





Lecture: Respiratory Fungal Infection

- important
- Extra notes
- Doctors notes

Objectives:

- Respiratory System
- > Rout of infection?
- Oral Cavity, any role?
- Respiratory fungal infections are less common than viral and bacterial infections.
- > Have significant difficulties in diagnosis and treatment.

Respiratory fungal infection - Etiology

| YEAST (Opportunistic) | Mould fungi (Opportunistic) | Dimorphic fungi (Primary infections) Common in travel |
|--|--|---|
| Candidiasis (Candida) | Aspergillosis (Aspergillus species) | Histoplasma capsulatum |
| Cryptococcosis (Cryptococcus neoformans, C. gattii) | Zygomycosis (y, e.g. Rhizopus, Mucor) | Blastomyces dermatitidis |
| | Other mould | Paracoccidioides brasiliensis |
| | | Coccidioides immitis |

Primary Systemic Mycoses

- Infections of the respiratory system that occur by 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, dimorphic fungi
- ✓ They are highly infectious

They include:

- ✓ Histoplasmosis,
- ✓ Blastomycosis,
- ✓ Coccidioidomycosis,
- ✓ Paracoccidioidomycosis

Aspergillosis

- Aspergillosis is a spectrum of diseases of humans and animals caused by members of the genus Aspergillus
- of mould fungi (Opportunistic).

These include:

- (1) Mycotoxicosis (such alpha toxin which produced by Aspergillus)
- (2) Allergy
- (3) Colonization (without invasion and extension) in preformed cavities
- (4) Invasive disease of lungs
- (5) Systemic and disseminated disease.

Aetiological Agents:

Aspergillus species, common species are:

A. fumigatus, (Glabellar)

A. flavus, (Regional)

A. niger,

A. terreus

A. nidulans.

Common airborne Fungi



CLASSIFICATION OF ASPERGILLOSIS:

Airways/nasal exposure to airborne Aspergillus

- Invasive aspergillosis
- Chronic aspergillosis
 Aspergilloma of lung
 Maxillary (sinus) aspergilloma
- Allergic:

Allergic bronchopulmonary (ABPA)
Allergic Aspergillus sinusitis

- Persistence without disease
 - colonisation of the airways or nose/sinuses

Risk factors:

- Bone marrow/ organ transplantation
- AIDS
- Diabetes
- others
- •Cancer: Leukemia, lymphoma,.. Etc

Aspergillosis:

Chronic Aspergillosis (Colonizing aspergillosis)

(Aspergilloma OR Aspergillus fungus ball) (Fungus Ball is a mass or clumping of hyphae +mucous + fibrin + cellular debris) usually inside cavity.

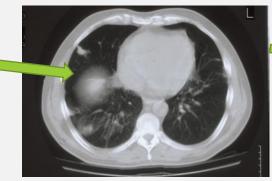
- Signs include: Cough, hemoptysis, variable fever
- Radiology will show mass in the lung , <u>radiolucent (air) crescent</u>

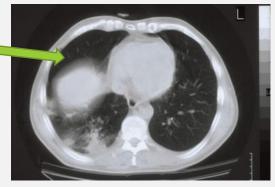
Invasive pulmonary Aspergillosis

Signs: Cough , hemoptysis, fever, Leukocytosis
Radiology will show lesions with halo sign

مهم

Invasive pulmonary aspergillosis





Note the Halo sign

Simple (single) aspergilloma



Note the Air crescent

Allergic bronchopulmonary (ABPA)

- Symptoms of Asthma
- Bronchial obstruction
- •Fever, malaise
- Eosinophilia
- Wheezing +/-

Also:

- •Skin test reactivity to Aspergillus
- •Serum antibodies to Aspergillus
- Serum IgE > 1000 ng/ml
- Pulmonary infiltrates

Fungal sinusitis

Clinical:

- Nasal polyps and other symptoms of sinusitis
- In immunocompromised, Could disseminate to \rightarrow eye \rightarrow craneum (Rhinocerebral)
- 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
- 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

^{*} A radioallergosorbent test is a blood test using radioimmunoassay test to detect specific IgE antibodies, to determine the substances a subject is allergic to.

Diagnosis of Aspergillosis

- Specimen:
 - ✓ Respiratory specimens: Sputum, BronchoAlveolar Lavage (BAL), Lung biopsy,
 - ✓ Other samples:
 - ✓ Blood, etc.
- Lab. Investigations:
 - **✓** Direct Microscopy:
 - Giemsa Stain, Grecott methenamine silver stain (GMS)
 - Will show fungal septate hyphae
 - ✓ Culture on SDA (Sabouraud Dextrose Agar is selective media)
 - ✓ Serology:
 - Test for Antibody
 - ELISA test for galactomannan Antigen
 - ✓ PCR: Detection of Aspergillus DNA in clinical samples

Choice of antifungal for aspergillosis: Usually we need surgery also

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



Cultures of Aspergillus



Smear: Septate fungal hyphae. Aspergillosis

Zygomycosis:

- Pulmonary zygomycosis
- Rhinocerebral zygomycosis

Risk factors

- ✓ Transplant patients
- ✓ Malignancy
- ✓ AIDS
- **✓ Diabetic ketoacidosis**
- ✓ Many others

Pulmonary Zygomycosis:

- Acute infection
- o Consolidation, nodules, cavitation, pleural effusion, hemoptysis
- Infection may extend to chest wall, diaphragm, pericardium.
 - Pulmonary infractions and hemorrhage
 - Rapid evolving clinical course
- Early recognition and intervention are critical

