Radiologist's view on Pedal Actinomycetoma: A Case Report with Comprehensive Review of Literature

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Abstract

Background: Tropical diseases include communicable and non-communicable diseases prevalent in tropical regions. Mycetoma is a chronic granulomatous infection involving the skin and subcutaneous tissue, commonly affecting the lower limbs. We present a case of actinomycetoma and a narrative review of the literature, focusing on diagnostic imaging.

Case presentation: A 36-year-old woman from eastern India presented with a six-month history of right foot swelling and a discharging wound. Multiple courses of antibiotics had been unsuccessful. Ultrasonography showed infiltrative hypoechoic soft tissue with nodular targetoid lesions. MRI demonstrated multiple nodular lesions with the characteristic dot-in-circle appearance, suggesting pedal mycetoma. Biopsy confirmed actinomycetoma.

Conclusion: Pedal mycetoma presents diagnostic and therapeutic challenges because of its insidious progression and delayed diagnosis. MRI helps assess soft tissue and bone involvement and disease extent. The dot-in-circle sign is characteristic and highly suggestive of mycetoma, but diagnosis requires histopathological and/or microbiological confirmation. Early recognition may improve treatment outcomes.

Keywords: *Pedal mycetoma, Madura foot, Actinomycetoma, Dot-in-circle sign.*

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Introduction

Tropical diseases include a panel of communicable and non-communicable diseases that are prevalent along and between the tropic of Cancer and tropic of Capricorn belt [1]. This includes infectious diseases like cholera, Malaria, HIV/AIDS, tuberculosis, leishmaniases, onchocerciasis, filariasis, trypanosomiasis, rickettsioses, etc and non-communicable diseases such as malnourishment, hypertension, diabetes, chronic obstructive pulmonary disease, myocardial infarction and cerebrovascular accident [2]. These diseases pose significant public health challenges in tropical areas, often exacerbated by factors such as climate, poverty, and limited access to healthcare. Mycetoma, initially reported in Madu-

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rai, Tamilnadu and termed as "Madura foot", has been classified by the WHO as an endemic disease of the subtropical and tropical areas [3]. Mycetoma is a chronic destructive granulomatous infectious disease involving the skin and subcutaneous tissue. It commonly affects the limbs, specifically the foot and ankle. However, it can also involve the abdominal wall, chest wall or head and neck region. Mycetoma of the foot is the most common form and is termed as mycetoma pedis or pedal mycetoma. Based on the causative agent, mycetoma is classified as actinomycetoma (caused by aerobic filamentous bacteria) or eumycetoma (caused by fungi). Owing to the nonavailability of any large-scale studies, the true incidence of mycetoma still remains uncertain. However, the proportions of actinomycotic and fungal aetiologies are approximately estimated as 60% and 40% respectively [4].

Early diagnosis guides appropriate management. USG and MRI help identify disease and its extent; cytology or biopsy can confirm mycetoma. Culture and molecular testing aid organism identification. Internal transcribed spacer (ITS) sequencing is used for fungal identification; bacterial identification requires appropriate bacterial culture and/or molecular methods [5].

In this report, we present a case of actinomycetoma, in a middle-aged female and review of existing literature with specific emphasis on multimodality diagnostic imaging.

Case Report

Clinical Details

A female patient of 36 years from the eastern part of India presented with swelling of the right foot and a discharging wound since 6 months (Figure 1). Initially, it was diagnosed as chronic bacterial osteomyelitis, and she was unsuccessfully treated with multiple courses of enteral and parenteral antibiotics from local hospitals. Her hematological parameters were unremarkable except for reduced hemoglobin concentration (9 g/dl).

Radiological Features

In line with the ongoing diagnosis, she was referred for an ultrasonography to detect and quantify localized collection, if any. Ultrasonography (USG) revealed infiltrative ill-defined hypoechoic soft tissue in the dorsum and sole of foot with inflamed adjacent fat. Multiple discrete and confluent nodular lesions, in solitary and clustered distribution were seen within the soft tissue (Figure 2). These nodular lesions showed a central hyperechoic focus surrounded by hypoechoic tissue with a peripheral hyperechoic rim, giving target/ dot-in-circle appearance. A linear hypoechoic sinus tract was seen reaching up to the overlying skin surface.

For further evaluation, magnetic resonance imaging (MRI) was performed. MRI revealed nodular infiltrative soft tissue, involving the subcutaneous tissue and muscles of the sole and dorsum of foot. The soft tissue exhibited low signal intensity on T1 and heterogeneously high signal intensity on T2/ PD FS/ STIR. Multiple variable sized welldefined nodular lesions were scattered within the soft tissue appearing hyperintense on T2/ STIR with a peripheral hypointense rim and central hypointense foci, representing dot-in-circle sign (Figure 3).

Extensive bone involvement was also seen (Figure 4). Moth-eaten pattern of bone destruction was seen involving the proximal ends of first, second and fourth metatarsals. Sclerosis of the adjacent bone was also seen. Solid periosteal reaction was seen along the second metatarsal. There was associated loss of normal T1 hyperintensity of the bone marrow with increase in PD FS/ STIR signal. Though the third and fifth metatarsals did not show obvious bone lysis or lesion, MRI revealed altered marrow signal intensity, representing involvement.

Histopathology

For confirmation of the diagnosis, a surface biopsy was performed. Histopathological examination with H&E staining revealed a focal colony of basophilic filamentous bacteria with peripheral Splendore-Hoeppli phenomenon. Filamentous bacteria stained positive on Grocott's methenamine silver (GMS) stain (Figure 5).

Management

Patient was started on multidrug antimicrobial regimen (dapsone, amikacin and cotrimoxazole). In view of extensive bone involvement and local spread, she was counseled regarding the need for prolonged antimicrobial therapy and the potential need for an above knee amputation if there was no response. Patient was reluctant for the same and subsequently defaulted the treatment.

