

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 μm
 - 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 2nd 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

- www.mycology.adelaide.edu (accessed June 14, 2007)
- www.doctorfungus.com (accessed June 14, 2007)
- Van Damme, P., Bierenbroodspot, F. Telgett, D.S., Kwakman, J., De Wilde, P.C., & Meis, J.F.G.M (2006). A case of imported paracoccidioidomycosis: an awkward infection in The Netherlands. *Medical mycology: official publication of the International Society for Human and Animal Mycology*, 44(1), 13-18.
- Pellegrino, A., de Capriles, C.H., Magaldi, S., Montes de Oca, I., Ruiz, M.E., Perez, C. et al. (2003). Case report: severe juvenile type paracoccidioidomycosis with hepatitis C. *The journal of tropical medicine and hygiene*, 68 (3), 301-303.