Case Resolution

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Diagnosis

Mycetoma pedis (Madura foot)

Discussion

In 1832, British researcher Johon Gill while working in Madurai (ex Madura), Indian district of the Tamil Nadu state, described a condition that he called "foot tumor". Later on in 1846, Colebrook reported the same condition with the name "Madura foot". It was not before 1860 that Vandyke Carter proved the mycotic nature of the condition and described several of its characteristics, such as its progression profile, the parts of the body most frequently affected, the color of the "grains" (particularly that of black grains), bone destruction, greater incidence in males, and surgical amputation as therapeutic option. It was him that gave the name of "mycetoma" (tumor caused by fungi) to this condition, term it is known as in medical literature.

Mycetoma pedis is a destructive granulomatous infection that affects the skin, subcutaneous soft tissues, muscle tissues, fascia tissues and, in severe cases, bone tissues. It is a chronic, slowly progressive condition. With respect to its etiology, it can be caused by true fungi (in such cases it is called "eumycetoma") or by aerobic actinomycetes (actinomycetoma) (Table). These microorganisms are considered to be soil contaminants, especially in tropical areas. The fungi portal of entry is through skin traumatism, and they usually affect rural individuals who do not use shoes due to their socio-cultural status.

From the clinical point of view, it is characterized by painless soft-tissue swelling with nodes which develop and discharge —through fistula— exudate fluids with purulent contents and grains containing the colonies from the etiologic agent. However, patients' clinic characteristics can vary according to the different etiologic microorganisms. If the agent belongs to the group of the actinomycetes, e.g. *Nocardia brasiliensis,* skin formation of fistulous granuloma is usually greater. Moreover, these ones tend to be more inflammatory lesions than eumycetoma is, and they show a greater degree of invasion into deep tissues.

These lesions are more frequently located in lower limbs, prevailing in patients' feet and their legs to a lesser extent. Lesion incidence decreases upwards. However, although not that frequent, there are reports on lesions in upper limbs, trunk, neck and head.

From the histological point of view, a typical mycetoma consists of focal granulomatous infiltration with a purulent center surrounded by a thick fibrous capsule containing the characteristic grains.

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Table. Madura foot etiology and characteristics

Agent	Frequency	Color of the grain	Approximate size
Actinomycetoma			
Actinomadura madurae	++++	White-pinkish	0.5-5 mm
Streptomyces pelletieri	+++	Red	0.3-0.5 mm
Streptomyces somaliensis	+++	Yellow	0.5-2 mm
Nocardia brasiliensis	++++	White-yellowish	<0.5 mm
Nocardia asteroides	++	Yellowish	25-150 µm
Nocardia caviae	++	White-yellowish	
Eumycetoma			
Madurella mycetomatis	++++	Brown-blackish	70 mm
Madurella grisea	++	Black	0.3-0.6 mm
Leptosphaeria senegalensis	++	Black	0.5-2 mm
Leptosphaeria tompkinsii	++	Black	0.5-2 mm
Pyrenochaeta romeroi	++	Black	
Exophiala jeanselmei	+	Black-brownish	0.2-0.3 mm
Pseudoallescheria boydii	++	White	
Neotestundia rosatti	+	White-brownish	0.5-1 mm

Mycetoma inflammatory reaction is unspecific, but the presence of grains is most useful to help identify the etiologic agent. If there are no sinuses with drainage it can be difficult to differentiate benign or malign soft-tissue tumors, cold abscesses and granuloma from a clinical point of view.

The condition is endemic in tropical (between 15°-South and 30°-North latitudes) and deserted regions, although there are also reports on cases in warm climate areas (Figure 8). There is a greater incidence in Mexico, Venezuela, Brazil, North of Argentina, some countries in Central America, Sudan, Senegal, India and Pakistan. Moreover, there are reports on sporadic cases in other countries in South America, the United States, Saudi Arabia, Yemen and Europe. The main etiologic agent in Argentina is *Nocardia brasiliensis*.

It is more frequent in males than it is in females: most authors agree on a 3:1 male: female ratio and it is believed that this male prevalence is due to males' greater exposure to contagious scenarios.

There are numerous reports on mycetoma diagnosis-making by conventional X-ray signs, which in frequency order are as follows: periosteal reaction, bone sclerosis, endosteal reaction, cortex erosion, lytic focal lesions, articular destruction, moth-eaten pattern, osteoporosis, and bone lysis. Some authors have set out classifications in stages. However, mycetoma characteristics in conventional X-rays are hardly specific, even when there are signs of chronic osteomyelitis; i.e. lytic lesions, sclerosis and remodeling in the affected bones in 50% of the cases. CT scan and MRI are more useful to visualize bone destruction, periosteal reaction and soft-tissue participation. Nevertheless, findings in CT scans are not specific either, and it is not possible to differentiate mycetoma infection from bacterial chronic osteomyelitis, granuloma, soft-tissue tumors, bone tuberculosis, and cold abscesses.

