



Case report

Long term follow-up of Maduromycosis treatment: A case review

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ABSTRACT

Maduromycosis is a rare deep fungal infection characterized by painless progressive destruction of limb caused by either fungal or filamentous bacteria. Its presentation is usually initiated by trivial penetration injury in farmers or laborers, worsen by immunocompromised status. Due to its painless course, this infection will severely destruct and deform hence leading to high morbidity of patient. We report a rare presentation of maduromycosis in 49-year-old housewife with no history of penetrating injury and no comorbid. Multi-disciplinary team was involved to establish the accurate diagnosis. The patient underwent surgical debridement and was given prolonged anti-fungal therapy. Combination of the treatments with patient's adherence lead to recovery without further recurrence and the patient was able to perform daily living activity.

1. Introduction and importance

Maduromycosis, also known as mycetoma, is an infectious inflammatory disease that affects the skin as well as connective tissue and bone in progression. It can caused by either filamentous bacteria (actinomycetoma), or fungi (eumycetoma) [1]. It might considered as "neglected prankster" since its painless progression yet high morbidity rate.

We present a case of otherwise healthy female with multiple painless ulceration on left foot that diagnosed with Maduromycosis, treated by surgical debridement followed by prolonged adjuvant anti-fungal medication.

2. Case presentation

A 49-year-old female presented with left foot ulcer presenting to our outpatient department. Initial lesion was recalled as a small callus on sole one year ago that ruptured and repeated in adjacent until nearly entire foot affected. Patient sought medical advice three months later and diagnosed with foot ulcer, treated using antibiotic but bring no improvement. Six months later the left foot became significantly swollen with mucopurulent discharge and painful that prevent patient from weight bearing. Patient is a housewife and denies any history of penetrated wound despite her habitual barefoot walking. There was no history of immunosuppressant medication, diabetes mellitus, tuberculosis, nor unexplained body weight loss. No familial history of similar issue was obtained. Patient has good hygiene and well educated.

On physical examination, there was marked swelling and deformity on her left foot. Numerous nodules with draining sinuses were found in plantar, medial and dorsal of left foot (Fig. 1). There was tenderness on deep palpation, however the distal neurovascular status was well preserved. Active and passive movement of ankle joints to distal are limited due to pain.

Her blood examination was within normal limits, unless erythrocyte sedimentation rate was elevated to 93/159 mm. Blood glucose level was within normal limit and HbA1c was 6.4%.

Radiographic examination revealed lytic lesion of tarsal bones and first ray, along with disuse osteopenia of calcaneus and remaining metatarsals (Fig. 2). On magnetic resonance imaging there was "dot-in-circle" sign observed on T2 image (Fig. 3).

Patient was later underwent surgical debridement and tissue sampling by authors team. Soft tissue coverage was highly respected to enable adequate envelope following the surgery (Fig. 4). Tissue sample was collected and sent to pathology department.

Histopathology finding shows filamentous structures with histiocytes, neutrophils, connective tissues and capillary perforation that consistent with eumycetoma characteristic (Fig. 5).

After Clinical Pathological Conference involving multi-disciplinary experts, diagnosis of maduromycosis was established and anti-fungal was commenced. Oral itaconazole 200 mg daily was administered for total 6 months, with serial evaluation for liver function. Patient was advised for routine and careful wound care, followed by partial weight-bearing until healing process had been completed. Routine follow-up for patient's adherence and tolerability to treatment was taken.

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Fig. 1. Clinical picture from pre-operative finding. Multiple nodes and sinuses were found as well as swelling and deformity of left foot. There were mucopurulent discharge from the lesion.



Fig. 2. Anteroposterior and oblique view of left foot shows lytic lesion of first ray, tarsals and calcaneus, along with disuse osteopenia over remaining metatarsals.

At the end of the treatment, the lesion healed by secondary intention, no recurrence was observed until 1 year after. Patient is satisfied and is able to perform daily living activity (Fig. 6).

