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Mycetoma at a tertiary care hospital in Saudi Arabia: correlation of histopathological and clinical findings

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PEER REVIEW

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Comments

This is a paper that gives a brief overview of mycetoma in a particular region of Saudi Arabia, offering insight on the type of condition that occurs in that particular region. It gives very precise information about the mycetoma in Saudi Arabia, and allows us to learn more about the etiology and clinical characteristics of mycetoma in that region.

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ABSTRACT

Objective: To present the histopathological and clinical correlation of mycetoma among patients attending King Abdulaziz University Hospital between 1998-2013.

Methods: The data of all histopathologically diagnosed mycetomas in the period between January 1998 and January 2013 were collected through a computerized database search of the anatomic pathology archives at King Abdulaziz University Hospital. The collected data were analysed. Identification of species were performed for five patients using 16S ribosomal DNA and internal transcribed spacer 2.

Results: There were 19 patients with mycetoma with an average age of 44.26 years and male: female ratio of 4:1. Actinomycetoma were 63.15% and eumycetoma were 36.84%. All patients presented with the classic lesions; presenting as painless subcutaneous mass, sinuses and discharge containing grains. The swellings were of slow evolution, with preferential foot localization. Species specification performed for samples from five patients with active lesions revealed species of *Actinomyces israelii* and *Madurella mycetomatis* in respective cases.

Conclusions: Actinomycetoma is more common than eumycetoma in this region. The fact that one of the patients with eumycetoma was a Saudi national raises the possibility of an indigenous species similar to *Maduraella mycetomatis* to be further explored for characteristics and pathogenesis. The disease has to be prioritized again and more robust and quick molecular diagnostic tools should be made available in order to save patients form disfiguring amputations.

KEYWORDS

Mycetoma, Madura, Cementing matrix, Actinomycetoma, Saudi Arabia, 16S rDNA

1. Introduction

Mycetoma is a chronic, granulomatous disease of the subcutaneous tissue invading the skin, which may involve muscle, bones and neighboring organs[1,2]. It is characterized by the triad of tumefaction, draining sinuses and presence of colonial grains in the exudates[3]. The most common site of occurrence is foot (approximately 70% cases), which explains the synonym "Madura foot"[4]. The term was coined by Gill after Madurai a district of Tamilnadu, India in 1842[5]. It can occur in almost any region of the body] and occasionally involves the hands, back or shoulders[1,6]. Mycetoma usually occurs in farm workers and people habituated to walking bare-footed[1]. The organisms enter the subcutaneous tissue by traumatic inoculation[4]. It is endemic in relatively arid areas such as tropical or sub-tropical regions[2,4].

Mycetoma is caused by variety of organisms that show wide geographic distribution with variable disease course that necessitates different therapies. In order to address this diversity

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mycetoma has been divided into two main groups according to causative agents: actinomycetic mycetoma caused by aerobic bacteria actinomyces, and eumycetoma caused by true fungi, most cases were caused by bacteria (50.8%) and a smaller percentage by fungi (41.7%), although the distribution varies in different countries. In many African countries more eumycetoma cases have been reported than those of actinomycetoma[7,8]. Both forms present as a progressive, subcutaneous swelling, although actinomycetoma has a more rapid course. Multiple nodules develop and may suppurate and drain through sinuses, discharging grains during the active phase of the disease[4]. Therapy of these two groups is dependent on the entity of causative agents. Actinomycetoma is amenable to treatment by antibiotics, either alone or in combination[9]. Eumycetoma is usually treated by aggressive surgical excision combined with antifungal treatment[4].

The diagnosis of mycetoma is often challenging as it gets delayed for a long time. It can lead to deformities and amputation of limbs. Diagnosis of mycetoma in Saudi Arabia requires a high degree of suspicion. The available reports on the frequency and pattern of mycetoma in Saudi Arabia can be dated back to 1999[10]. We present this study to update our understanding of mycetoma in this region.

