

# **Paracoccidioidomycosis**

- Paracoccidioidomycosis refers to the infectious, endemic disease caused by the fungi pathogen, *paracoccidioides brasiliensis*

Phylum: Ascomycota  
Genus: *Paracoccidioides*

- Wide spectrum of disease severity depending on strain
- Healthy individuals are affected

- Infections may include:
  - lungs
  - skin
  - buccal mucosa
  - nose
  - spleen/liver
  - GI tract

- **Dimorphic fungi**

- 25°C mold    37°C yeast
- mold form has no known sexual form (Fungi Imperfecti)

## **Species: *Paracoccidioides brasiliensis***

- **GEOGRAPHICAL DISTRIBUTION**

- Central and South America
- 23° north of Mexico down to Argentina
- NOT in Chile or the Caribbean
- most frequent in:
  - Brazil
  - Venezuela
  - Colombia

- **ECOLOGICAL NICHE**

- unknown!
- isolated 4 times in soil
- has been found in wood, fruit bats, armadillos

- **DIMORPHIC COMPARISON**

25°C Mold Form: slow growing  
flat, wrinkled  
yellowish brown  
septate hyphae (sterile)  
aleuriconidia  
do not sporulate

37°C Yeast Form: folded, wrinkled  
white  
multiple buds around mother yeast cell “steering  
wheel”  
buds form short chains

- Conversion occurs on enriched medium (brain heart agar)
- Needs 10-20 days of incubation to occur
- Observed conversion into yeast form is critical for diagnosis
  - DNA confirmation confuses w/ *Blastomyces dermatitidis*
  - Conidia formation similar and confuses w/ genus *Chrysosporium*

- **KEY CHARACTERISTIC**

- \* exo-cellular serine-thiol proteinase enzyme
  - enables the fungus to invade tissue better
- Strains vary geographically and exhibit varied severity of infection

## **Paracoccidioidomycosis: The Disease**

- Can lay dormant for years within the lymph nodes and appear later with relation to an immunodeficiency.
- **Risk factors**
  - Agricultural workers
  - Farmer/ hunter
  - Smoker/ Alcoholism
  - Immunocompromised conditions
- But effects healthy individuals as well
- Presumably acquired via inhalation of conidia

- **Histopathology**
  - Areas of granulomatous inflammation
    - Central caseation
    - Pyogenic abscesses
  - Giant cells are present in granulomata (contain yeast)
  - fungus occurs as budding yeast with cells 12-14  $\mu\text{m}$
  - Central cell surrounded by numerous blastoconidia varying in size, attached by narrow necks
- **Epididimology**
  - Very common among men
  - Women less commonly affected
  - Mean male to women ratio is 15:1
  - Rare in children and teens
  - Most patients are 30 years or older
  - Person to person transmission does not occur
- **Two major categories:**
  - Chronic adult form
    - 80-90% of cases
  - Acute or subacute juvenile form
- **Forms of disease:**
  - Asymptomatic
    - Occurs in most cases
  - Mucosal lesions
    - Ulcerative lesions of mouth and nose areas
  - Pulmonary
    - Affect central and basal zones of lungs
  - Skin
    - Ulcerative, crusty lesions
- **Diagnosis**
- Direct examination of:
  - Skin scraping
  - Sputum
  - Pleural fluid
  - Bone marrow
  - Material biopsies
  - Pus draining from lymph
- **Skin**
  - 10% KOH and Parker Ink
  - Or Calcofluor white mount

- **Tissue**
  - PAS
  - GMS
  - Gram stain
  
- **Exudates and Body Fluid**
  - 10% KOH and Parker Ink
  
- Chest X-ray used for key characteristics, BUT not diagnosis
  
- **Serology Test**
  - Western blot
  - ELISA
  - Immunodiffusion
  
- **Prognosis**
  - Good if treated
  - High mortality rate in acute juvenile type if not treated quickly
  
- **Antifungal Treatment**
  - Very long time
  - Frequent relapse
  
  - Azoles
    - Fluconazole
    - Ketoconazole
    - Itraconazole
  
  - Sulfas (5 years)
    - Sulfadiazine
    - Sulfamethoxypyridazine
    - Sulfadimethoxine
  
  - Amphotericin B
    - Not effective alone
    - Needed along with azoles or sulfas

### **Case Report 1**

- Pellegrino et al., The American journal of tropical medicine and hygiene, 68(3), 301-303.
- A 34 year old man, had a history of hepatitis C and he was a heavy smoker & drinker.

