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MED437
KING SAUD UNIVERSITY



Respiratory Fungal Infection



MICROBIOLOGY
437

Important!
Doctor's Notes
Only found in females' slides
Only found in males' slides
Extra Notes

"I'm not telling you it's going to be easy. I'm telling you it's going to be worth it."

Respiratory Fungal infections

A+B are opportunistic
C is primary infections

Etiology

- ❖ Respiratory System: Nose to alveoli
- ❖ Route of infection?
 - Inhalation of the spores
 - Aspiration like Candida
 - Hematogenous spread (blood)
- ❖ Oral Cavity, any role?
- ❖ Respiratory fungal infections are less common than viral and bacterial infections.
- ❖ Have significant difficulties in diagnosis and treatment.

A) Yeast

- Candidiasis (Candida and other yeast)
- Cryptococcosis (Cryptococcus neoformans, C. gattii)

B. Mould fungi

- Aspergillosis (aspergillus species)
- Zygomycosis (Zygomycetes, e.g. Rhizopus, Mucor)
- Other mould

C. Dimorphic fungi it existence depends on temperature; body temp. 37 → yeast / room temp. 25 → mould

- Histoplasma capsulatum
- Paracoccidioides brasiliensis
- Blastomyces dermatitidis
- Coccidioides immitis

Primary Systemic Mycoses

- ❖ Infections of the respiratory system (**Inhalation**)
- ❖ Dissemination seen in **immunocompromised hosts**
- ❖ Common in North America and to a lesser extent in South America. Not common in other parts of the World
- ❖ **Etiologies are dimorphic fungi**
 - In nature found in soil of restricted habitats.
 - Primary pathogens
 - They are highly infectious
- ❖ **They include:**
 - Histoplasmosis
 - Blastomycosis
 - Coccidioidomycosis
 - Paracoccidioidomycosis

Aspergillosis

Aspergillosis is a **spectrum of diseases** (group of diseases) of humans and animals caused by member of genus *Aspergillus*

These include:

1. **Mycotoxicosis** (like poisoning caused by toxins) we have many types of mycotoxins which depends on concentration, time of exposure) e.g **aflatoxin** which mostly poison the kidney
2. **Allergy**
3. **Colonization** (without invasion and extension) in preformed cavities
4. Invasive disease of lung (spread locally)
5. Systemic and disseminated disease (**extrapulmonary**) → hematogenous

Risk Factors :

1. Bone marrow/ organ transplantation
2. Cancer: leukemia/ lymphoma
3. AIDS
4. Drugs: cytotoxic drugs, steroids
5. Diabetes

Aetiological Agents: Aspergillus species → *A.fumigatus*, *A.flavus*, *A.niger*, *A.nidulans*, *A.terreus*

Classification

Invasive aspergillosis

Chronic aspergillosis:

1- Aspergilloma of lung

2- Maxillary (sinus) aspergilloma

Allergic aspergillosis:

1- Allergic bronchopulmonary (ABPA)

2- Allergic aspergillus sinusitis

Persistence without disease colonisation of the airways or nose/ sinuses

Aspergillosis

★ Chronic Aspergillosis (Colonizing aspergillosis) (Aspergilloma OR Aspergillus fungus ball)

Signs:

- Cough
- Hemoptysis
- variable fever

Radiology:

will show mass in the lung,
radiolucent crescent

★ Invasive pulmonary Aspergillosis

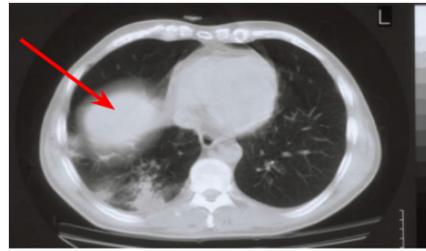
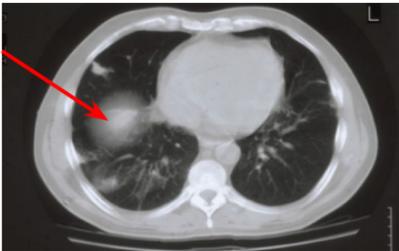
Signs:

