

Lecture ~ 06

Respiratory Fungal Infections ~ 01



Microbiology Team - 430

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❖ Rout of infection:

- Inhaled fungal spores. (Commonly).
- Oral cavity. "it contains 47 different types of fungi"

☒ Respiratory fungal infections are less common than viral and bacterial infections.

☒ Fungal infections are opportunistic infections.

“Diseases that affect immunocompromised patients mainly, rarely affect healthy hosts”

☒ Have significant difficulties in diagnosis and treatment.

❖ Factors increase susceptibility of Fungal infections:

- Inducing immunosuppression:
 - AIDS
 - Bone marrow/ organ transplantation.
 - Cancer: Leukemia, lymphoma.. etc
 - Drugs: Cytotoxic drugs, steroids.. etc
 - Endocrine related: Diabetes.
 - Failure of organs: multi-organ.
- Other factors:
 - Surgery.
 - Increased survival of premature neonates.
 - More elderly patients.
 - Long Stay in hospital/ ICU.
 - Devices.

Etiology:

❖ YEAST:

- *Candida* and other yeast causing **Candidiasis**
- *Cryptococcus neoformans*, *C. gattii* causing **Cryptococcosis**.
- *Pneumocystis jiroveci* causing **Pneumocystosis**.

❖ Mould fungi

- *Aspergillus species* causing **Aspergillosis** (most common).
- *Zygomycetes*, e.g. (*Rhizopus* & *Mucor*) causing **Zygomycosis**.
- Other mould.

Yeast & mould are opportunistic (affect immunocompromised patients)

❖ **Dimorphic fungi: (These Fungi cause Primary Systemic Mycoses)**

- *Histoplasma capsulatum* (causing **Histoplasmosis**).
- *Blastomyces dermatitidis* (causing **Blastomycosis**).
- *Paracoccidioides brasiliensis* (causing **Paracoccidioidomycosis**).
- *Coccidioides immitis* (causing **Coccidioidomycosis**).

Dimorphic fungi are primary infections (can affect a healthy individual).

Aspergillosis:

❖ **Definition:**

Is a spectrum of diseases of humans and animals caused by Members of the genus *Aspergillus*.

❖ **Etiological Agents:**

Aspergillus species

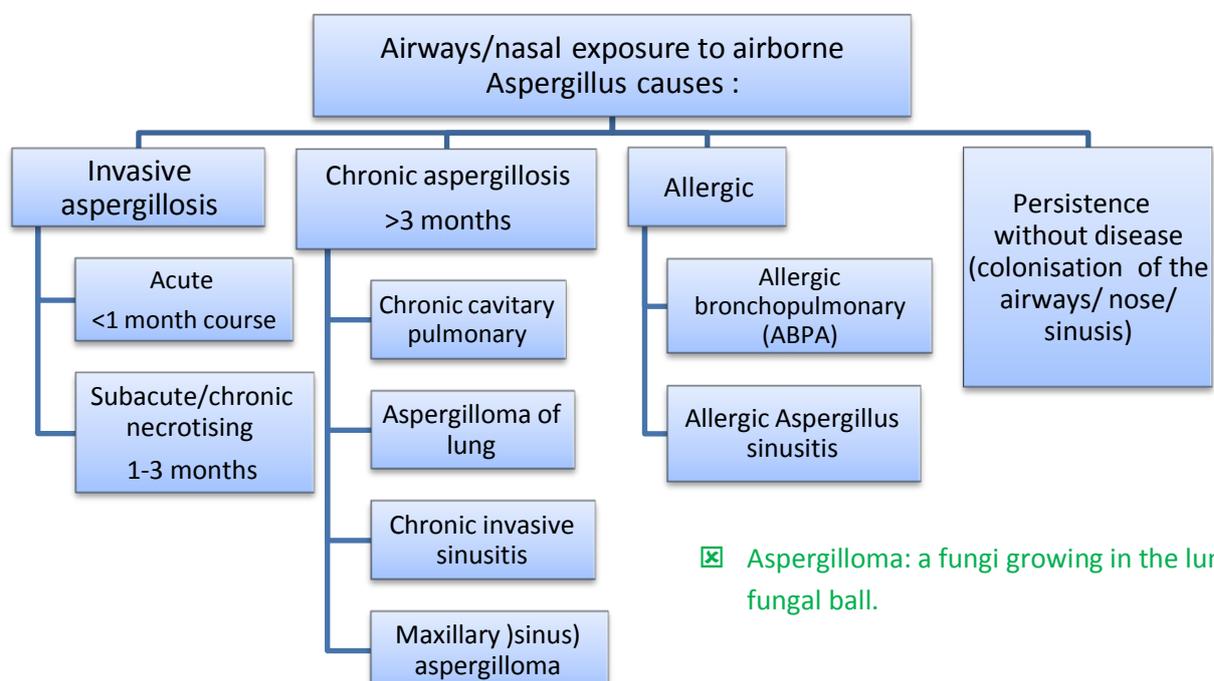
Common species are *A. fumigatus*, *A. flavus*, *A. niger*, *A. terreus* and *A. nidulans*.

