (RTR) and the clinical distinction of malignancy versus infection may be difficult in this patient population, with the need for further histological investigations. We report here on a 73-year-old male RTR who presented with such a suspicious lesion of 1 year's duration, in the absence of preceding trauma.

Case

The patient had been transplanted with a cadaver kidney 3 years earlier because of end-stage renal disease secondary to vascular nephropathy. There was no history of rejection, and the patient was taking the following long-term immunosuppressive drugs: tacrolimus (3 mg), mycophenolate mofetil (720 mg), and methylprednisolone (4 mg). In addition, he was treated with metoprolol, furosemide, and ramipril for chronic hypertension.

On clinical examination, there was a single crusted violaceous plaque on the back of the right hand (Fig. 1A). The lesion was painless, and no inoculation event could be identified. In order to further evaluate this process, a punch biopsy was performed, which showed necrosis and diffuse inflammation in the dermis, with granulomas and histiocytes, as well as an infiltrate of lymphocytes, neutrophils, and plasma cells (Fig. 1B and C). Periodic acid–Schiff staining further demonstrated fungal elements diffusely distributed in the dermis (Fig. 1C, inset). Mycological cultures remained negative.

However, real-time polymerase chain reaction (RT-PCR) assay combined with direct sequencing of 2 independent internal transcribed spacer domains of the rDNA gene (1) specifically identified *Alternaria infectoria* as the causative agent. [Correction added after online publication date August 5, 2009]. Itraconazole (200 mg/day) was first initiated for 6 months, in association with close follow-up of tacrolimus serum levels. The dosage of mycophenolate mofetil was reduced by half (360 mg/day). However, extension of the lesion required its surgical excision, and anti-mycotic therapy was administered for another 6-month period.

Discussion

Phaeohyphomycosis refers to subcutaneous and/or systemic infection caused by dark-walled hyphae that are

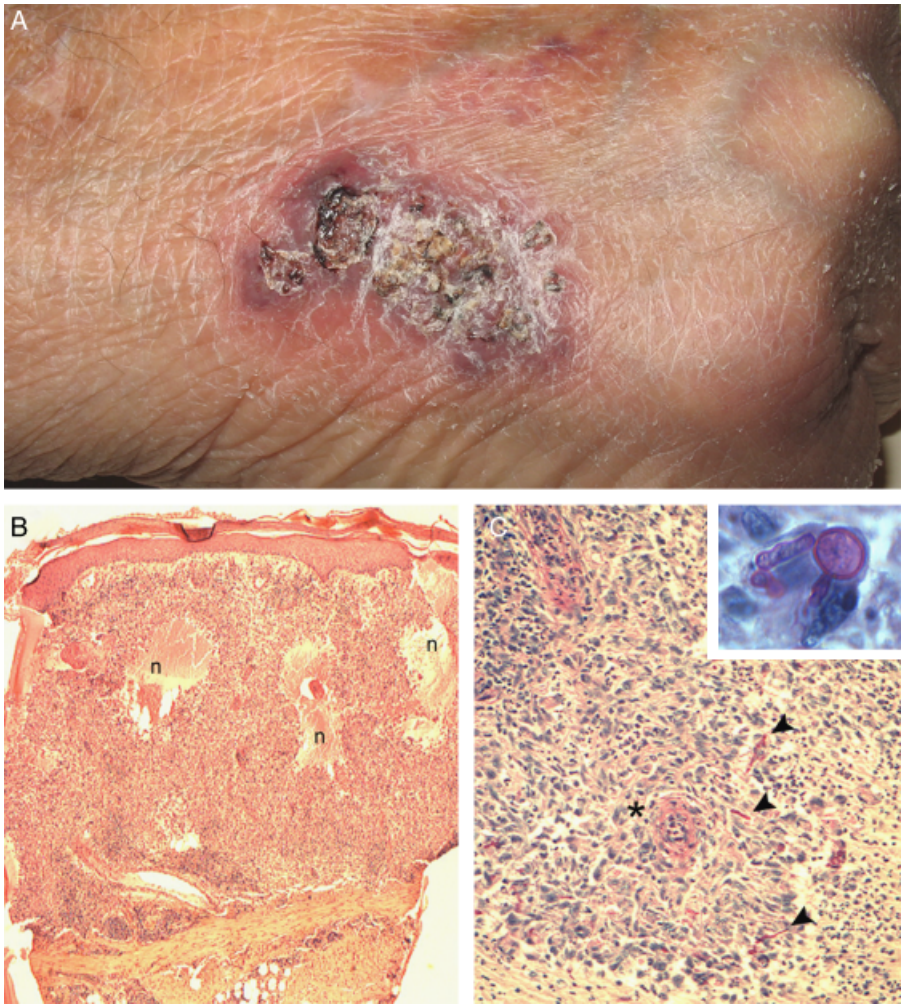

Fig. 1. Cutaneous alternariosis. (A) Clinical examination: a scaly violaceous plaque on the back of the right hand. (B–C) Histological examination (hematoxylin and eosin staining): at low magnification (B), presence of diffuse inflammatory infiltrates surrounding large necrotic areas (n) in the dermis. At higher magnification (C), identification of numerous granulomas (*) composed of lymphocytes, plasmocytes, and neutrophils, with scattered elongated structures (arrowheads) corresponding to fungal elements, as demonstrated by periodic acid–Schiff counterstaining (C, inset).

mostly regarded as plant pathogens, soil saprophytes, and contaminants (2). As an example, species of the genus *Alternaria* are ubiquitous plant-inhabiting saprobes and are increasingly associated with opportunistic phaeohyphomycosis in immunocompromised individuals. Alternarioses have indeed been described in patients with Cushing syndrome, lymphoproliferative disorders, acquired immunodeficiency syndrome, and after solid organ transplantation (3). *Alternaria alternata* represents the main cause of cutaneous alternarioses.

Two possible routes of infection have been described. In the exogenous form, mycosis results from direct inoculation of fungal elements, whereas in the endogenous type, infection occurs after inhalation of fungal conidia with subsequent systemic spread and cutaneous involvement (3). Hence, the clinical presentation may range from local skin lesions to invasive and disseminated infection (4). The cutaneous manifestations include verruciform, eczematous, or ulcerating plaques, as well as vegetating or nodular lesions. Skin lesions can be single, as described here, and mimic malignancy, or multiple—especially in disseminated disease.

Therefore, punch biopsy and culture are strongly recommended before treatment. Species of the genus *Alternaria* usually grow in routine laboratory media, except *A. infectoria*, which rapidly loses its ability to sporulate and proliferate (2). RT-PCR routinely performed from skin samples allow the selective amplification and identification of the causative mycotic agent, as described here (5). [Correction added after online publication date August 5, 2009].

In the absence of evidence-based recommendations, long-term itraconazole is regarded as the first-line treatment of cutaneous alternarioses. It must be noted that close follow-up of calcineurin inhibitors (CNI) serum level is critical, given the itraconazole-induced inhibition of CNI metabolism (4). Surgical excision of accessible lesions may help in cases resistant to classical antifungal therapy (6).

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