

Lecture 8:

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Opportunistic mycosis : Penicilloiosis

Penicillium :- is a genus of **ascomycetous** fungi of major importance in the natural environment as well as food and drug production.

Some members of the genus produce **penicillin**, a molecule that is used as an **antibiotic**, which kills or stops the growth of certain kinds of bacteria inside the body. Other species are used in **cheesemaking**.

Penicillium marneffei:- *Penicillium* species are usually regarded as unimportant in terms of causing human disease. ***Penicillium marneffei***, discovered in 1956, is different. This is the only known thermally dimorphic species of *Penicillium*, and it can cause a lethal systemic infection (**penicilliosis**) with fever and anaemia similar to disseminated cryptococcosis.

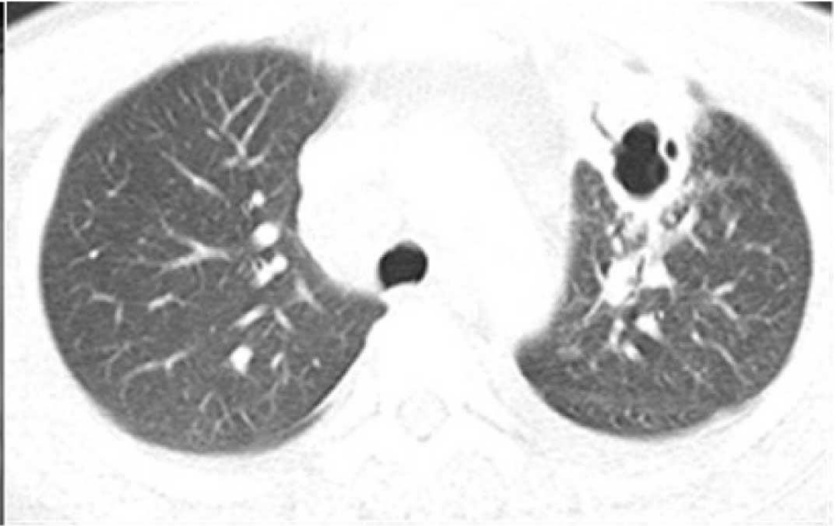
Epidemiology:- There is a high incidence of penicilliosis in AIDS patients in SE Asia; 10% of patients in Hong Kong get penicilloiosis as an AIDS-related illness. Cases of ***P. marneffei*** human infections (**penicilliosis**) have also been reported in HIV-positive patients in Australia, Europe, Japan, the UK and the U.S.

All the patients, except one, had visited Southeast Asia previously. Discovered in bamboo rats (***Rhizomys***) in Vietnam, it is associated with these rats and the tropical Southeast Asia area. ***Penicillium marneffei*** is endemic in Burma (Myanmar), Cambodia, Southern China, Indonesia, Laos, Malaysia, Thailand and Vietnam. Although both the immunocompetent and the immunocompromised can be infected, it is extremely rare to find systemic infections in HIV-negative patients. The incidence of ***P. marneffei*** is increasing as HIV spreads throughout Asia. An increase in global travel and migration means it will be of increased importance as an infection in AIDS sufferers.

Penicillium marneffei has been found in bamboo rat faeces, liver, lungs and spleen. It has been suggested that these animals are a reservoir for the fungus. It is not whether the rats are affected by ***P. marneffei*** or are merely asymptomatic carriers of the disease.

Clinical Presentation:-

Patients commonly present with symptoms and signs of infection of the reticuloendothelial system, including generalized lymphadenopathy, hepatomegaly, and splenomegaly. The respiratory system is commonly involved as well; cough, fever, dyspnea, and chest pain may be present, reflecting the probable inhalational route of acquisition. Approximately one-third of patients may also exhibit gastrointestinal symptoms, such as diarrhea.



Laboratory diagnosis:-

The fact that *Penicillium marneffei* is thermally dimorphic is a relevant clue when trying to identify it. However, it should be kept in mind that other human-pathogenic fungi are thermally dimorphic as well. Cultures should be done from bone marrow, skin, blood and sputum samples. Plating samples out onto two Sabouraud agar plates, then incubating one at 30 °C and the other at 37 °C, should result in two different morphologies. A mold-form will grow at 30 °C, and a yeast-form at 37 °C. Mycelial colonies will be visible on the 30 °C plate after two days. Growth is initially fluffy and white and eventually turns green and granular after

sporulation has occurred. A soluble red pigment is produced, which diffuses into the agar, causing the reverse side of the plate to appear red or pink. The periphery of the mold may appear orange-coloured, and radial sulcate folds will develop. Under the microscope, the mold phase will look like a typical *Penicillium*, with hyaline, septate and branched hyphae; the conidiophores are located both laterally and terminally.

Each conidiophore gives rise to three to five phialides, where chains of lemon-shaped conidia are formed. On the 37 °C plate, the colonies grow as yeasts. These colonies can be cerebriform, convoluted, or smooth. There is a decreased production in pigment, the colonies appearing cream/light-tan/light-pink in colour. Microscopically, sausage-shaped cells are mixed with hyphae-like structures. As the culture ages, segments begin to form.

The cells divide by binary fission, rather than budding. The cells are not yeast cells, but rather arthroconidia. Culturing isn't the only method of diagnosis. A skin scraping can be prepared, and stained with Wright's stain. Many intracellular and extracellular yeast cells with crosswalls are suggestive of *P. marneffei* infection. Smears from bone marrow aspirates may also be taken; this is regarded as the most sensitive method. These samples can be stained with the Giemsa stain. Histological examination can also be done on skin, bone marrow or lymph nodes.



The patient's history also is a diagnostic help. If they have traveled to Southeast Asia and are HIV-positive, then there is an increased risk of them having penicilliosis. Antigen testing of urine and serum, and PCR amplification of specific nucleotide sequences have been tried, with high sensitivity and specificity. Rapid identification of penicilliosis is sought, as prompt treatment is critical. Treatment should be provided as soon as penicilliosis is suspected.

Treatment:-

2 weeks of amphotericin B, then 10 weeks of oral itraconazole.

Genomics Sexual reproduction

P. marneffei had been assumed to reproduce exclusively by asexual means based on the highly clonal population structure of this species. However, studies by Henk et al.(2012) revealed that the genes required for meiosis are present in *P. marneffei*. In addition, they obtained evidence for mating and genetic recombination in this species. Henk et al. concluded that *P. marneffei* is sexually reproducing, but recombination in natural populations is most likely to occur across spatially and genetically limited distances resulting in a highly clonal population structure. It appears that sex can be maintained in this species even though very little genetic variability is produced.