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Case report

Soft tissue mycetoma: "Dot-in-circle" sign on magnetic resonance imaging

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ABSTRACT

A 36-year-old Mexican female with a slowly growing foot mass was referred to orthopedic surgery clinic for further evaluation. Foot magnetic resonance imaging revealed an infiltrative soft tissue mass along the dorsal aspect of the fourth metatarsal. T2-weighted images revealed multiple central low-signal "dots" surrounded by areas of bright signal intensity, known as the "dot-in-circle" sign, which is highly specific for mycetoma. Surgical biopsy confirmed the diagnosis of bacterial mycetoma in this patient. Mycetoma can lead to progressive deformity and loss of function, as well as possible limb amputation in the case of delayed diagnosis or misdiagnosis. The "dot-in-circle" sign on magnetic resonance imaging can assist in rendering a final diagnosis and distinguish mycetoma from other etiologies of a soft tissue mass, such as a sarcoma or benign soft tissue lesions.

Introduction

Mycetoma is a chronic progressively destructive granulomatous infection of the skin, underlying soft tissue, and sometimes bone acquired by direct inoculation of certain species of bacteria and fungi into the involved tissues [1]. The disease most commonly affects young adults in tropical or subtropical populations with a male predominance [2]. It generally involves parts of the body that come in direct contact with soil, with the foot being the most commonly affected site [1]. Some of the associated predisposing factors include low socioeconomic status, occupations such as farming, and lack of protective clothing [3].

Mycetoma diagnosis can be suggested either clinically or by histopathologic findings but definitive diagnosis requires positive tissue culture [4]. Mycetoma can result in significant morbidity and sometimes even mortality. Therefore, timely

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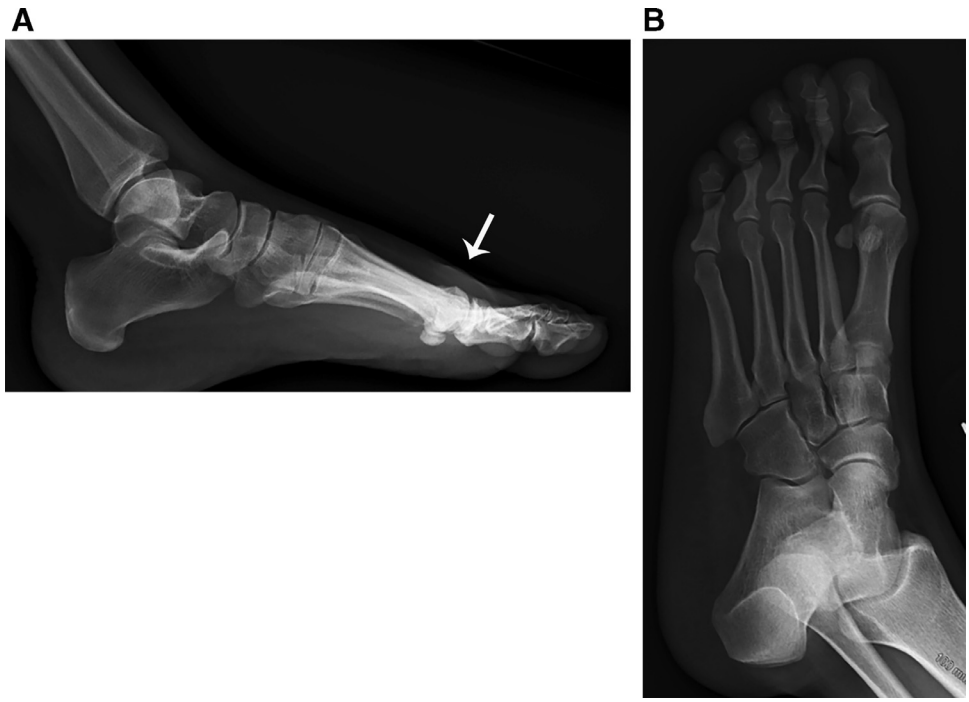

Fig. 1 – (a,b) Lateral and oblique radiographs of the left foot during prior visit (2 years before current encounter) show an area of nonspecific swelling and increased soft tissue density overlying the third and fourth metatarsal heads. There is no soft tissue calcification, osseous erosion, or periosteal reaction.

diagnosis and treatment is of utmost importance. Treatment includes antibiotics or antifungals after identification of the causative organism in localized infection. More severe infection may require surgical excision or amputation [5,6].