- **Complaints:**
  - Fever
  - Asthemia
  - Weight loss
  - Coughing
  - Abdominal Pain
  
- **Physical Examination**
  - Fever
  - No lesions
  - Right eye showed hemorrhage of the fundus with a white center
  
- **Lab Work**
  - Bone Marrow biopsy
    - Stained with H&E, showed abundant yeasts, similar to *P. brasiliensis*
  - Liver Biopsy
    - Stained with H&E and GMS, tissue showed reaction compatible to *P. brasiliensis*
  
- **Histopathology**
  - Double immunodiffusion test performed in serum was positive for *P. brasiliensis*
  - Isolated & cultured in Sabourad's glucose agar at 37°C for 18 days, showing budding yeast
  
- **Treatment**
  - 50 mg/day amphotericin B (AMB)
  - Then anemia and severe hypokalemia occurred
  - Amphotericin was decreased to 25 mg/day
  - Health worsened and thoracotomy and tube drainage was performed
  - Pleural liquid showed *P. brasiliensis*
  - So AMB was increased to 50 mg/day and 400 mg/day of intraconazol
  - 2 grams of AMB for the following six months
  - No recurrence of disease after one-year check up

## **Case Report 2**

- Van Damme, et al., Medical Mycology (2003) 68 (3), 301-303.
  
- In October 1998, a 60 year old Dutch man presented at the Department of Oral and Cranio-Maxillofacial Surgery
  
- **Complaints**
  - Painful ulceration on right side of face in the buccal vestibular mucosa

- **History**

- Past 3 months lesion persisted
- Dentist prescribed Corsodyl (mouth rinse), and Daktarin (oral gel)
- Heavy Smoker
- Worked as a carpenter with in third world aid programs in the jungles of Peru and Equador
  - 1967-1991

Lived in:

- Tocahe (12 years)
- Cuzco (5 years)
- West Ecuador ( 5 years)
- Check-up in Germany revealed in 1998 that he had an increase erythrocyte sedimentation rate
- Diagnosed with coughing and wheezing

- **Lab Work**

- Radiography of chest reveals a pattern of radiodensities
- CT scan of lungs showed sarcoidosis or bronchoillitis obliterans organizing pneumonia
- Lung tests and biopsies revealed pneumonia with restricted lung function
- \* NO EVIDENCE OF TUBERCULOSIS
- Diagnosed with endstage sarcoidosis

**5 months later**

showed no improvement

- Dentist noticed: irregular mucosa and gingiva on the right side of face  
teeth were loose  
showed signs of periodontitis

**1 week later**

no improvement; referred to oral surgeon

- Weight loss, fatigue, fever, and night sweats
- Sample from mouth showed:
  - pseudo-epithelial hyperplasia
  - inflamed cells
  - many large budding yeast cells
- A 2<sup>nd</sup> biopsy used direct fluorescence microscopy of a wet preparation stained with calcoflour white mount
- Finally, showed multiple peripheral buds characteristic of *Paracoccidioides brasiliensis*
- Complained of prostate pain – urine taken for cultures

- **Histopathology**

**Oral Culture**

- Mold grew after 3 weeks at 28°C
- Unicellular yeast grew at 37°C

- **Diagnosis**

- \* Chronic multifocal paracoccidioidomycosis

- **Treatment**

- Itraconazole oral solution initially
  - After 1 week peri-oral symptoms improved
  - After 3 weeks lung function improved
  - 5 years later was slightly dyspneic, but otherwise free of symptoms

### **References**

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