



MYCETOMA, A NEGLECTED TROPICAL DISEASE: A CASE REPORT WITH A REVIEW OF LITERATURE

Uchendu Obiora Jude^{1,2}, Otene Cletus Ikechukwu^{3,4} & Odokume Emanuel Igbo^{1,5}

¹Department of Pathology, Delta State University Teaching Hospital, Oghara, Delta State, Nigeria

²Department of Histopathology, Delta State University, Abraka, Delta State, Nigeria.

³Department of Surgery, Delta State University Teaching Hospital, Oghara, Delta State, Nigeria.

⁴Department of Surgery, Delta State University, Abraka, Delta State, Nigeria.

⁵Department of Human Anatomy, Delta State University, Abraka, Delta State, Nigeria.

Corresponding Author Name: Uchendu Jude Obiora

E-mail: ojlinksent@gmail.com

INTRODUCTION

Mycetoma is a chronic debilitating granulomatous infectious disease resulting from infection by either fungal organisms or fungus-like bacteria, but having essentially same pathogenesis and clinical feature.[1] About 60% of the cases are of bacterial origin, while 40% cases are of fungal etiology.[2] The fungal disease is known as mycotic mycetoma/eumycetoma and are caused mostly by *Madurella mycetomatis*, *Madurella grisea* and *Scedosporium apioapsermum/Pseudallescheria boydii*.{Nenoff;Lichon} The bacterial disease is known as actinomycotic mycetoma/actinomycetoma and are caused mainly by the anaerobic species of actinomycetes bacteria (*Nocardia*, *Streptomyces* and *Actinomadura*).[1,3] The disease is synonymous with Madura foot, a name coined from the region Madura in South India, where Gills, a French Missionary in 1842 reported and described the first clinical case, because over 70% of the lesions has foot involvement.[4] Clinically, the disease often presents as slow but progressive soft tissue swelling with chronic undulating plaques and multiple cutaneous sinuses that extrudes yellowish sulfur granules representing micro-colonies of the causative organism.[2] The pathogenesis is related to the ability of the causative agent to evoke chronic granulomatous inflammation in the dermis, subcutaneous tissue and sometimes, the underlying bones.[5].The predisposing factors to Mycetoma include systemic diseases, immunosuppression, low socioeconomic status, and malnutrition, walking on bare feet, trauma, farming occupation, poor hygiene and male gender.[6] It was recently included among the list of neglected tropical diseases by the World Health Organization in 2016, because it has long been ignored in the worldwide health agenda.[7] It's global incidence of Mycetoma is not known although an estimated incidence of 135 cases/year has been reported across 102 countries between latitudes 15° south and 30° north (The Mycetoma belt) with most of the global cases recorded in Sudan, Venezuela, Mexico and India Few cases have also been reported in some African countries such as Egypt, Nigeria, Kenya, Niger, Senegal, Mauritania, Ethiopia, Chad, Cameroon, Djibouti, and Somalia.[,8,9,10,11] To the best of our knowledge, this disease has never been encountered in this region. We therefore present the first clinically confirmed case of Madura foot in Delta State University Teaching Hospital, Nigeria.

CASE REPORT

A 42 year old male Nigerian business man, presented to the surgical department of Delta State University Teaching Hospital in January, 2021 with a left dorsal foot swelling of 10 years duration. The swelling was slowly progressive, firm in consistency, non-tender and measure 10x10x5cm, with occasional discharging sinuses. It was initially painless, but became gradually painful with dragging sensation, which is worse at night, but relieved with NSAID. There was no associated lymphadenopathy. The swelling was first noticed while he was in Ghana. He used to assist his father in farm work a decade ago. There was no history of fever, or night sweating, weight loss or chronic cough. There is no history of trauma to the leg or contact with anyone with similar swelling. He is not a known hypertensive or diabetic. He takes significant amount of alcohol and also used tobacco products. On examination, he is a middle aged man, afebrile, not pale, anicteric and not dehydrated. He had a hard mass on the dorsum of the left foot about 10 x 10 cm x 5cm, hard, not tender and not mobile. Routine blood investigations including total counts, differential counts, ESR, and alkaline phosphatase were within normal limits and X-ray examination excluded bone involvement. He had an excision biopsy under regional anaesthesia. A working diagnosis of soft tissue sarcoma was entertained and the tissue from the tumour was sent for histopathological evaluation.

Histopathology examination was in keeping with Mycetoma. Patient was placed on antifungal therapy for 6 months and follow-up evaluation has shown marked improvement.