It has been reported that mycetoma grains, its capsule and the inflammatory granuloma it is accompanied by have characteristic US appearances. Some publications also state that, on the other hand, US images can differentiate eumycetoma from actinomycetoma, and even myecetoma from lesions of different etiology. This way, eumycetoma lesions are visualized as multiple thick-wall cavities without dorsal acoustic enhancement and with hyperechogenic images within, which can be interpreted as black grains. In lesions due to actinomycetoma results are similar, but grains are less hyperechogenic —perhaps due to their lesser size and consistence—and they are typically grouped at the bottom of the cavity.

Mycetoma US diagnosis is more accurate and exact in the evaluation of lesions without sinuses. The size and extension of lesions can be accurately determined by US and it is useful for surgical techniques planning and interventional procedures. Publications focused on US usually come from African countries, where mycetoma is endemic and populations have less access to greater complexity techniques such as CT scan and MRI.

MRI is the best imaging study to evaluate the degree of bone destruction, periosteal reaction and soft-tissue compromise. On the other hand, it is also true that at the first stages findings are usually unspecific and, again, lesions cannot be differentiated from those in chronic osteomyelitis, and even soft-tissue tumors. However, there is an MRI image which is considered to be practically pathognomonic in mycetoma, which consists of a high-signal rounded or ovoid lesion with a hypointense focus within: it is the so-called sign of the "point within the circle" (Figures 2-7), which can be seen in 80% of the cases according to the original Sarris et al.'s description. These authors carried out histological correlations between the components of the sign of the point within the circle, and they found that the hyperintense focal image that can be seen in MRI represents the inflammatory granuloma, the little hypointense foci within granuloma represent the balls of fungi or grains, and the low-intensity tissues surrounding these lesions are characterized by fibrous matrixes (Figure 9). Other researchers have also studied the lesions from a histological point of view focusing on their correlation with MRI, and have stated that T1- and T2- hypointensity in the central focus is due to the magnetic susceptibility of the metabolic products within the grains.

Although this sign is clearly seen in T2-weighted images with or without fat suppression, it can also be seen in T1-weighted images with fat suppression after administering i.v. gadolinium contrast, as it is shown in images in the presentation of the cases.

Grains discharged from the different etiologic agents have different characteristics from the shape and size points of view. Consequently, the possibility to see the grains by MRI can help in rough identification of microorganisms. For example, *Nocardia brasiliensis* produces small kidney-shaped grains (50-150 µm) which can be difficult to see in images. On the other hand, *Actinomadura madurae* forms rounded or oval grains whose size varies between 1 and 10 mm.

Nevertheless, the possibility to see the grains by MRI depends on other factors, not only grains size, such as image quality (magnetic field power) and the parameters of the sequences in use. On other occasions, imagines cannot be identified in every granuloma, perhaps because of their variable size, independently of the MRI equipment resolution.

Like other authors, in our series of cases we have found the sign of the "point within the circle" in mycetoma locations outside the foot (Figures 6 and 7).

Figure 8. Geographic distribution of mycetoma.

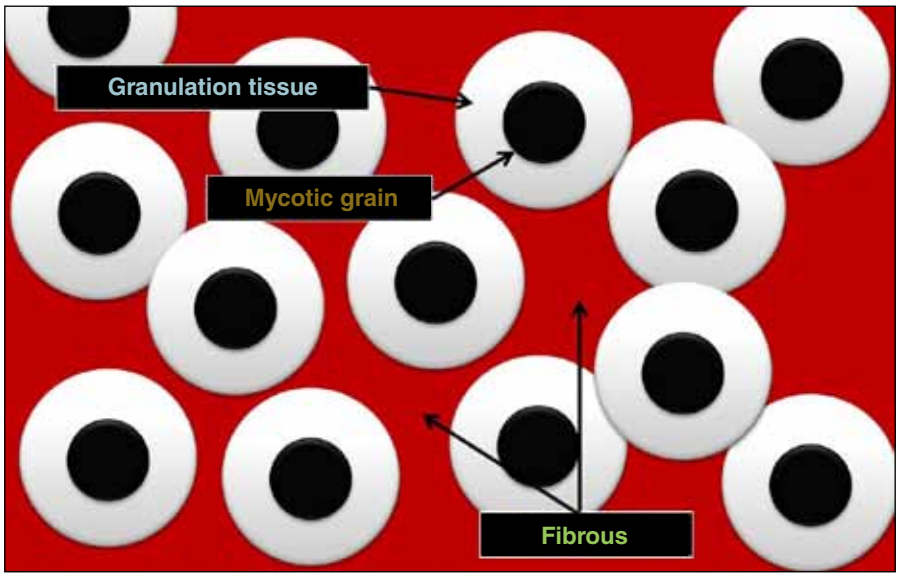

Figure 9. Diagram showing the different components of the sign of the "point within the circle".

Conclusion

Mycetoma should be one of the possible differential diagnoses in all cases of foot swelling, especially if there are nodes and fistula. When mycetoma only compromises feet soft tissues, many times anti-microbial therapies are curative. However, when there is bone compromise, anti-microbial drugs are usually ineffective and it may be necessary to resort to partial resection or amputation. Therefore, MRI is the best image study for mycetoma early diagnosis and bone compromise screening, what is essential for adequate management.