Mycetoma: Experience of 482 Cases in a Single Center in Mexico

Alexandro Bonifaz1*, Andrés Tirado-Sánchez1, Luz Calderón1, Amado Saúl1, Javier Araiza1, Marco Hernández1, Gloria M. González2, Rosa María Ponce1

1 Department of Mycology, Dermatology Service, General Hospital of Mexico, Mexico City, Mexico; 2 Departamento de Microbiologia, Facultad de Medicina, Universidad Autónoma de Nuevo León, Monterrey, Nuevo León, Mexico

Abstract

Mycetoma is a chronic granulomatous disease. It is classified into eumycetoma caused by fungi and actinomycetoma due to filamentous actinomycetes. Mycetoma can be found in geographic areas in close proximity to the Tropic of Cancer. Mexico is one of the countries in which this disease is highly endemic. In this retrospective study we report epidemiologic, clinical and microbiologic data of mycetoma observed in the General Hospital of Mexico in a 33 year-period (1980 to 2013). A total of 482 cases were included which were clinical and microbiology confirmed. Four hundred and forty four cases (92.11%) were actinomycetomas and 38 cases (7.88%) were eumycetomas. Most patients were agricultural workers; there was a male predominance with a sex ratio of 3:1. The mean age was 34.5 years old (most ranged from 21 to 40 years). The main affected localization was lower and upper limbs (70.74% and 14.52% respectively). Most of the patients came from humid tropical areas (Morelos, Guerrero and Hidalgo were the regions commonly reported). The main clinical presentation was as tumor-like soft tissue swelling with draining sinuses (97.1%). Grains were observed in all the cases. The principal causative agents for actinomycetoma were: Nocardia brasiliensis (78.21%) and Actinomadura madurae (8.7%); meanwhile, for eumycetomas: Madurella mycetomatis and Scedosporium boydii (synonym: Pseudallescheria boydii) were identified. This is a single-center, with long-follow up, cross-sectional study that allows determining the prevalence and characteristics of mycetoma in different regions of Mexico.

Introduction

Mycetoma is a chronic granulomatous disease, associated with a progressive, inflammatory reaction that clinically presents as tumor-like soft tissue swelling with sinus tract formation that drains purulent material containing grains. Mycetoma usually results of traumatic implantation of soil organisms on subcutaneous tissue; can be classified as eumycetoma or actinomycetoma depending on whether the infection is caused by filamentous fungi or aerobic filamentous actinomycetes, respectively [1,2,3].

Mycetoma represents a classical neglected disease that primarily affects the poorer populations and rural regions of Africa, Latin America, and Asia at latitudes defined as the “mycetoma belt” where higher mycetoma frequencies are observed. This region is located around the Tropic of Cancer, between latitudes 15° South and 30° North, encompassing the countries with the highest rates of infection including Sudan, Somalia, Senegal, India, Yemen, Mexico, and Venezuela [1,4,5]. The predominant climate of the “mycetoma belt” is subtropical and dry tropical with an annual average rainfall of about 300–1000 mm and temperatures ranged from 10–20°C to 20–40°C, respectively. This region is characterized by low humidity and low annual rainfall with well-defined alternating rainy and dry seasons. Actinomycetomas caused by Nocardia spp. occur mostly in regions with higher humidity, while actinomycetomas caused by Actinomadura spp. and Streptomyces spp. or eumycetoma occur in drier areas with low relative humidity [1,3,4,5].

Most causative agents of mycetoma, including fungi and actinomycetes, have been isolated from soil, decaying organic matter, plants and thorns; and, the disease is usually associated with traumatic injury followed by inoculation of the microorganism propagule. There are three main factors associated with the establishment of disease: inoculum size, immune status of the host, and hormonal adaptation (based on the observation that men typically develop the disease) [1,3,6,7,8,9].

Epidemiological data from different areas demonstrate that males are more affected (sex ratio 3–4:1), ranging in age between the third and fourth decades of life [6,10,11]. Mycetoma is common in persons that work in rudimentary conditions without protective garments or shoes leading to the presentation of the illness primarily in poor rural workers or homemakers that participate in outdoor activities. Nearly all cases affect the lower limbs (73%), especially the foot and lower limbs. The nature of the patient’s occupation also influences disease presentation, for example lumberjacks and sugarcane carriers generally present with mycetoma on the back [6,10,11].

