Case Report: Non-Invasive Management of Madura Foot with Oral Posaconazole and Ciprofloxacin

Amit M. Sharma, Namita Sharma, Amritpal Nat, Meghan Rane, and Timothy P. Endy*

Department of Medicine, State University of New York, Upstate Medical University, Syracuse, New York; Division of Infectious Disease, Department of Medicine, State University of New York, Upstate Medical University, Syracuse, New York

Abstract. Madura foot is a chronic infection caused by fungus and/or bacteria. Traditionally, treatment has been surgical debridement or amputation. Non-invasive management with long-term antimicrobials alone has been reported as successful. We report a case of Madura foot in a Somali refugee successfully managed with oral posaconazole and ciprofloxacin.

CASE PRESENTATION

A 22-year-old Somali male presented with right foot pain and swelling for 7 years and “tiny watermelon seeds” extruding out of the “puncture wounds” on the sole of the right foot (Figures 1–3). The patient gave a history of prolonged barefoot outdoor exposure in his native country and at his refugee camp in Kenya. Physical examination revealed swelling of the sole of his right foot and multiple sinus tracts along with evidence of recent drainage (Figures 1 and 2). Magnetic resonance imaging (MRI) of the right foot showed contiguous involvement of the skin and subcutaneous tissue over the medial and plantar aspects of the foot and reactive changes in the bone consistent with an underlying osteomyelitis. Subsequent biopsy showed ulceration and extensive fibrosis (Figure 3), focal granulomas (Figure 4), and clusters of darkly pigmented fungal hyphae (Figure 5). The patient was hospitalized and initially treated with intravenous trimethoprim-sulfamethoxazole (TMP-SMX) and liposomal amphotericin B. The patient was discharged home on an oral regimen of posaconazole while completing 3 weeks of ciprofloxacin.

Figure 1. Initial presentation of the patient. Swelling of the sole of his right foot and multiple sinus tracts along with evidence of recent drainage. Compared with normal left foot.

Figure 2. Eumycetoma triad: subcutaneous mass, sinus tracts, and grain discharge.

Figure 3. Histological appearance of the biopsy sample. Note the extensive ulceration and extensive fibrosis, focal granulomas.

*Address correspondence to Timothy P. Endy, Division of Infectious Disease, Department of Medicine, State University of New York, Upstate Medical University, Syracuse, 725 Irving Avenue, Suite 304, Syracuse, NY 13210. E-mail: endyt@upstate.edu
TMP-SMX 160 mg bid for 6 weeks, posaconazole 400 mg bid, and ciprofloxacin 500 mg bid. Five months into the treatment there was considerable improvement in his symptoms (Figure 6) and he continued with posaconazole and ciprofloxacin for 6 additional months. Twelve months into the treatment, his foot size was equivalent to his unaffected left foot (Figures 7 and 8) and his oral antibiotic treatment was stopped.

**DISCUSSION**

Madura foot is an ancient disease having been described in a 1,500-year-old skeleton recovered from Israel. Sir George Ballingall, a British military surgeon working in India, was the first to describe “Madura Foot” in the 1800s, sometimes called “Ballingall’s disease,” and documented the large burden of this condition in India. Mycetoma commonly involves the foot (Madura foot) and also known as maduramycosis, is a chronic subcutaneous polymicrobial bacterial (actinomycetoma) and/or fungal infection (eumycetoma) that is destructive and associated with severe morbidity and disability. The initial event is thought to arise from traumatic inoculation of fungus and bacteria into the skin or subcutaneous tissue. During the initial phases, a hard, painless papule forms that increases in size to form a tumor-like growth termed a mycetoma. As the tumor grows in size, sinus tracts form, and there is extensive soft-tissue involvement and eventual involvement down into the bone producing an osteomyelitis. Dark granules that form from dead organisms are discharged from the sinus tracts forming the “watermelon seeds” observed during the late states of the mycetoma.