Imaging is usually used when there is diagnostic ambiguity, to map the extent of the disease, and to exclude other pathologies. Radiograph, ultrasound, and computed tomography (CT) provide only limited evaluation due to poor soft tissue contrast and are often used for initial evaluation. MR imaging can effectively map the extent of disease and can be used to identify additional sites of infection as well as involvement of osseous structures; however, imaging features can be misleading. Mycetoma can have nonspecific appearance on MR imaging and may mimic a malignant or benign soft tissue mass such as a sarcoma or hemangioma; however, some imaging features are useful to narrow the differential diagnosis [7,8]. One highly specific imaging feature of mycetoma is the "dot-in-circle" sign, which consists of ring-like areas of high signal intensity lesions with a central low-signal "dot" representing small fungus balls or bacterial grains [8,9]. It is important for radiologists to be familiar with this imaging feature to be able to provide more precise diagnosis and prevent unnecessary surgical intervention.

Case report

A 36-year-old Hispanic female presents with a 1-year history of a growing mass on the dorsal left foot. She reported having pain in the left foot with exertion. She denied any systemic symptoms, purulent drainage, or trauma to her foot. The patient is originally from Mexico, but had been living in the US since she was a teenager. She reported walking barefoot as a child in Mexico, but not recently.

Radiograph of the foot showed mild diffuse soft tissue prominence with increased soft tissue density at the level of metatarsophalangeal joints (Fig. 1a and b). Contrast-enhanced MR imaging (Fig. 2) showed an infiltrative heterogeneously-enhancing soft tissue mass over the dorsal aspect of the distal fourth metatarsal and proximal phalanx with insinuation into the third and fourth webspaces. On T1-weighted images (Fig. 2a), the mass was predominantly isointense relative to muscle without internal fat signal intensity. T2-weighted images (Fig. 2b and c) and short tau inversion recovery (STIR) images (Fig. 2d) demonstrated a heterogeneous, predominantly bright signal intensity lesion with thin septations and surrounding hypointense borders, composed of multiple rounded foci with central low signal intensity dots. The lesion demonstrated avid postcontrast enhancement with central foci of nonenhancement (Fig. 2e).

The overall impression at that time was that the mass could be a neurogenic lesion; however, histologic correlation would be necessary to exclude more sinister pathologies such as synovial cell sarcoma. The patient underwent a surgical excision, with pathology subsequently revealing a soft tissue with multifocal abscesses, bacterial colonies, and extensive reparative changes with no evidence of malignancy. No bacterial culture or smear was done at that time and the patient was not given antibiotics except for 1 dose of 2 g intravenous cefazolin and 750 mg intravenous vancomycin perioperatively.