3. Clinical discussion

Mycetoma are steadily less common due to improved nutrition and hygiene status, hence its presentation -especially in otherwise healthy patient- become interesting. Skin and subcutaneous tissue infection are the classic presentations, while deep tissue infection is more commonly found in immunocompromised patient and related to higher patient morbidity.

Maduromycosis derives from Madura district in India where it was endemic, first described by Gill in 1842 and Carter in 1860 [2,3]. Nowadays maduromycosis are more commonly reported in tropical and subtropical climate regions. Body area predilections including foot (most often), hand, thigh, tibia, orbit, testes, ear, mandible, even craniocerebral [2,4-7].

Mycetoma shares similar clinical appearance, regardless various underlying causative agents. Most cases initiated by trivial penetrating wound in farmers, laborers, or barefoot walkers in rural areas, result in delayed presentation of this infection [8,9]. However, many patients have no previous history of trauma on infected site, making hypothesis that there is an unidentified intermediate host [10].

Initial lesions are usually small painless papules or nodules -suggesting the lesion produces anaesthetic substance- making patients presentation in early stage are uncommon. Pain presence is related to secondary infection with bacteria or late bony destruction, as shown in our patient. [10] Infections may progress to connective tissue and bone, while tendon, muscle and nerve are usually spared until late in the disease [10]. Subcutaneous lesion enlargement followed by rupture and sinus tracks formation that drain a mucopurulent exudate containing fungal colonies in the form of macroscopic grain [5,8]. It will develop and re-occurs in adjacent area, guiding to tentative diagnosis.

Three cardinal features associated with maduromycosis as described by McElroy et al. are tumefaction, formation of sinus tracts, and presence of grains in affected tissue. Some untreated mycetoma can eventually deforms the limb intensely [2,5].

The most important part in mycetoma diagnosis is determine the causative agent, whether eumycetomic (fungal) or actinomycotic (bacterial), as treatment of these pathogens is quite different [8]. Actinomycetoma agents include *Nocardia brasiliensis*, *Actinomadura pelletieri*, and *Streptomyces somaliensis*, whereas *Madura mycetoma* and *Pseudallescheria boydii* are identified as eumycetoma agents [4].

Microbiological culture is the gold standard for diagnosis, however, the causative organism is often difficult to be cultured; making histopathology evaluation become the next most reliable diagnostic method.

Under immersion oil, microscopic evaluation of 2-4 μm wide hyphae, chlamyospore and blastospore will be found in eumycetomic, while thin, 0.5 μm thin, branching hyphae will be found in actinomycetoma, both in hematoxylin and eosin staining. The abscess itself consists of pseudoepitheliomatous hyperplasia, abundant granulation and fibrous tissue, with hyphae containing grains [5].

Molecular diagnostic techniques such as polymerase chain reaction (PCR) will be the next promising modality though it is only limited to several centre recently. [5,11]

Radiological evaluation, especially bone involvement evaluation is important, since its presence will predict unsuccessful treatment unless surgical approach is performed [12]. Dot-in-circle appearance in our patient MRI finding, is pathognomonic to mycetoma, as explained by Parker Lee et al., central low signal "dot" in T2 corresponded to fungal element and high signal granuloma corresponded to fibrous tissue "circle" [4,5]. Dot-in-circle appearance might observed both on ultrasonography and MRI [4,5,13].

A multi-disciplinary team approach consists of orthopedic surgeon, internist, radiologist, pathologist, and microbiologist are required to establish correct diagnosis, as we applied in our patient by Clinical Pathological Conference. Differential diagnosis of this case could be extrapulmonary tuberculosis, Kaposi's sarcoma, fibroma and foreign body granuloma [10].

Treatment success and prognosis of mycetoma are determined by correct diagnosis, proper treatment regimen, aggressive surgical approach and patient adherence for prolonged medication [8]. Several cases even require limb ablation due to progressive worsening despite proper treatment in immunocompromised host, including diabetes mellitus, on-going immunosuppressant and pregnancy. Amputation is indicated in massive bone destruction, unrespond to prolonged medical treatment and severe drug side-effect [14].



