Mycetoma, Mycoses and Pregnancy

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Mycetoma is a chronic infection seen in countries in the tropics caused by either fungi (eumycetoma) or filamentous bacteria or actinomycetes (actinomycetoma). It presents with subcutaneous swelling confined to one site and over the surface there are draining sinus tracts discharging small microcolonies or grains, composed of the causative organisms. Tracts may also penetrate adjacent sites including bone, thereby spreading the infection. Accurate diagnosis of mycetoma depends on a combination of culture, and histopathology which is essential to distinguish between the two causal groups of organisms. Generally the actinomycetomas respond to combinations of antibiotics with a reasonable success rate whereas eumycetomas seldom respond well to antifungal drugs and often surgical intervention is necessary. While the disease is not common it is always disfiguring often leading to disabling deformity. Satisfactory treatment is complicated by a low level of recognition by health care workers even in endemic areas, unavailability of cost effective therapeutic drugs and poor treatment responses, particularly for eumycetoma. This problem has been exacerbated by the fact that there is only a small number of scientists and clinicians carrying out research or even collecting basic data on this potentially devastating infection. Work of small but determined groups such as the Mycetoma Research Centre (http://mycetoma.uofk.edu/) based in Khartoum, with international connections particularly in the Netherlands and Mexico has made our understanding of the disease much clearer. The centre runs a very comprehensive web site with clinical and epidemiological information on the disease and the challenges that face those working with mycetoma patients (1). It was therefore highly appropriate that mycetoma was recognised as a neglected disease by the World Health Organisation in 2013 (2).

The case described in this issue (3) presents many of the difficulties features of mycetoma. The patient had a eumycetoma (fungal) infection and the organism Madurella mycetomatis, while prevalent in Sudan and SubSaharan Africa, is not commonly described in South America. Recently the use of molecular tools has begun to make some sense of this situation, where it appears that organisms originally classified as M. mycetomatis may belong to one of several different species M. mycetomatis, M. pseudomycetomatis, M. tropicana, and M. fahalii. While resembling each other in cultural morphology they may exhibit different drug susceptibilities (4). It has also been shown that the dark melanin pigment surrounding the hyphae and grains of M. mycetomatis may also provide a sink for antifungal drugs which are bound to the melanin, thus reducing their bioavailability (5). Antifungal agents with low binding affinity are bioavailable in much higher concentrations. Voriconazole for instance is an example of a low affinity medication, making it a possible, albeit expensive, treatment option. There are now case reports documenting the efficacy of voriconazole in mycetoma in a few patients (6).

Little is known about factors that alter the clinical course of this infection. Sometimes mycetomas appear to enter a rapidly progressive phase with sudden local spread which can extend over a few months and the rare cases of fatal infection often belong to this group. However, previously, there have been few published records of the effect of pregnancy on the course of this disease. The case presented here is therefore unique in recording a severe deterioration in the clinical appearance and severity of an M. mycetomatis infection during pregnancy (3). This has been described elsewhere, as the authors point out, but seldom as a specific observation (7). Pregnancy is associated with increasing infection rates of other fungal infections notably those due to Candida species although interestingly in the latter, the presence of Candida in the vaginal mucosa is associated with a much higher asymptomatic carriage rate rather than infection due to tissue invasion in pregnant than non-pregnant women (8). Other infections from cryptococcosis, sporotrichosis to coccidioidomycosis are also more common or more aggressive in pregnant women. Explanations for worsening of these fungal infections during pregnancy include lymphopenia and changes in regulatory T-cell numbers (9). However, a major focus of investigation has been the shift from a Th1 to Th2 pattern of immune response in the first trimester which is a key mechanism in ensuring tolerance of the growing embryo but it may enhance susceptibility to certain infections (10). Whatever the reason, management of pregnancy-associated mycoses is problematic. In superficial infection reliance on topical treatment is usually advised. However in deep mycoses, such as mycetoma, treatment already associated with a high level of poor responses becomes even more difficult. Some of the oral azoles carry a risk, albeit very low, of birth defects. Established human cases of foetal deformity, e.g. with fluconazole, are fortunately very

© 2015 The Authors. doi: 10.2340/00015555-2037
Journal Compilation © 2015 Acta Dermato-Venereologica. ISSN 0001-5555
rare; other azoles may produce birth defects in animal models and their use are discouraged, where possible, in pregnancy (11). The treatment options here would therefore have been limited. Amphotericin B could have been used but generally its therapeutic effect in mycetomas is poor.

This case (3) is a sad reminder of a severe consequence of what is normally a happy event. Managing serious fungal disease in pregnant women can be difficult and the consequences to mother and child are grave. The therapeutic approach adopted here, amputation, seems drastic but in truth reflected the best of a number of bad options.

REFERENCES