SHORT REPORT: SUCCESSFUL TREATMENT OF BLACK-GRAIN MYCETOMA WITH VORICONAZOLE

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Abstract. Fungal mycetoma (or eumycetoma) are endemic diseases in tropical areas that have economic effects because of their chronic and disabling evolution. Classic treatments include surgery and antifungal drugs, but these have multiple side effects. We report a case of black-grain fungal mycetoma successfully treated with voriconazole without side effects. The duration of the treatment remains unclear, but must be prolonged because of the frequency of relapses.

Mycetoma is an infection caused by Actinomyces or environmental fungi. It results from implanting the pathogen into subcutaneous tissue through a penetrating injury (mostly in the foot because causative pathogens are found in soil), which may secondarily infect fascia, muscles, joints, and bones. This disease is endemic in tropical and subtropical regions, especially in west Africa and India. It is a major public health problem because of its prevalence and chronicity in young active workers.¹

Madurella sp. are one of the main microorganisms causing black-grain fungal mycetoma. Classic treatment consists in radical surgery, but treatment with ketoconazole or itraconazole,² occasionally with flucytosine, is considered marginal because of poor short-term efficacy and unacceptable high rate of recurrence and side effects.³ Voriconazole has been used in a few cases of mycetoma, but just once in Madurella mycetomatis mycetoma.⁴ We report the efficacy and long-term tolerance of voriconazole therapy in a patient with Madurella sp. foot mycetoma.

A 55-year-old man from Senegal who was living in France since 1980 was referred to Hôpital Necker-Enfants Malades in Paris in April 2005 for a swelling of the right foot that had evolved for six years. He never received any medical or surgical therapy for the swelling. A diagnosis of eumycetoma was made on the basis of clinical examination, emissions of small black grains, microscopic examination, and histopathologic findings. Culture was positive, but the fungus did not sporulate. Molecular identification of the isolate was performed at the National Reference Center for Mycology and Antifungals (Institut Pasteur, Paris, France).

Sequencing of the internal transcribed spacer region of ribosomal DNA was done after amplification of DNA with fungal universal primers.⁵ Based on the closer match obtained after comparison of the sequence with our database, the fungus was tentatively identified as a Madurella sp.

Antifungal susceptibility testing showed a high susceptibility to voriconazole (minimum inhibitory concentration [MIC] < 0.015 µg/mL). Susceptibilities to itraconazole and terbinafine were ≤ 0.015 µg/mL for both drugs. Voriconazole was used to treat this patient because of simplicity of use and its good long-term tolerance.⁶ Radiologic evaluation with conventional radiographs and magnetic resonance imaging (MRI) did not show any joint or bone involvement. An MRI showed sinus tracts in the internal side of the foot next to the tarsal bones (Figure 1).

Oral voriconazole therapy (200 mg twice a day) was started in April 2005. After three months, the wound had closed and the subcutaneous induration dramatically decreased. The patient could then walk without complaints. After one year of therapy, a minor induration persists and a recent MRI showed a major improvement in the subcutaneous lesions (Figure 2). Because of the lack of any side effects, treatment with voriconazole was continued.

Treatment of fungal mycetoma had not changed for years. Recently, terbinafine monotherapy was used for treatment of a few cases of eumycetoma in Senegal⁷ with encouraging results (80% clinical improvement in 20 patients). Posaconazole

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**Figure 1.** Coronal T1-weighted (A), axial T2-weighted (B), and axial contrast-enhanced T1-weighted (C) magnetic resonance images of the patient showing show marked soft tissue swelling associated with increased vascularity.
We report the efficacy of long-term voriconazole therapy for Madurella sp. foot mycetoma. This is consistent with the recent description of another patient with M. mycetomatis eumycetoma, without bone involvement, who also received voriconazole for 16 months and did not show any recurrence four years after treatment had ended. Voriconazole has also been successfully used for the treatment of eumycetoma caused by other fungi, such as Scedosporium apiospermum, S. prolificans, and Fusarium sp. Because of its good efficacy for treatment of fungal bone infection, at least for invasive aspergillosis, voriconazole may represent a major improvement in the management of fungal mycetoma because its use may prevent mutilating surgery and its functional consequences. Voriconazole efficacy during fungal mycetoma should now be further documented on a larger scale. Although voriconazole is an expensive drug, its use should be considered if results of additional studies are encouraging because mycetoma is endemic in some developing countries.

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