- Cough
- Hemoptysis
- Fever
- Leukocytosis**

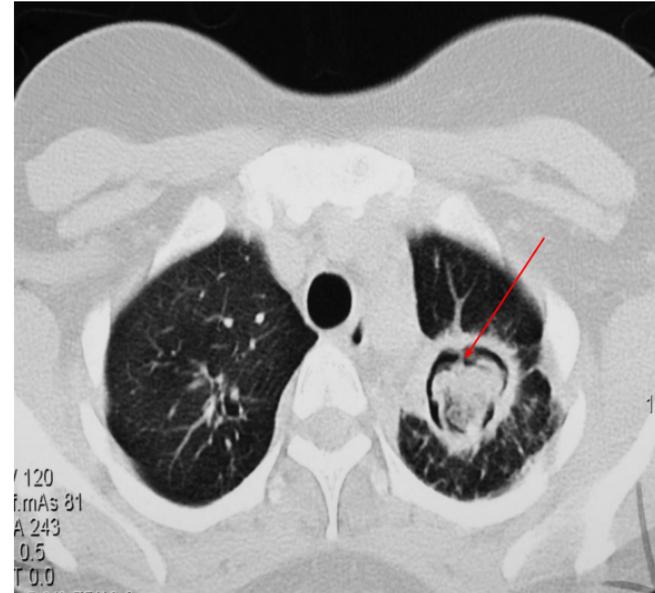
Radiology:

will show **lesions** with
halo sign

Invasive pulmonary Aspergillosis **Note the Halo sign**



Simple (single) aspergilloma **Note the air crescent** as we can see the ring shape means that this area is filled with air which means that its recovering



Allergic bronchopulmonary (ABPA)

Symptoms of Asthma

- ❖ Bronchial obstruction
- ❖ Fever, malaise
- ❖ Eosinophilia
- ❖ Wheezing +/-

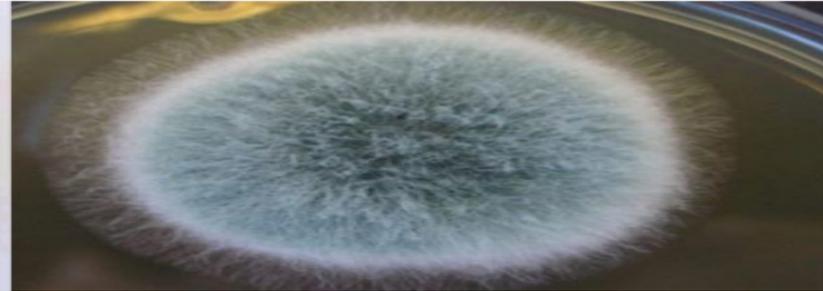
Also:

- ❖ Skin test reactivity to *Aspergillus* (positive)
- ❖ Serum antibodies to *Aspergillus*(positive)
- ❖ Serum IgE > 1000 ng/ml
- ❖ Pulmonary infiltrates

Common Airborne Fungi differ by color after culturing



Aspergillus niger (black-brownish)



Aspergillus fumigatus (greenish-yellow)

Fungal sinusitis

Clinical:

- ❖ **Nasal polyps** and other symptoms of sinusitis, **also headache and nasal stuffiness.**
- ❖ In immunocompromised, **could disseminate to eye** > cranium (Rhino cerebral)
- ❖ The most common cause in KSA is **aspergillus flavus**
- ❖ In addition to aspergillus there are other fungi that can cause fungal sinusitis
- ❖ Aspergillus sinusitis has the same spectrum of aspergillus disease in the lung

Diagnosis:

- ❖ Clinical and radiology
- ❖ Histology
- ❖ Biopsy
- ❖ Culture
- ❖ Precipitating antibodies useful in diagnosis
- ❖ **Measurement of IgE level, RAST test**