The burden of maduramycosis is not known though a recent systemic review of the literature and meta-analysis estimates that the prevalence can be as high as 3.49 cases per 100,000 in highly endemic countries such as Mauritania, Sudan, Mexico, Senegal, Niger, and Somalia. Most cases were described in men as compared with women with 70% of cases found in persons between 11 and 40 years of age. The
foot was the most affected body site (68.7%) followed in declining frequency by the leg (9.9%), trunk (6.1%), and arm (4.0%). Eumycetomas are endemic in Africa, the Indian subcontinent, and Latin America, whereas Actinomycetomas predominate in the Americas, with a majority of all cases in Mexico. In a meta-analysis of case reports conducted in 2013, almost 8,763 cases of Mycetoma were identified of which the majority of cases were reported from Mexico (2,607 cases), Sudan (2,555 cases), and India (1,392 cases). Countries with the highest prevalence include Mauritania (prevalence of 3.49 cases per 100,000 inhabitants) and Sudan (prevalence of 1.81 cases per 100,000 inhabitants). The hallmark of the infection is the ability of the offending organisms to form grains (i.e., black for eumycetoma and yellow for actinomycetoma). The bacterial and fungal causes of mycetoma also vary by region and includes most frequently the bacteria Actinomadura madurae, Streptomyces somaliensis, Actinomadura pelletieri, Nocardia brasiliensis, and the fungus Madurella mycetomatis, Scedosporium boydii, and Falciformispora senegalensis.

Clinical diagnosis of eumycetoma is based on the triad of subcutaneous mass, sinus tracts, and grain discharge (see Figure 2). The primary lesion is frequently a papule that grows slowly in size to give rise to secondary nodules, and triggers an inflammatory response of the deep dermis and subcutaneous tissue, resulting in draining sinuses communicating with overlying skin and osteomyelitis as shown in our patient. The color of the discharge is an indicator of the underlying pathogen; however, most infections are polymicrobial and can alter its appearance. Histological and microbial diagnosis is essential in the identification of the correct organism and instituting appropriate antifungal and antibacterial treatment. Serodiagnosis with enzyme-linked immunosorbent assay is not always diagnostic as a result of variable levels of humoral response to infection, and ancillary investigations such as polymerase chain reaction are not readily available at all centers. The MRI of the affected area has diagnostic value and usually shows a characteristic “dot-in-circle” sign (Figure 9).

Management for maduramycosis entails extensive debridement of the infected tissue combined with prolonged antifungal therapy with ketoconazole (400–800 mg/day) or itraconazole (400 mg daily). Long treatment periods, financial burden from the treatment complicated by drug resistance results in frequent failure of medical management and increases the probability of a surgical intervention such as amputation. The use of potent, extended-spectrum triazoles

![Figure 8](image_url)

**Figure 8.** Completion of 12 months of medical therapy. (A) Plantar view. Size of the right foot is almost similar to the left foot. Old sinus tracts have healed and no deformity of the right foot is noted. (B) Dorsal view. No residual deformity of the right foot. Patient did not have difficulty with weight bearing.

![Figure 9](image_url)

**Figure 9.** Magnetic resonance imaging, T2 weighted coronal images of a Madura foot. Shows inflammatory changes with multiple soft tissue and osseous small hyperintense lesions with peripheral hypointense rim corresponding to mycetoma grains (yellow arrows). Few of them showing “dot-in-circle” sign (thicker white arrow) characteristic of Madura foot. *Source of images from Reference 14.*
such as Posaconazole (800 mg/day) has produced high cure rates (80%) with remission up to 2 years after treatment.\textsuperscript{11,12} Posaconazole is a broad spectrum azole antifungal that has activity against a broad range of fungal pathogens, which includes yeasts and molds with use against \textit{Aspergillus} spp., \textit{Fusarium} spp., and Zygomycetes.\textsuperscript{11,13} It has good penetration to the bone and has been shown to be safe and well tolerated when administered long term. Our patient did not have any complications from long-term use with posaconazole and ciprofloxacin with good results. The efficacy of this approach with the prolonged use of oral azoles and antibiotics for this condition awaits formal efficacy studies.

Received May 30, 2014. Accepted for publication June 29, 2014. Published online October 27, 2014.

Authors' addresses: Amit M. Sharma, Namita Sharma, Amritpal Nat, and Meghan Rane, SUNY Upstate Medical University, Medicine, Syracuse, NY, E-mails: SharmaA@upstate.edu, SharmaN@upstate.edu, NatAm@upstate.edu, and RaneM@upstate.edu. Timothy P. Endy, Upstate Medical University, Syracuse, NY, E-mail: endyt@upstate.edu.

REFERENCES