Fig. 3. T2 sequence on magnetic resonance imaging of left foot shows dot-in-circle appearance adjacent to tarsal bone and base of first metatarsal.



Fig. 4. Surgical debridement was undergone by maintaining adequate soft tissue envelope.

Antibiotics are used in actinomycotic mycetoma as its bacterial nature, along with surgical debridement of infected tissue. Antibiotic classes including penicillin, dapsone, cotrimoxazole, macrolide and aminoglycoside with various supportive data [8,10,15].

Eumycetoma is more difficult to eradicate and drug

resistance give even more challenge. Previous recommendation of amphotericin B has shown widely ineffectiveness and major side effects [5,16]. Novel recommendations of fluconazole and itraconazole are established, as we administer to our patients for 24 months, along with periodical liver function evaluation. Surgical debridement was also performed prior, along with tissue sampling.

4. Conclusion

Maduromycosis diagnosis and treatment should be established by multi-discipline approach. Its rare prevalence along with painless progression and inadequate treatment lead to high morbidity rate, especially if bony destruction has been found in initial diagnosis. Accurate diagnosis combined with aggressive surgical approach, patient's adherence on prolonged adjuvant medication as well as its side effect evaluation will result in good prognosis.

By presenting complete history taking, multiple workup modalities, followed by treatment and its result, authors offer a simpler and more cost-effective approach for every next case with similar profile.

This work has been reported in line with the SCARE 2020 criteria [17].

Availability of data and materials

The authors respect the patient's right to privacy. We presented all important information in this published article.

Authors' contributions

AG, HSA, GDP was major contributors to the writing of manuscript and as the corresponding author. IN performed the procedure. RS

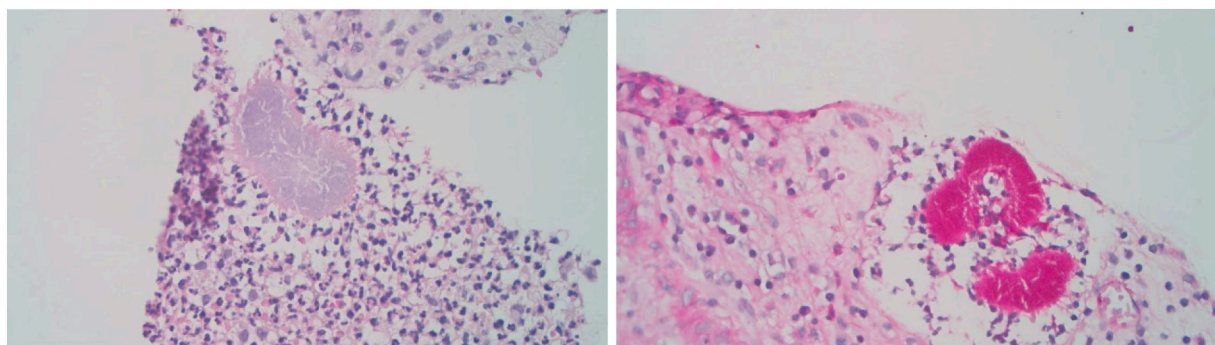


Fig. 5. Histopathological finding of tissue sampling shows filamentous structures between histiocyte inflammatory cells, neutrophil, connective tissue and capillary perforation, consistent with eumycetoma.



Fig. 6. Clinical pictures after 6 months oral itraconazole treatment. Lesion was healed by secondary intention with no recurrence and patient has already back to daily living activity.

revised the manuscript. All authors reviewed and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the ethical board of Hasanuddin University of Makassar.

Our patient has signed terms of consent to participate in the research of this case report.

The institutional ethical committee has approved the publication of this case report.

Consent for publication

Written informed consent was obtained from the patient for publication of this report and the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Guarantor

Ruksal Saleh & Astrawinata Guatama.

Provenance and peer review

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Declaration of competing interest

The authors declare that they have no conflict of interests.

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