Discussion

Pedal mycetoma was recognized as a disease entity by Gill in the year 1842 at Madurai, India and was later termed ‘mycetoma’ by Carter in 1880 [6]. It commonly affects those occupations that are in close contact with soil and vegetations such as farmers, cattle breeders, agricultural workers and poultry farmers. It usually involves parts of the body that are exposed to the soil like hands, feet and lower legs. Transdermal inoculation is the most common route of transmission, usually following trauma or penetrating injury [7].

It is prevalent in patients between 20 to 40 years of age and demonstrates male predilection with a reported male-female ratio of 3.5 to 1 [8]. It is a sinister disease that painlessly spreads through the soft tissue to involve bones, rendering conservative management options futile. Clinically, it presents with a triad of features- painless foot swelling, multiple sinuses and discharging specific-colored grains [4].

Though actinomycetoma and eumycetoma present with similar features, the former exhibits a rapid progressive course resulting in locally advanced and disseminated infection [9]. Infection progresses in four stages [4].

The first stage of the disease is incubation which can vary from a few weeks to years. Subsequently, the patients develop non-specific features of local cellulitis like swelling and pain. As the pathogen proliferates in the subcutaneous plane, microabcesses with surrounding granulation tissue result in formation of subcutaneous nodules. As these nodules increase in size, they erupt the overlying skin surface forming discharging sinuses. Eventually, the disease extends into deeper tissue planes and involves bones causing significant soft tissue and osseous destruction. Deformity soon ensues destruction.

In the advanced stages, diagnosis can be made readily based on classical clinical features. During the early indolent course of the disease, it is often misdiagnosed and unsuccessfully treated as common bacterial cellulitis. At the time of diagnosis, the disease is usually advanced with extensive soft tissue and bone involvement necessitating amputation. Hence, the challenge lies in early diagnosis of the disease.

Radiological investigations, especially ultrasonography (USG) and magnetic resonance imaging (MRI) are indispensable tools for early diagnosis. Plain radiographs can be normal in the early stage of disease but can demonstrate bone involvement and soft tissue thickening. However, computed tomography (CT) helps in better characterization of the pattern of bone involvement, periosteal reaction, presence of osteoporosis and bone destruction [10]. Magnetic resonance imaging (MRI) is the imaging modality of choice aiding in excellent characterization of the soft tissue, associated extensions and infiltration, bone involvement and bone marrow edema. It also plays an indispensable role in pretherapeutic staging, evaluation of associated complications and therapeutic response assessment. Bone scintigraphy is another valuable tool for assessment of therapeutic response [10].

The spectrum of radiological features comprises of various patterns of soft tissue and bone involvement. USG and MRI are the preferred tools for soft tissue characterization. On USG, it presents as an ill-defined hypoechoic infiltrative mass. Few authors have described increased color flow and Doppler signals within soft tissue which can be secondary to inflammation [11, 12]. On MRI, the soft tissue appears hyperintense on T2, PD FS and STIR sequences. It predominantly involves the subcutaneous tissue but frequently infiltrates the muscles and deeper soft tissue due to its aggressive nature [7], as observed in our case.

The presence of ‘dot-in-circle' sign has been described as a specific hallmark for pedal mycetoma [7, 11, 12, 13]. It has been described in cases of both eumycetoma and actinomycetoma. The basis of ‘dot-in-circle' sign depends on the pathological organization of the granuloma which comprises of a central core of microbial elements (fungal hyphae or filamentous bacteria) surrounded by granulation tissue and chronic inflammatory infiltrate with a peripheral rim of fibrosis (Figure 6) [14]. It was first described by Sarris et al in 2003 [15]. However, the earlier available case reports also describe similar findings [16, 17]. ‘Dot-in-circle’ sign, typically described on MRI, can also be appreciated with a similar appearance on USG. On USG, it appears as a hypoechoic lesion with a central hyperechoic core and peripheral hyperechoic rim (Figure 7). On MRI, this sign is best described on T2 FS, PD FS and STIR sequences in which these lesions appear hyperintense with a central hypointense focus and a peripheral hypointense rim (Figure 8).

T1 FS post contrast images have also been described to depict ‘dot-in-circle' sign but demonstrate no obvious advantage over non contrast sequences [14]. However, post contrast images can additionally demonstrate the actual extent of soft tissue infiltration, associated collections, disease activity and subtle bone involvement. Diffusion

weighted imaging (DWI) can aid in assessment of therapeutic response. Though few authors have not specifically reported ‘dot-in-circle' sign, Jimenez et al [18] reported the absence of the same in a case of eumycetoma which was initially misdiagnosed as synovial sarcoma.

In the cases reviewed by the authors, the dot-in-circle sign or a similar appearance was reported in 185 of 188 cases with ultrasonography and/or MRI findings (98.4%). This is a reported proportion in selected published cases, not an estimate of diagnostic sensitivity. No systematic search strategy or formal diagnostic-accuracy method was documented. Sinus tracts may appear hypoechoic on USG and hyperintense on T2/STIR.

Bone involvement includes bone destruction, sclerosis, periosteal reaction and resultant deformities. As a general observation, most authors have reported aggressive patterns of bone destruction of which moth-eaten pattern and permeative type are the most common [11, 19, 20, 21, 22, 23, 24]. Aggressive forms of periosteal reaction such as interrupted, lamellated and spiculated patterns have been described as frequent associations [11, 14, 19, 22, 23, 24]. As in our case, few authors have also reported nonaggressive solid form of periosteal reaction [11, 25, 26]. Martinez et al [27] described ‘snow melting’ pattern of bone involvement characterized by lytic bone destruction with surrounding florid dense sclerosis. The presence of bone marrow edema without obvious cortical involvement or bone destruction can represent early involvement. Hoogervorst et al [28] reported non-contiguous disseminated small hypointense lesions scattered within the tibial bone marrow in an immunocompromised patient without any bone involvement. Advanced long term disease results in extensive osteolysis, sclerosis and bony ankylosis [22]. The salient radiological features that have been described in the earlier literature are summarized in table 1.

