Topic 20: Paracoccidioidomycosis

Paracoccidioidomycosis

A chronic granulomatous mycosis with primary involvement of the lungs and leading to inapparent, acute or chronic and sometimes disseminating disease that usually involves reticuloendothelial tissue, and mucocutaneous tissue and more rarely other organs, which is caused by the asexual fungus *Paracoccidioides brasiliensis*.

Synonyms

- **Lutz-Splendore-Almeida's disease**
- **South American Blastomycosis**
- **Brazilian Blastomycosis**

Lutz described 2 cases in 1908

***most often seen as chronic progressive in normal host Thus, somewhat like blastomycosis. Produces fibrotic sequelae.**

Paracoccidiodes brasiliensis

Fungi Imperfecti
Hyphomycetes*
Thermally dimorphic
- **yeast-like forms @ 37ºC**
- **mold @ 25ºC**

South American endemnecy
- their most prevalent deep1º mycosis, but only with few U.S. hospitalizations ~ 10-12/year

Single form-species with only poorly understood ecology
- **few isolations from nature**
- **e.g., soils of mountain forests of Venezuela**

Original binomial:
- ***Zymonema brasiliensis*** **~ 1912 (illegal)**

***partial 28S rRNA sequencing suggests Onyginales affinity**

Early History

Brazilian Adolfo Lutz in 1908 described two disease cases involving extensive lesions in the nasopharyngeal regions

- **fungus in tissue somewhat like *Coccidiodes immitis* spherules but budded**
- **called disease pseudococcidioidal granuloma vs coccidioidal granuloma**
- **didn't name fungus**

Many others also thought *in vivo* phase was a spherule having endospores that remained attached to spherule wall*

***"cryptosporulation"**

Almeida* & Lacaz 1927 & 1929

Clarified organism was not a type of *Coccidiodes* and that the disease was very different from Coccidioidomycosis. So-called "cryptosporulation" was a misinterpretation and that yeast cell in tissue instead enlarged many diameters, accompanied by many mitoses, and then the nuclei migrated into numerous multiple buds on yeast mother cell surface.

***changed name from *Zymonema brasiliensis* to *P. brasiliensis*, 1930**

Origin of Disease

Early misconceptions - because most early cases associated with lesions in nasopharyngeal regions (particularly mucocutaneous tissues of nose or mouth) it was assumed that disease began:

1. **by traumatic inoculation of the fungus into oral mucosa**
2. **by ingestion of fungus**

More recent efforts finally established that majority of cases have pulmonary origins (1960s and 70s)*

Skin testing has shown there are many subclinical and resolved infections in endemic regions

85% of cases show lung involvement 35% of those only lungs.

Skin testing results

1. **Equal male/female skin testing & case rates for children, or skin testing for adults (exposure rates?)**

2. **Adult serious forms 7 to 70:1 male/female ratio. Greater than 90% of serious cases in males**

   reason: 1) occupational?/probably not because exposure rates ~ same as/skin test
   2) female hormones inhibit conidia or mycelial conversion to yeasts*

***mediated (?) by specific estradiol receptors in fungus cytoplasm**

Clinical Picture

85% of all patients seeking medical help have evidence of pulmonary disease

60% have skin or mucus membrane involvement. Of these, 25% have lymph node involvement.

Of the patients seeking medical help, ~50% are concerned about skin lesions and 50% about respiratory condition.

Lesions usually begin as papules or vesicles in nose which ulcerate; also tongue. Can be painful.

Clinical Types of Paracoccideoidomycosis

A. Primary benign disease — **normal patients**
- **1. Primary pulmonary paracoccidioido- mycosis**
- **2. Pulmonary reinfection with allergic manifestations** — **(1^{o})**
  resolution does not → obvious protective immunity

B. Acute and chronic <u>progressive disease</u>
- **1. Acute and <u>chronic progressive</u> pulmonary disease* (adult type)**
- **2. Disseminated disease (latent or active) involvement** — **opportunistic forms(?) (2^{o})**
  - **a. Mucocutaneous lymphangitic****
  - **b. Extracutaneous single organ involvement**
  - **c. Generalized disease (rarer)**
- **3. Acute <u>juvenile</u> paracoccidioidomycosis**

***fever, rales, chest pain, productive cough, only**
****most common to nose cavities**
From Rippon, p 510
For B1 &B3 see handout for details!

Secondary Progressive Paracoccidioidomycosis

5. Acute or subacute form (juvenile type) -- this form probably develops as a direct and rapid evolution of the primary complex. The patients, usually both young males and females, deteriorate swiftly, presenting a systemic disease affecting mainly the reticulo-endothelial system. Patients tend to develop a good humoral immune response, but fail to present adequate cellular immunity. Histopathology is characterized mostly by a non-specific inflammation which shows a poor organization towards a loose granulomatous pattern. Fungi are numerous in lesions, showing intense budding.

6. Chronic form (adult type) -- other patients are able to localize the disease in the lungs, mucocutaneous areas and/or other organs. This form of the disease is highly prevalent among adult males and can affect only one organ or system (unifocal form) or two or more organs (multifocal form). Patients usually raise an adequate specific humoral immunity and a less depressed cellular immune response than that seen in the acute form. Histopathology shows a typical epithelioid granuloma, which surrounds and impairs the multiplication of fungi.

Generalized dissemination, usually in very immunocompromised adults.

Therapy*

pre-1940 none and recognized disease often advanced to death

1940s -> 50s, sulfanamides; variable effectiveness

1960 --> Amphoteracin B; traditional drug of choice

1990 azoles?? triazoles; 1992 itraconazole drug of choice in S.A., 100mg/ for 6 mo. --> 99% clinical cure rate
Serology

- **-CF Tests**
- **-tube precipitin tests**
- **-recently ID and FA tests too**

Disease like the systemic endemic U.S. diseases being controlled with good success.

AIDS association - still rare disseminated.

***all clinically detectable cases should be treated with systemic antifungals**