Mycetoma: retrospective study of 13 cases in Tunisia

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SUMMARY

Mycetomas are inflammatory pseudotumors of chronic and progressive evolution, of fungal (Eumycetoma), or bacterial (Actinomycetoma) origin. We conducted a retrospective study of patients who have been consulted for mycetoma over a period of 28 years.
Thirteen cases of mycetomas were collected during the 28-year period, 10 patients were of rural origin. The lesions were localized on the foot in all instances. There was no male predominance.
Histopathological examination confirmed mycetoma in all 13 cases and the determination of the infectious agent in 9 cases: 4 actinomycotic and 5 fungal. Microbiological examination identified the species in 7 cases. Bone involvement was found in 10 cases. Eumycetomas were treated by ketoconazole. The other cases were treated as actinomycetomas by antibiotics. The antibiotic treatment was associated with surgical excision in 4 cases and with amputation in 1 case.
Mycetomas are rare in Tunisia, and only observed sporadically, for this reason the diagnosis is usually late, with severe functional, psychological, and socioeconomic consequences.

KEY WORDS

mycetoma, skin, clinical study, Tunisia

Introduction

Mycetomas are inflammatory pseudotumors of chronic and progressive evolution affecting the skin, subcutaneous tissues and sometimes, the underlying bone. They are usually accompanied by multiple fistulas and by secretion of grains. The causative agents are exogenous, either fungi (eumycetoma) or aerobic bacteria (actinomycetoma). The grains result from host-parasite interactions and their morphology is complex (1).

The causative agents are barely identifiable clinically. The color of grains allows a diagnostic orientation: red grains are always actinomycotic, black grains are always fungal and white or yellow grains should be identified by histology and microbiological examination.

In all cases, the confirmation of the diagnosis depends on the finding of the causative agent by histological, bacteriological, and mycological examinations.

Microscopically, fungal grains appear as branched filaments, 2 to 4 µm in diameter, usually displaying

Table I. Summary of mycetoma cases observed in the Department of Dermatology of Charles Nicole Hospital in Tunis.

Cases n°	Sex	Age at the beginning	Histopathology	Culture
1	M	17	Black-grain mycetoma (fungal)	M. mycetomatis
2	M	18	White-grain mycetoma	Negative
3	F	28	White-grain mycetoma	N/D
4	M	16	White-grain mycetoma	Pseudallesheria boydii
5	F	31	White-grain mycetoma	Pseudallesheris boydii
6	F	60	Yellow-grain mycetoma	N/D
7	M	12	Black-grain mycetoma (fungal)	M. mycetomatis
8	F	24	Actinomycotic white-grain mycetoma	Negative
9	F	38	Mycetoma	N/D
10	F	42	Actinomycotic white-grain mycetoma	Streptomyces somaliensis
11	M	26	Actinomycotic yellow-grain mycetoma	N/D
12	F	56	Actinomycotic white-grain mycetoma	Actionomadura madurae
13	M	62	Black-grain mycetoma (fungal)	M. mycetomatis

N/D: not done

vesicle-like structures at their ends. Concerning actinomycotic grains, filaments are less than 1 µm in diameter. Histopathological examination is particularly interesting in the absence of grains in atypical lesions with cysts. The elementary histological manifestation is a granuloma surrounding the grain. For some causative agents such as. *Actinomadura* (A) *mycetomatis, Streptomyces somaliensis*, *A. madurae*, and *A. pelletieri* the histopathology of grains allows the species to be identified , while in others it suffices only to define the genus. For the diagnosis of species the culture is usually needed.

Mycetomas are frequent in hot and dry tropical, subtropical and temperate regions, where they represent a substantial public health problem. They are however, rare in Tunisia (2).

Our aim was to elucidate the epidemiological and clinical aspects of this condition in Tunisia through a study of cases of mycetoma collected in the Department of Dermatology of the Charles Nicolle Hospital in Tunis.