Treatment:

Depends on the type and severity of the disease and the immunological status of the patient

Diagnosis of Aspergillosis

Lab investigations

- **Direct Microscopy:**

Giemsa Stain, Grecoth methenamine silver stain (GMS)

Will show fungal septate hyphae

- **Culture on SDA**

- **Serology:**

Test for Antibody or Antigen
ELISA test for galactomannan
Antigen

- **PCR:**

Detection of Aspergillus DNA in clinical samples

Specimen

- **Respiratory specimens:**

Sputum, BAL,
Lung biopsy,

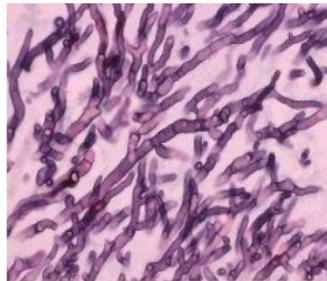
- **Other samples:**

Blood, etc.

Cultures of aspergillus



Smear: septate fungal hyphae. Aspergillosis



Choice of antifungal for aspergillosis

- **Voriconazole**
- **Alternative therapy:**
Amphotericin B,
Itraconazole, Caspofungin

Zygomycosis

Clinical forms of Zygomycosis:

- ❖ Pulmonary zygomycosis
- ❖ Rhinocerebral zygomycosis (can extend to adjacent structures)

Risk factors:

- ❖ Transplant patients, malignancy, AIDS, diabetic ketoacidosis, and many others.

Pulmonary Zygomycosis



Diagnosis:

- ❖ Acute
- ❖ Consolidation, nodules, cavitation, pleural effusion, hemoptysis
- ❖ Infection may extend to chest wall, diaphragm, pericardium.
 - Pulmonary infarction and hemorrhage
 - Rapid evolving clinical course

Early recognition and intervention are critical

- ❖ **Specimen:**
 - Respiratory specimens: Sputum, BAL, Lung biopsy,
 - Other sample
- ❖ **Lab. Investigations:**
 - Direct Microscopy: Giemsa, Grocott methenamine silver stain (GMS)
 - Will show broad non-septate fungal hyphae
 - Culture on SDA (no cycloheximide)
- ❖ **Serology:** Not available because the specie doesn't contain antigen

Etiology:

Zygomycetes (Non-septate hyphae) e.g Rhizopus

Treatment:

- ❖ Amphotericin B
- ❖ Surgery

Pneumocystis (PCP)

❖ Pneumocystis pneumonia (PCP)

- Opportunistic fungal pneumonia
- It is **interstitial pneumonia of the alveolar area.**

- Previously thought to be a protozoan parasite, but later it has been proven to be a fungus
- **Does not grow in laboratory media e.g. SDA**
- **Naturally found in rodents (rats), other animals (goats, horses), Humans may contract it during childhood**

Affect:

compromised host (especially common in AIDS patients.)

Etiology:

Pneumocystis jiroveci

Laboratory Diagnosis:

- **Patient specimen:** Bronchoscopic specimens (B.A.L.), **Sputum**, Lung **biopsy tissue.**
- **Histological sections or smears** stained by **GMS stain.**
- **Immunofluorescence** (better sensitivity)
- If positive will see cysts of **hat-shape, cup shape, crescent**