DISCUSSION

Like all Neglected tropical Diseases, closing the research gap on Mycetoma is highly desirable. Our extensive literature search showed that the first written reference of mycetoma was in the Ancient Indian religious book *Atharva Veda*, where it was described as Anthill foot.[12] Dr John Gill, in 1842, published the first detailed clinical description of the disease.[4] Corebrook took a step further by coining the name Madura foot, inspired by the site of the lesion and the region where the disease was first discovered.[13] With more insight into the disease, Vandyke Carter was convinced that it was a fungal tumor, after identifying fungal filaments in the discharge from the sinus tracts and therefore gave it the name Mycetoma.[14] Pinoy, in 1913 divided the etiological causes into



actinomycosis (bacterial cause) and the 'true Mycetoma' (fungal cause). [15] In this report, we intend to, in our little way to the body of already existing body of knowledge.

Although available literature attests that this disease has been reported mainly in Asia, South America and Africa, [9,10] our online search reveals that there is paucity of confirmed cases in Nigeria. We are of the opinion that this is probably the first confirmed case in Delta State, Nigeria, although absence of microbiological and histopathology services in most primary and secondary health care centers are major setback to success of surveillance to this rare and neglected tropical disease.

In the index case, the patient agreed that he first noticed the disease symptoms while in Ghana. It can be adduced that the organisms were already inoculated into the host before the patient departed to Nigeria. Invariably, this highlights the role of travelling on the epidemiology of chronic diseases, as a disease contacted in one country can be diagnosed later in a different country. Travelling history should therefore always be considered in the evaluation of chronic diseases, as the distribution can be as far reaching as the human vector can travel. We think that the ease of migration, tourism and trading across the globe is important in the explanation of the disease incidence outside the Madura belt, especially in Europe.

Earlier studies show that fungal causes of Madura foot usually lives as saprophytes in the soil. The fungal spores are inoculated into the body through abrasions and trauma to the skin. [16]. This may explain why the foot is the most common site of Mycetoma and why wearing barefoot, thorn pricks, trauma to the foot and even being a farmer, herdsman, builders, landworkers or fieldworker increases the risk. [10] History of involvement with farm activity was obvious in the index case. As observed in this report, there seem to be an overall male predominance in the distribution of the disease with as much a male to female ratio of 3.7:1 [17] This is expected as the male is the favored gender for all the mentioned risk factors above such as polarized involvement in agricultural and outdoor activities.

Once inoculated, the organism multiplies progressively within the site, and spreads along facial planes, involving the skin, subcutaneous tissue and underlying tissues.[16] It is a general observation that eumyceta is a slowly progressive disease.[16] As observed in the present case, it took a time space of 10 years before the growth got to the size of 10x10x6cm. The disease progression is a complex interplay of host and the pathogen, resulting in failure of the immune system to engulf the pathogen and a consequent chronic granulomatous inflammation and foreign body reaction to the granules with protracted tissue destruction that may spread into bony structures.[5,16] Rupture of the micro-colonies of the organisms through the skin eventually results in discharging sinuses as seen in his case.[18] The X-ray result however excluded bony involvement, further attesting to the slow progression of the disease. Late presentation therefore seems to be the major underlying factor to the disease morbidity.

The clinical presentation of Mycetoma consists of a triad of symptoms, namely tumefaction (swelling), multiple draining sinuses and the presence of granules.[2,19] In the index cases, the sinuses were few and the discharge/granules less often. A high index of suspicion is therefore important in deciding the next line of action to confirm diagnosis. Distinguishing eumycetoma from actinomycetoma is possible through microscopic evaluation of the granules in the discharge, culture of organism and histopathological evaluation of hematoxylin and eosin as well as Glucott Methenamine-Silver stained tissue sections. On light microscopic examination, granules of eumycetoma appear as septate hyphae while those of actinomycetoma appear as fine branching filaments or bacillary forms.[20] Gram stain are positive for actinomyces and negative for fungi(Eumycetoma).[21] The colour of granules are specific for different species of eumycetoma.[Sahu,2016] Histopathological evaluation of Hematoxylin and eosin stained tissue sections will demonstrate the presence of sulfur granules, with dense neutrophilic infiltrates, surrounded by nodules of chronic granulomatous inflammatory response with or without foreign body giant cells.[23] Special histological stains such as GMS will highlight the fungal hyphae in cases of Eumycetoma.[24] Both were positive in the present case. PCR based diagnosis using biopsy specimen is a rapid diagnostic technique that allows sequencing of the DNA sequencing can also be used in correct identification of



the organism.[25] CT scan and MRI are useful in determining extent of deep tissue and bone involvement, while ultrasonography can help distinguish eumycetoma/actinomycetoma/non-mycetoma lesions.[26] Earlier radiological studies has identified osteoporosis, loss of cortical margin, bone erosion, lytic lesions and expansion and basic changes on affected bony structures.[27]

