

Clinico-radiological-pathological correlation in eumycetoma spectrum: Case series

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ABSTRACT

Maduramycosis or mycetoma is one of the chronic granulomatous diseases commonly seen in tropical regions. Microbiological cultures and biopsy are done for definitive diagnosis of the disease but they are time consuming methods. The purpose of this study was to correlate clinical, radiological and pathological features in eumycetoma cases to emphasize the role of "dot in circle" sign leading to early imaging based diagnosis. Imaging plays an important role in early diagnosis of mycetoma which has therapeutic implications. "Dot in circle" sign is a recently described sign in mycetoma cases on ultrasound (USG) and magnetic resonance imaging (MRI). We diagnosed 4 cases of eumycetoma based on clinical and imaging features which were confirmed with histopathology. Differential diagnosis which may mimic this sign are also discussed. The "dot in circle" sign is seen on both ultrasound and MRI. This sign is highly specific for mycetomas. Knowledge of this sign can help in early diagnosis of mycetomas preventing misdiagnosis and further complications.

Keywords: Dot in circle; granulomatous; magnetic resonance imaging; mycetoma; ultrasound.

Cite this article as: Yadav T, Meena VK, Shaikh M, Khhera S, Sureka B, Garg P, et al. Clinico-radiological-pathological correlation in eumycetoma spectrum: Case series. *North Clin Istanbul*

In 1842, Gill first recognized Madura foot or mycetoma as a disease entity in Madurai, India and in 1880, Carter coined the term "Mycetoma" [1]. Mycetoma can be caused by, the *Eumyces*, or true fungi (eumycetoma), or *Actinomyces*, filamentous bacteria of the Order actinomycetales (actinomycetoma) [2]. Mycetoma occurs more commonly in tropical climate regions. It frequently involves exposed areas of the body which come in direct contact with soil, so commonly occurs in feet, lower legs and hands. Thorn prick with direct inoculation of the infecting organism is the most common mechanism. Mycetoma is a chronic localized granulomatous disease, which is slowly progressive in nature. It is characterized by excessive formation of granulation tissue and discharging

sinuses however, in later course of the disease, it can also involve the bone. Appearance of discharging sinuses is very important for making clinical diagnosis of mycetoma but in early stages of the disease without the formation of discharging sinuses, clinically it looks similar to chronic bacterial infections or soft tissue neoplasms. So, imaging plays an essential role in the early diagnosis [2]. USG and MRI both demonstrate recently described "dot in circle" sign (Fig. 1). The specificity of "dot in circle" sign on MRI and USG for the detection of mycetoma is high [3–5].

Case 1 – A 35-year-old male, teacher by occupation, presented with complaints of swelling in dorsum of right foot over the region of middle toe (Fig. 2A), which was

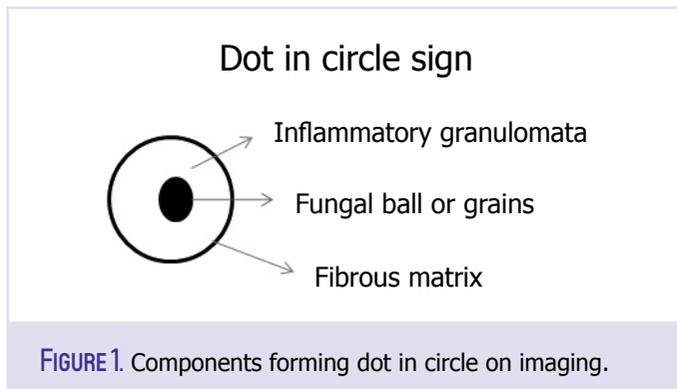
Received: January 23, 2019 Accepted: May 14, 2019 Online: July 12, 2019

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gradually increasing in size over a period of 2 years. He had a past history of thorn prick over middle toe while gardening in his farmhouse. Swelling was also associated with discharge from multiple sinuses. Radiograph of the foot did not reveal any abnormality except soft tissue density over dorsum of middle toe (Fig. 2B). During further work up, ultrasound showed multiple lesions with hyperechoic foci in center and hypoechoic wall in periphery of lesions (Fig. 2C). MRI of foot confirmed multiple hyperintense lesions with central hypointense dots and surrounding hypointense tissue (Fig. 2D, E). Bone marrow involvement or osteomyelitis was absent.



