Localized Recurrence of Ankle Mycetoma after Surgical Excision: A Case Report

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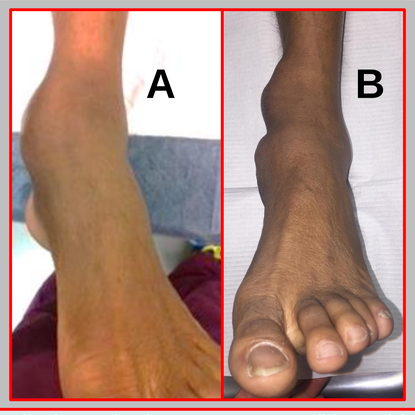
Purpose & Literature Review

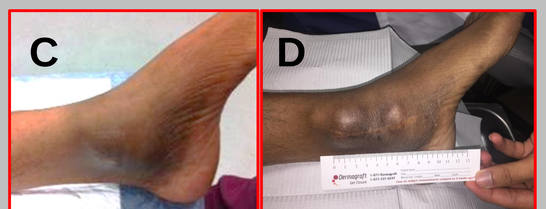
Mycetomas are chronic, localized, progressive, and potentially devastating infections with a predilection for the lower extremity. Accurate identification of the causative organism is critical in providing appropriate treatment. This study presents a case of left ankle eumycetoma, with recurrence 23 months after surgical excision. This report aims to increase awareness of adequate diagnostic approach and management of this unique, neglected tropical disease.

There is a paucity of literature concerning mycetomas and the disease is rarely reported in North American literature. This disease is endemic in tropical and subtropical countries. Localized infection typically occurs by traumatic inoculation of skin from contaminated soil, shrubbery or even contaminated shoes. Infection evolves from small subcutaneous nodules that progress into draining sinuses. Patients often present with advanced disease, including destruction of surrounding tissue and subsequent loss of function. The two causative pathogens are Actinomycetes (actinomycetoma) bacteria or Eumycetes (eumycetoma) fungi; diagnosis is confirmed by histopathologic exam. Cultures and DNA sequencing are needed for speciation of organisms **(1).** In this particular case, histopathology was used to identify *Pseudallescheria boydii* (*P. boydii*) as the causative agent of the eumycetoma. *P. boydii* is increasingly recognized as a significant opportunistic fungus, especially for disseminated infections occurring in immunocompromised patients **(2).** We present a recurrent case of a localized subcutaneous fungal mycetoma in a patient with non-insulin-dependent diabetes mellitus (NIDDM).

Clinical Appearance



Preoperative photographs. Fig A: Mass over anteromedial aspect left ankle anterior view (October 2015), Fig B: recurrence of mass 23 months postoperatively (September 2017); Fig C: medial view (October 2015), Fig D: medial view (September 2017)



Case Report

A 52-year-old Haitian male who had emigrated to the United States in 2001 was referred to our podiatric office March 2013. Patient presented with a painless, enlarging soft tissue mass to the left anteromedial ankle present for five months duration. Denied weight loss, fever, any other constitutional symptoms. The mass was freely movable, with firm consistency, no fluctuation, and intact skin.

Past medical history was significant for NIDDM for three years. Patient denied any recent trauma to area. Social history revealed no previous history of agricultural or field work. The only instance of soil-related injury was left ankle sprain/injury while playing soccer in Haiti 18 years prior (1995).

Left ankle X-rays showed lobulated soft tissue mass to left medial ankle. On initial office visit, needle aspiration was attempted with no fluid retrieved. Magnetic resonance imaging (MRI) without contrast was performed (June 2013) revealed a lobulated, encapsulated heterogeneous soft tissue mass inferior to medial malleolus. Mass measured 2.5 x 1.0 cm **(Figure 1)**, confined to subcutaneous tissue.

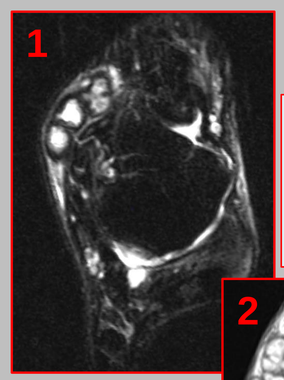
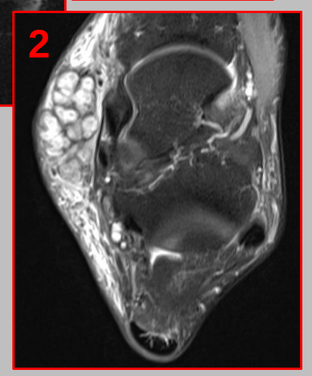


Fig 1: MRI Ankle (left) without contrast - Axial T2 fat saturated sequence - June 2013;