Patients and methods

We conducted a retrospective study dealing with patients diagnosed in our Department as having mycetoma, from January 1976 to December 2003. The diagnosis of mycetoma was suspected due to the presence of inflammatory lesions with multiple fistulas, and especially in cases discharging grains. Histological examination was systematically performed, while an X-ray examination of the affected area allowed the detection of bone involvement.

In the most recent seven cases, the grains were identified after culture on Sabouraud medium for fungal grains and on Lowenstein medium for actinomycetes.

Results

Thirteen cases of mycetomas were collected during the period under consideration. The mean-age at the onset of the disease was 33 years (range from 12 to 62 years). The mean duration before the first medical evaluation was 12.2 years. Six patients were males and seven females. Table 1. Ten patients came from rural areas, two were from urban areas and one was an immigrant from Mauritania. The localization was in all instances on the feet. A history of preceding minor trauma was reported in 3 cases. Clinically, mycetomas presented chiefly as chronic infiltrated lesions penetrating deep into subcutis with sinuses discharging a serous secret or pus, with grains in 12 out of 13 cases (Fig.1). Grains were black in 3, white in 7 and yellow in 2 cases. Histopathology allowed the confirmation of mycetoma in all instances and the determination of the infectious agent in 9 cases: 4 actinomycetic and 5 fungal. Microbiological examination identified the species in 7 cases. The actinomycotic origin was noticed in two of the four histopathologically detected cases: *Actinomadura madurae* in 1 case, *Streptomyces somaliensis* in 1 case.

The fungal origin was observed in 5 cases: *Madurella mycetomatis*: in three and *Pseudallescheria boydii* in two cases. Table 1.

Bone involvement was found in 10 cases (76.9%). This affection was of variable severity ranging from osseous demineralization (2 cases), to osteitis in 7 cases,

and metatarsal atrophy in one case.

Eumycetomas were treated with ketoconazole (Nizoral®) 200mg/day. The other cases were treated as actinomycetomas. The combination of cotrimoxazole/ampicillin was used in four cases, cotrimoxazole/amoxicillin in one case and cotrimoxazole/dapsone in one case. Three patients were lost for follow up before treatment. The outcome was favorable in 7 patients, with complete recovery in 3 of them. Antibiotic treatment was combined with surgical excision in 4 cases and with amputation of the foot in one case.

Discussion

Mycetomas are rare in Tunisia, and only appear sporadically. Since the first Tunisian case reported by Gemy and Vincent in 1892, only 36 cases were reported up to 1992 (3). The published Tunisian series reveal the rarity of this condition: 11 cases over 20 years (4), 12 cases over 27 years (2), and 3 cases over 10 years (5). In contrast, a series from Senegal included 109 cases over a period of 5 years (6). On both sides of the 15th north parallel, mycetomas represent a real public health problem. Geographic factors and the rainfalls intervene in the selection of causative agents of mycetomas (1). Actinomycotic mycetomas predominate in the relatively more rainy areas (Central Senegal, Niger, Mali), while eumycetomas prefer the regions with modest annual rainfall such as North Senegal or Mauritania (7).

Fungal and bacterial agents are saprophytes in soil or on plants. The inoculation of the agent is generally secondary to minor injuries inflicted with a spine, fish bone or a soiled tool (8), which explains the relative frequency in rural populations. In our patients the pedal affection was due to the habit of walking barefoot. A history of a minor injury was found in 3 of our patients. In literature, trauma has been reported in only one third of cases (6-9).

In the series reporting a larger number of cases, male predominance is estimated at 80% (6), which is probably because of their agricultural activities. In rural regions women also participate in agricultural activities. For this reason some authors have suggested the existence of a hormonal resistance factor in women (8). This hypothesis seems to be reinforced by the exceptional occurrence of mycetomas before puberty and by the onset or aggravation of the condition during pregnancy (6-8).

In our series a male predominance was not observed, the sex ratio F/M was 1.17. The ratio ranges from 1 to 3 in the other Tunisian reports (2, 4, 10). Cheikh noted only three women in his study (5). A Mexican study yielded similar results, except that 60% of the patients were women (8).