The differential diagnosis of mycetoma include chronic osteomyelitis, tuberculosis, buruli ulcers, blastomycosis, coccidiomycosis, leishmaniasis, botromycosis, leprosy, syphilis, foreign body reactions and messenchymal tumour.[28]. Therapeutic approach and prognosis depends on the causative agent, the duration of the disease and presense of complications. Surgical intervention may not be necessary in early disease. Actinomycetoma are successfully treated with only drugs (Co-. Drutrimoxazole, Co-amoxiclav and Amikacin). Eumycetoma usually requires use of antifungal drugs such as ketoconazole, itraconazole and voriconazole, in combination with surgical excision.[29] In the present case, the tumour was successfully excised, while patient is currently on itraconazole 200 mg BD which is to be continued for the period of 6 months.

CONCLUSION

We report the first case of Madura foot in a 42 year old male in Delta State, Nigeria. It is important for Clinician to consider Mycetoma for any slowly growing foot tumours with discharging sinuses. The present case has also emphasized the role of travelling histology in the epidemiology of rare tropical diseases.

REFERENCES

1. Nenoff P, van de Sande WW, Fahal AH, Reinel D, Schöfer H. Eumycetoma and actinomycetoma - an update on causative agents, epidemiology, pathogenesis, diagnostics and therapy. *J Eur Acad Dermatol Venereol.* 2015; 29:1873-83.
2. Arora V, Handa B. Actinomycetoma of temporal bone: A rare case report. *Indian J Otol.* 2015; 21:298-302.
3. Lichon V, Khachemoune A. Mycetoma : a review. *Am J Clin Dermatol.* 2006; 7:315-21.
4. Gill: India army medical reports. London, Churchill, 1874.

5. Fahal AH, el Toum EA, el Hassan AM, Mahgoub ES, Gumaa SA. The host tissue reaction to *Madurella mycetomatis*: New classification. *J Med Vet Mycol.* 1995;33:15–7.
6. Ali RS, Newport M, Bakhiet SM, Ibrahim ME, Fahal AH (2020) Host genetic susceptibility to mycetoma. *PLoS Negl Trop Dis.* 2020; 14(4): e0008053.
7. Mycetoma is added to WHO List of 'Neglected Tropical Diseases'–DNDi [Internet]. [cited 2020 Jan 24]. Available from: <https://www.dndi.org/2016/media-centre/press-releases/mycetoma-who-ntd-list-response/>
8. Emery D, Denning DW. The global distribution of actinomycetoma and eumycetoma. *PLoS Negl Trop Dis.* 2020; 14(9): e0008397. <https://doi.org/10.1371/journal.pntd.0008397>
9. Ahmed AO, van Leeuwen W, Fahal A, et al. Mycetoma caused by *Madurella mycetomatis*: a neglected infectious burden. *Lancet Infect Dis.* 2004; 4 (9): 566-74.
10. Fahal AH. Mycetoma: A thorn in the flesh. *Trans R Soc Trop Med Hyg.* 2004; 98:3-II.
11. Relhan V, Mahajan K, Agarwal P, Garg VK. Mycetoma: An update. *Indian J Dermatol* 2017;62:332-40
12. Kwon-Chung KJ, Bennett JE. Mycetoma. In: Cann C, editor. *Medical mycology.* Malvern (PA): Lea & Febiger; 1992: 560-93.
13. Ventatswami S, Sankarasubramanian A, Subramanyam S. The Madura Foot: Looking Deep. *The international Journal of Lower Extremity Wound.* 2012;11(1):31-42.
14. Carter HV. On a new striking form of fungus disease principally affecting the foot and prevailing endemically in many parts of India. *Trans Med Phys Soc Bombay* 1860; 60: 140-2.
15. Pinoy E. Actinomycoses and mycetomas. *Bull Inst Past.* 1913; 11: 929-38.
16. Zijlstra EE, van de Sande WWJ, Welsh O, Mahgoub ES, Goodfellow M, Fahal AH. Mycetoma: a unique neglected tropical disease. *Lancet Infect Dis.* 2016;16(1):100–12.
17. Fahal AH, Suliman SH, Hay R. Mycetoma: The spectrum of clinical presentation. *Trop. Med. Infect. Dis.* 2018;3(3):97.