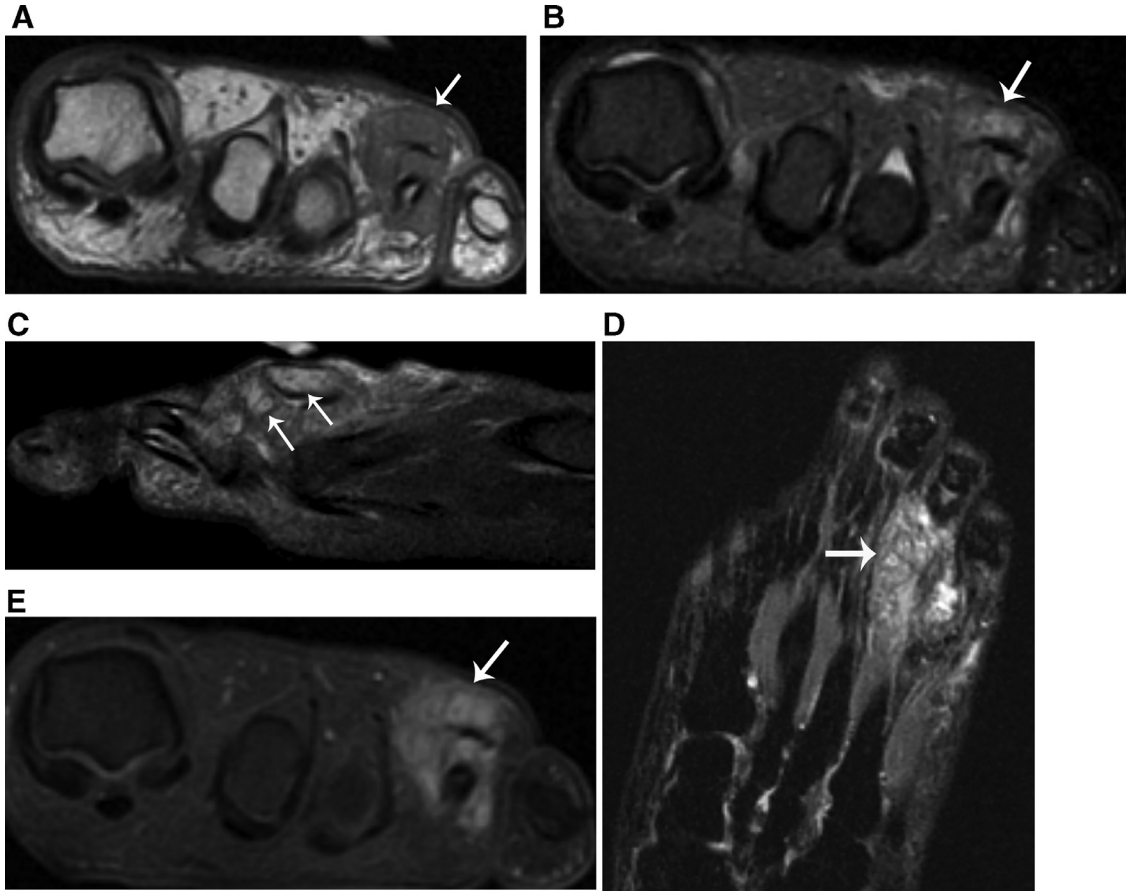

Fig. 2 – (a–e) MR imaging performed on prior visit (2 years before current encounter). Axial T1-weighted image (3a) shows a soft tissue lesion dorsal to the fourth metatarsal head insinuating into the third and fourth web-spaces. Axial (3b) and sagittal (3c) T2-weighted fat-saturated images and coronal STIR image (3d) show a heterogeneously bright signal intensity lesion with multiple rounded foci encircling small low signal intensity dots. Axial T1-weighted fat-saturated image obtained after intravenous administration of gadolinium-based contrast (3e) shows enhancement of the lesion. The central dots lack significant enhancement.

Two years later, the patient returned to orthopedic clinic, stating that the mass on her left foot never completely resolved after surgery, and had been increasing in size over the past few months. She had also developed a new papule medial to the site of swelling within the last few months.

On physical exam, vital signs were within normal limits. There was a 0.5 × 0.5 cm erythematous papule over the dorsum of the left forefoot at the level of the third metatarsal head, as well as a palpable nonmobile mass over the fourth metatarsal shaft. The incision over the dorsum of fourth metatarsal from the previous surgery was well healed (Fig. 3). Laboratory studies, including basic metabolic panel, complete blood count, and C-reactive protein were within the reference ranges.

Radiograph of the left foot showed mild nonspecific forefoot soft tissue swelling. There was no acute pathology such as fracture, dislocation, or radiopaque foreign body (Fig. 4a and b). MR imaging before and after administration of gadolinium-based contrast agent was requested and performed for further evaluation of the lesion using our institutional MR imaging protocol for neoplastic processes (Fig. 5). MR imaging again showed an infiltrative heterogeneously-enhancing soft tissue mass centered over the dorsal aspect of the distal fourth metatarsal and proximal phalanx with insinuation into the third and fourth webspaces. The mass abutted the fourth metatarsal without evidence of osseous invasion or marrow signal changes. T1-weighted images demonstrated isointense signal intensity to muscle (Fig. 5a). T2-weighted (Fig. 5b and c) and STIR (Fig. 5d) images showed a heterogeneous predominantly bright signal intensity lesions with foci of rounded hyperintense signal with a “central dot” of lower signal intensity. Postcontrast, fat-suppressed T1-weighted images (Fig. 5e) show moderate, heterogeneous enhancement of the mass with some internal low-signal nonenhancing foci. Time-resolved angiography with stochastic trajectories MR angiography (Fig. 5f) showed an area of increased vascularity along the dorsal forefoot at the area of the space-occupying lesion. Given the imaging appearance and history of regional infection, soft tissue mycetoma was diagnosed, and the possibility of benign or malignant neoplastic processes was favored to be less likely.