Example of the diseases they induce:

- Mycotoxicosis.
- Allergy.
- In preformed cavities Colonization (without invasion and extension).
- Invasive, inflammatory, granulomatous, necrotizing disease of lungs.
- Systemic and disseminated disease.

❖ The type of disease and severity depends upon the physiologic state of the host and the species of *Aspergillus* causing the disease.

❖ **Classification of Aspergillosis:**



1. Chronic Aspergillosis “Aspergilloma”

(Colonizing aspergillosis or Aspergillus fungus ball)

- Clinical presentation:

Cough, hemoptysis (coughing up of blood or of blood-stained sputum)

Variable fever

- X-ray findings:

Radiology will show mass in the lung,

Air crescent



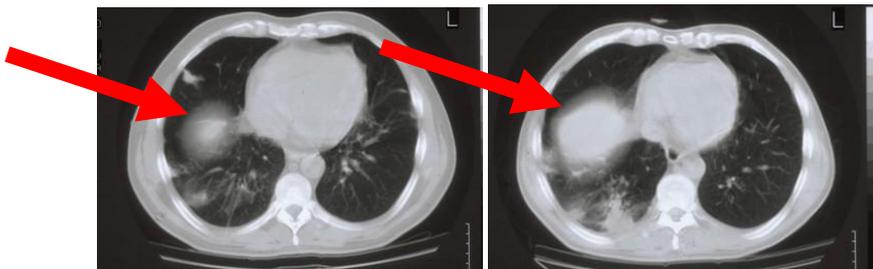
2. Invasive pulmonary Aspergillosis:

- Clinical presentation:

Cough, hemoptysis, Fever, Pneumonia & Leukocytosis.

- X-ray findings:

Halo sign



3. Aspergillus sinusitis:

- Etiology:

Aspergillus flavus (Most Common).

- Clinical presentation:

Nasal polyps – sinusitis

Could disseminate to → eye-craneum (Rhino cerebral).

→ Brain causing (cerebral aspergillosis).

4. Allergic bronchopulmonary aspergillous (ABPA) :

- Clinical presentation:

- Have history of Asthma and Bronchial obstruction.
- Fever, malaise (feeling of general discomfort).
- Eosinophilia
- Wheezing +/-

Also:

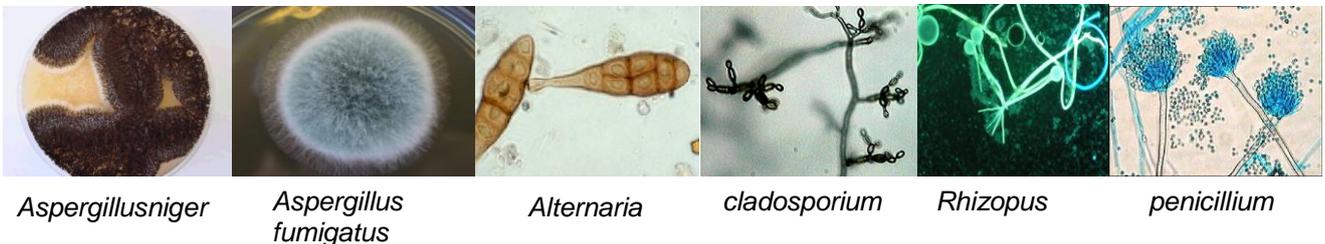
- Skin test reactivity to Aspergillus.
- Serum antibodies to Aspergillus.
- Serum IgE > 1000 ng/ml (because it is a type1 hypersensitivity reaction).
- Pulmonary infiltrates.

