

Lecture ~ 06

Respiratory Fungal Infections ~ 01



Microbiology Team - 430

Done By:

Ghadeer Al-Wuhyad

Hanan Al-Rabiah

Khawla Al-Othman

Ibrahim Al-Faris

Hatim Al-Ansari

Hussam Al-Razqan

Mohammed Al-Kurbi

❖ 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

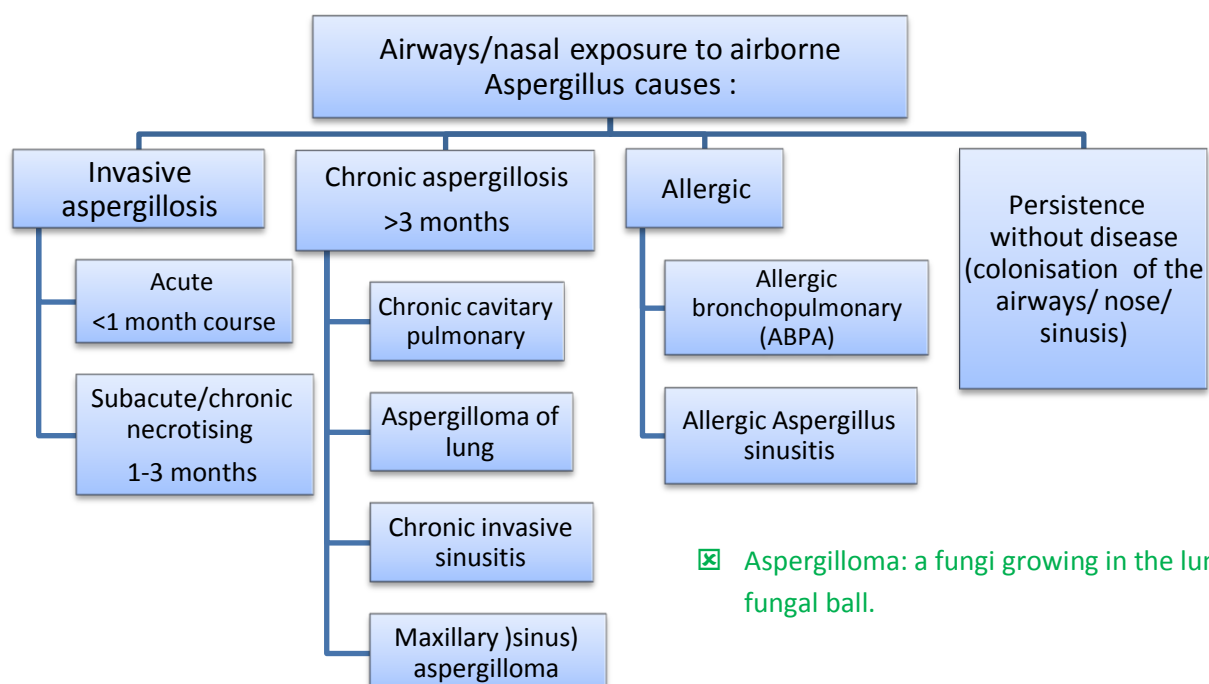
Common species are A. fumigatus, A. flavus, *A. niger*, *A. terreus* and *A. nidulans*.

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:**

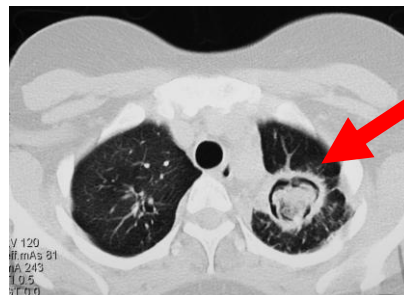
Cough, hemoptysis (coughing up of blood or of blood-stained sputum)

Variable fever

- **X-ray findings:**

Radiology will show mass in the lung,

Air crescent



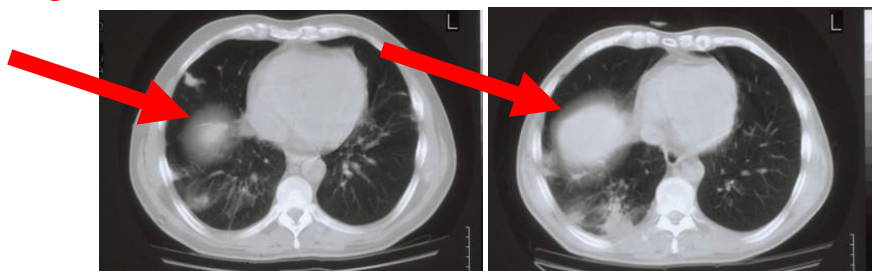
2. Invasive pulmonary Aspergillosis:

- **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-cranium (Rhino-cerebral).

→ Brain causing (cerebral aspergillosis).

4. Allergic bronchopulmonary aspergillosis (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*, *Scedosporium*
(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, Grecoff, (methenamine silver stain)GMS
- a. Result: will show septate fungal hyphae with Dichotomous branching (V shaped branching of hyphae 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:

Chronic Aspergillosis

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

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 Flavus 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: <u>Septate fungal hyphae</u> | 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 But in Sinusitis we only look for : <u>mucin</u> | - Immuno compromised : 1.AIDS 2.Cancer 3. Drugs 4. Diabetes - Other : - <u>Surgery</u> |
| Zygomycosis | Stained smear , Result will show : Non-septate fungal hyphae | | _____ | _____ | | 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 effective)
 - In some cases surgery is required such as sinusitis.

Zygomycosis (mucormycosis) :

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