Distinctive patterns of bone involvement in actinomycetoma and eumycetoma have been observed [14, 19]. Eumycetoma is associated with larger [usually > 1 cm in size] intraosseous cavities while Actinomycetoma causes moth-eaten pattern of bone destruction i.e., multiple punctate well-defined cavities. Gameraddin et al [29] studied the differential sonographic and Doppler characteristics of eumycetoma and actinomycetoma. They reported that eumycetoma was associated with multiple aggregated grains, more heterogeneous echotexture and higher vascularity in comparison to actinomycetoma.

Radiological staging of the disease is imperative for planning the treatment and patient counseling. In 2003, Abd El Bagi [30] devised a radiographybased system for staging bone involvement in pedal mycetoma (Table 2). Subsequently in 2012, El Shamy et al [31] proposed a detailed MRIbased mycetoma skin, muscle, bone (MSMB) grading system (Table 3) which comprises of three subscores- skin (scores 0-4), muscle (0-3) and bone (0-3). Out of a total score of 10, a score of 1-3 is considered mild, 4-7 is considered moderate and 8-10 is considered severe.

Imaging also aids in evaluating the therapeutic response in patients on conservative management [10, 32]. Radiological features of healing are remodeling and sclerosis of the active edges of erosions, ossification of bone cavities and solid periosteal reaction, generalized bone sclerosis, resolution of bone marrow signal alteration, disappearance of granulomata (showing ‘dot-incircle' appearance), reduced heterogeneity of soft tissue enhancement, normalization of diffusion restriction and normalization of increased uptake on bone scintigraphy.

Due to painless and quiescent progression of the disease, numerous patients present with complications even at the time of initial diagnosis. Complications include periostitis, osteomyelitis, arthritis, bone destruction resulting in deformity, secondary bacterial infection, bacteremia and septicemia [9, 33]. Differential diagnoses include diabetic foot, localized bacterial cellulitis, osteomyelitis, Charcot arthropathy, venous thrombosis, tuberculosis and vascular tumors and malformations. Among these conditions, soft tissue collection with bone fragments in osteomyelitis, rice bodies in tuberculosis and phleboliths in vascular malformations can mimic ‘dot-in-circle' appearance. Clinicoradiological features that aid in differentiating these conditions are enumerated in table 4.

Treatment of pedal mycetoma depends on the causative pathogen and stage of the disease. Actinomycetoma is treated with a combined regimen of antimicrobial agents including cotrimoxazole, dapsone, amikacin and tetracycline [34, 35].

Eumycetoma requires antifungal therapy, commonly itraconazole, with surgical excision when indicated. Treatment is tailored to the organism and disease extent [32, 34, 35].

Age > 59 years, lesion of size > 10 cm, duration of disease > 5 years and positive family history are predictors of recurrence following surgical debulking or excision [37].

Locally advanced disease with bone involvement, multiple recurrences and non-response to medical therapy might require amputation of the limb [38].

Conclusion

Pedal mycetoma is a chronic granulomatous infection caused by aerobic filamentous bacteria or fungi. USG and MRI help characterize lesions and assess soft tissue and bone involvement, disease extent, and response to therapy. The dot-in-circle sign is characteristic and highly suggestive, but mimics occur; histopathological and/or microbiological confirmation is required. Early recognition may improve treatment outcomes.

Abbreviations

HIV/AIDS: Human immunodeficiency virus/ Acquired immunodeficiency syndrome
WHO: World Health Organization
FNAC: Fine needle aspiration cytology
PCR: Polymerase chain reaction
USG: Ultrasonography
MRI: Magnetic resonance imaging
PD FS: Proton density fat saturation
T2 FS: T2 fat saturation
T1 FS: T1 fat saturation
STIR: Short tau inversion recovery
DWI: Diffusion weighted imaging
CT: Computed tomography
H&E: Hematoxylin & Eosin
GMS: Grocott's methenamine silver
MSMB: Mycetoma skin, muscle, bone grading.

Table 1:
Salient radiological features of Pedal mycetoma described earlier in the literature

