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Case report

Madura foot and a continued diagnostic enigma: Dot-in-circle sign on magnetic resonance imaging and ultrasound

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ABSTRACT

Madura foot is a chronic granulomatous disease of the skin and underlying tissues caused by fungi or bacteria. Early diagnosis is important to avoid disfiguring limb deformities. Low clinical suspicion, limited availability of diagnostic tools, and infection with fastidious organisms may lead to misdiagnosis and delayed treatment. Imaging tests can help to make a timely diagnosis in a non-invasive manner. Here we report two patients with a non-classical clinical presentation and a more favorable differential diagnoses who were correctly diagnosed as cases of Madura foot based on the ''dot-in-circle sign'', a specific finding on magnetic resonance imaging and ultrasound.

Introduction

Mycetoma is a granulomatous tropical disease caused by either bacteria (actinomycetoma) or fungi (eumycetoma), which predominantly affects poor communities in rural areas, especially young males [1–3]. Most mycetoma cases are reported from endemic countries comprising the ''mycetoma belt", of which Ethiopia is a part [3]. The classical triad of the disease is subcutaneous swelling, multiple discharging sinuses, and the presence of macroscopic granules within the sinuses. Muscle and bone involvement occur in chronic untreated cases without eliciting pain [1,3].

Early diagnosis before the appearance of classical sinuses and grains is difficult because of non-specific features common to many etiologies in the tropics [1,4] . The available diagnostic tests for mycetoma are few, mainly histopathologic examination of tissue biopsies and staining or culture of grains, and these are not without limitations [4,6]. In addition, many endemic regions simply do not have the financial resources to carry out these necessary tests [3]. Imaging offers a non-invasive aid to diagnosis [5]. In this report, we demonstrated the diagnostic utility of "dot-in-circle" sign on either magnetic resonance imaging (MRI) or ultrasound (US) in the absence of typical clinical features of the disease or amidst more appealing differentials.

Case 1

A 15-year-old male patient from the Afar region, Ethiopia, presented to our hospital with a chronic wound on the dorsum of his right foot with sinus tracts that intermittently drained brown purulent discharge. Eight years earlier, he had stepped on a wood while walking barefoot; otherwise, he has no symptoms suggestive of tuberculosis (TB) or close contact with TB patients and is HIV seronegative. He was treated with several courses of antibiotics at a local health center for the above complaints, but the symptoms continued to worsen. On physical examination at presentation, he had a large, nodular, nontender mass on the dorsal aspect of the right foot with multiple sinus tracts that were not draining fluid (Fig. 1).

Right foot radiographs of the patient showed well-defined semicircular erosions on the lateral margin of the first proximal phalanx with adjacent solid periosteal reaction and associated soft-tissue swelling over the forefoot (Fig. 2).

Further examination of the patient with US of the right ankle and foot revealed a lesion with a heterogeneous echo pattern on the dorsum of the right foot, containing multiple hypoechoic thick-walled lesions with small sharp hyperechoic foci (dot-in-circle sign) (Fig. 3). Color Doppler showed increased vascularity in the surrounding soft tissue. An MRI was planned, but the patient's parents could not afford the cost. A

Abbreviations: MRI, Magnetic resonance imaging; MTP, Metatarsophalangeal; US, Ultrasound; PD, Proton Density; SPAIR, Spectral Attenuated Inversion Recovery.

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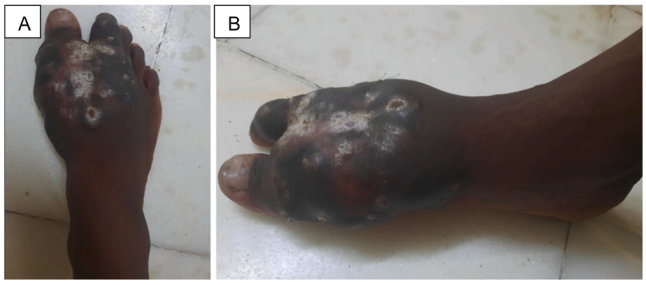

Fig. 1. Pictures demonstrating the gross appearance of the right foot of the patient (A and B). There was diffuse swelling and multiple nodularities, as well as dry sinus tracts.