5. Other diseases caused by Aspergillus:

- Corneal ulcer (inflammation of cornea involving disruption of its epithelial layer)
- Endophthalmitis (inflammation of the internal coats of the eye).
- Otitis externa – otitis media (caused by A. niger).
- Nail & skin infection (caused by A. niger).

☒ **Most common source of fungi is airborne** (carried through air).

- Common airborne Aspergilli :



- Air quality in hospitals:

Can cause:

- Nosocomial pulmonary Aspergillosis (hospital acquired infection).
- Post-Operative Aspergillosis >500 cases (After operation infection).

Fungal sinusitis:

❖ Treated with:

Chemotherapy, after treatment Biopsy show **hyphal invasion**

1. Acute invasive *Aspergillus* sinusitis:

❖ Diagnosis:

Requires both biopsy and preferably culture for *mucormycosis*, *Scedopsporium*
(Other micro organism which affects the sinus and causes the same disease)

❖ Differential Diagnosis:

Infection / Fusarium

❖ Treatment:

- Tissue requires systemic antifungal therapy to minimize eye, mouth and destruction, including spread to face, brain and cure
- Some cases require surgical removal **such as Nasal polyp**.

2. Allergic *Aspergillus* sinusitis

❖ Clinical presentation:

Nasal obstruction, recurrent sinus infections, loss of smell and nasal polyps.

❖ Diagnosis:

- *Aspergillus* precipitins (a laboratory test to detect antibodies in the blood resulting from exposure to the fungus *Aspergillus*).
- Result appear +ve for *Aspergillus* antibodies in 85% of patient.
- Surgical handling of specimen very important – mucus versus tissue: allergic or chronic invasive.

3. Chronic invasive *Aspergillus* sinusitis:

❖ Complications in immunocompromised:

- Orbital apex syndrome (an orbital infection).
- Generalised proptosis (Forward protrusion of one or both eyeballs) and blindness.
- Cavernous sinus thrombosis (formation of a blood clot within the cavernous sinus, a cavity at the base of the brain).
- Osteomyelitis of the base of the skull.
- Cerebral aspergillosis.

❖ Diagnosis of Fungal Sinusitis :

1. Specimen:

- a. Respiratory specimens: Sputum, BAL (Bronchio alveolar lavage), Lung biopsy.
- b. Other samples: depend on the site e.g. CSF → CNS
- c. Blood: For serolog.

2. Lab investigations:

1. Direct Microscopy:

- Stained smear : Periodic Acid Schiff (P.A.S)(a staining method used to detect glycogen in tissues); KOH, Giemsa, Greccott, (methenamine silver stain)GMS

- a. Result: will show septate fungal hyphae with Dichotomous branching (V shaped branching of hyphea in aspergillous).

2. Culture: on SDA (no cycloheximide).

This is insensitive to fungal infections.

3. Serology:

- Test for antibody: Using I.D (Immunodiffusion).
- Test of Antigen: ELISA test for galactomannan Antigen_(antigen associated with aspergillous)

Antigen test is available with a better sensitivity than Immunodiffusion .

4. PCR (polymerase chain reaction).

Real-time molecular based in vitro diagnostic tests for Aspergillus spp.

❖ Treatment :

By Antifungal drugs: Voriconazole

Amphotericin B (AmBisome)

If cannot use these drugs we can use Caspofungin

Zygomycosis (mucormycosis)

❖ Classification:

- Pulmonary zygomycosis.
- Rhinocerebral zygomycosis.

❖ Risk factors:

- **Diabetic ketoacidosis.**
- Granulocytopenia.
- Corticosteroid therapy.
- Malignancy.

❖ Etiology:

- **Zygomycetes which is Non-septate hyphae**
- Mainly of the order Mucorales (Rarely Entomophthorales) e.g. Rhizopus, Mucor,

❖ Complications:

- *Angioinvasion, Thrombotic invasion of blood vessels*
- *Pulmonary infarctions and hemorrhage*
- *Rapid evolving clinical course*
- *High mortality*

❖ Clinical presentation of acute zygomycosis:

- Fever, pulmonary infiltrates "refractory (resistance) to antibacterial therapy", Consolidation, nodules, cavitation, pleural effusion and hemoptysis.
- If not treated, infection may extend to chest wall, diaphragm, and pericardium
☒ That is why early recognition and intervention are critical.

