Mycetoma & Other Subcutaneous Mycosis

TEAM 439

MICROBIOLOGY

VERSION 1

Objectives

- Acquire the basic knowledge about mycetoma and the clinical features of the disease.
- Acquire the basic knowledge about other common subcutaneous mycosis and their clinical features.
- Know the main fungi that affect subcutaneous tissues, muscles and bones.
- Identify the clinical settings of such infections.
- Know the laboratory diagnosis, and treatment of these infections.

Colour index:

Red: Important.

Grey: Extra info & explanation.

Purple: Only in girl's slides.

Green: Only in boy's slides.

Any future corrections will be in the editing file, so please check it frequently.

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Subcutaneous Mycoses

- **Subcutaneous Mycoses**: Fungal infections involving the dermis, subcutaneous tissues, muscle and may extend to bone (if treatment is delayed).
- **Initiation**: skin trauma (NOT CONTACT ONLY)
- **Treatment**: difficult to treat , surgical intervention is frequently applied
- **Affects** both healthy host, and immunocompromised host (*more severe*), (not opportunistic pathogen)

❖ Examples of Subcutaneous Mycoses

- **Mycetoma** (Most common)
- **Subcutaneous zygomycosis**
- **Sporotrichosis**
- **Phaeohyphomycosis**
- Chromoblastomycosis
- Rhinosporidiosis (Rare)
- Lobomycosis (Rare)

1) Mycetoma

A Chronic granulomatous disease of the skin and subcutaneous tissue which sometimes involves muscle and bones.

★ **Characterized By:**

- **Swelling in the site of trauma**
- **Abscess Formation**
- **Multiple draining sinuses that exude characteristic grains (granules) of clumped organisms**

- **Typically affects** : *"depending on the site of trauma"*
  1. The lower extremities (mainly foot).
  2. Other areas of the body (e.g. hand , back , neck).

- Mycetoma is endemic in **tropical**, **subtropical**, and **temperate** regions. **Sudan**, Senegal, Somalia, India, Pakistan, Mexico, Venezuela.

- Common in people who work in rural areas, framers.

- It is more common in men than in women (3:1).

- The disease was first described in the Madura district of India in 1842, and called by (Madura Foot). → "Madura Foot or Mudura mycosis is another name for Mycetoma".

1) Mycetoma, contd..

1 Classification & Etiology

Mycetoma is classified to 2 things. First, If it was caused by **fungi**, we call it **Eumycetoma**.
But if it was caused by aerobic filamentous **bacteria**, we call it **Actinomycetoma**.

Eumycetoma

❖ **Etiology of Eumycetoma** chronic granulomatous fungal disease.

Caused by a several mould fungi → mold, or Filamentous fungi.

The most common are:

1) Madurella mycetomatis Most common in our region.
2) Madurella grisea
3) Pseudallescheria boydii

★ **Color of grains:** black or white → usually black

Actinomycetoma

❖ **Etiology of Actinomycetoma**

Caused by Aerobic filamentous bacteria, Gram positive.

1) Actinomadura madurae (Most common)
2) Streptomyces somaliensis.
3) Nocardia brasiliensis. (Partially acid fast bacillus,requires a special stain), (rare)).

★ **Color of grains:** yellow, white, yellowish-brown, pinkish- red

Do not confuse it with Actinomycosis (which is an infection caused by Actinomyces → it's Gram +ve **anaerobic** bacteria).

الـ Filamentous bacteria هي مجموعة وسطية بين الفطريات والبكتيريا، مثلا عندها hypha وتتكاثر بالكونيديا (Asexual reproductive spore of fungi, remeber?)
وبنفس الوقت هي وحيدة خلية نفس البكتيريا. الزبدة أنه في الماضي كانت تعتبر من الFungi لكن حاليًا وبعد النظر لتركيبتها وتكوينها الكيميائي قرروا انها بكتيريا. كول صح؟

➔ **Color, shape and size of grains helps in diagnosing the causative organism**

2 Pathogenesis / Clinical Presentation of Mycetoma.

Mycetoma acquired via trauma of skin

Trauma (break skin barrier)