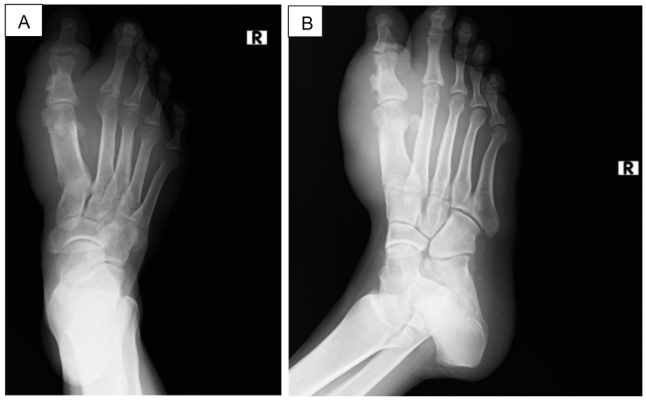

Fig. 2. Frontal (A) and oblique (B) radiographs of the right ankle and foot of the patient show soft tissue swelling and erosion on the 1st proximal phalanx medial cortex giving a half-moon appearance with adjacent solid periosteal reaction.

core needle biopsy was taken from the lesion, and it was suggestive of an actinomycetoma. The patient received treatment with itraconazole and co-trimoxazole for eight months with little improvement in symptoms. He is transferred to orthopedic surgery unit for possible surgical intervention.

Case 2

A 50-year-old female patient presented to our hospital- Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia- with worsening pain in her right foot and difficulty walking for 2 months. The patient had a history of TB treatment two years ago after an x-ray diagnosis of right ankle joint TB was made at a remote hospital after she presented with pain and swelling in the right ankle for five years. However, she saw only minimal improvement after completion of anti-TB treatment.

On physical examination at her presentation to our hospital, she appeared healthy and had normal vital signs. There was swelling and mild tenderness in the right ankle and metatarsal tenderness in the right foot, but no deformity or swelling.

Laboratory tests revealed a normal complete blood count with a white blood cell count of 6.1×10^3 cells per microliter and hemoglobin of 10 g/dl. The ESR was 10 mm/h and the renal and liver function tests and urinalysis were normal. Uric acid level was determined to be 2 mg/dl and Fasting blood sugar was 95 mg/dl. Gram stain of the lesion was positive for gram positive cocci. No growth was evident in the bacterial culture. Histopathologic examination was not done due to an inadequate tissue sample. A plain radiograph showed lytic lesions involving the navicular and cunifom bones as well as the metatarsal bases. (Fig. 4).

With a diagnosis of non-specific arthritis, she was started on a 100 mg suppository of indomethacin to be taken as needed. However, a follow-up visit three months later found no improvement in symptoms. At this time, an ankle MRI was also done to make a diagnosis and look for complications such as osteomyelitis. There were multiple rounded lesions of varying sizes diffusely involving the subcutaneous tissue, muscles, and bones of the right ankle and foot. The lesions were hyperintense having a central hypointense dot and a peripheral rim of hypointensity in T2 and PDW SPAIR, and showed contrast enhancement (Fig. 5). There were also diffuse marrow changes of the hind, mid, and forefoot bones, except the calcaneous and cuboid. A minimal amount of ankle joint fluid collection was also seen. Tendons, ligaments, and aponeurosis appeared normal.

A diagnosis of Madura foot was made and the patient was treated with fluconazole and cotrimoxazole and indomethacin was continued. The patient is complying well with her medications and has seen significant improvements after six months of treatment.

Discussion

Mycetoma infection occurs in humans through the entry of organisms from the soil into subcutaneous tissue, and the foot is considered to be the most common site, with the forefoot preferentially affected [6,7]. The disease may take the most devastating form through the involvement of muscle and bone, causing osteosclerotic or osteolytic lesions if no treatment is initiated at an appropriate time [8]. Tendon and nerve structures appear to be resistant until late in the disease course. When clinically suspected, the presence of the characteristic grains in histopathologic sections and culture of grains on specific media establish the diagnosis and allow definitive identification of the causative agent [3,9]. However, low clinical suspicion and difficulty identifying the causal agents with a biopsy or culture often lead to a delayed diagnosis. Imaging is a fast and affordable diagnostic tool that can offer a non-invasive diagnosis and be used to evaluate the extent of the disease [9].

Radiographs may be normal or show soft tissue swelling, bone sclerosis, bone cavities with a moth-eaten appearance, periosteal reaction, cortical scalloping, fanning of the rays, or osteoporosis [6,9]. Eumycotic lesions tend to form a few cavities in bone that are ≥ 1 cm in diameter, while actinomycetes often form smaller but more numerous cavities, leading to a moth-eaten appearance [7]. Radiograph findings of bone involvement are common in mycetoma patients and do not necessarily indicate actual bone invasion [8]. However, erosions and cavities can be due to the replacement of osseous tissue and marrow by masses of the pathogen. Periosteal reactions can be seen in up to 72% of patients and can cause some concern when they take the shape of a codman's triangle, lamellar pattern, or sunray speculation, which may be indistinguishable from osteosarcoma and Ewing's tumor [8]. Overall, if radiographic changes are present, osteomyelitis and benign and malignant bone conditions must be excluded [10]. In both cases, bony erosion was evident on the radiographs, with an associated solid periosteal reaction seen in the first case and lytic lesions present in the second case.

