Rev Iberoam Micol 1999; 16: 57-59

Mycetoma caused by *Exophiala jeanselmei*. Report of a case successfully treated with itraconazole and review of the literature

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We report a case of black grain mycetoma in a 74-years-old man who presented with a 50-yr. history of sinus-tract formation in the right foot. This is the first case of an *Exophiala jeanselmei* mycetoma successfully treated with itraconazole. In addition a review of the literature on this subject was done.

Key words *Exophiala jeanselmei*, Mycetoma, Itraconazole

Micetoma causado por *Exophiala jeanselmei*. Descripción de un caso tratado exitosamente con itraconazol y revisión de la literatura

Resumen Describimos un caso de micetoma de grano negro en un hombre de 74 años, con historia de formación de trayectos fistulosos en el pie derecho durante 50 años. Este es el primer caso de un micetoma por *Exophiala jeanselmei* tratado exitosamente con itraconazol. Presentamos tambien una revisión de la literatura sobre el tema.

Palabras clave *Exophiala jeanselmei*, Micetoma, Itraconazol

The first case of mycetoma caused by *Exophiala jeanselmei* was reported by Jeanselmei *et al.* [1]; and, the isolated fungus was named *Torula jeanselmei* by Langeron [2] who studies it. In human tissue *E. jeanselmei* may be present as dematiaceous hyphae, or as muriform bodies, or, also, as grains. These three different tissual forms characterize three groups of mycosis: phaeohyphomycosis, chromoblastomycosis and mycetoma. The organism is the most important agent of subcutaneous phaeohyphomycosis [3]; exceptionally it causes chromoblastomycosis [4]; and, it is an infrequent agent of mycetoma [5]. The fungus is also known to cause keratomycosis [6] and visceral phaeohyphomycosis [7]. Subcutaneous phaeohyphomycosis, chromoblastomycosis and mycetoma due to *E. jeanselmei* have been observed in Brazil [4,8,9].

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Aceptado para publicación el 25 de noviembre de 1998

1130-1406/99/5.00 Euros

The opportunity to publish the second reported Brazilian case of mycetoma by *E. jeanselmei* led us to add a review of this subject.

CASE REPORT

This patient (JS), a 74 year-old negro farmer, is native of the Southernmost State of Brazil. He was admitted with a complaint of a tumefaction on the right foot (Figures 1 and 2). The lesion began 50 years ago, after a traumatism by a stone fragment while he was working on the field. Since that time he was hospitalized six times and was treated with topics and clotrimazole. Besides, he was also submitted to surgeries (15 and 19 years ago).

Physical examination showed a tumor-like process on the foot. The lesion was distributed over the lateral aspects of dorsum of the foot, extending over the lateral aspects of the ankle. The tumefaction was indurated, covered by an irregular surface due to many depressed scars and some fistulae. Some fistulae drain a yellowish secretion containing many small black grains.

MYCOLOGICAL FINDINGS

Grains were teased and mounted in 20% potassium hydroxide solution. They were mainly composed of rounded thick-walled vesicles (clamydoconidia) and few short fragments of dematiaceous hyphae (Figure 3). Cultures

Figure 1. Tumefaction on the right foot.

Figure 2. Sinus tract expelling black grains.

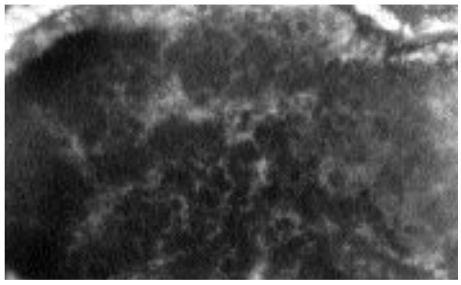

Figure 3. Granule made up of compact brown, swollen cells. Direct examination by KOH mount (100X).

Figure 4. Clinical healing, after 27 months' therapy with itraconazole.

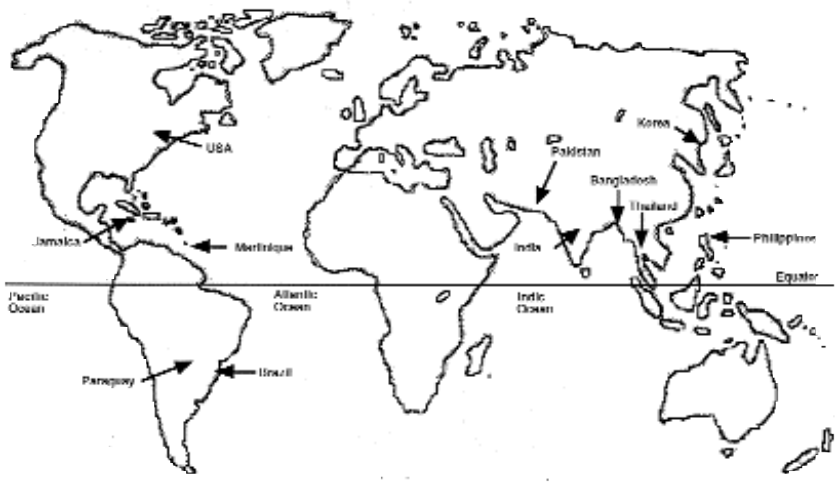

Figure 5. Geographic distribution of the reported cases of mycetoma due to *E. jeanselmei.*

