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See also Commentary, p. 259–260

SHORT COMMUNICATION

Eumycetoma on the Foot Caused by *Madurella mycetomatis*: Amputation After Significant Worsening During Pregnancy

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Mycetoma is a chronic, subcutaneous infection caused by traumatic inoculation through the skin of some types of filamentous aerobic bacteria (actinomycetoma) and true fungi (eumycetoma) (1, 2). It is considered a neglected disease with high morbidity and major effects on the patient's quality of life (1–3). Few published cases have examined mycetoma during pregnancy (4–7). We report here a case of a patient with eumycetoma on her foot that exhibited significant clinical worsening during pregnancy, which illustrates the difficulty of treatment of this infection during pregnancy, when consideration of the teratogenic and toxic effects of antifungal drugs is paramount.

CASE REPORT

A 27-year-old woman presented with a 3-year-history of a slowly growing mass on the calcaneus and plantar regions of her right foot, which exhibited erythematous nodules, cutaneous sinuses, exudate and black grains, with no pain or constitutional symptoms (Fig. 1A, B). She had a history of local trauma that involved walking barefoot under a waterfall in Rio de Janeiro, Brazil, two months prior to the onset of symptoms. Cutaneous biopsy was performed. Histological findings included grains composed of pigmented hyphae, surrounded with a cement material, mixed inflammatory infiltrate, with abscesses, multinucleated foreign body giant cells and granulation visible on haematoxylin and eosin (H&E) and Grocott methenamine silver stains. The diagnosis of eumycetoma caused by *Madurella mycetomatis* was confirmed by the presence of a brownish diffusable pigment on Sabouraud dextrose agar and thermotolerance test (37ºC). Treatment with itraconazole (200 mg twice daily) for 5 months resulted in some improvement; however, treatment was suspended following a 2-week delay in menstruation. Liposomal amphotericin B was prescribed, but was suspended after 5 weeks due to hypokalaemia, nausea, vomiting and syncope. During pregnancy, the infection was exacerbated, and the number of lesions increased dramatically (Fig. 1C, D). Intense pain due to recurrent episodes of secondary bacterial infections prohibited the patient from walking. Computed tomography and magnetic resonance imaging, performed before and after the patient became pregnant, revealed worsening of her condition and increasing bone destruction. The patient had a normal delivery and gave birth to a healthy baby. She decided to interrupt lactation in the second month to reintroduce itraconazole. After 2 months, below-knee amputation

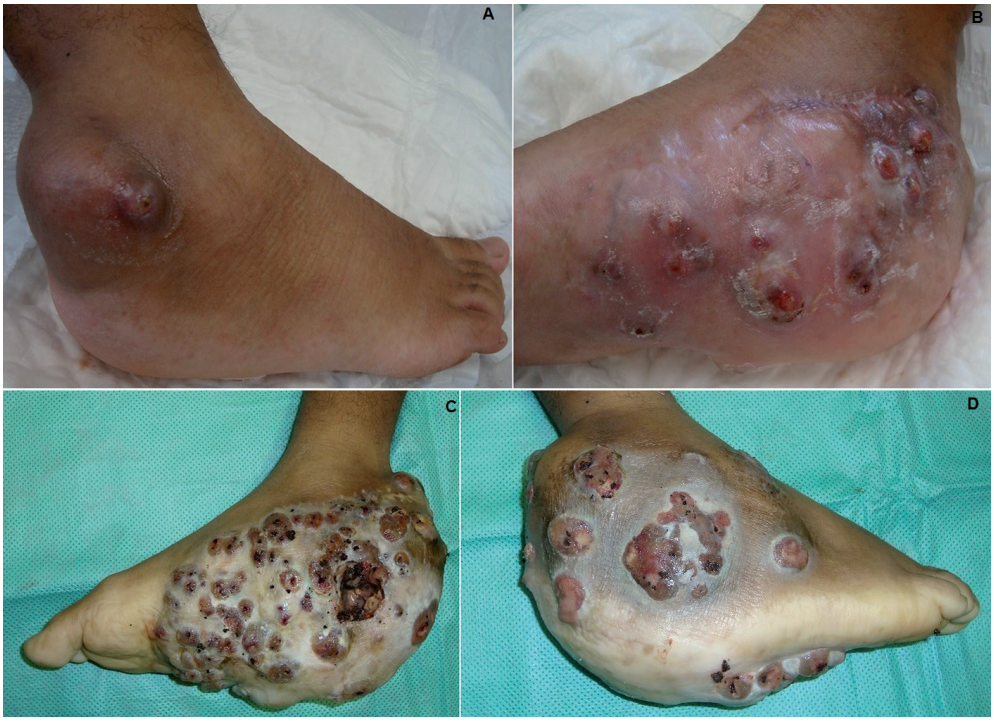

Fig. 1. (A, B) Eumycetoma of the right foot before pregnancy and (C, D) after pregnancy.

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was indicated due to massive bone destruction, clinical worsening and the request of the patient. The antifungal treatment was maintained for 3 months following surgery in order to minimize the risk of local recurrence.

DISCUSSION

Pregnant and non-pregnant women are likely to be susceptible to the same fungal infections (8). However, certain fungal, bacterial and parasitic infections tend to exhibit more aggressive, atypical and exuberant courses in pregnant women (8, 9). Cutaneous leishmaniasis (10), phaeohyphomicosis (9), nocardiosis (6, 7), coccidioidomycosis (8, 11), paracoccidioidomycosis (8), blastomycosis (8) and histoplasmosis (8) are some examples. We found only 4 reported cases of mycetoma during pregnancy (4–7), all of which involved significant clinical worsening. Bone destruction was reported in 2 of them, both eumycetoma, and only one case exhibited indications for amputation. We were unable to find any cases of eumycetoma in the placenta or cases that threatened the foetus. The immunological mechanisms underlying this phenomenon are incompletely understood, probably because of the immunocompromised state of pregnant women due to hormonal influences or the suppression of cell-mediated immunity due to the decrease in the CD4/CD8 ratio (5–7, 11). Elagab et al. (3) suggested that the Th2 cytokine profile might be associated with the development of eumycetoma, because he showed that patients with eumycetoma have increased concentration of circulating interleukin (IL)-10.

Although itraconazole is the drug of choice for *M. mycetomatis*, the US Food and Drug Administration (US FDA) classifies azole agents as category C drugs during pregnancy (5, 12). Flucytosine and echinocandin are insufficient for the treatment of *M. mycetomatis* and are contraindicated during pregnancy (8, 12–14). Terbinafine is classified by the US FDA as a category B drug during pregnancy; however, *in vitro* studies have demonstrated high minimum inhibitory concentrations for *M. mycetomatis* (13). Amphotericin B in a lipid formulation remains the drug of choice for the treatment of systemic fungal infections during pregnancy (8). However, the US FDA classifies this drug as a category B drug during pregnancy, and it has many side-effects and the susceptibility of *M. mycetomatis* is low (12). Surgery is indicated for the treatment of local and disseminated lesions with or without bone involvement, as it reduces the number of lesions and the duration of drug treatment. Amputation is indicated for cases with massive bone destruction, massive disease that does not respond to prolonged medical treatment and for patients who experience severe drug side-effects (2, 15). The use of orthopaedic aids as soon as possible after amputation is essential for achieving a high quality of life.

In our case, we believe that the pregnancy was responsible for the clinical worsening of the mycetoma infection. In addition, during pregnancy, treatment is usually stopped because of the lack of safe and effective drugs that do not result in risks for the foetus or the mother.

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