Lecture - 07

Respiratory Fungal Infection 02

Microbiology Team - 430

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Candidiasis:

Candidiasis is a fungal infection (mycosis) of any of the genus *Candida* species (all yeasts), of which *Candida albicans* is the most commonly responsible for Candidiasis

Candida are yeasts, some of them have pseudohyphae

Other species include

- Candida glabrata
- Candida tropicalis
- Candida parapsilosis
- Candida krusei

Candida:

- Part of the endogenous "normal" flora which are present in the Skin, Gut or mucosal surface
- Most infections are due to person's own flora "Endogenous source"
- The Candida infection maybe by exogenous transmission

Portal of entry:

- Breach in skin or mucosa by catheters, trauma, surgery

Candidiasis

High-risk patients

AIDS
Surgery
Malignancy
Leukopenia
Burns
Premature infants

Exposures

ICU >7 days
CVCs
(Central venous catheters)
Antibiotics
TPN
(Total Parenteral Nutrition)
Colonization

Disease spectrum:

1.Infections of the skin and nail	**2.Gastrointestinal infections** (oral cavity, esophagus)
3.Infection of genitalia (vulvovaginal candidiasis) dr. said he won't ask about it	**4.Urinary tract infection** (lower and upper UTIs) dr. said he won't ask about it
5.Ocular infections (Keratitis, endophthalmitis)	**6. Candidemia** (Candida in the blood)
7. CNS infection (infection of the brain)	**8. Deep organ Candidiasis**
9. Pneumonia	**10. Endocarditis**
11. Bone and joint infections	**12. Chronic Mucocutaneous Candidiasis (CMC)** (congenital, immunological defect)

Mucocutaneous & Cutaneous infections

- **Oral thrush**:

White or grey Pseudomembranous patches on oral surfaces especially .tongue with underlying erythema **(redness of the skin)**

Common in: neonate, infant ,children , elderly , compromised host and AIDS

- **Esophagitis** (The infection of the esophagus very common)
- **Diaper rash**

Pulmonary Candidiasis (pneumonia)

- Primary pneumonia is less common and could be a result of Aspiration
- **Secondary pneumonia commonly seen with:** - Hematogenous Candidiasis
  - Immunocompromised patients

Diagnosis:

- Isolation of *Candida* from sputum
  (When we find the yeast in the sputum **doesn't** always mean there is an infection, because the sputum has normal flora but if we have a large number of yeasts this mean there is an infection)
- BAL (Bronchioalveolar Lavage) :
  (Is a medical procedure in which a bronchoscope is passed through the mouth or nose into the lungs and fluid is squirted into a small part of the lung and then recollected for examination)
- Radiology and clinical features
- Lung biopsy

(if we find yeast in the lung's tissue) → this mean there is infection, because the lung doesn't has normal flora (it is sterile)

Other yeast causing pulmonary infections: *Trichosporon and Geotrichum*

Candidemia

- Candidemia : when the blood has Candida
- Increased colonization (endogenous or exogenous factors) Damage in host barriers by Catheters, trauma, surgery and Immunosuppressant

*Central venous catheters (CVC) (major source to cause Candidemia)

Disseminated "spread" Candidiasis (involvement of any organ)

can cause:

- Septic shock
- Meningitis
- Ocular involvement (retinitis) inflammation of the retina of the eye

Symptoms:

Fever could be the only clinical manifestation

Candida – nosocomial bloodstream infection:

Candida is the fourth in causing nosocomial bloodstream infections) BSI.

Have very high mortality levels (47% in ICU) (29% in non ICU)

Diagnosis of Candidiasis

1. **Laboratory Diagnosis**

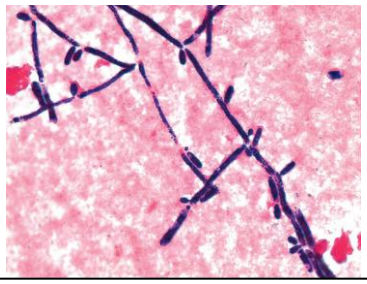
   Specimen depend on site of infection

- **Blood for serology**
- **Swabs → pharyngitis , oral trush**
- **Urine → UTI**
- **CSF (Cerebrospinal Fluid) → meningitis**
- **Sputum and lung biopsy → Pulmonary Candidiasis**

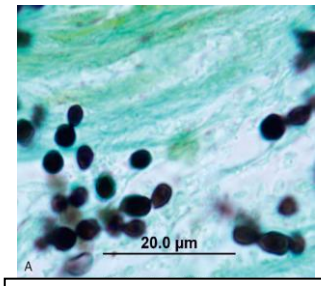
2. Direct microscopy

Gram stain, KOH, Giemsa, GMS, or PAS stained smears.