The incubation period is unknown, disease symptoms present months to years after traumatic inoculation, depending on the
Author Summary

Mycetoma is a chronic, subcutaneous granulomatous disease that usually begins after traumatic inoculation with causative microorganisms. Based on its etiology, mycetoma is referred to eumycetoma when the infection is caused by filamentous fungi, and actinomycetoma when the infection is due to aerobic actinomycetes (in Mexico predominantly Nocardia brasiliensis). Establishing the etiology is extremely important since it impacts treatment regimens. Mycetoma typically presents around the Tropic of Cancer between latitude 15° South and 30° North (also known as “mycetoma belt”) affecting poor populations in Africa, Asia, and Latin America, including Mexico, which represents a highly endemic area with higher frequencies of actinomycetomas. Mycetoma usually affects males (male:female ratio of 3:1), agricultural or rural workers (age range 20–40 years) that typically do not have access to protective equipment. The main clinical presentation is as soft tissue swelling with sinus tract formation draining grains, which leads to diagnosis. The foot is the most commonly affected localization; however, when disease presents in high risk areas, such as the trunk, it can disseminate to the lungs and spinal cord. This report represents a single center study which provides epidemiologic, clinical, and microbiological data of mycetoma cases in different regions of Mexico.

Materials and Methods

The Institutional Review Board approved the retrospective (cross-sectional) analysis of the database and clinical records of the Mycology Department of the Dermatology Service at the General Hospital of Mexico, patients were enrolled between January 1980 and December 2013 (34 years). We included all cases of mycetoma confirmed by microscopic observation of grains by direct examination with 10% potassium hydroxide (KOH), saline solution, and lugol solution. The culture media used were Sabouraud dextrose agar and Yeast extract agar, however, when infection by Actinomadura madurae was suspected, Lowenstein-Jensen agar, and BHI agar (Brain Heart Infusion) were used. Histological examination was performed in some cases using hematoxylin and eosin (H&E), Grocott’s methenamine silver (GMS), and Periodic acid–Schiff (PAS).

Actinomycetes identification was carried out using micro morphological criteria (Gram and Kinyoun stains) as well as biochemical and major phenotypic tests such as urease production, hydrolysis of casein, gelatin, tyrosine, xanthine, hypoxanthine substrates and, growth at 45°C [12,13]. Fungal agent identification was based on morphological and reproductive form criteria and on biochemical tests. Some strains were identified using molecular techniques (by amplification and sequence analysis of ribosomal DNA, the internal transcribed spacer region (ITS), the translation elongation factor 1 alpha (EF1-α), the partial beta tubulin gene (TUB), and the small subunit of the nuclear ribosomal RNA gene [nucSSU]). General epidemiologic and clinical data were extracted from clinical records. All patients remained anonymous and descriptive statistics were used to analyze the data.

Results

A total of 482 mycetoma cases were included in the present study, one patient presented simultaneously two different mycetomas. Demographic data are described in Table 1.

Figure 1 illustrates the age distribution of mycetoma, and Figure 2 the geographic mycetoma distribution in Mexico. The Pacific Ocean zone including Morelos, Guerrero, and Oaxaca accounted for 284 cases (58.92%) and the Gulf of Mexico zone (including Hidalgo and Veracruz) accounted for 162 cases (33.60%). The remaining 36 cases presented in other states including Chiapas, Tabasco, Michoacan, Colima, Jalisco, San Luis Potosi, Durango, Chihuahua, and Baja California.

Most cases were actinomycetomas (92.11%) with a male to female ratio of 2.8:1. However, this ratio changes in cases due to Actinomadura madurae, of the 42 cases (30.06%) were males and 29 (69.04%) were females with a male:female ratio of 1.2:2. Age ranges were classified in decades, the mean age was 34.5 years old (range 7–92 years). Pediatric cases (<18 years old) were 20/482 (4.14%) and 5/482 cases (1.03%) were younger than 15 years old.