The patient was elected by the surgical team for operative removal of the mass. Surgical excision was performed and the patient was given a 1-week course of Bactrim (160 mg, twice

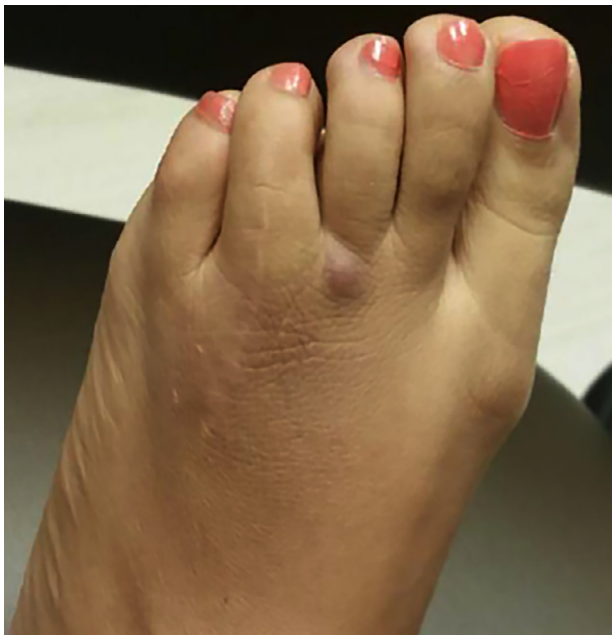

Fig. 3 – Photograph of the left foot at the time of current clinical visit demonstrates a surgical scar from prior resection. There is diffuse soft tissue swelling at the surgical bed with a small papule at the of third metatarsal head.

daily by mouth) after the surgery. Surgical pathology result showed filamentous gram-positive rods on Gram stain, suggesting bacterial mycetoma. Acid-fast bacilli smear and culture and Fite stain (to identify Mycobacterium leprae) were negative. The organisms seen on Gram stain did not grow in aerobic culture. Anaerobe, fungal, and bacterial blood cultures were also not able to grow the organism.

Patient followed up at the infectious disease clinic 3 weeks after surgery. Based on clinical and pathologic findings, antibiotic therapy was started for bacterial mycetoma. The patient completed 11 weeks of Bactrim (160 mg, twice daily by mouth) and Ceftriaxone (2 gm, single dose daily intravenously). Over this period, the soft tissue mass and papule decreased in size; however, the patient developed Bactrim-induced pancytopenia. Therefore, Bactrim and ceftriaxone were discontinued and the patient was started on Augmentin (125 mg, twice daily by mouth), which she took for 2 months. Over this period, the mass disappeared and the papule continued to decrease in size. The remaining small papule that was observed on follow-up exam was suspected to be just a residual scar. At this point, the antibiotics were discontinued. The patient followed up 3 months after stopping the antibiotics (Fig. 6). At this time, the papule had remained unchanged in size and she was symptom-free.

Discussion

Mycetoma is a localized mass-like soft tissue granulomatous lesion which can gradually develop draining sinuses with discharging grains of contagious material. Mycetoma is either caused by fungi (eumycetoma) or bacteria (actinomycetoma) [3]. It is a progressively destructive disease and can lead to loss of function, morbidity, or even unnecessary limb amputation; therefore, timely diagnosis is important. Mycetoma is more common in tropical and subtropical regions [10]. In Mexico, most mycetoma cases occur in rural areas and are mostly caused by Nocardia brasiliensis [2].