We will see under microscope:



Budding yeast cells and pseudohyphae +/-



Budding cells only

3. Blood culture

We do this culture to diagnosis if there is blood infection whether by bacteria or fungal on SDA and blood agar

Because *C. albicans* is the most common species to cause infection and it is different from other yeast. In addition easy to identify it from other yeast, we use special investigations to diagnose it

We use the following tests to identify *C. albicans*:

1. Germ tube test (Formation of germ tube when cultured in serum at 37^{0})
2. Chlamydo-spores production in corn meal Agar (CMA)

If these positive ⟶ yeast is *C.albicans*
If these negative ⟶ it could be any other yeast

Diagnosis by culture on SDA between C.albicans and other candida

Candida albicans	Other candida
1. **Gram test tube** Will germinate 2. **Chlamidospores production** In corn meal agar	1. **Biochemical tests** " Carbohydrate assimilations" 2. **Culture on chromogenic media** 3. **Serology** "mannan antigen" 4. **PCR**
If these were negative we use these ⟶	so we know it's not c.albicans

To identify other yeasts we will do:

1. **Biochemical test :**
   Use Carbohydrate assimilations and fermentation
2. **Culture on Chromogenic Media CHROMagar™ Candida**
   In this media you can see each specious of yeast with a special color.
3. **Serology**
   (Detect the antibody and antigen in the serum)
   Test for Antigen, e.g. Mannan antigen by ELISA Test for Antibodies
4. **PCR**

Management of the systemic fungal infection:

Guidelines in treatment:

- **Begin antifungal! Therapy – EARLY**

(When we begin with thereby early, the risk of mortality will be decrease to 10%)

But when it's late, the risk will increase and may lead to death

- Control the underlying disease
- Remove/decrease immunosuppressant
- Restore Immune Function

Treatment of the Candidiasis:

- **Oropharyngeal**: Topical Nystatin suspension
  Clotrimazole troches ,Miconazole, Fluconazole suspension.
- **Vaginitis:** Topical; Miconazole, Clotrimazole, Nystatin

Systemic treatment of Candidiasis:

- Fluconazole
- Voriconazole
- Caspofungin
- Amphotericin

Treatment of Candidemia:

- Treat for 14 days after last positive culture and resolution of symptoms
- Remove all intravascular catheters, if possible
- **(don't stop the therapy even if the sign and symptoms disappeared)**

In vitro "in lab" susceptibility of Candida spp:

Antifungal susceptibility testing isn't done routinely in the microbiology lab

(We do this test when the Candida is not albicans)

Points to consider

- *C. glabrata* can be less susceptible "resistant" to Fluconazole
- *C. krusei* is resistant to Fluconazole

Pulmonary cryptococcosis

- **Causative agent yeast with a thick capsule**
  - *Cryptococcus neoformans*
  - *C. gattii*

- **Source of infection**
  From birds droppings & contaminated soil
- **Pathogenesis:**
  - Human infected by inhalation
  - **In the normal person**: the infection could be asymptomatic

In immune-compromised person: may be developed pneumonia, disseminate to CNS **causing meningitis** ⟶ (Cryptococcus neoformans)

- **Lab Diagnosis:**
  -India Ink preparation
  Show yeast cell with capsule
  -Culture on SDA
  -Serology (Excellent sensitivity)
  Capsular Antigen by latex agglutination

- **Treatment**

Systemic fungal agents

- Amphotericin B
- Combination of Amphotericin B & flucytosine

Pneumocystosis (PCP)

"Opportunistic fungal pneumonia"

It is interstitial pneumonia of the alveolar area

Affect compromised host, especially common in AIDS patients

- **Etiology**

Pneumocystis jiroveci

- Previously thought to be a protozoan parasite
  (Because it has cysts and a way of parasite growth)
- It has been proven to be a fungus
  (Because it has DNA structure and molecular biology of the fungal)

It does not grow in laboratory media e.g. SDA

Naturally found in rodents (rats), other animals (goats, horses)
Humans contract it during childhood

• Lab Diagnosis

- **Patient specimen**:
  Bronchoscopic specimens, B.A.L., Sputum, Lung tissue biopsy

- **Histologic sections or smears stained by** Silver stain (GMS),
  If positive will see **cysts** of hat-shape/cup shape crescent

- Immunofluorescence has better sensitivity.

• Treatment :

Trimethoprim – sulfamethoxazole**.**

Summary

Invasive candidiasis: these infections happen in immune-compromised patients and healthy person.

Risk factor of Candida: (surgery, age, long stay in hospital/ICU)

infection	Clinical presentation	Risk factors	diagnosis	Treatment
Mucocutaneous and cutaneous **" Oral thrush "**	White patches on tongue	Neonate and >65yrs patients Immunocompromised patients **AIDS**	**Swabs**	**Fluconazole** **Voriconazole** **Amphotericin B**
Pulmonary **" Pneumonia"**	Chills Fever Productive cough rusty sputum	Aspiration of organism Hematogenous Candidiasis Immunocompromised patients	**Sputum** **Lung biopsy** **B.A.L**	
Blood **" candidemia"**	Fever **Complications:** Septic shock - retinitis	Catheters trauma surgery Immuno-suppressants	**Blood culture** **1-Germ tube test.** **2-Chlamydia-spores production in corn meal agar.** **If it is – (do biochemical test).**	

Direct microscopy with stains e.g. GMS "silver stain" will show Budding yeast cells and pseudohyphae +/-

Infection	Organism	Risk factors	Diagnosis	Treatment
Pulmonary Cryptococcus	Cryptococcus neoformans **C. gattii**	Immunocompromised patients *cause **meningitis**	**India Ink** (capsule) **Serology** (Capsular Antigen by latex agglutination)	**Combination of Amephotericin B & Flucytosine.**
Pneumocystosis "PCP"	*Pneumocystis jiroveci*	AIDS patients	**Sputum** **BAL** **PCR** **Microscopy** (cysts) **Immunofluorescence** (more sensitive and it is better than silver stain)	**Trimethoprim - sulfamethoxazole**