Lower limbs were affected in 341 cases (70.74%), Three hundred one cases (62.44%) occurred in the foot, 70 cases (14.52%) affected the upper limbs (36 cases on the hands [7.46%] and 34 on the arms [7.05%]). The trunk was involved in 49 cases (10.16%), 38 (7.88%) of those included back and shoulders. All cases involving multiple sites were associated with multiple traumatic inoculations. In regards to clinical presentation, mycetomas were classified as follows: 468 cases as tumor-like with draining sinuses (97.1%); eight cases as tumor-like without sinuses (1.65%); four cases as verrucous plaque (0.82%) and two as cystic form (0.41%). Eight patients (1.6%) presented lymphatic spread from the original mycetoma lesion: six from the foot to the inguinal area and two from the back to the axillary region.

(Figure 3) One patient presented with two mycetomas, each with a distinct causative agent: the one affecting the right foot was caused by Madurella mycetomatis, and the second one affecting the left foot was caused by Fusarium solani complex.

Etiological agents were identified in 472/482 cases (98.34%). The agent was found in all of the actinomycetoma cases (n = 444 cases). In 430 cases (89.2%) the microorganisms were isolated and identified, and the remaining 14 cases were classified according to the grains observed during direct examination and/or histopathologic analysis. Two cases had double concurrently causative agents: N. asteroides s. l.+N. brasiliensis [14] and N. brasiliensis+ A. madurae. Thirty-eight cases were eumycetomas and in 30/38 cases the etiological agents were isolated. Of the remaining seven cases (four hyaline and three melanized-type) only grain observation at direct microscopy was detected without identifying the causative fungi (Table 2) [15,16].

Discussion

Mycetoma is a chronic granulomatous disease generally affecting low-income people including agricultural workers, peasants, or rural workers laboring with limited or no protective garments and soiled tools. The majority of cases (62%) described
in this report affected the foot, supporting previous reports [3,5,6,10] and one meta-analysis [11] that described foot as the most common site of infection (68.7% of cases). Since mycetoma presented most often on the feet of individuals living in the Indian endemic region, it explains why initial reports mentioned it as “Madura foot” [11,17,18,19]. Due to the predilection for feet, mycetoma control could be achieved by using appropriate footwear and clothing that protects the limbs. However, it should be emphasized that people living in endemic regions sometimes wear open-toed shoes, mainly due to the warm climate and therefore are less protected against potential trauma [1,5,20,21].

Mycetoma is associated with high morbidity and low mortality; however, the socioeconomic impact is significant; therefore patients are unable to work, resulting in decreased family income. In addition, treatments are expensive and difficult to maintain due to prolonged course of the disease. Almost all countries located in

| Variables               | Number of cases (%) |
|-------------------------|----------------------|
| **Type of Mycetoma**    |                      |
| Actinomycetoma          | 444 (92.11)          |
| Eumycetoma              | 38 (7.88)            |
| Total                   | 482 cases (100)      |
| **Gender**              |                      |
| Male                    | 358 (74.27)          |
| Female                  | 124 (25.72)          |
| Male:female ratio       | 2.8:1                |
| **Evolution**           |                      |
| Shortest                | 2 months             |
| Longest                 | 36 years             |
| Average                 | 2.2 years            |
| **Anatomical localization** |                  |
| Lower limbs (feet, legs)| 341 (70.74)          |
| Upper limbs (hands, arms)| 70 (14.52)          |
| Trunk (anterior and posterior thorax, abdomen) | 49 (10.16) |
| Head and neck           | 4 (0.82)             |
| Several locations       | 10 (2.07)            |
| Lymphatic dissemination (e.g., foot-inguinal region) | 8 (1.65) |

Figure 1. Age distribution of the mycetoma patients.
doi:10.1371/journal.pntd.0003102.g001
Figure 2. Geographical location of the five states with the higher incidence of mycetoma in Mexico.
doi:10.1371/journal.pntd.0003102.g002

Figure 3. a) Foot mycetoma due to *A. madurae*. b) Back mycetoma with multiple sinuses caused by *N. brasiliensis*. c) Extensive mycetoma in an adolescent due to *N. brasiliensis*. d) Exophytic or tumoral mycetoma caused by *Fusarium solani* complex.
doi:10.1371/journal.pntd.0003102.g003
the “mycetoma belt” do not provide free quality health services or medical insurance [5,20,21].

