



## Case report

Mycetoma due to *Madurella mycetomatis*

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## ABSTRACT

Mycetoma is a progressive destructive disease causing severe disability, if untreated, in otherwise healthy people. Susceptible populations are usually adult males and disease is characterized by the triad of tumor formation, presence of grains and draining sinuses. Here, we report a case of mycetoma of a young female, manifested only as a painful swelling over left ankle which was initially suspected as a malignancy. The preliminary diagnosis of mycetoma came with the presence of characteristic “dot in circle” sign in radiological evaluation which was confirmed by the positive fungal culture of 2nd biopsy for *M. mycetomatis*.

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## Introduction

Mycetoma is a disfiguring chronic inflammatory disease, which is endemic in tropical and subtropical regions of the world. It has been identified as a neglected tropical disease recently. The offending agent could be either bacteria (actinomycetoma) or fungi (eumycetoma). More than 20 different moulds are responsible for eumycetoma and four fungi namely, *Madurella mycetomatis*, *Pseudallescheria boydii*, *Leptosphaeria senegalensis* and *M.grisea* are responsible for approximately 95 % of eumycetoma. The effective management of mycetoma is based on early and accurate diagnosis of the causative organisms.

## Case report

A 22 year old, previously healthy female presented with dull pain and swelling of her left ankle for five years. Although initially she had relief with analgesics, subsequently did not respond and associated with swelling over the left ankle which affected her daily work and sleep. There were no pustules or sinuses with granules at this stage. She did not have fever, loss of appetite or

loss of weight and denied of previous traumatic injury to the affected site.

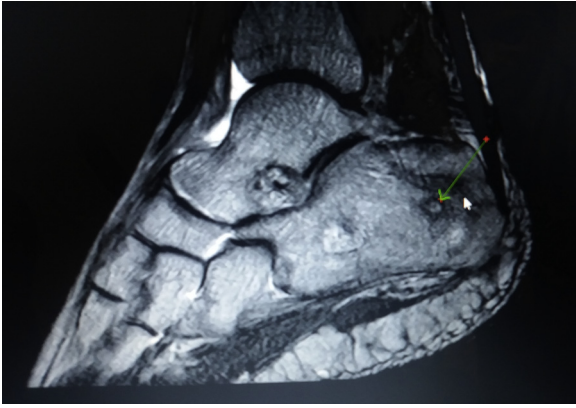
Basic investigations, X ray, ESR and full blood count, were within normal range. Her symptoms did not improve with the initial management with analgesics and she was further evaluated radiologically with the clinical suspicion of malignancy of bone or soft tissue. The MRI findings of the left ankle showed multiple linear and rounded lesions in the left calcaneus. The lesions showed a contrast enhancing center with a hypointense rim. There was hypointense dot noted at the centre of the lesion in T2 weighted image giving rise to “dot in circle sign” (Fig. 1: MRI of the left ankle showing “dot in circle sign”). Cortical erosions noted in the superior, posterior and the lateral aspect of the calcaneus. There was no sinus tract to the skin. The rest of the tarsal bone and distal tibia and fibula were normal. All the above radiological features were suggestive for maduromycosis of the foot.

With the radiological supportive evidence of maduromycosis, a punch biopsy of the skin was obtained and sent for mycological evaluation. Although both direct smear and culture were negative, she was started with oral itraconazole 200 mg twice daily and cotrimoxazole. It appeared to be responding and she was informed to continue the antimicrobials further. However, after about 4 months, she noted reappearing of throbbing pain and few pustular lesions over the affected area. These pustules subsequently ruptured and secreted clear fluid containing black dots. With the new clinical picture, a repeat biopsy was obtained for fungal studies. The direct smear of the biopsy with 10 % KOH revealed septate fungal filaments.

After 2 weeks, a scanty growth of filamentous fungi was seen in the Sabouraud Dextrose agar incubated in 26 °C and 37 °C. The

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**Fig. 1.** MRI of the left ankle showing “dot in circle sign”.

obverse view of the colony was yellowish brown with wooly consistency. Reddish brown pigment was diffusing in to the medium. The lactophenol cotton blue mount of the growth revealed sterile dense melanized mycelia. No sporulation was noted. The slide culture also showed sterile mycelium. Based on above characteristics the diagnosis of *M. mycetomatis* was made.