➤ <u>Etiology:</u>

• Zygomycetes , Non-septate hyphae e.g. Rhizopus,

Note:

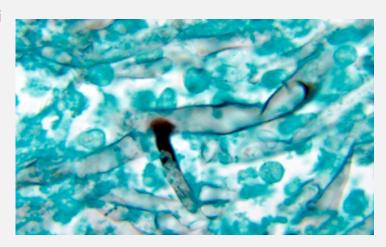
Aspergillosis –septate hyphae p.Zygomycosis – non-septate hyphae

Diagnosis:

- > Specimen:
 - Respiratory specimens: Sputum, BAL, Lung biopsy,
 - Other samples
- **>** Lab. Investigations:
 - Direct Microscopy:

Giemsa, Grecott methenamine silver stain (GMS)

- ➤ Will show broad non- septate fungal hyphae
- Culture on SDA (no cycloheximide) because it may inhibit the growing of this fungi
- > Serology: Not available
- > Treatment:
 - Amphotericin B
 - Surgery



Pneumocystosis (PCP):

- Pneumocystis pneumonia (PCP)
- Opportunistic fungal pneumonia
- It is interstitial pneumonia of the alveolar area that effect immunocompromised hosts.
- Affect compromised host
- Especially common in AIDS patients.
- Etiology: Pneumocystis jiroveci
- 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 (only we can use silver \ IF stain which is more sensitive)
- Naturally found in rodents (rats), other animals (goats, horses), Humans may contract it during childhood

Pneumocystosis:

Laboratory Diagnosis:

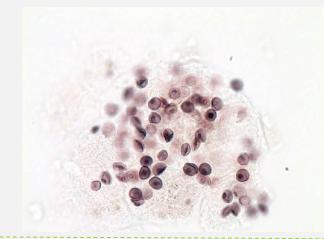
- Patient specimen: Bronchoscopic specimens (B.A.L.), Sputum (not very good), Lung biopsy tissue.
- Histological sections or smears stained by GMS stain.
 - Immunuofluorescence (better sensitivity)

If positive will see **cysts** of hat-shape, cup shape, crescent.

Treatment:

Trimethoprim – sulfamethoxazole (the two drugs are combined and known as co-trimoxazole)

Dapsone



Pulmonary Candidiasis

Candida causing Pneumonia but Not Common.

Has Primary and Secondary

Secondary Dissimination of blood

Diagnose: don't depend on Sputum

Treatment: Fluconazole

Voticonazole if resistant to fluconazole

summary:

Etiology

Classification

Respiratory Fungal Infections

| Opportunistic | | Primary infections |
|--|--|------------------------------|
| Yeast | Mould Fungi | Dimorphic fungi |
| Candidiasis (candida, and other yeast) | Aspergillosis (Aspergillus species) Zygomycosis (Zygomycetes eg. Rhizopus, mucor) | Histoplasma capsulatum |
| | | Blastomyces dermatitidis |
| Cryptococcosis (Cryptococcus neoformans, C. gatti) | | Paracoccidiodes brasiliensis |
| | Other mould | Coccidioides immitis |

(1) Primary Systemic Mycoses

(Inhalation)

Primary pathogens

Highly infectious

Etiology: Dimorphic fungi:

Histoplasmosis

Blastomycosis

Coccidioidomycosis

Paracoccidioidomycosis

(2) Aspergillosis

(next slide)

(3) Zygomycosis

- Rhinocerebral zygomycosis
- Pulmonary zygomycosis (Acute)

Etiology:

Zygomycetes (rhizopus)

Diagnosis:

Specimen (sputum, BAL, biopsy)

Lab (direct microscopy: GMS and Giemsa stain = broad non-septate fungal hyphae)

(culture = SDA)

(serology= not available)

Treatment:

Amphotericin B

Surgery

(4) Pneumocystosis (PCP)

Opportunistic fungal pneumonia

Etiology:

Pneumocystis jiroveci

Diagnosis:

Specimen (sputum, BAL,

biopsy)

Histology (GMS stain)

Immunofluorescence

Treatment:

Trimethoprim –

Sulfamethoxazole

Dapsone

summary:

Invasive aspergillosis

Signs:

cough, hemoptysis, fever, leukocytosis.

Radiology:

Lesions with halo signs

Chronic aspergillosis (colonizing apergillosis)

- Aspergilloma of lung
- Maxillary (sinus) aspergilloma

Signs: cough, hemoptysis,

variable fever

Radiology: mass in the lung, radiolucent crescent

Persistence without disease colonization of the airways or nose/sinuses

(2) Aspergillosis

Etiology: (Aspergillus species)

- A. fumigatus
- A. flavus
- A. niger
- A. terreus
- A. nidulans

Diagnosis:

Specimen (Sputum, BAL, biopsy, blood, etc)

Lab (direct microscopy: GMS and

Giemsa stain = septate hyphae)

fungal

(culture = SDA)

(Serology = test for antibody,

ELISA)

(PCR = detection of aspergillus

DNA in clinical sample)

<u>Treatment:</u>

Voriconazole

Alternative: Amphotericin B,

Itraconazole, Caspofungin

Allergic

- Allergic aspergillus sinusitis
- Allergic bronchopulmonary Aspergillosis (ABPA):

Symptoms of asthma, bronchial obstruction, fever, malaise, eosinophilia, wheezing +/-

Fungal Sinusitis

Signs: nasal polyps and other symptoms of sinusitis

Most common cause:

Aspergillus flavus

Diagnosis:

clinical and radiology, histology, culture, RAST, IgE levels

Treatment:

Varies according to severity and type of the disease and the immunological status of the patient

GOOD LUCK!

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