The classical clinical presentation of mycetoma should lead to simple diagnosis based on the identification of a swelling zone with multiple sinus tracts; however, there is a significant lack of information between patients and clinicians, leading to delayed diagnosis and late referral to hospital, and consequently inadequate therapeutic response [5,7,8].

This study examined nearly 500 mycetoma cases from a single public hospital, helping to control for variables and facilitated the isolation and identification of the causative agents (the causative agent was classified in most of the cases). Ninety two percent were actinomycetoma and 8% were eumycetoma, in accordance with previous studies [10]. This result differed from one report [6] that identified 3.5% eumycetoma cases this is probably due to the difficult diagnosing these cases until they are finally referred to specialty hospitals. Reports from Latin America [22,23,24,25] and, particularly, studies conducted in Mexico show a predominance of actinomycetoma, in contrast to those made in Africa, India, and Asia where cases of eumycetoma predominate [17,20,26,27,28,29]. This epidemiological difference can be explained by differences in climate and other environmental factors. The effect of climate is observed in mycetoma cases reported in India [17,18,19] where the majority of actinomycetoma occur in the northern region, where the climate is subtropical and has a higher annual rainfall; while, eumycetomas occur more often in the southern where the climate is dry tropical, has a low relative humidity, and more constant temperatures. In Mexico, eumycetomas occur in drier areas. This study provides a more accurate number of cases of mycetoma in Mexico (73 new cases per-year) [6], we believe that mycetoma remains difficult for clinicians to diagnose, for that several cases may be under diagnosed and therefore underreported [1,3,11].

In our study, we observed that mycetoma primarily affects men, with a male:female ratio of almost 3:1 in our study, in concordance with a previous report about mycetoma incidence in Mexico [6]. We believe that mycetoma remains difficult for clinicians to diagnose, for that several cases may be under diagnosed and therefore underreported [1,3,11].

### Table 2. Etiologic agents of actinomycetoma and eumycetoma.

| Etiologic agent | Number (%) |
|-----------------|------------|
| **Actinomycetomas** | | |
| Nocardia brasiliensis | 377 (78.21) |
| Nocardia asteroides complex | 4 (0.82) |
| Nocardia otitidiscaviarum (Syn. Nocardia caviae) | 2 (0.41) |
| Nocardia spp | 4 (0.82) |
| Actinomadura madurae | 36 (7.46) |
| Actinomadura pelletieri | 2 (0.41) |
| Streptomyces somaliensis | 3 (0.62) |
| A. madurae grains (Identified by KOH and biopsy) | 6 (1.24) |
| Nocardia spp. grains (Identified by KOH and biopsy) | 8 (1.65) |
| Double etiology | | |
| N. brasiliensis+N. asteroides s.l. [14] | 1 (0.20) |
| N. brasiliensis+A. madurae | 1 (0.20) |
| **Eumycetomas** | | |
| Black grains (total) | 26 (5.39) |
| Madurella mycetomatis | 15 (3.11) |
| Trematospheria grisea (Syn. Madurella grisea) | 4 (0.82) |
| Medicopsis romeroi (Syn. Pyrenochaeta romeroi) | 1 (0.20) |
| Exophiala jeanselmei | 1 (0.20) |
| Cladophialaphora bantiana (CBS 16363) [15]* | 1 (0.20) |
| Cladophialaphora mycetomatis (CBS 122637) [16]* | 1 (0.20) |
| Not identified. (Confirmed by observation of black grains with KOH and biopsy) | 3 (0.62) |
| Hyaline grains (white or yellowish): total | 12 (2.48) |
| Scedosporium boydii (Syn. Pseudallescheria boydii) | 3 (0.62) |
| Fusarium solani complex (CBS: 135554) | 2 (0.41) |
| Acremonium sp | 1 (0.20) |
| Aspergillus nidulans | 1 (0.20) |
| Microsporum canis | 1 (0.20) |
| Not identified | 4 (0.82) |

* [14,15,16] previously reported.

doi:10.1371/journal.pntd.0003102.t002
change of male:female ratio in cases of mycetoma caused by *A. madurae* (male:female ratio of 1:2.2) is partly due to this microorganism is not affected by progesterone and testosterone as with *Nocardia brasiliensis* [8,9].