The presence of bone erosions without demineralization that are well defined with sclerotic or overhanging margins and periosteal new bone formation can be seen in chronic gout [11,12]. Joint effusion and synovitis, bright dotted foci, and hyperechoic stippled aggregates can also be found on US [11]. Some of these imaging findings were present in the first case, which made chronic gout a possible differential diagnosis. However, his young age and skin findings led to a diagnosis other than chronic gout being considered. The absence of soft tissue or articular tophi, double contour signs, or hyperechoic cloudy areas in the synovial fluid also speak against this diagnosis [11,12].

The "dot-in-circle" sign, seen as tiny hypointense foci on all sequences on MRI within the hyperintense spherical lesions represents the small central foci of the fungal balls or grains within inflammatory granulomas [6]. The sign is suggested to be highly specific for this infection [6,7]. As previously reported, the sign was most clearly demonstrated in our case

on the T1-weighted sequence following intravenous contrast, although it was still visible in T2-weighted and PD SPAIR images [5,13]. The ability to visualize the grains on MRI depends on multiple factors, including grain size, image quality, and imaging parameters, and small grains may not be visible if they are beyond the resolution of the scanner [13]. Diffuse hyperintensity involving the majority of the bones of the foot secondary to marrow edema can be seen [5]. MRI is the gold standard to evaluate both the soft tissues and early bone involvements [9].

The differentials include soft tissue hemangioma with the "dots" resembling phlebolith and osteoarticular TB with the ‘’dots’’ masquerading rice bodies, hypointense foci seen in the synovial fluid of patients [7]. However, in hemangiomas, pooling of contrast material with arteriovenous shunting, the presence of multiple enlarged feeding vessels, and the presence of phleboliths on plain radiographs are give-aways [14]. Rice bodies seen in tuberculosis and other inflammatory arthritides appear as small, low-signal foci in the synovial fluid on T2-weighted images but do not show contrast enhancement [15].

US findings of "dot-in-circle" sign are similar to the MRI sign, with multiple round hypoechoic lesions containing hyperechoic foci that corresponded to the grains [5,7,13]. Eumycetoma grains produce sharp hyperechoic foci, while actinomycetomas produce fine hyperechoic foci that commonly settle at the bottom of the rounded lesion [7]. Gameraddin et al. recently reported that features including multiple cavities, separated grains, and heterogeneous echotexture were more notable in eumycetoma, in addition to significantly increased soft tissue vascularity [2]. In our first case, the hyperechoic foci were located at the center of the rounded lesion and there was markedly increased soft tissue vascularity, which are characteristic features of eumycetoma, although the biopsy result suggested otherwise. Thus, we may not rely on sonographic findings to make an etiologic diagnosis. US allows for guided aspiration biopsy and can help determine the size and extent of the lesion for surgical planning [10].

Medication treatment is successful in treating actinomycetoma, but lesions caused by fungal pathogens tend to have a worse prognosis and respond poorly to the few effective medical therapies that exist [3,14]. The poor response to medications seen in our first patient can be due to an inadequate medication regimen or underlying immune compromise from malnutrition [10]. Late diagnosis can also be a factor, as it increases the need for invasive surgical treatment [3].

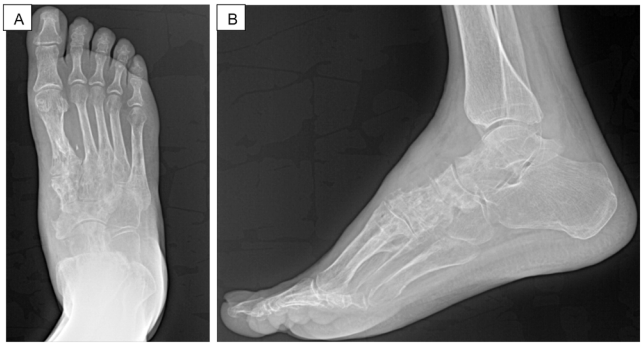

Fig. 4. Anteroposterior (A) and lateral (B) radiographs of the right foot and ankle show lytic lesions involving the navicular and cunifom bones as well as the metatarsal bases.

As demonstrated in the present report, the diagnosis of Madura foot is challenging to make, particularly if the classical foot swelling with nodularity and draining sinuses are absent. Regardless of how soft tissue masses appear clinically, one should always consider the possibility of this diagnosis in chronic lower extremity complaints in endemic areas. The dot-in-circle sign on MRI and US are highly specific signs and help in making an early diagnosis if visualized [13].