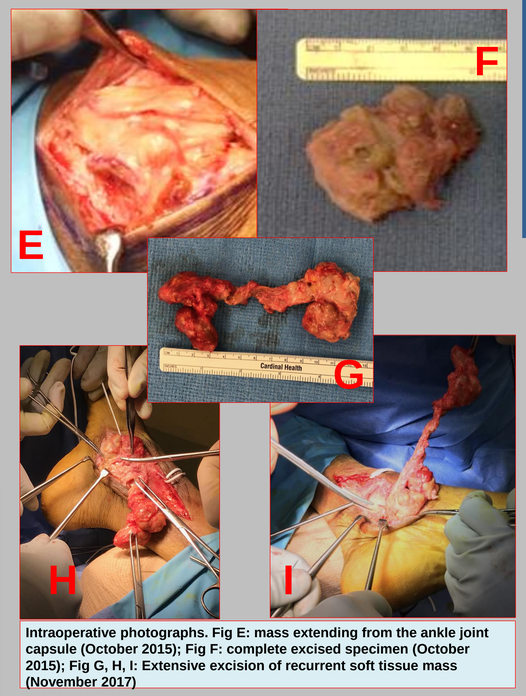
Fig 2: MRI Ankle (left) with/without contrast - Axial T2 proton density (PD) fat saturated (FS) sequence - October 2017.



Based on MRI results, conservative and surgical treatment options were discussed in detail. Recommendation made for excisional biopsy. Patient elected to have soft tissue mass closely monitored, and was amenable to surgical resection in the event of mass enlargement. Patient was then lost to follow-up for more than two years. Patient next presented to office (October 2015) with complaints of enlargement of mass over two months duration **(Fig A,C)** and concomitant onset of a small lesion to the overlying skin with clear drainage; however no evidence of ulceration or sinus was seen clinically. Recommendation again made for surgical intervention. Patient now amenable, scheduled for soft tissue mass excision. Routine laboratory tests were unremarkable, all vital signs stable preoperatively.

Surgical Procedure

A linear anteromedial incision at the ankle joint was made overlying the soft tissue mass. Gross physical findings revealed a large subcutaneous soft tissue mass extending from the ankle joint capsule **(Fig E)**. An intraoperative frozen section was sent for pathological analysis. Once identified benign, the soft tissue mass was meticulously dissected from underlying soft tissues, and excised in toto. The mass was freed from underlying soft tissue without evidence of violation to ligamentous/tendinous structures. Gross specimen was sent for histological analysis **(Fig F).** The operative site was flushed and closed using standard operative technique.



Intraoperative photographs. Fig E: mass extending from the ankle joint capsule (October 2015); Fig F: complete excised specimen (October 2015); Fig G, H, I: Extensive excision of recurrent soft tissue mass (November 2017)

Postoperative Results

Final pathology revealed negative AFB and gram stains. PAS-D stain was positive for non-pigmented fungal hyphae with acute-angle branching and septations **(Fig A2).** Final pathologic diagnosis was reported as Eumycetoma with suppurative and focally necrotizing granulomatous inflammation; likely *Pseudallescheria boydii* **(Fig A1, A2).** The patient was referred to outpatient Infectious Disease (ID) clinic. Since fungal species of *P.boydii* could not be confirmed by culture, ID, microbiology, and podiatry all agreed the best treatment would be to monitor patient at regularly scheduled intervals, without starting empiric antifungal treatment. With any evidence of recurrence, a new specimen would be obtained to select appropriate antifungal therapy.

After initial postoperative course with ID and podiatric surgery, patient failed to follow-up. Patient returned to podiatric office 23 months postoperatively (September 2017), with recurrence of a much larger soft tissue mass at the same anatomic location **(Fig B, D).**

Results continued

Per primary care physician records, recent routine laboratory values (including HA1c) were within normal limits. Patient reports he noticed re-appearance of mass on left ankle approximately 4 months prior. Although recurrent masses remained painless, he was prompted to return to clinic after noticing a "rupture" of skin overlying the returning mass, with clear drainage. Patient denies any constitutional symptoms. Clinical exam confirms recurrence of left medial ankle soft tissue mass, with corresponding area of superficial ulceration to the proximal aspect of the mass. No acute signs of infection were noted to the ulceration. Repeat MRI of left ankle with/without contrast (October 2017) again revealed lobulated partially enhancing soft tissue mass **(Fig 2, 3, 4).** The repeat study also demonstrated the pathognomonic ("dot-in-circle sign") appearance of multiple high intensity circles with a central hypointense dot **(Fig 3)**, corresponding with grains of a mycetoma **(3).** Patient again consented for surgical excision of left ankle mass. Need for future compliance emphasized including follow-up testing and treatment postoperatively for best possible postoperative outcome. The patient shortly thereafter underwent left medial ankle soft tissue mass excision (November 2017).