Figure 1 shows mycetoma is most prevalent in the third decade of life (63.28%), which represents the most productive ages. The mean age was 34.5 years, similar to observations were made by van de Sande [7]. Some cases were reported in elderly, however we must consider that the infection may have started many years ago, suggesting that these individuals may have acquired the disease in youth. Moreover, only 4% of the cases were reported in patients <15 years old similar to previously reported studies [6,30]. The percentage of children infected in our study (and other reports [6,30]) differed from a report by Fahal et al. [31] that described a 15% infection rate (n = 722) in children in Sudan, this was probably due to their outdoor work activities. However, the same study reported trauma in only 22.5% patients suggesting that different mechanisms of infection that deserve to be clarified [1,31].

The main clinical presentation was tumor-like with draining sinuses; cases presented as tumor-like without sinuses and cystic form were all eumycetomas; verrucous-plaque presentation was rare, the last one is very important since its differential diagnosis include verrucous-tuberculosis, chromoblastomycosis and nontuberulous mycobacterial diseases. Although lower limbs (predominantly feet) were most commonly affected by mycetoma in our population (similar to the majority of previous reports [6,10,25]) it is interesting that the trunk was affected in about 10% of cases (predominantly back and shoulders). A previous Mexican report [6] described and incidence rate of the trunk in 19% of the cases, which was significantly different from the 1.4% rate described for these cases in Sudan [11]. These differences in anatomic regions affected may be explained due to occupation differences; patients in Mexico usually carry wood, sugarcane, or diverse materials on their backs. Mycetoma affecting the trunk should be considered of poor prognosis because of the proximity of lungs, spinal cord, and viscera [32]. It is also important to emphasize that cases presenting with multiple infections were described in immunocompetent patients that suffered multiple traumatic inoculations. Cases associated with lymphatic spread (1.65%) are typically seen in immunocompromised patients (malnutrition, immunosuppressants, malignant tumors, and chronic alcoholism).

*Nocardia* spp. was the main etiological agent (82.32% of cases), being *N. brasiliensis* the predominant species (78.21%). The strains were identified using phenotypic tests that lead to the identification of two more species: *N. asteroides* complex and *N. otitidiscaviarum* (formerly *N. caviae*) [14,33]. Molecular biology techniques such as PCR and sequencing of 16S rRNA and the hsp65 gene allow the correct identification and classification of *Nocardia* species [15]. For example, *N. mexicana*, *N. harenae*, and *N. takedensis* were isolated from Mexican patients [34,35,36]. The second most common causative agent was *A. madurae*; distributed worldwide [11], which is easily identified due to the larger (1–3 mm) white-yellowish, soft, wide-fringed border grains. Regardless, *A. madurae* is more difficult to isolate than *Nocardia* species, which regularly grow in rich culture media such as Lowenstein-Jensen, BHI-agar. Morphologic analyses leads to the identification of the causative agent, however, confirmation is carried out using phenotypic and temperature tests [12]. Other etiologic agents include *A. pelletieri* and *S. somalensis* commonly found in Africa and Asia. Remarkably, the two cases presented with mixed infections following traumatic inoculation were due to *N. brasiliensis*+*N. asteroides* s.l. and *N. brasiliensis*+*A. madurae*, respectively, both presented in immunocompetent patients [14].