The mean age at the onset of the disease was 33 years in our series, while it was 32 years in another review from Tunisia (2). This matches with data from medical literature setting the age of onaset as being the active period of life, between 15 and 40 years (1).

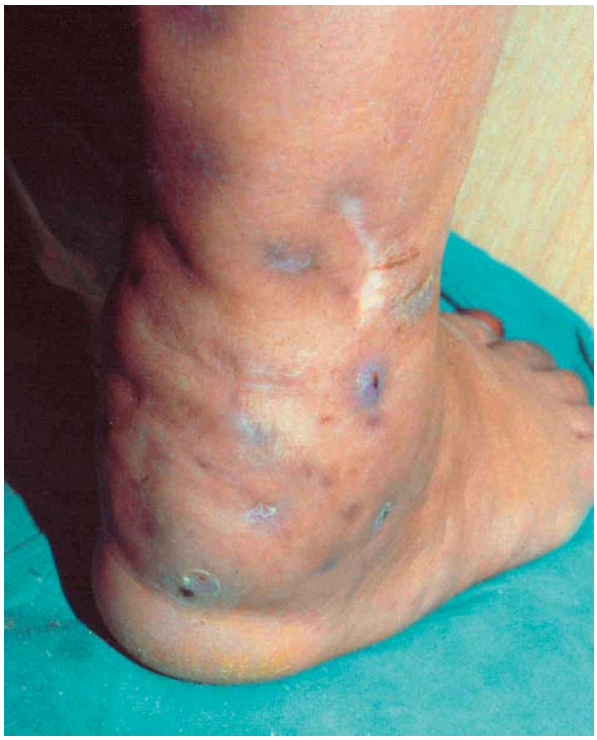

Figure 1. Multifistulated inflammatory tumor of the foot.

The mean-duration before first consultation is rather long; it was 12.2 years in our series and more than 5 years in 53.6% of cases in Mexico (8). This is explained by the slow evolution of the disease and its indolence in the beginning. In the early phase the only signs are a sensation of discomfort and a mild pain at the inoculation site. Later on a small nodule appears progressing slowly into the subcutaneous tissues (1).

The diagnosis is usually evident: on first consultation: a nodule or infiltrated plaque with multiple fistulas discharging pus and often grains of variable size and color.

The pedal localization is the most frequent; and justifies the historical designation of the condition as "*Madura foot*". Localizations outside the foot or lower leg seem to be rare (6). The infections of legs, thighs, and forearms are less deep, while the affection of hands progresses often rapidly to the bones. When the knees, elbows and buttocks are affected cysts may develop, but multiple sites of infection are exceptional, and are rather due to a lymphatic dissemination from the initial site (7).

In Tunisia, the actinomycotic agents seem to be predominant, and in particular *Actinomadura madurae* (2) which is also detected in Algeria and Morocco (2).

In cases of supposed bone involvement the prognosis is serious. An x-ray examination is essential, and eventually also a CT scan and MRI (7). The risk of bone involvement increases with the duration of the disease (11), and was found in 76.9% of our patients, probably due to pedal localization and the late diagnosis. Visceral localization is rare, but a lethal outcome is possible.

Treatment depends on the causative agent. Eumycetoma requires frequently surgery, sometimes a large excision or amputation combined with anti-fungal treatments. Just ketoconazole, 200 to 400 mg daily during several months, seems to be less effective. Itraconazole may also be used.

Treatment with dapsone-streptomycin, cotrimoxazole-streptomycin or cotrimoxazole only seem to yield good results. A combined treatment with trimetoprime and sulfametoxazole as well as tetracycline's or rifampicine are also mentioned in the literature. In all cases, medical supervision is necessary for several years..

The prophylaxis of mycetoma is based on disinfection of the post-traumatic lesions and especially on a preventive wearing of shoes.

Conclusion

Mycetomas remain a serious problem in endemic areas. They are rare, in Tunisia. The diagnosis is often late with functional, psychological, and socioeconomic after-effects. This situation calla for efficient preventive measures and early diagnosis.

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