18. Mohammad N, Arif C, Ruksana P, Rokon U, Abdur R, Moydul H; The Madura foot - A Case Report. *N Dermatol Online* 2011; 2(2): 70-73.
19. Bonifaz A, Tirado-Sánchez A, Calderón L, Saúl A, Araiza J, Hernández M, González GM, Ponce RM. Mycetoma: Experience of 482 Cases in a Single Center in Mexico. *PLoS Negl Trop Dis*. 2014;8:e3102.
20. Taralakshmi VV, Pankajalakshmi VV, Arumugam S, et al. Mycetoma caused by *Madurella mycetomii* in Madras. *Australas J Dermatol* 1978;19:125.
21. Zaias N, Taplin D, Rebell G. Mycetoma. *Arch Dermatol* 1969; 99:215.
22. Sahu AA, Patri B, Agarwal S et al. Eumycetoma - a rare case report in present ERA. *Int J Health Sci Res*. 2016; 6(7):432-434.
23. Siddig EE, Fahal AH. Histopathological Approach in Diagnosis of Mycetoma Causative Agents: A Mini Review. *J Cytol Histol*.2017; 8: 466.
24. Guarner J, Brandt ME. Histopathologic diagnosis of Fungal Infection in 21st century. *Clinical microbiology Review*.2011;24(2);247-80.
25. Arastehfar A, Lim W, Daneshnia F, van de Sande WWJ, Fahal AH, Desnos-Ollivier M, et al. *Madurella* real-time PCR, a novel approach for eumycetoma diagnosis. *PLoS Negl Trop Dis*.2020; 14(1): e0007845]
26. Fahal et al. Ultrasonographic imaging of Mycetoma. *British journal of Surgery*.1997.84; 1120-2.
27. Yaghoobi R, Ranjbari N, Nasaii S, Actinomycetoma. Report of 4 cases of Mycetoma from Khoozeston (Ahwaz). *Quarterly dermatology Journal*. 1999; 2(4):43-8.
28. Emmanuel P, Dumre SP, John S, Karbwang J, Hirayama K. Mycetoma: a clinical dilemma in resource limited settings. *Ann Clin Microbiol Antimicrob*. 2018; 17:35.
29. Fahal AH. Mycetoma Management Guidelines [Internet]. Available from: <http://www.mycetoma.edu.sd/index.php/mycetoma-management-guidelines>