FIGURE 3. Eumycetoma of the great toe. **(A)** Swelling at lateral aspect of great toe with discharging sinus and foci of hyperpigmentation. **(B)** Radiograph of the foot (AP view) image shows soft tissue density over lateral aspect of great toe (black arrow). **(C)** On ultrasound, multiple lesions (white arrows) are evident with thick hypoechoic walls and hyperechoic foci in center. **(D)** Axial T2-weighted MRI shows multiple hyperintense lesions with central hypointense dots (white arrows).

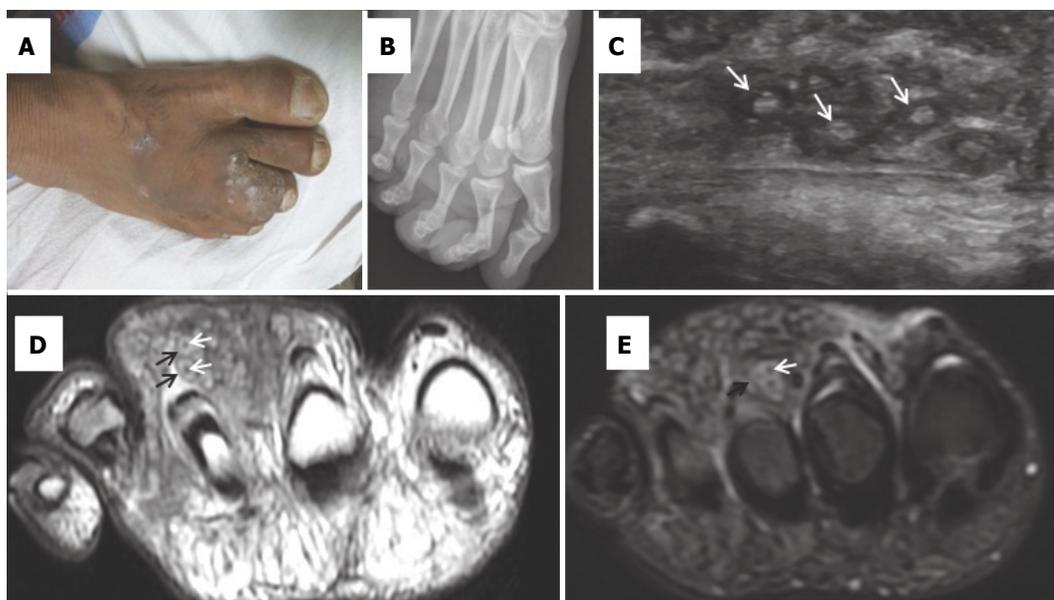


FIGURE 2. Eumycetoma of the foot. **(A)** Soft tissue swelling at dorsum of right middle toe and foot region with multiple encrusted skin sinuses. **(B)** Radiograph of the foot (AP view) appears normal except a soft tissue density shadow over heads of 2nd–4th metatarsals. **(C)** Ultrasound image shows multiple lesions (white arrows) with hypoechoic walls (circle) and hyper echoic foci in center (dots) giving the appearance of “dot in circle”. **(D, E)** Axial T2-weighted **(D)** and STIR **(E)** MRI images showing multiple hyper intense lesions with hypointense periphery (black arrows) with central hypointense dots (white arrows) giving the appearance of “dot in circle”.