↓

Painless Subcutaneous firm nodule is observed

↓

Massive swelling + skin rupture + sinus tract formation

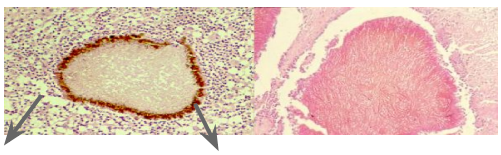
- Old sinuses close and new ones open , draining exudates with grains (granules)
- **Grains** may sometimes be seen with the naked eye

1) Mycetoma, contd..

3 Diagnosis

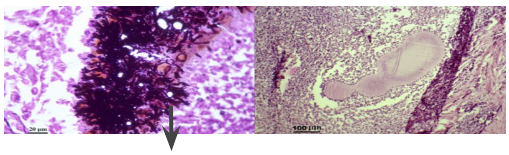
Clinical Samples:

1. **Biopsy tissue** (swaps or superficial samples of the draining sinuses are inadequate). **(BEST)**
2. Pus.
3. Blood (for serology only "antibody/antigen").



Inflammatory reaction

Clumped organisms



Filaments

Diagnosis	**Culture**		**1-Media such as Sabouraud dextrose agar (SDA) to isolate fungi** Fungi are identified based on the macroscopic and microscopic features. **2-Blood agar to isolate bacteria.** For Actinomycetes biochemical and other tests are used for identification (eg:coagulase, Hydrolysis)
	Direct Microscopic Examination	**Histological Sections**	Hematoxylin-Eosin
		Smears	**Fungi**: Stain with 1. Giemsa 2. Gomori 3. methenamine silver **Actinomycetes:** Stain with Gram, ZN (ziehl neelsen) stain (actinomycetes)
		Grains	(Observing the size of the filaments , the color grains) ➢ **White-to-yellow** grains indicate: P boydii, Nocardia species, or A. madurae infection. ➢ **Black grains indicate**: Madurella species infection. ➢ **Red-to-pink** grains indicatie: A. pelletieri infection
	Serology		Detect the antibodies using culture filtrate or cytoplasmic antigens of mycetoma agents Antibodies can be determined by immunodiffusion, enzyme-linked immunosorbent assay Helpful in some cases for diagnosis and follow-up

4 Treatment

Most common and first line

- **Eumycetoma** (treated with antifungal): **Itraconazole** Also Voriconazole and (Amphotericin B (same as subcutaneous zygomycosis))
- **Actinomycetoma** (treated with antibiotics): Trimethoprim-sulfamethoxazole \ Dapsone \ Streptomycin.
  (Combination of 2 drugs is used).

➔ **Therapy** is **suggested** for several months or years (1-2 years or more) .

➔ **Actinomycetoma** generally respond better to treatment than Eumycetoma.

➔ **Radiologic tests** (bone radiographs) **if bone involvement is suspected**
(important for all mycetoma patients for management and follow up).

➔ **Surgical Care:** In Eumycetoma, surgical treatment **debridement** (tissue removal) or **amputation** in patients:

- Not responding to medical treatment alone
- If bone is involved.

2) Subcutaneous Zygomycosis

What is it?	**Chronic localized** firm Subcutaneous masses. Painless + nodules.	
Location	Facial area or other like hand, arm, leg, thigh. Could be anywhere in the body	
Etiology	**Mould fungi of the Zygomycetes** (Could be everywhere, even in the air)	**2- Entomophthorales** : Mostly in immunocompetent. - Conidiobolus coronatus. - Basidiobolus ranarum.
		3- Mucorales : Mostly in immunocompromised. عفن الخبز - Rhizopus - Mucor.
Acquired via	**Traumatic implantation of spores**: needle-stick, tattooing, contaminated surgical dressings, burn wound. (Inhalation of spores).	
Clinical Features	- Firm swelling of site with intact skin-Distortion. Unlike mycetoma, there is no discharge, pus, and sinus formation. + **necrosis** is seen. - Direct spread to adjacent bone and tissue.	
Laboratory Diagnosis	- **Specimen**: Biopsy tissue. ★ **Direct microscopy**: stained sections or **smears**: broad **non-septate hyphae.** - **Culture**: Culture on SDA (Sabouraud dextrose agar)	
Treatment	- Oral Potassium iodide(KI) - **Amphotericin B. (DRUG OF CHOICE)** - Posaconazole (the other alternative)	