S. No.	Study	Country	No. of cases	Type	Soft tissue characteristics		Presence of Dot-in-circle	Pattern of bone involvement	Periosteal reaction	Deformity
					USG	MRI				
1	Lewall DB et al. 1985 [19]	Saudi Arabia	30	19- A 11- E	NR	NR	NR	Sclerosis, cortical erosions, intraosseous cavities, moth-eaten pattern, osteoporosis	Present (laminated/ spiculated/ bizarre)- 67%	NR
2	Fahal AH et al. 1997 [16]	Sudan	100	NR	Hyperreflective grains surrounded by single or multiple thick -walled cavities	NR	NR	NR	NR	NR
3	Czechowski J et al. 2001 [10]	UAE	20	13- A 7- E	NR	Loss of normal signal intensity of the soft tissue with increased T2 signal	NR	Bone marrow abnormalities in 15 patients Bone destruction, erosions and coarsening of trabeculae	Present	NR
4	Ispoglou SS et al. 2003 [17]	Greece	1	A	NR	Altered signal intensity of the affected soft tissue and bones, T1/ T2 hypointense ovoid lesions within the affected bones	NR	Mottled destruction of tarsals and metatarsals, sclerosis and bone marrow involvement	Absent	NR
5	Sarris I et al. 2003 [15]	Reported in UK	2	E						
	Case 1	Pakistan		E	Hypoechoic lesion with hyperechoic foci	Hyperintense lesions separated by hypointense stroma on STIR with central low signal intensity evident on T1FS post contrast images.	Yes	NR	NR	NR
	Case 2	Nigeria		E	NR	Follow up MRI- nonspecific inflammation with T2 hyperintense lesion showing central hypointensity	Yes	NR	NR	NR
6	Salamon LM et al. 2006 [39]	USA	1	E	NR	Hyperintense subcutaneous lesion with internal hypointense foci	NR	Absent	Absent	NR
7	Cherian RS et al. 2009 [7]	India	3	E						
	Case 1				NR	Conglomerate areas of multiple discrete, small round hyperintense lesions with peripheral low signal rim and central dot	Yes	Absent	Absent	NR
	Case 2				NR	Infiltrative lesion involving the subcutaneous and muscular planes	Yes	Absent	Absent	NR
	Case 3				NR	Extensive altered signal intensity involving the tarsals and soft tissue	Yes	Chronic osteomyelitis of tarsals	NR	NR
8	Asly M et al. 2010 [21]	Morocco	1	E	NR	NR	NR	Bone resorpiton and permeative bone destruction diffusely involving the tarsals, metatarsals and phalanges	NR	NR
9	Jimenez AL et al. 2011 [18]	USA	1	E	NR	Multiloculated well defined subcutaneous mass at the dorsum of distal foot	Absent	Absent	Absent	Absent
10	Elmaataoui A et al. 2011 [25]	Morocco	2	E	NR	NR	NR	Geographic bone ill-defined bone destruction with sclerosis	Present (solid)	NR

Table 1:
Salient radiological features of Pedal mycetoma described earlier in the literature

11	Jain V et al. 2012 [20]	India	1	E	NR	Extensive soft tissue and osseous inflammation, multiple discrete and confluent spherical lesions with hypointense rim, few showing central hypointense focus	Yes	Moth eaten type of bone destruction with articular erosions	NR	NR
12	El Shamy EM et al. 2012 [31]	Sudan	42 (foot involvement in 25 patients)	A- 24 E- 18	NR	Ill-defined infiltrative soft tissue with multiple lesions showing peripheral hypointense rim and hypointense center, macro and microabscesses	Yes	Bone marrow edema, intraosseous cavities, destruction	Yes	NR
13	Laohawiriyakamol T et al. 2014 [40]	Thailand	8	A- 4 E- 4	Central hyperreflective area surrounded by hypoechoic tissue with increased vascularity	Multiple small discrete round-to-oval hyperintense lesions separated by hypointense rim and central hypointense dot	Yes	Bone marrow abnormality	NR	NR
14	Brufman T et al. 2015 [26]	Israel	1	E	NR	NR	NR	Infiltrating destructive lesion of first metatarsal with bone remodelling	Present (solid)	NR
15	Martinez EI et al. 2016 [27]	Spain	1	A	Hypoechoic lesions with central hyperechoic foci	Soft tissue mass with multiple discrete and conglomerate hyperintense lesions with central hypointense foci	Yes	1. Lytic destruction with surrounding sclerosis- Snow melting pattern 2. Articular erosions	NR	Present (at second interphalangeal joint)
16	Neelakantan S et al. 2016 [41]	India	1	E	Multiple conglomerate hypoechoic lesions with hyperechoic center and diffusely increase Doppler signal	Increased T2/ STIR signal of the subcutaneous and muscular planes with multiple conglomerate T2/ STIR hyperintense lesions with hypointense rim. Few of the lesions showed central hypointense foci.	Yes	Absent	Absent	Absent
17	Sidhu R et al. 2017 [24]	India	1	E	Multiple hypoechoic lesions with hyperechoic centers	Multiple T2 hyperintense lesions with low signal rim and central hypointense foci	Yes	Moth- eaten pattern of bone destruction with sclerosis	Present (aggressive)	NR
18	Guerra-Leal JD et al. 2019 [42]	Mexico	6	A	Multiple hypoechoic nodules with extensive soft tissue inflammation	Inflammatory changes with soft tissue abscesses	Yes	Punched out lesions seen in 4 of 6 patients	Present in 4 patients	NR
19	Yadav T et al. 2020 [14]	India	4	E						
	Case 1				Multiple lesions with central hyperechoic foci and peripheral hypoechoic wall	Multiple hyperintense lesions with hypointense foci	Yes	Absent	Absent	Absent
	Case 2				Multiple hypoechoic lesions with central hyperechoic foci	Multiple hyperintense lesions with central hypointense dots	Yes	Absent	Absent	Absent
	Case 3				Multiple clustered lesions with peripheral hypoechogenicity and hyperechoic center	Multiple hyperintense lesions with hypointense dots	Yes	Absent	Absent	Absent
	Case 4				Ill-defined lesions with central hyperechoic foci and peripheral hypoechoic wall	Multiple hyperintense lesions with dot in circle sign in the soft tissue and bones	Yes	Multiple osteolytic lesions with diffuse sclerosis	Present (aggressive)	NR

Table 1:
Salient radiological features of Pedal mycetoma described earlier in the literature