The causal agents of eumycetoma represented only 8% of our series, melanized fungi was the most commonly observed (26 cases, 5.39%). Of these, *Madurella mycetomatis* was the foremost isolated fungi, found in 15 cases, and also considered responsible for 25% of cases worldwide, mainly in Africa and Asia [11]. Some cases have a well-defined history of trauma (e.g., thorn pricks) prior to mycetoma development; however, in some cases a well-defined traumatic event was not identified, de Hoog [37] recently noted that *M. mycetomatis* is a close relative to dung-inhabiting fungi and suggested that the natural habitat of this fungus could therefore also be dung; trauma or repeated contact with cattle dung could act as an adjuvant for inoculation of causative agents of mycetoma. Identification of *Madurella* species has been hampered by the absence of sporation leading to confusion during the identification process. The use of molecular techniques for the identification of specific regions and genes (e.g., rRNA ITS, partial β-tubulin gene, RNA polymerase II subunit 2 gene) has defined *Madurella* species as a cryptic complex belonging to the order Sordariales, consists primarily of *M. mycetomatis*, *M. fahalii*, *M. tropicana*, and *M. pseudomy- cetomatis* [38]. Identification of the infecting agent is critical since differences in thermal adaptation and susceptibility to antifungal agents exist between strains. *M. grisea* has been reclassified and now belongs to the order Pleosporales and named *Trematosphaira grisea*. It should be noted that the latter was more frequently reported as a cause of mycetoma than *M. mycetomatis* in a recent report from Mexico [6]; however, difficulties in morphological and phenotypic identification could have led to confusion. Other melanized fungi further characterized by molecular biology techniques was *Exophiala jeanselmei* and *Cladothialophora bantiana*, which are common agents of phaeohyphomycosis [15]; and *Cladothialophora mycetomatis*, considered new species [16]. Regarding hyaline fungi, *Scedosporium boydii* (Syn: *Scedosporium apiospermum*, *Pseudallescheria boydii*), was the foremost isolated strain (similar to other studies) [6,11,24,26]. Mycetomas due to *Fusarium* have been previously described [39,40], we found *F. solani* in two cases; interestingly, one of them was microscopically classified as *F. chlamydosporum*, but was reclassified using molecular biology as part of the *Fusarium solani* complex (CBS 135554). One case resulted from infection with *Aspergillus nualnus*, an agent rarely reported [41] and identified morphologically for the presence of Hulle cells. A case resulting from *Microsporum canis* infection was classified as pseudomycetoma [42] because of the rarity of the agent as a mycetoma pathogen and usually developed as consequence of a chronic tinea capitis, typically seen in immunocompromised patients in the absence of traumatic inoculation [42,43].

The study has limitations inherent to its design, however, provides important information about the status of mycetoma in Mexico. The study results can be generalized only to our population (Mexico); although the geographical areas studied has similarities with other world regions in terms of climate, distribution of etiologic agents and sociocultural conditions. Mycetoma fulfills all the criteria of a neglected tropical disease [20,21,44]. It is extremely important to monitor cases and their causative agents, as a mean to understand the epidemiology of the disease, and to establish interventions for prevention, treatment and rehabilitation.

**Supporting Information**

**Checklist S1** STROBE Statement list in reports of cross sectional studies is completed and attached. (DOC)
Author Contributions
Conceived and designed the experiments: JA MH GMG. Performed the experiments: JA MH GMG. Analyzed the data: AB ATS LC.