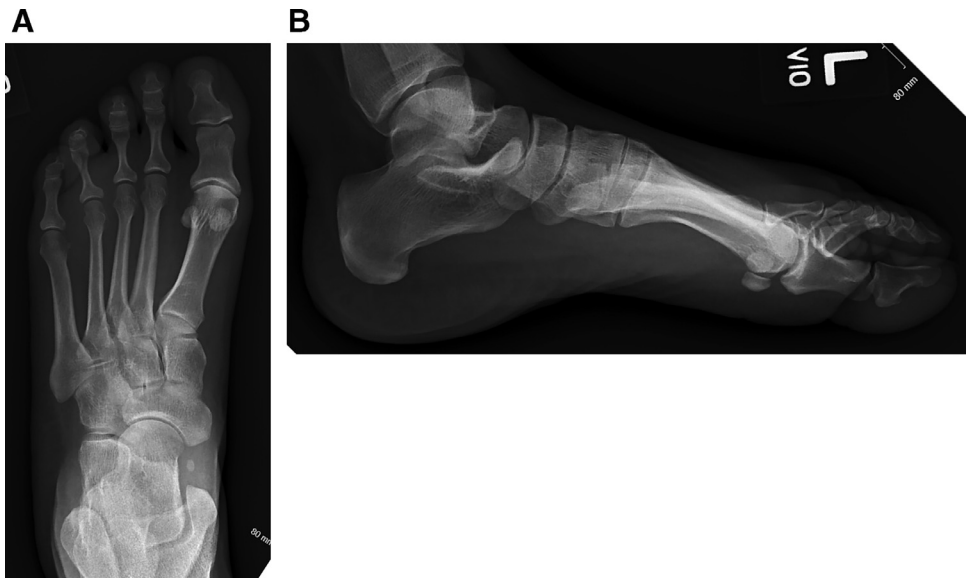

Fig. 4 – (a,b) Anterior posterior and lateral radiographs of the left foot during current encounter again show a nonspecific sift tissue density overlying the third and fourth metatarsal heads. There is no soft tissue calcification, radiodense foreign body, osseous erosion, or periosteal reaction.