20	Serfaty A et al. 2020 [22]	Brazil	1	E	NR	NR	NR	Multiple bone cavities with permeative bone destruction and sclerosis	Present (aggressive)	Bony ankylosis of small joints of foot
21	Karrakchou B et al. 2020 [4]	Morocco	1	E	NR	Multiple soft tissue collections	Yes	Absent	Absent	NR
22	Gameraddin M et al. 2020 [29]	Sudan	60	A & E	Multiple cavities and aggregated grains (E > A) Heterogeneous ehcotexture (E > A) Vascularity (E > A)	NR	NR	NR	NR	
23	Sahu BK et al. 2021 [43]	India	3 (Radiological features have been described in one case)	E	NR	NR	Yes	NR	NR	NR
24	Jolu A et al. 2021 [44]	France	1	A	NR	Intraosseous conglomerated foci and microabscesses within calcaneum	NR	Lytic bone cavities with sclerosis of calcaneum	Present	Absent
25	Tarafdar S et al. 2022 [23]	India	7 (4 cases of pedal mycetoma)	E						
	Case 1			E	NR	Extensive soft tissue involvement	Yes	Punched out lytic lesions with diffuse sclerosis of bones	Present	NR
	Case 2			E	NR	Interarticular soft tissue showing increased PD FS signal	Yes	Punched out lytic areas	Absent	NR
	Case 3			E	NR	Soft tissue mass showing areas of diffusion restriction with homogeneous enhancement	Yes	Permeative bone destruction	Present (aggressive)	NR
	Case 4			E	NR	Serpinginous high signal mass infiltrating the soft tissue of foot	Yes	Marrow edema in metatarsal	Absent	NR
26	Hoogervorst LA et al. 2022 [28]	Netherlands	1 (immunocompromised)	E	NR	Multiple nodules in soft tissue and multiple intraosseous lesions	Yes	Absent	Absent	NR
27	Bentaleb D et al. 2022 [12]	Morocco	2	A						
	Case 1				Hyperreflective area surrounded by hypoechoic soft tissue showing increased vascularity	Multiple small hyperintense lesions with peripheral fibrosis and central hypointense foci, infiltration of surrounding soft tissue	Yes	Joint effusion in metatarsophalangeal joint	NR	NR
	Case 2				Echogenic nodules with hypoechoic halo	Multiple round to spherical hyperintense lesions with separated by hypointense tissue and few showing hypointense center, infiltration of plantar fascia and muscles	Yes	Bone marrow edema in metatarsals	NR	NR
28	Nabih OO et al. 2023 [13]	Morocco	1	A	NR	Scattered and contiguous rounded T2 hyperintense lesions with hypointense border and central hpointense foci	Yes	Osteolysis of tarsals and metatarsals	NR	NR
29	Hailemariam T et al. 2023 [11]	Ethiopia	2	E						

Table 1:
Salient radiological features of Pedal mycetoma described earlier in the literature

	Case 1				Heterogeneous lesion containing multiple hypoechoic thick- walled lesions with small hyperechoic foci, increased vascularity in surrounding soft tissue	NR	Yes	Well-defined coritcal erosions	Present (Solid)	
	Case 2				NR	Multiple variable sized lesions involving soft tissue and bones, lesions were hyperintense with a central dot and peripheral hypointense rim	Yes	Permeative bone destruction	Present (aggressive)	NR
30	Present case	India	1	A	Infiltrative ill-defined heterogeneously hypoechoic soft tissue, multiple variable sized hypoechoic lesions with central hyperechoic foci and hyperechoic rim	Ill-defined heterogeneous infiltrative soft tissue involving the subcutaneous tissue, muscles and bones with multiple variable sized lesions appearing hyperintense on STIR/ PD FS with hypointense rim and central hypointense foci	Yes	Moth eaten pattern of destruction with surrounding sclerosis and bone marrow edema	Present (solid)	Absent

Legend of Table 1: A- Actinomycetoma; E- Eumycetoma; NR- Not reported.

Table 2: Radiography-based staging system proposed by Abd El Bagi ME et al [30]

Stage	Radiographic feature
Stage 0	No bone involvement
Stage I	Displacement or cortical scalloping
Stage II	Isolated periosteal reaction or reactive cortical sclerosis
Stage III	Solitary bone involvement
Stage IV	Longitudinal spread along single ray
Stage V	Horizontal spread but limited to forefoot, midfoot or hind foot
Stage VI	Multidirectional spread involving multiple rays and rows of bones

Table 3: MRI-based mycetoma skin, muscle, bone (MSMB) grading system proposed by El Shamy ME et al [31]

Score	MRI Feature
Skin and subcutaneous tissue	
0	No skin or subcutaneous involvement
1	Obliteration of skin and fascial planes
2	Abscess formation
3	Formation of sinus tract without grains
4	Formation of sinus tract with grains
Muscle	
0	No muscle involvement
1	Muscle oedema
2	Formation of micro-abscess
3	Formation of macro-abscess
Bone	
0	No bone involvement
1	Bone oedema
2	Bone cavitation
3	Bone destruction

Table 4: Common differential diagnoses for pedal mycetoma with distinguishing clinicoradiological features