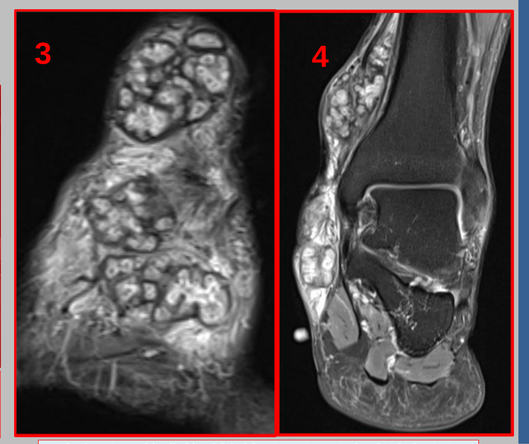


Fig 3. MRI Ankle (left) with/without contrast - Sagittal short T1 inversion-recovery (STIR) sequence - October 2017

Fig 4. MRI Ankle (left) with/without contrast- Coronal PD FS - October 2017

The soft tissue mass was resected in its entirety **(Fig G, H, I)** Under direct instruction of ID and microbiology, the following specimens (6 total) were sent to pathology and microbiology, respectively: Pathology (fresh): mycetoma; Pathology (in formalin): mycetoma; Aerobic and Anaerobic Gram Stain/Culture; AFB Gram Stain/Culture; Fungal Gram Stain/Culture.

Final pathologic diagnosis for both specimens were reported as soft tissue showing acute and chronic inflammation, abscess formation, and necrosis; with numerous clusters of non-septate fungal organisms/molds present. GMS and PAS stains were positive for fungal organisms/non-septate molds. To date, all three preliminary reports for Aerobic, Anaerobic and Fungal Cultures confirm mold isolated from cultures. Definitive identification of fungal species is pending final growth. Patient was also started on oral fluconazole daily after his repeat surgical intervention.

Histopathology

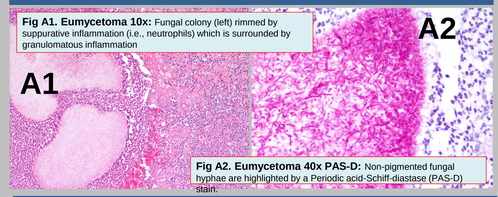


Fig A1. Eumycetoma 10x: Fungal colony (left) rimmed by suppurative inflammation (i.e., neutrophils) which is surrounded by granulomatous inflammation

Fig A2. Eumycetoma 40x PAS-D: Non-pigmented fungal hyphae are highlighted by a Periodic acid-Schiff-diastase (PAS-D) stain.

Discussion

Mycetoma is a chronic, slowly developing mycosis that results in large painless tumor-like masses in the subcutaneous tissue. Incidence occurs in the "mycetoma belt" stretching between the latitudes of 15 South, 30 degrees North **(4).** The typical demographic are agricultural workers, those living in rural areas and those who participate in outdoor activities. Minor traumatic inoculation typically allows the pathogen to enter skin through soil. This is followed by subcutaneous nodule formation that will slowly progress into draining sinuses and granule formation. If left untreated, bone invasion is common which can lead to amputation. Each species produces a specific type of granule that histopathologically can be used to help identify the causative agent. *P.boydii* was identified as most likely offending agent in this case based on histopathology. However, there are pitfalls in this diagnosis alone as grains of many species have overlapping morphological features **(1).** Therefore, cultures are needed to confirm identification of the offending pathogen for appropriate targeted anti-fungal therapy. Several actinomycetes and fungi have been implicated as causative agents of mycetoma; it is important to speciate organisms to ensure correct antimicrobial therapy. Early diagnosis and adequate long-term antifungal treatment following surgical excision of eumycetoma appear to be the most important steps for successful outcome. Frequent radiographic and clinical examination should continue even after postoperative course and cessation of antifungals. The present case underscores the importance of considering epidemiological clues for diagnosis and the multidisciplinary teamwork involved in effective treatment of mycetomas of the lower extremity

References

1) Alam, K., Maheshwari, V., Bhargava, S., Jain, A., Fatima, U., & Haq, E. ul. (2009). Histological Diagnosis of Madura Foot (Mycetoma): A Must for Definitive Treatment. *Journal of Global Infectious Diseases*, *1*(1), 64–67. http://doi.org/10.4103/0974-777X.52985

2) Cortez, K. J., Roilides, E., Quiroz-Telles, F., Meletiadis, J., Antachopoulos, C., Knudsen, T., … Walsh, T. J. (2008). Infections Caused by *Scedosporium* spp. *Clinical Microbiology Reviews*, *21*(1), 157–197. http://doi.org/10.1128/CMR.00039-07

3) Laohawiriyakamol, T., Tanutit, P., Kanjanapradit, K., Hongsakul, K., & Ehara, S. (2014). The "dot-in-circle" sign in musculoskeletal mycetoma on magnetic resonance imaging and ultrasonography. *SpringerPlus*, *3*(1), 1-7.

4) Fahal, A. (2004). Mycetoma: A thorn in the flesh. *Transactions Of The Royal Society Of Tropical Medicine And Hygiene, 98*(1), 3-11.

5) Van de Sande WWJ. Global Burden of Human Mycetoma: A Systematic Review and Meta-analysis. Vinetz JM, ed. PLoS Neglected Tropical Diseases. 2013; 7(11):e2550. doi:10.1371/journal.pntd.0002550.

6) Zijlstra, E., Van de Sande, W., & Fahal, A. (2016). Mycetoma: A Long Journey from Neglect. *PLoS Neglected Tropical Diseases, 10*(1), E0004244.

Acknowledgements

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