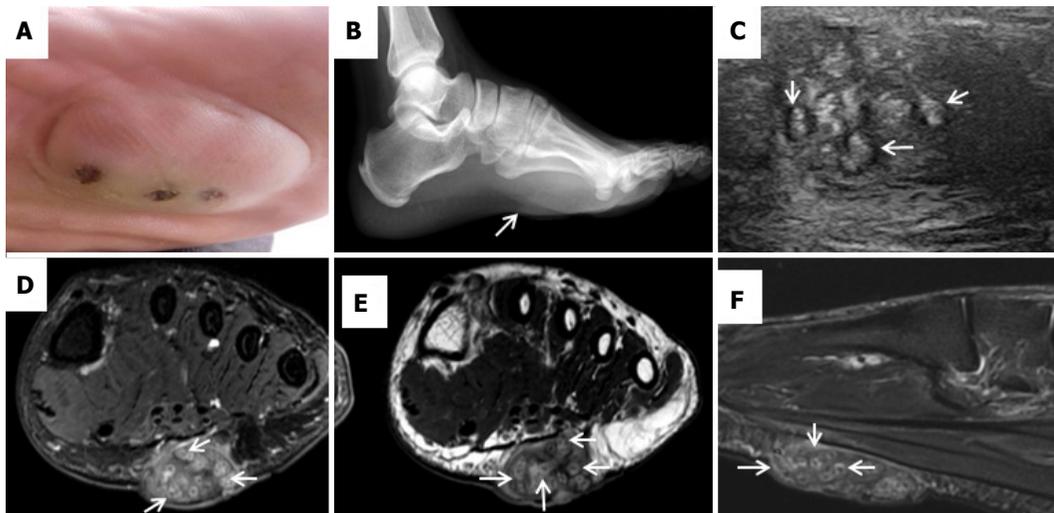


FIGURE 4. Eumycetoma at the plantar aspect of foot. **(A)** A protuberant swelling at plantar aspect of foot with few encrusted sinuses. **(B)** Lateral radiograph of the foot appears normal except a soft tissue density shadow on the plantar aspect (arrow). **(C)** On high resolution ultrasound, multiple clustered lesions are noted, which have hypoechoic periphery and hyperechoic center. **(D–F)** Axial STIR **(D)**, T2WI **(E)**, and Sagittal STIR **(F)** MRI images show multiple hyperintense lesions with central hypointense dots (white arrows) showing typical “dot in circle” sign in the subcutaneous plane.



FIGURE 5. Eumycetoma with bone involvement. **(A)** Soft tissue swelling at ankle on the medial side, extending into plantar aspect of foot with few encrusted sinuses and hyperpigmented patches in skin. **(B, C)** AP and lateral radiographs of ankle show multiple osteolytic and sclerotic lesions in calcaneum with periosteal reaction (white arrows) at lower end of tibia and fibula. **(D)** Ultrasound image shows multiple lesions with dot in circle sign (black arrows).

Case 2 – A 27-year-old male, came with complaints of soft tissue swelling and few discharging sinuses in dorso-lateral aspect of right great toe (Fig. 3A). He noticed this swelling 6 months back. He had no significant occupational history or history of thorn prick. Foot radiograph showed mild soft tissue density along the proximal phalanx in lateral aspect of great toe (Fig. 3B). On ultrasound, multiple hypoechoic lesions with hyperechoic foci in center were seen (Fig. 3C). On MRI of foot, multiple hyperintense lesions with central hypointense dots

consistent with dot in circle sign were seen (Fig. 3D).

Case 3 – A 32-year-old male, presented with a soft tissue swelling in plantar aspect of left foot (Fig. 4A). Swelling was partially exophytic in appearance. Three discharging sinuses were present at the dome of swelling. He was farmer by occupation. Foot radiograph showed no significant abnormality except soft tissue density shadow (Fig. 4B). On ultrasound, multiple clustered lesions with hypoechoic wall in periphery and hyperechoic foci in cen-

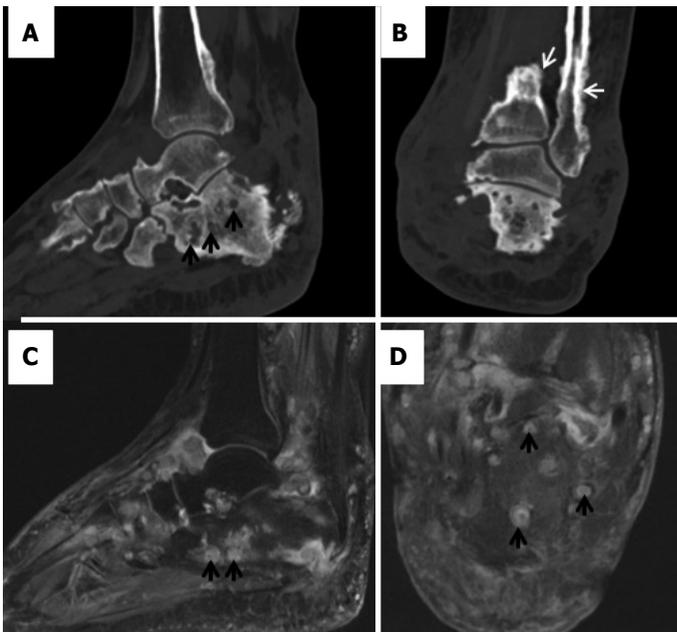


FIGURE 6. CT and MRI of ankle of the patient with eumycetoma in figure 5. **(A, B)** Sagittal and coronal reformats of CT of ankle show multiple osteolytic areas (black arrows) in calcaneum with periosteal reaction at lower end of tibia and fibula (white arrows) with soft tissue involvement, respectively. **(C, D)** Sagittal and coronal STIR MRI images show multiple lesions in calcaneum and soft tissues with dot in circle sign (arrows).

ter were seen (Fig. 4C). MRI of foot demonstrated multiple lesions with dot in circle sign (Fig. 4D–F).

