Penicillium marneffei Infections

- Jenee Thurston, Kelly Bees, Adam Speerstra

Courtesy of: www.doctorfungus.com

Courtesey of:
Penicillium marneffei

- Discovered in 1959 by G. Segratain in Paris
- Only known thermally dimorphic species of Penicillium
- Can cause penicilliosis with fever and anemia
- Dimorphic saprophyte of soil and decomposing organic matter.

Taxonomy Includes:
- Kingdom: Fungi
- Phylum: Ascomycota
- Class: Euascomycetes
- Order: Eurotiales
- Family: Trichocomaceae
- Genus: Penicillium
Geographic Distribution

- **Widespread**
  - Specifically in Southeast Asia
    - Burma (Myanmar), Cambodia, Southern China, Indonesia, Laos, Malaysia, Thailand and Vietnam

- Cases were reported in HIV-positive patients in Australia, Europe, Japan, the UK and the U.S.
  - All, except one traveled to Southeast Asia.
Epidemiology

- Affects HIV-infected & immunosuppressed patients
- Discovered in bamboo rats (Rhizomys & Cannomys)
- Epidemiological markers and reservoirs for human infections
- High mortality and morbidity rates
- 10% of HIV patients in Hong Kong affected
- Soil exposure, especially during the rainy season, is a critical risk factor.

- Third most common opportunistic infection (after extrapulmonary tuberculosis and cryptococcosis) in HIV-positive individuals

Courtesy of: http://animaldiversity.ummz.umich.edu/site/accounts/pictures/Rhizomyinae.html
Life Cycle

- Thermally dimorphic
- Divided into three distinct phases:
  1. a multicellular, filamentous (mold) vegetative form
  2. asexual reproductive stage (conidiogenesis)
  3. a unicellular yeast-like/arthroconidial phenotype
- Temperature and nutrition are key factors to determine which specific phase is displayed
Life Cycle

- Young colonies are grown on Sabouraud glucose agar
  - rapid growing, flat, filamentous, and velvety, woolly, or cottony in texture
  - Usually appear bluish gray-green
  - Mature colony is reddish yellow, producing a pink or red-rose pigment that diffuses into the surrounding medium

Morphologies of *P. marneffei* under a microscope

Courtesy of: http://cmr.asm.org/cgi/content/full/19/1/95
Pathogenesis

- Pathogen found in bamboo rat feces, liver, lungs and spleen
- Higher incidence during rainy season
  - Favorable for production of fungal spores (conidia)
- Airborne spores inhaled by susceptible individuals
- Unclear whether people get the disease by eating infected rats, or by inhaling fungi from their feces

Courtesy of: http://medicine.med.nyu.edu/pulmonary/node/673
Diagnosis and Histopathology

- Biopsy of skin lesions, lymph nodes or bone marrow
- The organism can also be identified on peripheral blood smear or bone marrow aspirate
- Fungi shown:
  - spherical or oval in shape
  - basophilic intracellular or extracellular yeastlike appearance on Wright stain, often with clear central septation
- Histopathologic features include granulomatous, suppurative, or necrotizing inflammation
- Polymerase chain reaction (PCR) assay is under evaluation for rapid diagnosis of \textit{P marneffei} infection
Clinical Manifestations

- Fever 99%
- Anemia 78%
- Weight loss 76%
- Skin lesions 71%
- Lymphadenopathy 58%
- Hepatomegaly 51%
- Pulmonary disease/symptom 49%
- Diarrhea 31%
- Splenomegaly 16%
- Oral lesions 4%
Clinical Manifestations cont....

- Duration of symptoms before presentation is 4 weeks.

- Other common manifestations:
  - Skin lesions, anemia, lymphadenopathy, and hepatomegaly with or without splenomegaly.
  - Skin lesions are present in two thirds of cases
    - Include papular eruptions, central umbilicated papules, acnelike lesions and folliculitis.
    - Found on the face, trunk, and extremities.
  - Pharyngeal and palatal lesions
  - Subcutaneous nodules

- Pulmonary symptoms (cough and dyspnea) occur in about 50% of cases.

Courtesy of: http://www.med.cmu.ac.th/student/patho/Kamthorn/050.html
Treatment & Prevention

- Mortality is at a 20% rate with treatment
- Amphotericin B with or without flucytosine, or itraconazole
- Ketoconazole & miconazole
- Newer azoles (posaconazole, ravuconazole, and voriconazole)
- Clinical failure rates:
  - fluconazole (63.8%)
  - amphotericin B (22.8%)
  - itraconazole (25%)
- Primary prophylaxis with itraconazole 200 mg daily can prevent the occurrence of penicilliosis among patients with AIDS
Case 1.

- **Patient:**
  - Located in India
  - 27-year-old male
- Recently developed multiple nodules on his face
- **Other Symptoms:**
  - fever, weight loss, anorexia, and general weakness.
- General examination revealed multiple molluscum contagiosum-like papules of various sizes with central umbilications mainly on his face, trunk, and upper and lower limbs.
Case 1.

- He was diagnosed seropositive for HIV infection.
- Mild anemia, leukopenia, and a raised erythrocyte sedimentation rate (ESR).
- A chest X-ray revealed bilateral patchy pneumonitis, and an ultrasonogram (USG) of the abdomen revealed mild hepatomegaly.
Case 1.

- A portion of the fine needle aspirate (FNA) when cultured yielded a *Penicillium* species
  - red diffusible pigment was produced

- Giemsa-stained smears of the aspirate
  - numerous intracellular and extracellular oval, elongated or sausage-shaped yeast-like cells,
  - cells divided by fission rather than by a budding process.

- Three days before initiation of treatment, the patient died.
Case 2.

- 29 year old
- Male
- Tay Ninh province, Vietnam
- Presented weight loss and a maculopapular rash on his genitalia.
- No previous testing for HIV antibody or virus.
- On examination, the only momentous findings were oropharyngeal candidiasis, cervical lymphadenopathy, and the maculopapular rash on his genitalia.
Case 2.

- Examination of chest and abdomen revealed no abnormalities.
- A chest radiograph appeared normal.
- Blood samples were collected for microbiological culture and HIV testing.
- On the second day of hospitalization, he developed generalized maculopapular rash with pustules and lesions with central necrotic umbilication.
- Results confirmed patient to be HIV positive.
- Culture of his blood sample yielded a red pigment–producing fungus that was subsequently identified as *P. marneffei*.
- Patient died ten hours after discharge.
References


Questions.

1. *P. marneffei* grows best in:
   - Dry temperature
   - Rainy seasons**
   - The cold
   - Heat

2. *P. marneffei* usually affects:
   - The elderly
   - HIV infected patients**
   - Infants
   - Women

3. *P. marneffei* is located in:
   - Southeast Asia**
   - Africa
   - South America
   - The Caribbean

4. All except one are common symptoms of this disease:
   - Cough
   - Fever
   - Lesions
   - Depression**

5. Which is a life cycle stage in *p. marneffei*?
   - Multicellular
   - Unicellular
   - Asexual
   - All of the above**