Oral itraconazole (200 mg twice daily) and terbinafine (250 mg daily) were started and continued for 7 months while monitoring liver functions. Her symptoms subsided gradually so that itraconazole dose was reduced up to 100 mg twice daily. After 16 months from the starting therapy, she was free from pain, swelling and discharging sinuses and she is being followed up at the clinic.

## Discussion

Mycetoma is a chronic granulomatous subcutaneous infection characterized by triad of tumor formation, presence of grains and draining sinuses [1]. It is frequently observed in lower limbs (80%), hands (8%) and other exposed areas of the body [2]. Mycetoma may confuse with malignancy or tuberculous infection in the absence of characteristic clinical features [3]. Although mycetoma targets the skin and subcutaneous tissues primarily, it progresses slowly in to adjacent tissues such as muscles, bones and joints resulting severe deformities, pathological fractures, osteopenia and osteoporosis [4,5]. Mycetoma can be complicated by secondary bacterial infections and the process has a high recurrence rate even after prolonged antifungal treatment [5].

Identification of the etiological agent and degree of disease extension are important in proper management [6]. Radiological evaluation is important in diagnosis and assessment of disease extension [6]. The soft tissue swelling and osteolytic changes are considered the most common radiological evidence of eumycetoma [6]. Vast array of radiographic findings including sclerosis, endosteal bone cavitation, extrinsic cortical scalloping, periosteal reaction, osteoporosis, soft tissue swelling, osteolysis, demineralization and osteomyelitis are associated with mycetoma [6,7]. CT shows higher sensitivity for early mycetoma while MRI has sensitivity towards late presentation [6]. A “dot in circle” sign observed in T2 weighted sequence of MRI is considered as a specific sign of mycetoma [6]. The “dot-in-circle” sign provides early, noninvasive clue in diagnosis of mycetoma [7]. Each ‘dot in circle’ sign comprises the low signal intensity rim surrounding the high signal foci with small central hypointense area representing fibrous septa, granulation tissue and fungal grains respectively [8].

Two deep biopsy samples, one for mycological diagnosis and one for histopathological diagnosis, should be obtained [9,10]. The mycological evaluation of the direct smear and culture takes 2–3

weeks and are not widely available especially in the developing world [9,10].

*M. mycetomatis* is the most common causative agent for eumycetoma [11]. *M. mycetomatis* is a melanized fungus belonging to the order Sordariales [12]. It has a moderate growth rate and unlike other *Madurella* spp, grows well at 37 °C [13]. The macroscopic view of yellow to brown colonies diffusing brown pigment in to the medium with wooly consistency and the microscopic view of mostly sterile dense melanized mycelium, provide essential clues for identification [13].

Prolonged antifungal treatment and surgical debridement generally produce satisfactory outcome [14]. *M. mycetomatis* is usually susceptible to itraconazole and ketoconazole, so these are frequently used during management [15,16]. For example, Kloezen et al. found that MIC values for itraconazole and ketoconazole of *M. mycetomatis* range from 0.016 µg/mL to 0.25 µg/mL and 0.031 µg/mL to 1 µg/mL respectively [3]. According to studies new azoles such as isavuconazole and ravconazole showed MICs ranged from <0.016 µg/mL to 0.125 µg/mL and <0.002 to 0.031 µg/mL respectively, indicating potential use against *M. mycetomatis* [15]. *M. mycetomatis* is less susceptible to echinocandins and amphotericin B and their effectiveness in treatment is doubtful [16].

## Conclusion

Mycetoma may confuse with other disease conditions such as malignancy or tuberculous infection. Radiological evaluation is important in early diagnosis and “dot in circle” sign observed in MRI is considered as a specific sign of mycetoma. This promotes early treatment before the disease progress to an advance stage leaving the patient disabled.

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