were obtained on Sabouraud dextrose agar and incubated at 25°C. Velvety black colored colonies were obtained. Slide culture showed the rudimentary and the well developed annelophores, with many single celled annelloconidia at their apex characteristic of *E. jeanselmei*. Diagnosis of the fungus was confirmed by Dr. KJ Kwon-Chung (NIH, Bethesda, MD, USA).

TREATMENT

The patient received itraconazole (200 mg every twelve hours). Fistulae were closed in four months; in one year the patient could wear closed shoes; and it was considered clinically cured after 27 months (Figure 4), but the treatment continued for six months.

DISCUSSION

Fourteen cases of mycetoma caused by *E. jeanselmei* could be gathered in the literature. Patient's data, country where the mycosis was acquired and duration of the disease were shown in Table 1.

The geographic distribution of mycetomas by *E. jeanselmei* is very interesting (Figure 5). It does not occurs in African and American countries (Americas) where mycetoma are quite frequent. In Asia it is more frequently seen in countries localized in the South or

Table 1. Data on 14 reported cases of mycetoma due to *Exophiala jeanselmei.*

Case	Patient's		Lesion		Country
No [Ref.]	Sex	Age (yrs)	Localization	Duration (yrs)	
01 [1,2]	M	49	Right foot	3	Martinique*
02 [19]	M	67	Right hand	2	USA
03 [10]	M	35	Right ankle	8	Korea
04 [12]	M	Middle age	Right ankle	30	Pakistan **
05 [14]	M	49	Right foot	?	India
06 [14]	M	28	Left thigh	?	India
07 [13]	M	35	Right foot	1	Philippines
08 [25]	F	39	Right foot	5	Paraguay***
09 [17]	F	19	Left index finger	5	Thailand
10 [15]	M	65	Right foot	15	Bangladesh
11 [26]	M	53	Right ankle	10	Jamaica **
12 [11]	M	35	Left foot	8	India
13 [8]	M	49	Left foot	?	Brazil (PR)
14****	M	74	Right foot	50	Brazil (RS)

Reported when the patient lived in France*, England**, and Argentina***. Present case****
The case reported by Neumeister *et al.* [7] was not quoted because they described a botriomycosis caused by *Mycobacterium chaelone* associated with phaeohyphomycosis by *E. jeanselmei.*

Southeast. In the Americas, with the exception of the Caribbean cases it was observed in USA (one case) and in the temperate zone of South America (four cases). The three Brazilian cases occurred in the states below the Tropic of Capricorn, where eumycetoma are very rare and caused only by *Pseudallescheria boydii.*

Another interesting commentaries could be added. The grain of this polymorphic fungus is very characteristic: In histological sections it seems to be the result of a grain that breaked up into fragments. Every fragment is composed of many round or polyhedral, thick walled dematiaceous cells (chlamydoconidia) and very few small hyphal fragments [2,10-15]. Based on the histological aspects, two other cases can be added to those yet reported. One occurred in Kenya [16]; another one occurred in the Southernmost Sate of Brazil (unpublished, personal communication from Dr. Raul Krebs, UFRGS, who kindly gave histological documentation).

Isolates of *E. jeanselmei* growth up as a yeast like colony, later on changing to a mould [10,11,13,15,17]; sometimes the yeast phase is not observed, as in our case. However, in slide culture of the filamentous isolate, the characteristic rudimentary and well developed annellophores were easily observed. In culture Nielsen *et al.* [13] and Emmons [18] observed also rare phialidic conidiophores, muriform bodies were seen in cultures by Nielsen *et al.* [13], and Carrion *et al.* [10] described chlamyconidia. These structures were not seen in our isolates.

Clinically, the involvement of patient's periostal tissue or bone were observed by Symmmers [19], Thammaya and Sanyal [15], and Hemashettar *et al.* [11]. Osseous involvement is not related to the duration of the disease.

In vitro studies demonstrate the sensitivity of *E. jeanselmei* to itraconazole [7,20] and promising results were obtained in cases of phaeohyphomycosis cause by *E. jeanselmei* [7,21-24]. Based on these results we used itraconazole which revealed to be highly effective in eumycetoma by this organism.

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