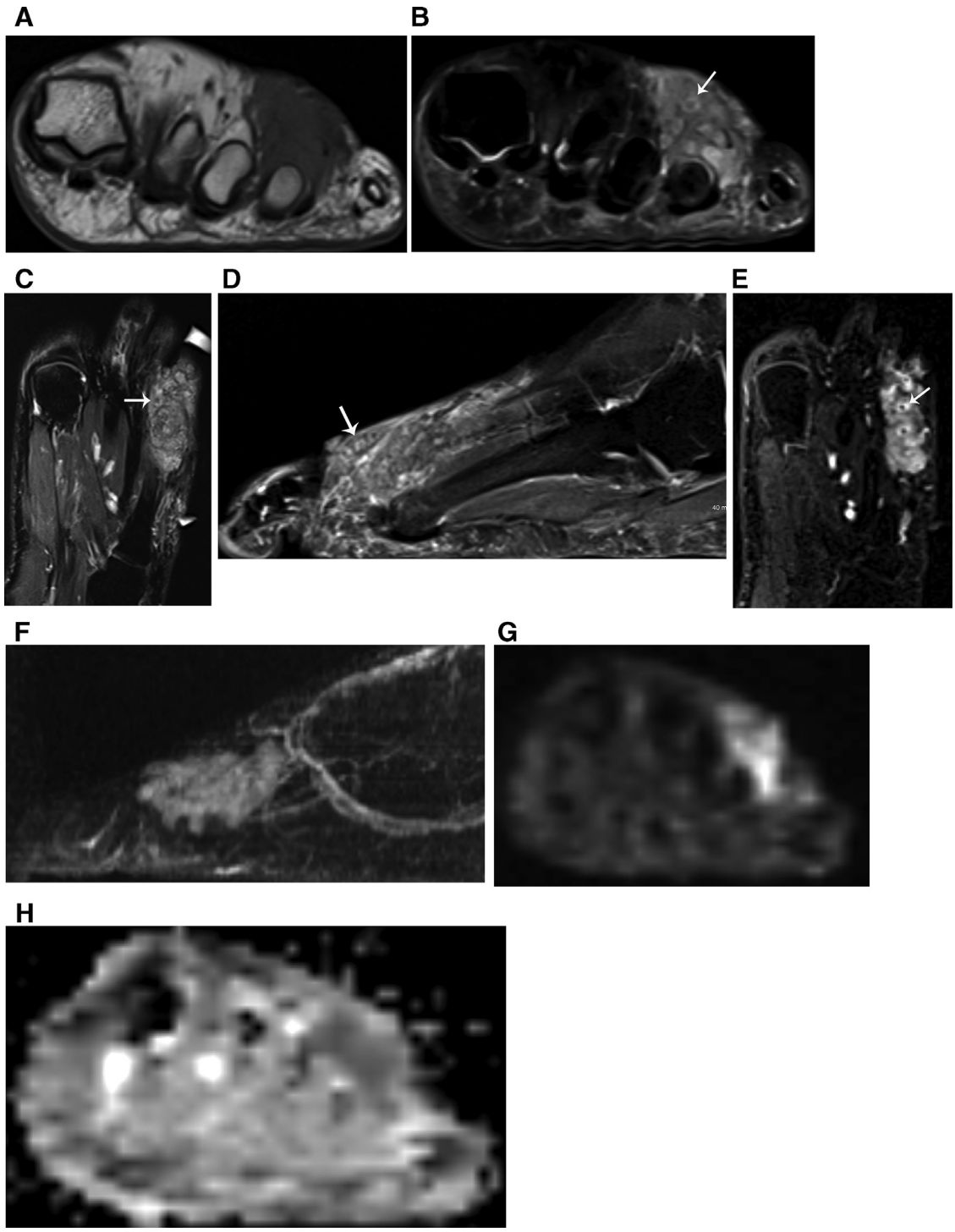

Fig. 5 – (a–h) MR imaging obtained on current encounter shows a soft tissue lesion at the area of prior surgical resection dorsal to the fourth metatarsal head. The lesion is isointense to muscle on T1-weighted image (a) insinuating into the third and fourth web-spaces. The lesion appears larger compared to the prior MR imaging. Axial (b) and sagittal (c) T2-weighted fat-saturated images and coronal STIR image (d) demonstrate a conglomerate of rounded bright signal intensity foci with central low signal intensity (dot-in-circle sign). This sign is even more conspicuous on postcontrast coronal T1-weighted fat-saturated VIBE subtraction image (e). TWIST MR angiography (f) shows an area of hypervascularity corresponding to soft tissue lesion. The lesion demonstrates mild diffusion restriction with bright signal intensity on b800 diffusion image (g) and ADC value of 0.95 ($\times 10^{-3}$ mm^2/s) (h). ADC, apparent diffusion coefficient; TWIST, time-resolved angiography with stochastic trajectories.

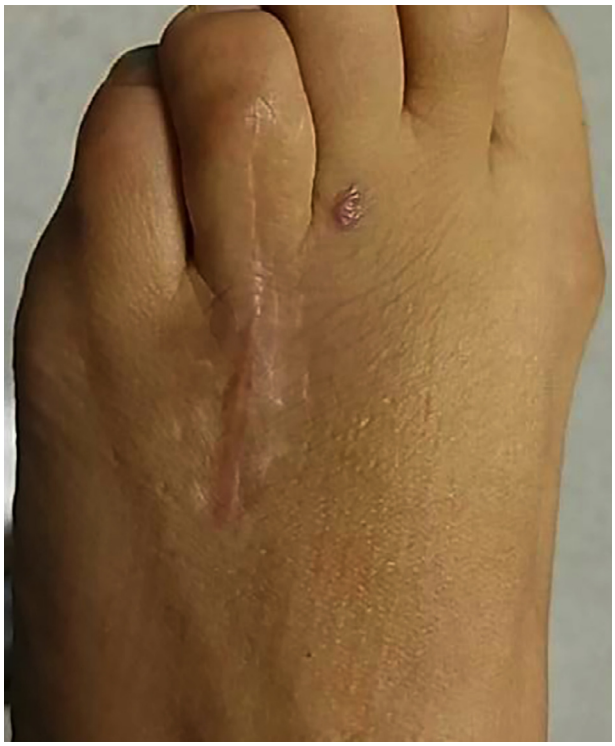

Fig. 6 – Photograph of the left foot after current surgery and completion of the course of antibiotics. Longitudinal surgical scar is again seen. Soft tissue swelling has significantly improved. There is a small area of scar at the area of prior skin papule at the third metatarsal head.

The organisms responsible for mycetoma are normal habitants of soil. The inoculation can occur after trivial trauma. The incubation period is highly variable and ranges from several months to 10 years [11]. When the infection is introduced into soft tissues, the causative agent organizes into small granules, called grains. Bacterial grains can be white, yellow, or red, while fungal grains are usually pale or black [12]. Surrounding soft tissues form inflammatory granulomas around these grains with a thin rim of fibrous matrix. Bone involvement is common in pedal mycetoma due to the superficial location of osseous structures [13].

Clinical diagnosis of mycetoma can be established by the presence of the triad of soft tissue mass, draining sinuses, and macroscopic grains; alternatively, it may be diagnosed histologically by microscopic examination of the grains, either in purulent discharge or in surgical specimens. Definitive diagnosis can be made based on positive culture; however, tissue culture can be time-consuming and burdensome because of rigorous growth requirements as well as the small numbers of viable pathogens present in a long-standing inflammatory lesion [4,14]. In our case, cultures failed to identify the etiologic pathogen despite positive histopathologic findings. Clinical diagnosis can be challenging, especially in nonendemic areas, or prior to development of the characteristic draining sinuses, as in our case [1,4–6]. Treatment depends on the causative organism and extent of the disease. It usually includes antibiotics or antifungals. More severe infection, especially with bone involvement, may require major surgical resection or amputation [5,6]. Recurrence rate after surgery is usually high, especially in cases of incomplete excision or underestimation of the extent of the disease, such as in our case.