Case 4 – A 37-year-old male, had history of minor trauma over left ankle 10 years back which was followed by swelling over left ankle and was associated with black

grain discharge. Foot radiographs revealed multiple osteolytic lesions in calcaneum, associated with periosteal reaction in tibia and fibula (Fig. 5B, C). Ultrasound of ankle showed few ill defined lesions with hyperechoic foci in center and hypo echoic wall in periphery (Fig. 5D). CT ankle confirmed multiple osteolytic lesions in calcaneum with periosteal reaction in tibia and fibula (Fig. 6A, B) confirmed. MRI ankle demonstrated multiple hyperintense lesions with dot in circle sign in both soft tissues and in calcaneum (Fig. 6C, D).

In all 4 cases, final diagnosis was eumycetoma which was confirmed on histopathology (Fig. 7). In the first three cases, surgery was done followed by antifungal therapy. In the 4th case, patient did not give consent for surgery and is on antifungal therapy since last 8 months.

DISCUSSION

Mycetoma is chronic granulomatous infection of the dermis and epidermis. It can be caused by the bacteria *Actinomyces* (*Actinomycetoma*) or by true fungi (*eumycetoma*) [6–9]. Mycetoma is more prevalent in tropical regions and is endemic in India. All of our cases belonged to western Rajasthan, in India which is a tropical area. Eumycetoma is more prevalent in areas with less rainfall, while actinomycetoma is more prevalent in areas with heavy rainfall. It is presumed that there is direct introduction of infecting organism after trauma or direct penetration of skin with sharp objects. This infection more commonly involves feet because they are more prone to trauma. First of all, soft tissue swelling occurs with inflammation in surrounding tissues due to forma-

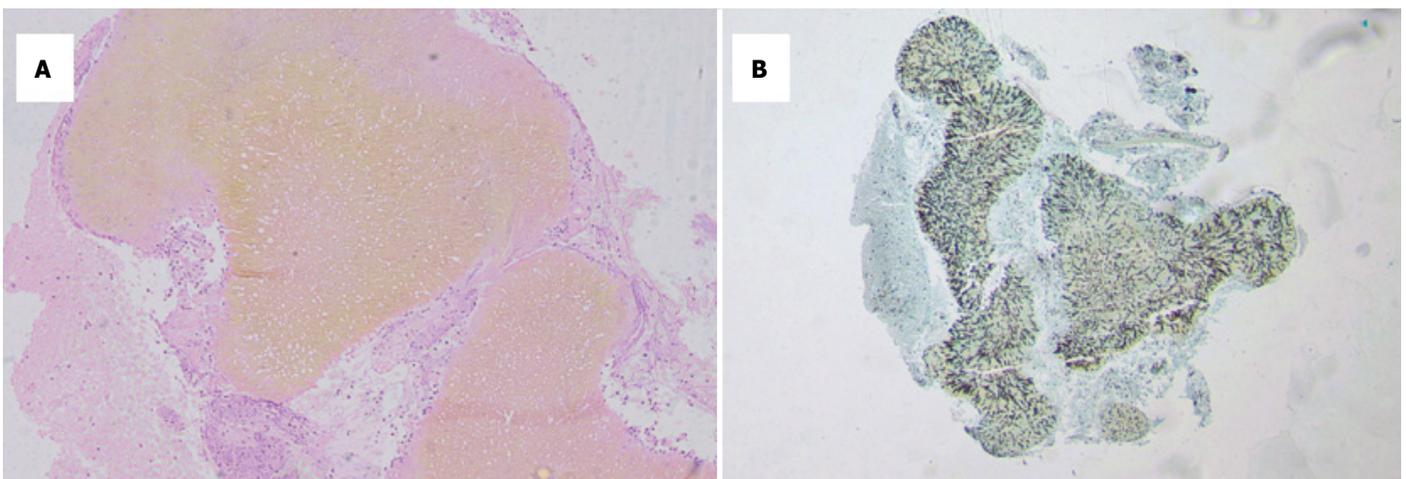


FIGURE 7. Eumycetoma on histology. **(A)** Haematoxylin and eosin (H&E) stain, low magnification, shows cluster of fungal hyphae surrounded by inflammatory response **(B)** GMS staining positive for fungal hyphae.

tion of granulation tissue. This granulation tissue further leads to the formation of multiple discharging sinuses. Bone involvement may occur in later course of the disease after many years [1, 6].

