University of Khartoum
Faculty of Medicine
Department of community medicine

In collaboration with

Mycetoma Research Centre (MRC)
Under supervision of:
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Group A1 – 2006 present:
Introduction
Mycetoma is a chronic granulomatous progressive inflammatory disease, that involve the subcutaneous tissue after a traumatic inoculation of the causative organism.
It could be caused by various genera of true fungi or by higher bacteria.
The characteristic triad of

- a painless subcutaneous swelling,
- sinuses
- and the discharge of grains

is pathognomonic of mycetoma.
The lesion usually presents as a slowly progressive painless swelling at the site of pervious trauma and gradually increases in size.
- Madura foot.
- Maduromycosis.
- Fungal Mycetoma.
- Eumycotic Mycetoma.
- Melanoid Mycetoma.
- Ochroid Mycetoma.

In Sudan:
Nabit – Shamam.
Gill who worked at a dispensary in the southern Indian province of Madura was the first to recognized mycetoma as a disease entity in 1842.

Godfrey first documented a case of mycetoma in Madras, India.
• In 1872 Carter further proposed the terms melanoid and ochroid in an attempt to classify the disease into two varieties.
Mythology
A patient believed that he acquired the disease by stepping on donkey’s urine.
A patient who was wounded by dry piece of wood thought that the swelling is an inflammatory response to it and the black grains are the remaining parts of the wood.
● A patient believes that drinking or eating hot food like tea, hot kesra.............will increase the swelling, pain and sinuses.

● He also thinks that the electrical lights are harmful to the lesion.
In some areas they treat mycetoma by applying Donkey’s feces to the lesion.

Others treat it by Cauterization.
Mycetoma is a painless, slowly progressive and with late clinical presentation in majority of patients, so the true incidence and the geographical distribution through the world is not yet exactly known.
Mycetoma is an important disease in tropical and subtropical regions around the world, and occurs in a mycetoma belt (15 south---30 north)
These regions are known by their hot and dry climate with rain only 3-4 months a year, which favors the growth of big thorny trees especially Acasia. These trees can be parasitized by the organism causing mycetoma.
Regarding Sudan, mycetoma is an endemic disease.
When going back to the report done by National Health Information centre of the FMOH, all reported cases are located in Khartoum, this is not true but maybe it is due to the fact that the only specialized centre in mycetoma is located in Khartoum.
Age: 20-45 years old
Gender: male > female (ratio 3:1)
Discharge patient
age and gender
**Occupation**: no occupation is immune but more commonly seen among agricultural workers and wood cutters.

**Predisposing factor**: in people with cell mediated immunity deficiency

**Source**: usually exogenous,

It is non- infectious and not zoonotic.
mycetoma is divided into two main categories according to the causative agents:
Eumycetoma
Actinomycetoma.
Eumycetoma agents

Madurella mycetomatus  70%  Black
Madurella grisea  ???  Black
Pseudallescheria boydii  ???  White, yellow
Leptosphaeria species  ???  Black
Curvuleria lunata  black
Asperigellus nidulans  White
Asperigellus flavus
Others:
Fusarium sp.
Cylindrocarpon sp.
Acremonium sp.
Actinomycetoma
Streptomyces somaliensis 18%  yellow
Actinomadura madurae 5%      white
Actinomadura pelletierir 3%   red
Nocardia brasiliensis      orange
Others:
Nocardia caviae
Nocardia otitidiscaviarum
Nocardia transvalensis
Nocardiopsis dassonvillei
Any trauma to the skin allow Mycetoma organisms enter human subcutaneous tissue as spores or small parts of the filaments of fungi or actinomycetes when the condition is favorable the organisms start replication forming colonies
sinus
The immune responses in mycetoma lesions were characterized by immunohistochemistry.

In sections stained with H&E, the inflammatory reaction around the grain was of 2 types.
In type I there were 3 zones:

**Neutrophil zone** immediately around the grains (CD15+).

**Intermediate zone** containing mainly macrophages (CD68+), and T-lymphocytes (CD3+).

**Peripheral zone** consisting of B-lymphocytes, plasma cells (CD20+) and fibroblast.
In the type II reaction, there was no Neutrophil zone, the grains being surrounded only by macrophages and giant cells.
IgG and IgM and complement were demonstrated on the surface of the grain and on filaments inside the grain.

Neutrophil and macrophages were recruited into the lesion by complement and were involved in the fragmentation of the grain.

The cytokine profile in the lesion and regional lymph nodes was of a dominant Th2 pattern (interleukins-10 and 4).
polysaccharide fraction (F1) and the lipid fraction reproduce the fundamental lesion of actinomycotic mycetoma.
polysaccharide fraction F1 isolated from Nocardia brasiliensis induced an inflammatory response with (PMN) and (MN) leucocytes between the 2nd and 4th days.

On the 8th day, a typical granulomatous reaction was observed involving large numbers of epithelioid cells.
Intravenous injection of the lipid extract induced an inflammatory reaction similar to that described above.
Clinical Features
clinical presentation

* Ahmed alamin
* Ebtehal M Hasan
* Islam Mustafa
* Islam Seddeq
*Mycetoma may cause no pain but it often itches or burns.