in mycetoma, etiology is trauma + plant material or something in the environment. However, subcutaneous zygomycosis is caused by trauma + something contaminated with zygomycetes. |||| Regarding microscopic examination, if you see grains this it is mycetoma, but if you see non-septate hyphae the it is subcutaneous zygomycosis

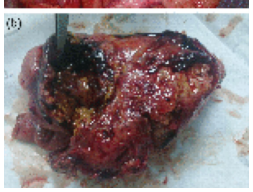
❖ Basidiobolomycosis (Gastrointestinal)

-Basidiobolus is a spp of filamentous fungi that belongs to the order Entomophthorales, Zygomycete

Patient comes with abdominal mass + pain, and commonly this is misdiagnosed as tumor.
It will be surgically removed. However, later on it appears to be fungi. And it is common in KSA!!

Symptoms

1. Abdominal pain.
2. Swelling.
3. Constipation.
4. Fever.
5. Weight loss.
6. Abdominal mass.



Misdiagnosis (presumptive diagnosis)

1. Abdominal malignancy.
2. Crohn's disease. Type of inflammatory bowel disease (IBD) that may affect any segment of the gastrointestinal tract from the mouth to the anus.

3) Sporotrichosis

Location	- Subcutaneous. - Deep cutaneous. - Systemic fungal infection. From 437:This infection is common in **gardeners**. اللي يشتغلون بالحدائق وخصوصًا لو فيه ورد بسبب الأشواك، ويكون فيه fungi بالورد أصلًا
Etiology	★ Sporothrix schenckii (**Dimorphic fungus**). Can be yeast / filamentous fungi depending on temperature.
Clinical Features	Can present as - plaque (subcutaneous nodules). - Lymphangitic. - Disseminated . The primary lesion can spread and often develop a unilateral lymphocutaneous lesions or, rarely, disseminated disease (diffuse disease-process, generally either infectious or neoplastic). By Inoculation into the skin
Laboratory Diagnosis	- **Specimen:** Biopsy tissue, pus. ★ **Direct Microscopy:** smear will show **Finger-like** yeast cells or **Cigar shaped**. - **Culture:** On SDA at room temperature and at 37C.
Treatment	- **Itraconazole (best)**, KI (Potassium iodine).

4) Phaeohyphomycosis:

01

What is it?

group of fungal infections caused by **dematiaceous** (Black fungi, darkly pigmented) fungi widely distributed in the environment.

02

Etiology:

-Dematiaceous mold fungi. **Common**
- Cladosporium.
- Exophiala.
- Wangiella.
- Cladophialophora.
- Bipolaris.

03

Location:

Thigh, Legs, Feet, and Arms.

04

Clinical Features:

Subcutaneous or **brain abscess**. **Presents as** nodules or erythematous plaques with no systemic involvement.

05

Diagnosis:

Specimens: Pus, biopsy tissue.
Direct Microscopy: KOH & smears will show brown septate fungal hyphae.
Culture: On SDA.

06

Treatment:

-Always **Surgical excision** of the lesion
-**Antifungal** (Itraconazole, Posaconazole).

5) Chromoblastomycosis (Only in Boys slides):

- Subcutaneous chronic fungal infection different dematiaceous fungi.
- The initial lesion is single nodule, then new nodules appear.
- The lesions become large with a cauliflower aspect and black dots, hyperkeratotic,Verrucous, Ulcerative.
- Treatment: Surgery and antifungal therapy

6) Bone and joint infections (Only in Girls slides):

- Osteomyelitis.
- Joint infections.