Clinically, when any patient presents with soft tissue swelling and discharging sinuses, then diagnosis of mycetoma should be considered [3]. Mycetoma is a slowly progressive disease. If proper treatment is not initiated in early stages of the disease then, it can lead to multiple complications like osteomyelitis, abscess formation, fistula formation and formation of multiple draining sinuses tracts with deformity of the involved body part [2]. In early stages of the disease, in the absence of discharging sinuses, clinical diagnosis of mycetoma is difficult. It can be misdiagnosed as soft tissue tumor or chronic indolent bacterial to tubercular infection. However, imaging plays an important role in early detection of mycetoma. “Dot in circle” sign is seen in mycetoma and this sign is very specific for mycetoma [7] (Fig. 1). All 4 of our cases demonstrated “dot in circle sign” on both ultrasound and MRI. In later course of the disease, bone involvement with destruction can occur which may require surgical management and has bad prognosis. So, for better prognosis of the patient, early detection of mycetoma is important. Imaging, particularly ultrasound and MRI play a crucial role in early detection of mycetoma and differentiate it from other pathologies.

Radiographs are helpful in detection of bone changes in cases of mycetoma. However, they may be normal if no bone involvement is present especially in early stage

of the disease. Common findings present on radiographs are bone sclerosis, periosteal reaction, bone cavities, cortical scalloping, osteoporosis and soft tissue thickening [7]. Sometimes bone changes on radiographs are helpful in differentiation of eumycetoma and actinomycetoma. Lesions of eumycetoma have a tendency to form few cavities in bone which are more than one centimeter in diameter. Bone lesions in actinomycetes usually have more number of cavities but are small in size which leads to moth-eaten appearance [2]. Bagi et al. has given a radiographic classification based on extent of bone involvement (stages 0–6) [7]. Computerized tomography (CT) scan depicts the extent of bone changes involvement better than radiographs. Initially Czechowski et al., in 2001 observed small foci of low-signal intensity on both T1- and T2- weighted images, and assumed that the low-signal intensity of these foci is due to susceptibility from the metabolic products of the “grains” [8].

In 2003 Sarris et al., described the “dot in circle” sign, as tiny hypointense foci with in the hyperintense spherical or circular lesions on T2W and STIR sequences [8–10]. Further correlation with histopathological findings revealed that high signal intensity on MRI is due to inflammatory granulomata, central low signal intensity part is composed of fungal balls or grain and outer hypointensity is due to fibrous matrix. Finally they too concluded that “dot in circle” sign is highly specific sign for mycetoma. Later, “dot in circle” sign was also reported by Kumar et al., in 2007 and Lee Parker et al., in 2009 [3, 9]. T1-weighted post contrast (gadolinium) images

TABLE 1. Differences between eumycetoma and actinomycetoma

Features	Eumycetoma	Actinomycetoma
Etiology	True fungi	Filamentous bacteria
Epidemiology	In drier areas	With abundant rainfall
Course of disease	Slowly progressive	Rapidly progressive, with more destruction
Size and Color of grains	Coarse, Black or pale	Fine, white, yellow or red
Radiographic changes	Few cavities in bone that are ≥1 cm in diameter	Early bone involvement. Smaller but more numerous cavities, leading to a moth-eaten appearance
Muscle involvement	Uncommon	May be present
Ultrasound	The grains are numerous and appear as very sharp hyperechogenicities. Single or multiple, hypoechoic, thick-walled cavities with no acoustic enhancement	The grains are fine, hazy, closely aggregated and commonly settle at the bottom of the cavities
Treatment	Antifungals with or without surgery	Antibiotics with or without surgery