Figure 1: Left foot mass with discharging sinuses and skin excoriation

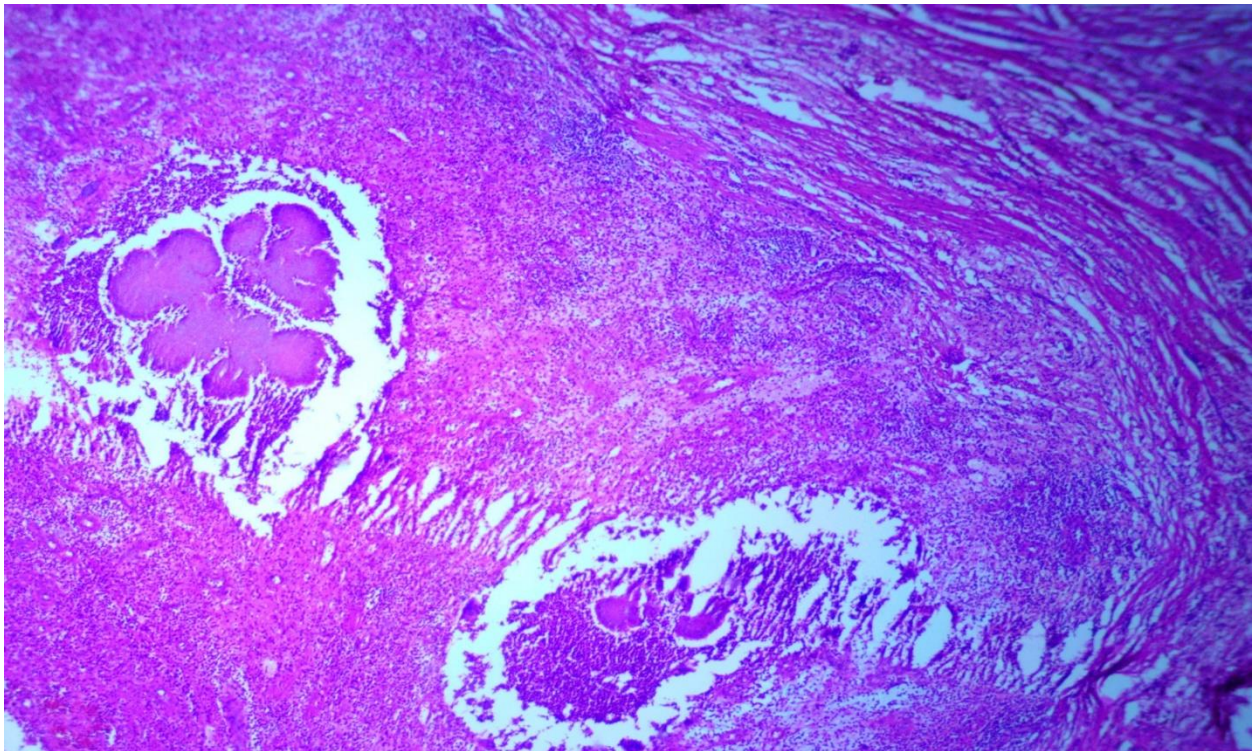


Figure 2: Microphotograph showing two areas with necrosis in a background of chronic granulomatous inflammatory response. Few foreign body-type giant cells are also present.

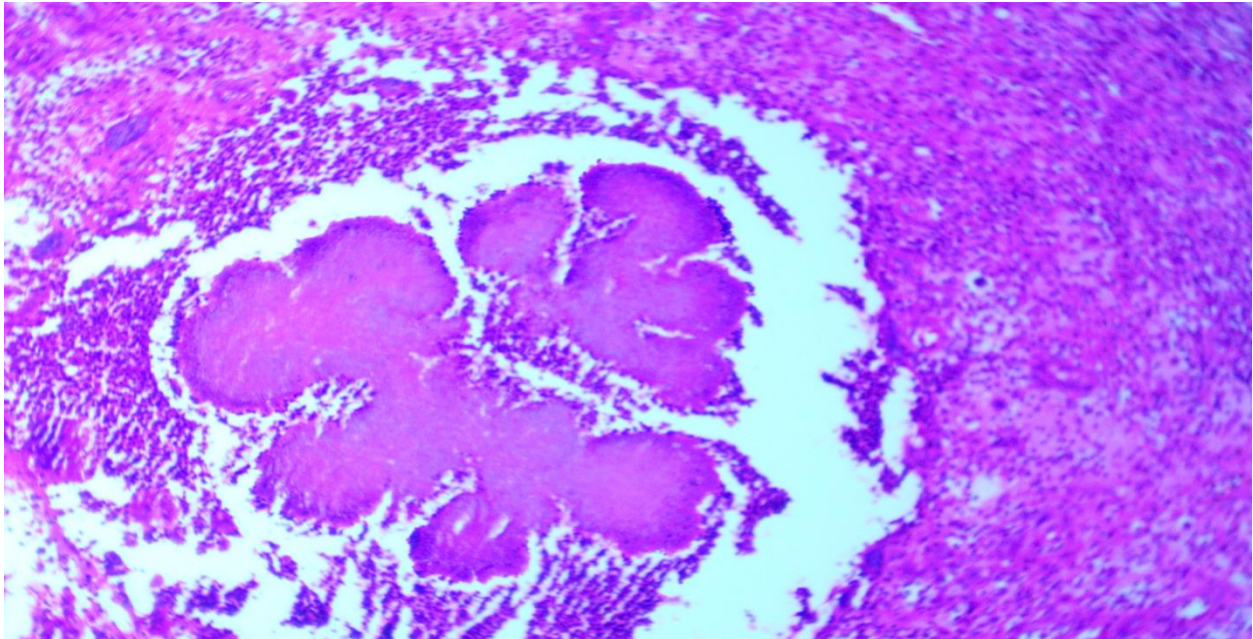


Figure 3: Microphotograph showing the Cauliflower pattern of necrosis, closely surrounded by neutrophils, characteristic of Mycetoma. The fungal hyphae are embedded within the area of necrosis



Figure 4: Microphotograph showing branching fungal hyphae using Glucott Methanamine Silver stain



Figure 5: Two weeks post op picture