The aim of this retrospective study was to present the histopathological and clinical correlation of mycetoma among patients attending King Abdulaziz University Hospital between 1998-2013.

2. Materials and methods

2.1. Study setting and population

A retrospective study of all histopathologically diagnosed mycetoma patients in the period between January 1998 and December 2013 was performed through a computerized data base search of the anatomic pathology archives at King Abdulaziz University Hospital (KAUH), Jeddah.

2.2. Data collection

The data was filtered using appropriate morphology Systematized Nomenclature of Medicine codes indicating the following parameters: Date of receiving biopsy, demographics, clinical diagnosis, morphology and radiography. Nineteen cases of mycetomas were retrieved and classified into eumycetoma and actinomycetoma. The diagnosis was based on clinical examination, radiological evidence, histopathological examination and correlation with grain cultures. Sufficient blocks for each specimen were submitted in order to ensure sampling adequacy. All cases were processed as per standard histopathological techniques, which include paraffin embedding, hematoxylin and eosin staining followed by Grams stain for actinomyces, Gomori methenamine silver (GMS) and periodic acid Schiff (PAS) stains for fungi. Microscopic examination was done by two pathologists separately to arrive at consensus. 16S ribosomal DNA (16S rDNA) and internal transcribed spacer 2 (ITS2) sequencing to identify bacteria and fungi to species level were performed in five cases with active lesions. And the treatments for the patients were recorded.

We analyzed the Medline literature search of the reported studies including epidemiological studies and diagnostic articles about mycetomas in the English literature from 2000-2013 through the national library of medicine, Pubmed, and OVID search engines. We used key words “Madura foot”, “mycetoma” “eumycetoma”, “actinomycetoma” and “*Madurella mycetomatis*” (*M. mycetomatis*), “Saudi Arabia” for Medline search.

3. Results

There were 19 patients with mycetoma with an average age of 44.26 years and male: female ratio of 4:1. Five among the nineteen patients (26.31%) studied were of Saudi origin with 80% of these being affected by actinomycetoma. The only Saudi patient with eumycetoma gave no history of farming enterprise. Detailed age and sex, demographic distribution, location of lesion, culture findings and radiological findings of all patients are presented in Table 1. Actinomycetoma were 63.15% and eumycetoma were 36.84%. All patients presented with classic lesions preferentially in the foot (73.6%). All cases in the study group were agriculture and farming workers.

Among twelve cases microscopic examination on hematoxylin and eosin (H & E) stained sections showed small to large actinomycetoma grains. These were ill-defined and multilobated, surrounded by neutrophils, epithelioid cells, plasma cells and multinucleated giant cells at the outer border. Macrophages were also seen at the periphery along with minimal fibrosis. Colonies showed slightly pale central eosinophilia. Outer border was deeply basophilic with ill-defined but delicate, radiating and branching filaments. The basophilia was demarcated by a fringe of hyaline-like material known as Splendore-Hoeppli phenomenon (Figure 1). Gram’s stain showed branching filaments, 1 micron thick, not breaking into bacillary or coccoid forms, in all cases (Figure 2), while special stains such as PAS and GMS were negative. Although grain cultures performed (on eight cases) were negative on two occasions, a histological diagnosis of actinomycetoma was given on the combination of the clinical picture of indurated swelling of soft tissue exhibiting multiple discharging sinuses with macroscopically typical grains, radiological evidence and the characteristic histopathological appearance .

Among the remaining seven cases grain culture was positive for *Madurella* species in two cases. Microscopic examination on H & E) stained sections among all seven cases showed rounded well demarcated colonies of eumycetoma. These were also surrounded by suppurative granulomas in between fibrotic tissue. The colonies had intricate filaments and were embedded in amorphous brownish cementing matrix (Figure 3). The matrix was highlighted by PAS stain imparting a grainy aspect to the colony (Figure 4). PAS (Figure 4) and GMS (Figure 5) stained sections highlighted interlacing septate hyphae 2 to 3 microns thick with rounded polygonal chlamydospores.