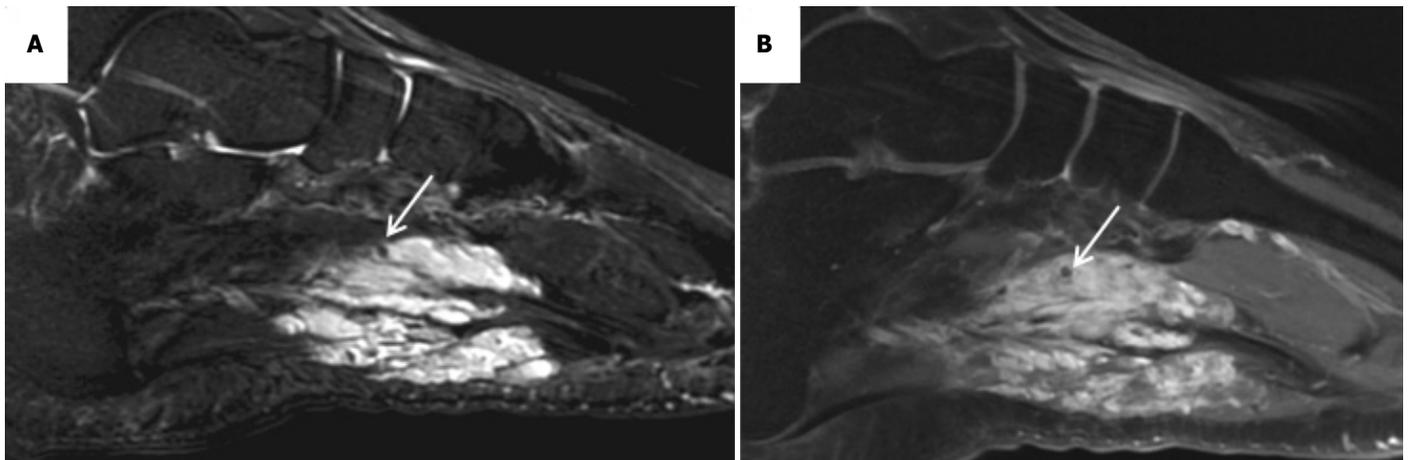


FIGURE 8. Dot in circle sign mimic – Phleboliths in a case of soft tissue hemangioma in foot (case not described in this series). **(A)** Sagittal STIR and **(B)** post contrast T1W images show small phlebolith (arrow) in a hemangioma on the plantar aspect of foot which can give similar appearance as dot in circle sign.

may also show dot in circle sign however, do not appear to have any advantage over sequences without contrast. We did not do post contrast MRI in any of our cases. Dot in circle sign can be seen in mycetomas involving soft tissues as well as bones, as seen in our case number four.

Ultrasound features of mycetoma were first described by Fahal et al., and they described that hyper-reflective echoes represent grains which is surrounded by hypoechoic tissue [4, 11]. Eumycetoma grains generally produce sharp hyperechoic foci while hyperechoic foci in actinomycetoma are usually seen at bottom of the lesions. “Dot-in-circle” sign in USG is similar to the MRI. Differences between eumycetoma and actinomycetoma are listed in Table 1.

Histopathological examination of lesion reveals that lesion is composed of grains of fungal hyphae or bacteria in the background of granulomatous reaction [12, 13]. Multiple methods are available for distinguishing actinomycetoma from eumycetoma like gram stain, periodic acid-Schiff, Gomori methenamine silver and lactophenol blue stain [13]. Biopsy or staining and culture usually give the definitive diagnosis but these are time consuming methods. Sometimes, making the correct diagnosis with the help of biopsy and staining is difficult, mainly in fastidious organisms.

Imaging mimics for dot in circle sign are phleboliths in hemangiomas and rice bodies. Sometimes, hemangiomas or low flow vascular malformations may mimic as dot in circle sign (Fig. 8) due to the presence of phleboliths which are seen as hypointense foci in the background of hyperintense lesion. However, clinical history, lesser



FIGURE 9. Dot in circle sign mimic - Rice bodies (case not described in this series). Oblique sagittal STIR image of elbow joint in a patient with articular tuberculosis. Multiple small hypointense nodular “rice bodies” are seen distending the joint and can mimic as dot in circle sign.

number of dot in circles, absence of sinuses, absence of inflammation in surrounding tissues should favour the diagnosis of vascular malformation [8].

Rice bodies are also hypointense nodular foci formed due to chronic synovial inflammation. These are seen in the synovial fluid of patients of rheumatoid arthritis or tuberculosis [9] (Fig. 9).

Conclusion

To conclude, the “dot in circle” sign is seen on both ultrasound and MRI. This sign is highly specific for mycetomas. Knowledge of this sign can help in early diagnosis of mycetomas preventing misdiagnosis and further complications.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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