References
1. Fahal AH. (2004) Mycetoma: a thorn in the flesh. Trans R Soc Trop Med Hyg 98: 3–11.
2. Webb O, Vera-Caballero L, Salinas-Carmona MC (2007) Mycetoma. Clin Dermatol 25:195–202.
3. Fahal AH (2006) Mycetoma Clinicopathological Monograph. Khartoum, Sudan: Khartoum University Press.
4. Lichou V, Khachemoune A (2006) Mycetoma: a review. Am J Clin Dermatol 7: 315–321.
5. Ahmed AA, van de Sande WW, Fahal A, Bakker-Weekdenburg I, Verbrugh H, et al. (2007) Management of mycetoma: major challenge in tropical mycoses with limited international recognition. Curr Opin Infect Dis 20: 146–151.
6. López-Martínez R, Méndez-Tovar LJ, Bonifaz A, Arenas R, Mayorga J, et al. (2013) Update on the epidemiology of mycetoma in Mexico. A review of 5,933 cases. Gac Med Mex 149: 506–592.
7. Poncio Mendes R, Negroni R, Bonifaz A, Pappagianis D (2000) New aspects of some endemic mycoses. Med Mycol 38 Suppl 1: 237–241.
8. Méndez-Tovar R, López-Martínez R, Méndez-Tovar, Manzano-Gayoso P (1995) Nocardia brasiliensis: In vitro and in vivo growth response to steroid sex hormones. Mycopathologia 132: 79–85.
9. Bout G, Lalanne P, Mariani F, Suchil P (1987) Etude épidémiologique de l’actinomycète de la mycetome au Mexique. A propos de 502 cas. Bull Soc Path Ex 80: 329–339.
10. van de Sande WW (2013) Global Burden of Human Mycetoma: A Systematic Review and Meta-analysis. PLoS Negl Trop Dis 7;7(11):e2550. doi: 10.1371/journal.pntd.0002550.
11. Mahgoub ES, Murray IG (1973) Mycetoma. London, William Heinemann Medical Books.
12. Brown-Elliott BA, Brown JM, Conville PS, Wallace RJ Jr (2006) Clinical and laboratory features of the Noeardia spp. based on current molecular taxonomy. Clin Microbiol Rev 19: 259–282.
13. Bonifaz A, De Hoog S, McGinnis MR, Saul A, Rodriguez-Cortes O, et al (2009) Eumycetoma caused by Cladosporium botulinum successfully treated with itracanazole. Med Mycol 47: 111–114.
14. Badali H, Gueidan C, Najafzadeh MJ, Bonifaz A, van den Ende AH, et al. (2012) Nocardia takedensis, a new pathogen isolated from human mycetomas. J Med Microbiol 61: 4530–4535.
15. Kresch-Tronik NS, Carrillo-Casas EM, Arenas R, Atoche C, Ochoa-Carrera LA, et al. (2012) Nocardia harmae, an uncommon causative organism of mycetoma: report on two patients. J Med Microbiol 61: 1153–1155.
16. de Hoog GS, van Diepeningen AD, Mahgoub el S, van de Sande WW (2012) Nocardia brasiliensis, an unusual etiologic agent by DNA sequencing. J Clin Microbiol 40: 113–136.
17. Kresch-Tronik NS, Carrillo-Casas EM, Arenas R, Atoche C, Del Río-Avila G, et al. (2013) First case of mycetoma associated with Nocardia takedensis. J Dermatol 40:133–136.
18. de Hoog GS, Ahmed SA, Najafzadeh MJ, Sutton DA, Keisari MS et al. (2013) Phylogenetic findings suggest possible new habitat and routes of infection of human eumycetoma. PLoS Negl Trop Dis 16;7(5):e2229. doi: 10.1371/journal.pntd.0002229.
19. de Hoog GS, van Diepeningen AD, Mahgoub el S, van de Sande WW (2012) New species of Madurella, causative agents of black-grain mycetoma. J Clin Microbiol 50: 988–994.
20. Yera H, Bougouze ME, Jeannet C, Baixench MT, De Pinieux G, et al. (2003) Mycetoma of the foot caused by Fusarium solani: identification of the etiologic agent by DNA sequencing. J Clin Microbiol 41: 1903–1908.
21. Kastkar VJ, Tanikwade SS, Kothare A (2011) Fusarium solani mycetoma. Indian J Dermatol 56: 315–317.
22. Joshi KR, Mathur DR, Sharma JC, Vyas MC, Sanghvi A (1985) Mycetoma caused by Aspergillus nidulans in India. J Trop Med Hyg 88: 41–44.
23. Botteril F, Romand S, Cornet M, Recanati G, Dupont B, et al. (2001) Dermatophyte pseudomycetoma of the scalp: case report and review. Br J Dermatol 145: 151–153.
24. Hotez PJ, Bottazzi ME, Franco-Paredes C, Ault SR, Periago MR (2008) The neglected tropical diseases of Latin America and the Caribbean: a review of disease burden and distribution and a roadmap for control and elimination. PLoS Negl Trop Dis 24;2(9):e300. doi: 10.1371/journal.pntd.0000300.