Treatment: **ANTIBACTERIAL**

- Trimethoprim - sulfamethoxazole
- Dapsone
- **Cotrimoxazole**

Summary

Aspergillosis

Aetiological Agents	1- A. fumigatus -2-A. flavus 3- A. niger -4- A. terreus 5- A. nidulans	Treatment	Voriconazole <i>Alternative therapy:</i> Amphotericin B, Itraconazole, Caspofungin
Risk Factors	<ul style="list-style-type: none"> ○ Bone marrow - organ transplantation ○ Cancer: Leukemia, lymphoma ○ AIDS ○ Drugs: Cytotoxic drugs, steroids ○ Diabetes 	Diagnosis	Specimen: Respiratory: Sputum, BAL, Lung biopsy. Other samples: Blood Lab: Direct Microscopy: Giemsa Stain, GMS stain Will show fungal septate hyphae Culture on SDA Serology: Test for Antibody ELISA test for galactomannan Antigen PCR: Detection of Aspergillus DNA
Classification	1- Invasive aspergillosis 2-Chronic aspergillosis A-Aspergilloma of lung. B-Maxillary (sinus) aspergilloma.	3- Allergic A- Allergic Aspergillus sinusitis B - Allergic bronchopulmonary (ABPA) 4- Persistence without disease: colonization of the airways or nose/sinuses.	

Primary Systemic Mycoses	
Transmission	Inhalation – highly infectious
Etiology	Dimorphic fungi: (Primary infections) Histoplasmosis Blastomycosis Coccidioidomycosis Paracoccidioidomycosis

Pneumocystis pneumonia (PCP): Opportunistic fungal pneumonia	
	It is interstitial pneumonia of the alveolar area.
Etiology	Pneumocystis jiroveci
Diagnosis	Laboratory Diagnosis: <ul style="list-style-type: none"> ○ specimen: BAL, Sputum, Lung biopsy tissue. ○ Histological sections stained by GMS stain. ○ Immunofluorescence If positive will see cysts of hat-shape, cup shape, crescent
Treatment	Trimethoprim – sulfamethoxazole Dapsone

Summary

Zygomycosis (Mould fungi) (opportunistic)	Pulmonary zygomycosis (Acute)	Rhinocerebral zygomycosis
Clinical Findings	Consolidation, nodules, cavitation, pleural effusion, hemoptysis	-
Prognosis	Infection may extend to chest wall, diaphragm, pericardium.	-
Etiology	Zygomycetes, e.g. Rhizopus	-
Diagnosis	1-Specimen: Respiratory specimens: Sputum, BAL, Lung biopsy 2-Lab: Direct Microscopy: Giemsa stain, GMS stain * Will show broad non- septate fungal hyphae Culture on SDA (no cycloheximide) Serology: Not available	
Risk factors	Transplant patients - AIDS Malignancy - Diabetic ketoacidosis	
Treatment:	Amphotericin B - surgery	

Aspergillosis (Mould fungi) (opportunistic)	Chronic Aspergillosis	Invasive pulmonary Aspergillosis	Allergic bronchopulmonary (ABPA)	Fungal sinusitis
Symptom	Cough <u>hemoptysis</u> variable fever	Cough hemoptysis fever <u>Leukocytosis</u>	Symptoms of Asthma Bronchial obstruction Fever, malaise Eosinophilia - Wheezing+/-	Nasal polyps other symptoms of sinusitis
Diagnosis	Radiology: mass in the lung, radiolucent crescent	Radiology: lesions with halo sign	- Skin test reactivity to Aspergillus - Serum antibodies to Aspergillus - Serum IgE > 1000 ng/ml - Pulmonary infiltrates	Clinical and Radiology Histology - Culture Precipitating Measurement of IgE level RAST test
Etiology	-	-	-	Aspergillus flavus
complication	-	-	-	In immunocompromised could lead to cranium (Rhinocerebral)
Treatment	-	-	-	depends on the type and severity and the immunological status of the patient

Quiz

4-D
3-C
2-A
1-C

1- which of the following is opportunistic?

A-Histoplasma capsulatum B-Coccidioides immitis

C-Cryptococcosis D-Blastomyces dermatitidis

2- a patient labs shows a fungal septate hyphae he most likely has?

A- Aspergillosis B- Zygomycetes

C- Histoplasmosis D-*Pneumocystis jiroveci*

3- which of the following tests is not effective in case of patient with *Pneumocystis pneumonia* ?

A-GMS stain B-IF

C-Culture D-PCR

4- a patient with Aspergilloma radiology result should show ?

A- halo sign B- nothing

C- pleural effusion D-radiolucent crescent

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