Conclusion

Mycetoma should always be considered in a chronic, perplexing lower extremity complaint in endemic areas, regardless of how soft

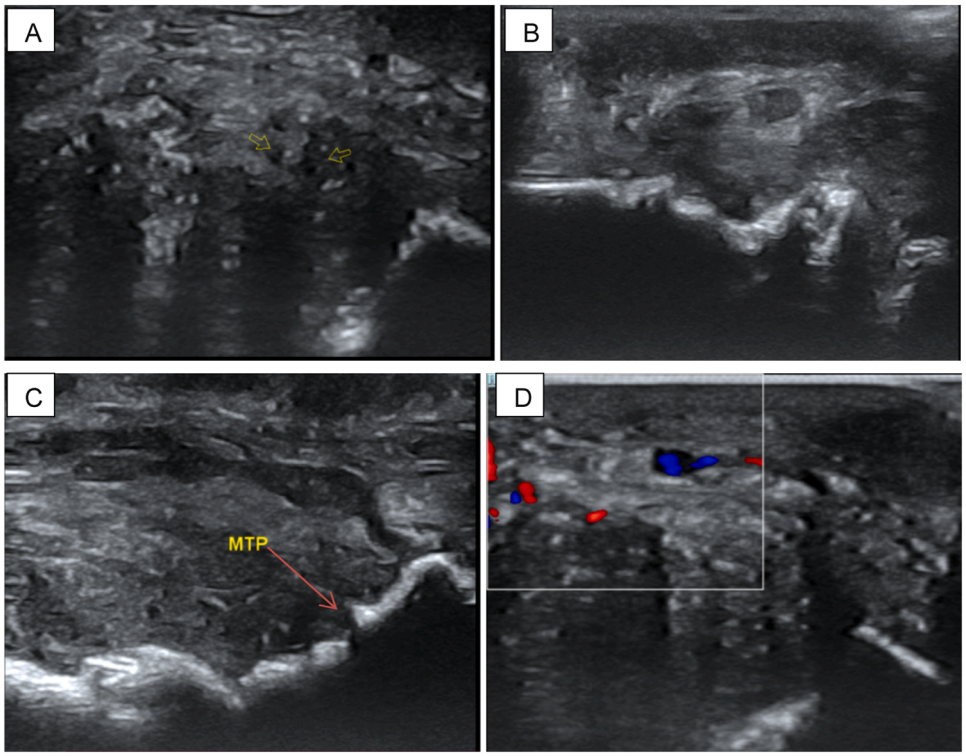

Fig. 3. A right ankle US shows multiple lesions (arrows) with thick hypoechoic walls and hyperechoic foci in the center giving the appearance of a ‘‘dot in a circle’’ (A) suggestive of a Madura foot. There is cortical irregularity over the right 1st metatarsus and proximal phalanx (B and C). A color Doppler examination (D) shows hypervascularity of the surrounding soft tissue.

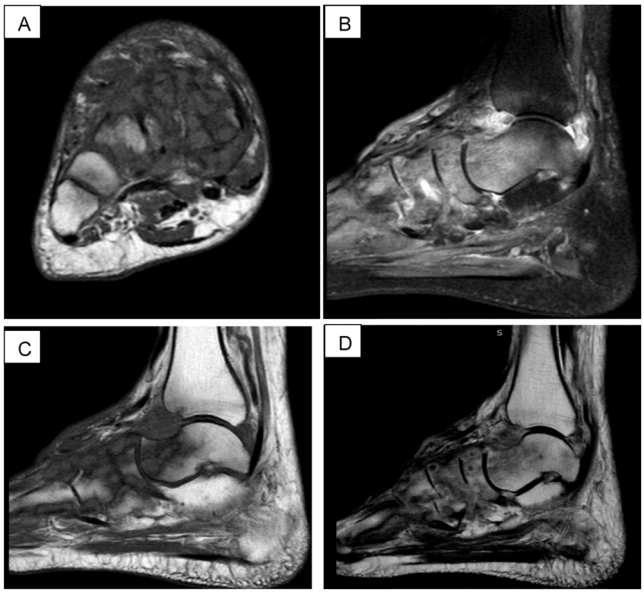

Fig. 5. A T1-weighted coronal MRI scan of the right ankle (A) shows multiple hypointense nodules of various sizes, diffusely affecting subcutaneous tissue, muscle, and bone. The lesions are hyperintense, with a central and peripheral border of hypointensity on the PDW SPAIR sagittal section (B). T1W sagittal sections pre (C) and post (D) contrast administration show contrast enhancement of the lesion with the "dot-in-circle" sign.

tissue and bones appear clinically or on imaging. The US and MRI findings of ''dot-in-circle'' sign are diagnostic of Madura foot and confirm the diagnosis early, which has significant treatment outcome implications.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient's parents for anonymized patient information to be published in this article.

Author contribution

All authors contributed to the conduct of this research and read and approved the final version of the manuscript.

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Declaration of Competing Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Data Availability

The data supporting the findings of the case are available upon request to the corresponding author.

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