Examples

Result From

Rarely comes as isolated clinical problem, it comes as a part of other disease, such as:

- Hematogenous dissemination.
- Foreign body.
- Direct inoculation of organism (trauma, surgery, etc..).
- Spared through direct extension of infection to the bone. (e.g. Rhinocerebral zygomycosis, Aspergillosis, mycetoma).

Etiology

- Candida species.
- Aspergillus species.
- Mould fungi.
- Dimorphic fungi:
- Blastomyces dermatitidis.
- Coccidioides immitis.
- Histoplasma capsulatum.
- Paracoccidioides brasiliensis.

LAST BUT NOT LEAST

Click Here to Check Our Summary

CASES / SAQ + MCQs

CASE 1:
36 years old man came to the hospital with localized firm subcutaneous masses on his face, no sinus formation, and no discharge. A biopsy was taken and sent to the lab. Result showed broad non-septate hyphae. What is the most likely diagnosis? What is your choice of treatment?

CASE 2:
19 years old girl came to the doctor complaining of prolonged fever and swelling in her abdomen. Her medical history was obtained and it revealed that she suffered from Constipation and huge weight loss. MRI was taken and it showed an abdominal mass. The patient was taken to the OR and the mass was removed. Later on, microbiology lab reported that the mass was fungi. What is the name of this condition?

CASE 3:
A girl who pricked her finger while pruning some rose bushes develops a deep cutaneous followed by systemic fungal infection. Later on, development of superficial cutaneous lesions that progress along dermal and subcutaneous lymphatics was detected. What is the most likely diagnosis? The most likely agent is?

CASE 4:
A 45 years old sudanese farmer came to the hospital complaining of massive swelling in his foot accompanied by sinus tract formation and black grains that are visible by naked eye. What is his most likely diagnosis? How will you treat him?

Q1: Which one of the following is not true about mycetoma?
A- if it was Eumycetoma, antifungal is used
B- if it was Actinomycetoma, combination of antibiotics is used.
C- Painful subcutaneous firm nodules are observed.
D- Commonly seen in farmers.
E- it is chronic and subcutaneous disease.

Q2: Treatment of Sporotrichosis is..
A- Posaconazole
B- Itraconazole
C- KI
D- (B+C)

Q3: Drug of choice to treat subcutaneous zygomycosis is..
A- Streptomycin
B- Voriconazole
C- Itraconazole
D- Amphotericin B

Q4: Madura foot is another name for..
A- Subcutaneous mycosis
B- Sporotrichosis
C- Mycetoma
D- Phaeohyphomycosis

Q5: Which one of the following cause brain abscess?
A- Phaeohyphomycosis
B- Sporotrichosis
C- Subcutaneous zygomycosis
D- Mycetoma

Q6: Direct microscopy findings of subcutaneous zygomycosis is..
A- Broad non-septate hyphae
B- Cigar shaped hyphae
C- Brown septate hyphae
D- Broad septate hyphae

Q7: Phaeohyphomycosis is group of fungal infections caused by..
A- Black & darkly pigmented fungi
B- dematiaceous
C- hyaline hyphomycetes
D- (A+B)

Q8: Which one of the following causes Eumycetoma?
A- Streptomyces somaliensis.
B- Actinomadura madurae
C- Pseudallescheria boydii
D- Nocardia brasiliensis.

Q9: Microscopic feature of Sporotrichosis is believed to be..
A- Brown septated hyphae
B- Brown non-septated hyphae
C- Cigar shaped yeast cells
D- Cigar shaped bacterial cells

Q10: To isolate fungi we use....
A- Chocolate agar
B- Blood agar
C- Sabouraud dextrose agar
D- Neomycin agar

Answer Key

Case 1: Subcutaneous zygomycosis, Amphotericin B
Case 2: Basidiobolomycosis
Case 3: Sporotrichosis, Dimorphic Sporothrix schenckii
Case 4: Eumycetoma, Itraconazole (anti-fungal)

1-C
2-D
3-D
4-C
5-A
6-A
7-D
8-C
9-C
10-C

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