Feature	Pedal mycetoma	Diabetic foot	Localized cellulitis	Osteomyelitis	Charcot arthropathy	Venous thrombosis	Tubercular arthropathy	Vascular malformation
Clinical								
Fever	-	+/-	+	+	-	+/-	+	-
Pain	-	+/-	+	+	-	+/-	+/-	-
Signs of inflammation	+	+	+	+	-	+	+	-
Discharging sinuses	+	+/-	-	+	-	-	+/-	-
Lymphadenopathy	+/-	+	-	+/-	-	-	+	-
Presentation	Subacute/ chronic	Acute/ subacute	Acute	Chronic	Chronic	Acute	Subacute/ chronic	Subacute/ chronic
Inflammatory Markers	Normal	Elevated	Elevated	Elevated	Normal	Normal	Elevated/ normal	Normal
Radiological								
Soft tissue characteristics	Ill-defined infiltrative, hypoechoic, T2/STIR hyperintense	Soft tissue edema and heterogeneity	Soft tissue edema and heterogeneity	Soft tissue edema and heterogeneity	Atrophy	Edema	Inflammatory changes	Ill-defined/ well defined lesion, insinuating across tissue planes, phleboliths
Associated collections	+/-	+	+	+	-	-	+/-	-
Sinuses	+	+/-	-	+	-	-	+/-	-
Bone involvement	Moth eaten/ permeative destruction and sclerosis	Permeative bone destruction, osteolysis, fragmentation and resorption	Normal	Sequestrum with surrounding sclerosis, involucrum	Sclerosis, osteolysis, fragmentation, resorption, intraarticular loose bodies, dislocation	Normal	Periarticular osteopenia, joint space narrowing, peripheral erosion, rice bodies	Venous- hypoplasia, scalloping, osteopenia Arterial- bone resorption, erosions
Periosteal reaction	Aggressive / solid	Aggressive / solid	Absent	Aggressive	Solid	-	Aggressive/ solid	Solid
Deformity	+/-	-	-	+/-	+	-	+/-	-
Dot-in-circle sign	+	-	-	Mimic	-	-	Mimic	Mimic



Figure 1: Clinical photograph of the patient [A and B] showing swelling of the foot with a discharging wound in the lateral aspect [A].

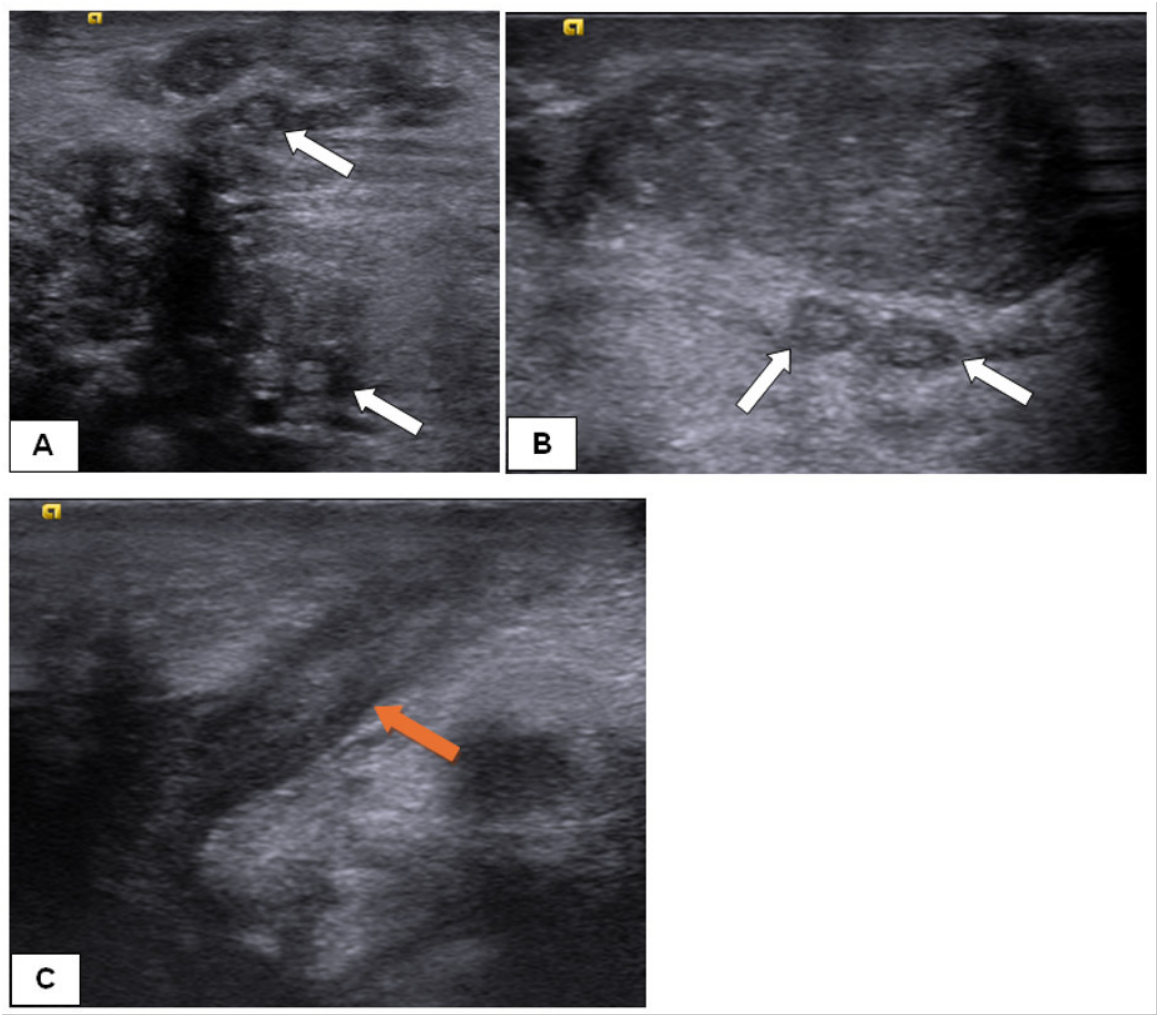


Figure 2: *Ultrasonographic images of the foot. Grey scale ultrasonographic images of the foot show infiltrative soft tissue with multiple discrete and conglomerate nodular lesions showing 'dot-in-circle' appearance [white arrows in A and B]. A linear hypoechoic sinus tract was also seen [orange arrow in C].*