Imaging is usually used when definitive diagnosis is not yielded clinically, especially when there is no discharging sinus. In addition, imaging is needed to evaluate the extent of the disease, involvement of deep tissue structures, recurrence, and to exclude other pathologies such as benign or malignant neoplastic diseases. Although radiograph is less sensitive to detect soft tissue findings, it is widely used due to low cost and wide availability. Initially, there is no osseous involvement and there could be displacement or bowing of the bones with slowly growing granulomatous mass. When lesions irritate the bone, periosteal reaction or reactive osseous sclerosis may occur. Finally, infection may penetrate the bone causing cortical erosion and cavities. In pedal mycetoma, infection usually spreads contiguously along a single ray of metatarsal bone and phalanx, or 2 adjacent rays. In cases of neglected or uncontrolled infection, infection can spread multidirectionally leading to severe mutilation and disorganization of the osseous structures [12]. Disease extension to osseous structures is always of important clinical concern. Early osseous changes are better depicted on CT; however, CT provides limited evaluation of soft tissue and bone marrow involvement due to poor soft tissue contrast [15].

MR imaging is the modality of choice for evaluation of mycetoma due to high soft tissue contrast, and capability of multiparametric evaluation with contrast studies and quantitative sequences such as diffusion weighted imaging (DWI). Mycetoma has characteristic features on MR imaging. It appears as a conglomerate of small rounded foci of high signal intensity on T2-weighted images with central small "dot" of low signal intensity ("dot-in-circle" sign) and a thin rim of dark signal intensity. T1-weighted images of mycetoma typically reveal predominantly isointense mass to muscle with mild hyperintensity of the central "dot" component. Postcontrast images typically demonstrate intense peripheral enhancement of the lesion with unenhanced central "dot" components, giving a honeycomb appearance [12]. DWI can also be a useful adjunct in suspected cases, with the central component of the mass demonstrating diffusion restriction. The role of DWI has not been evaluated comprehensively in musculoskeletal mycetoma. There is mild diffusion restriction in areas of enhancement and granulomatous clusters in our case with an apparent diffusion coefficient value of 0.95 ($\times 10^{-3}$ mm^2/s) (Fig. 5g and h).

The "dot-in-circle" sign was first described in 2001, when Czechowski et al studied MR images of 20 patients with mycetoma. They noticed low-signal "dots" in 16 cases. They suggested that the observed "dots" are mycetoma grains [16]. Two years later, Sarris et al used the term "dot-in-circle" sign for the first time to describe this finding [17]. The "dot-in-circle" sign is present in 80% of patients with musculoskeletal mycetoma and is highly suggestive of this disease entity. The high-intensity "circles" correspond to granulomata and the central low-signal "dots" correspond to bacterial or fungal grains. The peripheral rim of low signal intensity presents a thin rind of fibrous matrix. This sign can be seen on

T2-weighted, proton-density, STIR, and gadolinium-enhanced T1-weighted fat-saturated images [12].

Overall, imaging features can vary in accordance with the stage and extent of disease, degree of tissue necrosis, and possible postoperative changes. The differential diagnosis for clustered cyst-like soft tissue lesion includes benign entities such as lymphatic and vascular malformations including hemangioma, and malignant lesions such as myxoid sarcomas or synovial cell sarcomas. Other infectious etiologies such as tuberculosis, hydatic infection, and pyomyositis are among the differentials [12,18–19]. In our case, the lesion was misdiagnosed based on imaging as a "neurogenic tumor with the possibility of malignancy such as synovial cell sarcoma not entirely excluded" on the patient's first clinical encounter.

Overall, the "dot-in-circle" sign on MR imaging is a specific indicator for mycetoma. Familiarity of radiologists and infectious disease specialists with this imaging finding is important to avoid unnecessary invasive treatment or intervention. Imaging can help with early diagnosis and post-treatment surveillance.

Disclosures

Majid Chalian; Medical advisor Imagen Technology Ltd.

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