*Patients may complain of a deep itching sensation.
Painless subcutaneous swelling which is firm but it can be soft rarely cystic.

multiple nodules which suppurate through multiple sinuses
The old sinuses may heal completely while new ones open and start discharging.

- The discharge is serous or purulent, or bloody
- It contains grains and the colour of them depends on the causative agent.
diffuse edema, scaling, and thickening of the skin with multiple clustered warty nodules and abscesses
When the lesion increase in size the skin over it becomes hyper pigmented.

And there may be areas of hyperhydrosis.
Clinical presentation of mycetoma differs in that:

eumycetoma infection grows slowly with clear defined margins capsulated and the bone involvement is late.

Actinomycetoma infection is rapid, progressive more inflammatory more destructive and invade the bone at the early stage.
The foot is the most common affected site.
The left foot is more affected than the right.
THE HAND
The Arm
The Shoulder
The Gluteal region
The knee and the thigh
The abdominal wall
Regional lymphadenopathy due to:
* genuine bacterial infection
* pigment deposition
* immune complex deposition

when the object, the periosteum is stretched and the patient complain of pain.
Lymphatic obstruction and fibrosis can cause erythema and lymphedema.

Cachexia and anaemia can be seen in the late stage.
Differential diagnosis:

- Botryomycosis
- Thorn granuloma
- Fibrolipoma
- Neurofibroma
- Cold abscess
FEATURES OF SPECIAL MYCETOMA SPECIES
Acremonium is one of the causative agents of eumycotic white grain mycetoma.

Rare cases of onychomycosis, keratitis, endophthalmitis, endocarditis, meningitis, peritonitis, and osteomyelitis due to Acremonium have also been reported.

- It is known to cause opportunistic infections in immunocompromised patients, such as bone marrow transplant recipients. Infections of artificial implants due to Acremonium spp. are occasionally observed.
Exophiala spp. can cause **phaeohyphomycosis**.

Subcutaneous infections such as **mycetoma** and **chromoblastomycosis** may develop due to *Exophiala* isolates.

They are associated with the existence of local or systemic immunosuppression, such as organ transplantation.

Prosthetic valvular vegetations, fungemia, and disseminated infections due to *Exophiala* spp. have also been reported.
• Pseudallescheria spp.

- pseudallescheriasis.
- The affected host is commonly immunosuppressed due to various reasons, such as hematological malignancies, organ transplantation or AIDS.
- A causative agents of white grain mycetoma
- Acquired via contact with soil and follows a minor trauma.
It can cause:
• cutaneous infections,
• sinusitis,
• keratitis,
• Lymphadenitis,
• endophthalmitis,
• meningoencephalitis
• brain abscess,
• endocarditis,
• pneumonia, lung abscess, pulmonary fungus ball, allergic bronchopulmonary fungal disease,
• bursitis,
• arthritis osteomyelitis,
• urethritis,
• and disseminated infections

Cerebral infections are commonly encountered as a complication in near-drowning patients.
Diagnosis
Diagnosis of mycetoma

- clinical
- radiology
- laboratory
Clinical diagnosis

Taking good history
where pt. come from
history of trauma
occupation

The stage of lesion can help in proper diagnosis

The probability of the population of endemic area to diagnose the condition
Radiological diagnosis

- x-ray
- CAT SAN
- MRI
- Ultrasound
- BONE SCAN

the extend of the lesion and whether there is bone involvement or not. This can differentiate between eumycetoma and actinomycetoma lesions.
Lab diagnosis

SPACEMEN

grains

blood

site of collection

Method used in collection
In X-ray film you see many changes
1) Soft tissue granuloma
2) Periosteal reaction
confirmation of causative agent

MACROSCOPY;

Except in: case of examination the grains of:

*aspiragillus nidulans

*actinomadurae madurae
CULTURE:

*using: grains

*As a compare b/w the primary isolation of:

Eumytoma grains

Actinomycetom grains
MODIFIED Z.N STAINS & BIOCHEMICAL TEST:

*Applied for Actinomycetes colonies

using: Z.N stain

For purpose of differentiation, as:

Nb

& Others: N.asteroid

Biochemical tests
DIRECT MICROSCOPIC EXAMINATION:

*prepare the grains for the examination of microscope

*The examination result in differentiation between:

_Eumycetoma & _Actinomycetoma
Examination of the colonial morphology:
principle: depending on the grains

Results can be get from the examination of the colonies of the grains:

**Mm**: brown black

**Ss**: dirty yellow, dry wrinkle

**Ap**: red, dry wrinkled

**Am**: white, smooth

**Nb**: creamy, dry wrinkled
Specimen: biopsy

*Purpose: mycological & histopathological diagnosis

*Properties: should contain the grains
  & stain it by the H&E

*Procedure:
On examination the grains which stained by H&E, then the differentiation b/w the grains:

<table>
<thead>
<tr>
<th>Component around grains</th>
<th>Ss</th>
<th>Am</th>
<th>Ap</th>
<th>Nb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grains shape</td>
<td>Round, bilobed, trilobed</td>
<td>Larg. irregular</td>
<td>Round, semi lunar</td>
<td>irregular, margins</td>
</tr>
<tr>
<td>Grains color</td>
<td>Brown blue</td>
<td>Deep blue</td>
<td>Deep purple</td>
<td>Light blue</td>
</tr>
<tr>
<td>PMNL, chronic inflammatory cells</td>
<td>PMNL, giant cells</td>
<td>PMNL, chronic inflammatory cells</td>
<td>PMNL embedded in the pus</td>
<td></td>
</tr>
</tbody>
</table>
**Asp.nidulans:**
- Grains large with viscles inside it
- Broad hyphae

**M.mycetomatus:**
- Grain shape & size: large, brown with irregular margins
- Two types be formed here:
  - **Vesicular grains:** periphery part brown pigment
    Central part filled with vesicle
  - **Filamentous grains:** matrix full with brown substance
    Matrix embedded with broad segmented
    Hyphae + chlamydospores

Component around the grains:
- *PMNL*
- *Granuloma cells*
SEROLOGY:

*Using:  
  - ID
  - CIE
  - ELISA

ID: Immuno_Diffusion test

*Principle of test  : precipitation test
*procedure of test

*Type of test: semiquantitively
*Purpose of test : following up the pt.
CIE: Counter Immuno Electrophoresis

*Principle of test: precipitation test

*Procedure of test

*Purpose of test: following up the pt.

The sensitivity of serological tests:

ID & CIE: have the same sensitivity

ELISA: have high sensitivity
Treatment of Mycetoma
Depends mainly on its etiological agent, the extent of the disease & patient compliance.

Treatment of Eumycetoma usually needs chemotherapy & surgery, while Actinomycetoma needs chemotherapy only EXCEPT in advanced lesions.
TREATMENT OF ACTINOMYCETOMA
1- Streptomycin sulphate (14 mg/kg daily) and (Dapsone) Diaminodiphenyl sulphone (1.5 mg/kg twice daily).

- Co-trimoxazole (14 mg/kg twice daily) or Rifampicin (15-20 mg/kg daily). May replace Dapsone in cases of no response & persistent side effects.

2- Amikacin sulphate (mg/kg) alone or in combination with Co-trimoxazole (14 mg/kg twice daily) is a second line for mycetoma treatment.

- In resistant cases:
  1- Fansidar (Sulfadoxine-pyrimethamine)
  2- Sulphonamides
• The cure rate varies between 60% and 90%.
• Duration is usually more than one year.
• Drug resistance and recurrence are common in incomplete & interrupted treatment.
• Medical treatment is useful in all stages of actinomycetoma even with advanced disease.
Treatment of Eumycetoma:

- First line (Drugs):
  - 1. Ketoconazole (Nizoral)
  - Dose is 400-800 mg daily
- Contra indication:
  Documented hypersensitivity; fungal meningitis
  - Safety for use during pregnancy has not been established
2. Itraconazole (Sporanox)
- Has a good success & a low recurrence rate.
- Recommended dose: 100-400mg daily
- Contraindication: known hypersensitivity
- Safety during pregnancy has not been established.

Itraconazole & Ketoconazole perform their action by inhibiting ergosterol synthesis (an important component of fungal cell wall)

Griseofulvin + Procaine Penicillin (given to financially deprived people)
Surgical excision is recommended for small localized lesions, debulking of massive lesions; for better response to medical treatment and for lesions became well encapsulated by medical treatment.
Amputation rarely done nowadays. It is done for very advanced lesions with bad general condition and as a life saving
Clinically:

1- reduction of the size of the swelling

2- closure of sinuses.

3- return of the skin back to normal
Radiological:

1- absence of cavities
2- new bone formation
Serologically

reduction of number and intensity of precipitation line till disappear

Three consecutive CIE with the interval of six weeks. If the three were –ve we consider the patient cured.
Examine after 3 months, then after 6 months, & then annually, may extend up to years following up is both clinically & serologically. the recurrence appear first in the later
prevention
*No Vaccine.

*No prophylaxis.

*No 1st aid (disinfectant are not protective).

*many researches was done in Sudan in experimental animals but it is not finished.
With all these risks
& all this work
We have nothing to do !!!!
SO

ALL THESE PEOPLE IN THE ENDEMIC AREA
JUST
NEED TO BE INFORMED
wear shoes to avoid skin-penetration (Thorn Pricks)
Detection of early cases when Swellings are small, then excision with concurrent medical treatment to prevent recurrence.
The Mycetoma Research Centre

specialized academic and scientific centre interested in various aspects of mycetoma. The centre was established in 1991 in Khartoum-Sudan under the umbrella of University of Khartoum.
To eradicate Mycetoma as a life-mutilating disease through the advancement of:
Education