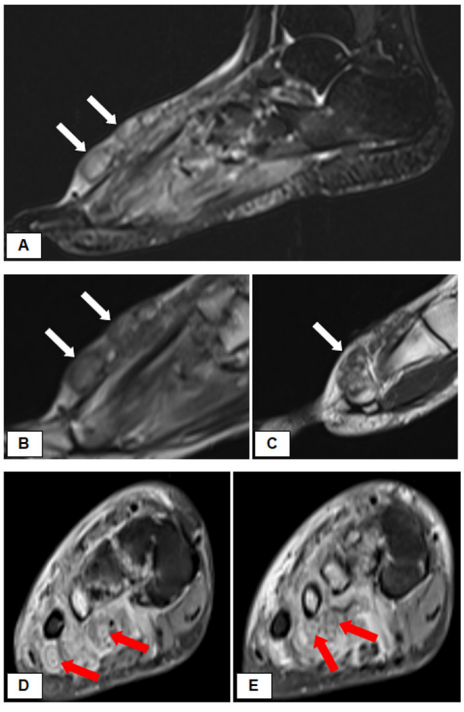


Figure 3: *MRI images of the foot. Sagittal STIR [A], sagittal T2 [B and C] and coronal PD FS [D and E] images show ill-defined infiltrative hyperintense soft tissue with variable sized nodular lesions [white arrows in A-C] with several showing 'dot-in-circle' appearance [red arrows in D and E].*

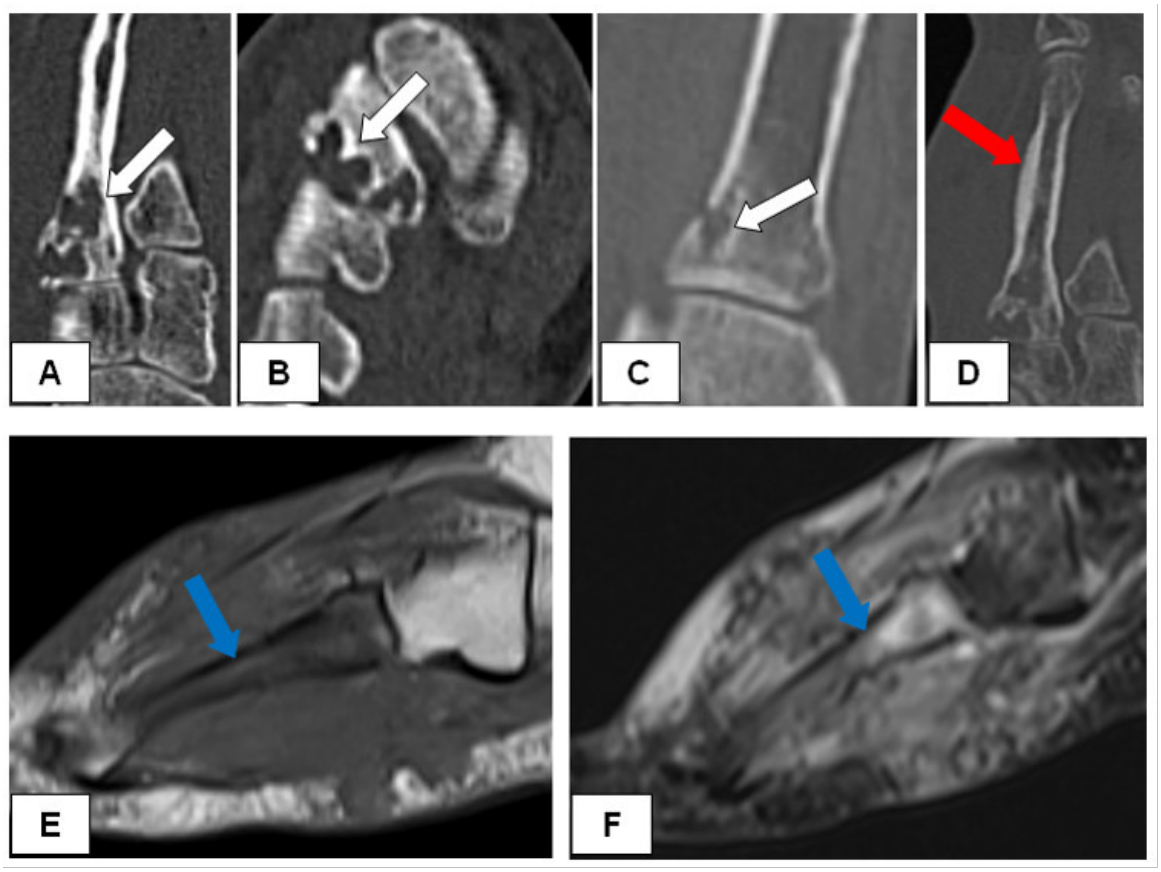


Figure 4: *Radiological images showing various forms of bone involvement. Reformatted computed tomographic [CT] images in bone window [A-D] show moth- eaten pattern of bone destruction [white arrows in A- C] involving the tarsals and metatarsals and solid periosteal reaction [red arrow in D]. Coronal T1 [E] and STIR [F] images show loss of normal T1 hyperintensity of the bone marrow of the metatarsal with diffuse increase in STIR signal [blue arrows in E and F].*

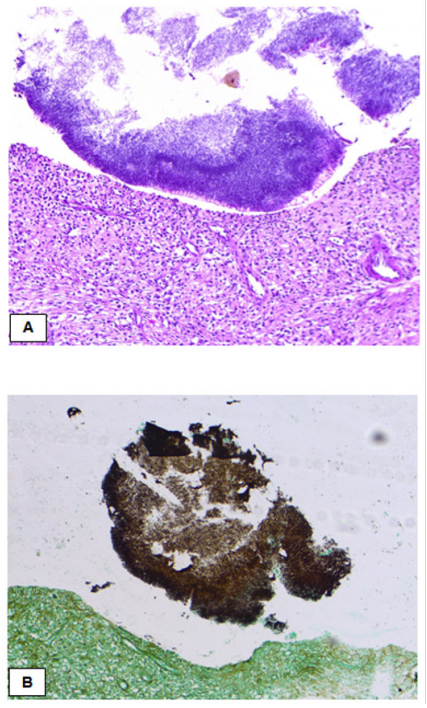


Figure 5: *Microscopic images of the histopathological sample. Magnified [10x] image of H & E staining [A] shows focal colony of basophilic filamentous bacteria with peripheral Splendore-Hoeppli phenomenon. Magnified [10x] image of GMS histochemical staining [B] demonstrates positively highlighted [brown stain] filamentous bacteria.*