❖ Diagnosis:

- Specimen:

- Respiratory specimens: Sputum, BAL, Lung biopsy.
- Other samples: in severe cases skin biopsy is required.

- Lab Investigations:

1. Direct Microscopy:

- Periodic Acid Schiff (P.A.S), KOH, Giemsa, Grecoth methenamine silver stains (GMS).
- Will show broad **non- septate fungal hyphae.**

2. Culture:

(On SDA) no cycloheximide.

3. No Serology available.

❖ Treatment:

Generally:

Amphotericin B ,

Posaconazole (Other azoles are not effective in fungal infections).

In some cases surgery is required **such as sinusitis**.

Summary

Fungal that affects the lungs:

- **Clinical presentation** : Cough, **Hemoptysis** & variable fever
- **X-ray Findings** : Air crescent

Chronic Aspergillosis

Invasive Pulmonary Aspergillosis

- **Clinical presentation** : Cough, Hemoptysis, Fever, Pneumonia & Leukocytosis
- **X-Ray Finding** : Halo Sign

Allergic bronchopulmonary aspergillosis (ABPA)

- **Clinical presentation** :
History of Asthma and Bronchial obstruction.
Fever, malaise (feeling of general discomfort).
Eosinophilia, Wheezing +/-
- **Also have** :
Skin test reactivity to Aspergillus.
Serum antibodies to Aspergillus.
Serum IgE > 1000 ng/ml
Pulmonary infiltrates.

Other diseases caused by Aspergillosis

- Corneal ulcer
- Endophthalmitis
- Otitis externa – otitis media (caused by *A. niger*).
- Nail & skin infection (caused by *A. niger*).

Fungal Sinusitis:

	Clinical Presentation	Complications in Immunocompromised	Different Diagnosis
Acute Invasive Aspergillus Sinusitis	- Nasal obstruction, recurrent sinus infections, loss of smell and nasal polyps. - Aspergillus Flavis is the most common	1. orbital apex syndrome 2. generalised proptosis and blindness 3. cerebral aspergillosis	Mucormycosis, Scedosporium, Fusarium infection
Allergic Aspergillus Sinusitis			_____
Chronic Invasive Aspergillus Sinusitis			_____

Respiratory Fungal Infection: (Diagnosis + Specimen)

	Direct Microscopy	Culture : on SDA	Serology	PCR	Specimen	Risk Factors
Aspergillus	Stained smear Result will show: Septate fungal hyphae	No cycloheximide	- Test for antibody: Using I.D - Test for Antigen : ELISA test for galactomannan Antigen	Just in invasive Asp.	Sputum, BAL, Lung Biopsy, Blood, CSF	- Immuno compromised : 1.AIDS 2.Cancer 3. Drugs 4. Diabetes - Other : - Surgery
Zygomycosis	Stained smear , Result will show : Non-septate fungal hyphae		_____	_____	But in Sinusitis we only look for : mucin	1. Diabetic ketoacidosis. 2.Granulocytopenia. 3. Corticosteroid therapy. 4. Malignancy.

- ❖ In Allergic Aspergillus Sinusitis Diagnosis we use : Aspergillus precipitins
- ❖ **Treatment** for Aspergillus: Voriconazole & Amphotericin B.
- ❖ Treatment for Zygomycosis: Amphotericin B & Posaconazole(other azoles are not affective)
 - In some cases surgery is required such as sinusitis.

Zygomycosis (mucormycosis) :

Classification	Complications	Clinical presentation of acute zygomycosis
<p>1. Pulmonary zygomycosis.</p> <p>2. Rhinocerebral zygomycosis. (initially the Zygomycosis affect the eye and the spread to the brain)</p>	<p>1.Angioinvasion, Thrombotic invasion of blood vessels</p> <p>2.Pulmonary infarctions and hemorrhage</p> <p>3.Rapid evolving clinical course</p> <p>4.High mortality</p>	<p>- Fever, pulmonary infiltrates, Consolidation, nodules, cavitation, pleural effusion and hemoptysis.</p> <p>- If not treated, infection may extend to chest wall, diaphragm, and pericardium</p>