Figure 6: *Schematic representation of the granuloma showing 'dot-in-circle' appearance. Granuloma shows a central core comprising of the microbial elements [shaded in red] surrounded by granulation tissue [shaded in yellow] with a peripheral fibrotic rim [red solid line], giving the characteristic 'dot-in-circle' appearance.*

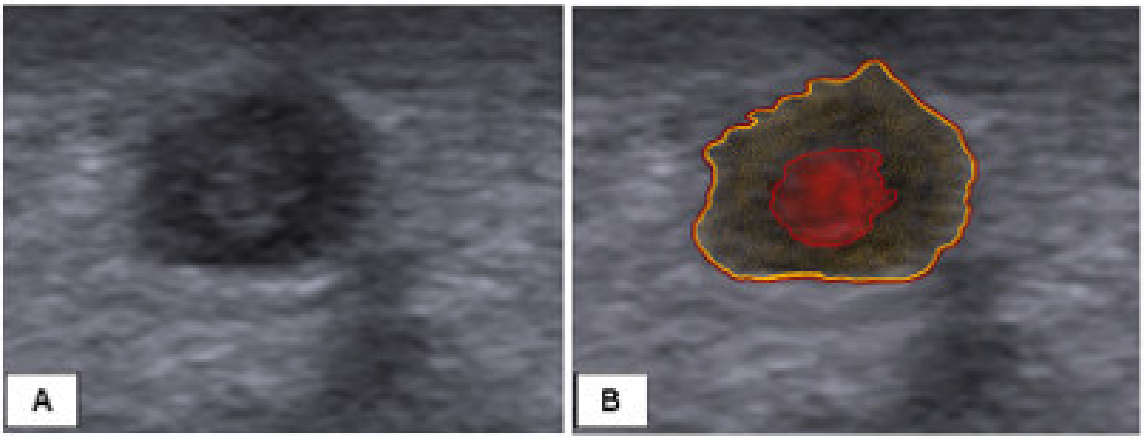


Figure 7: *Ultrasonographic appearance of the granuloma showing 'dot-in-circle' appearance. Grey scale ultrasonographic image [A] with annotation [B] shows a lesion with central hyperechoic core [shaded in red] surrounded by hypoechoic granulation tissue [shaded in yellow] and a peripheral hyperechoic rim of fibrosis [solid red-yellow line].*

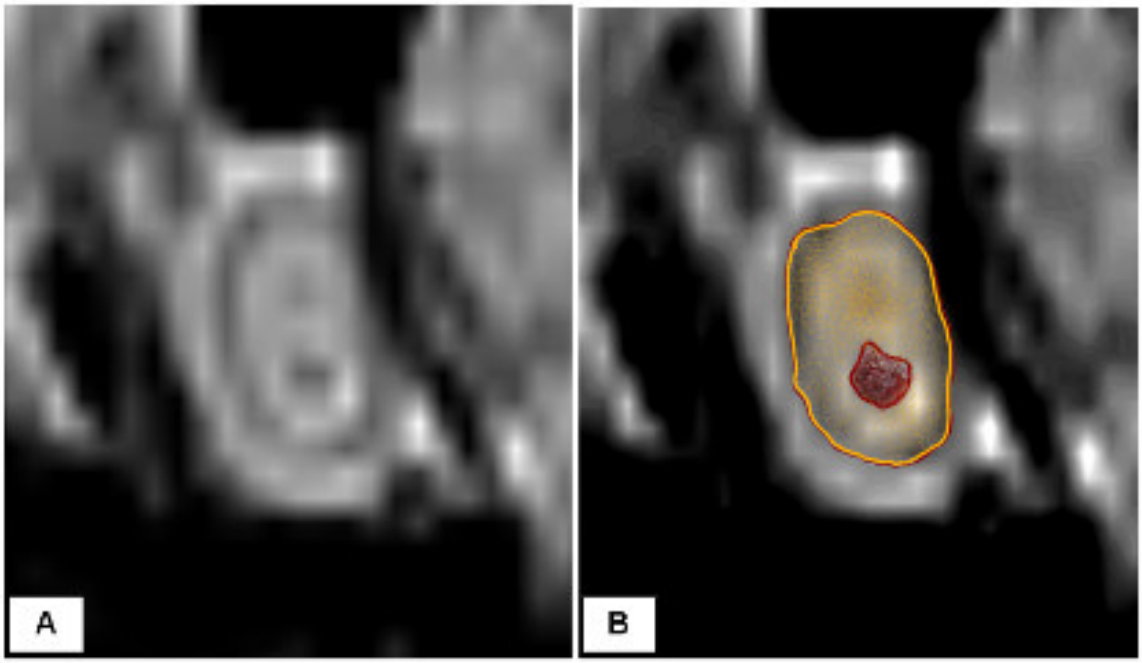


Figure 8: *MRI appearance of the granuloma showing 'dot-in-circle' appearance. PD FS MRI image [A] with annotation [B] shows a well-defined lesion with a central hypointense dot [shaded in red] surrounded by hyperintense granulation tissue [shaded in yellow] and a peripheral hypointense fibrotic rim [solid red-yellow line].*

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