Disseminated Penicillium marneffei infection presenting as cavitary lung lesions in a HIV sero positive patient.

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Abstract: Disseminated Penicillium marneffei infection is an AIDS defining illness in South East Asia and typically presents as pyrexia of unknown origin with pulmonary and skin manifestations and organomegaly. Although pulmonary involvement is a common finding, cavitary lung lesions are an unusual presentation. This paper reports a 30 year old lady from Assam, diagnosed to be HIV sero positive with disseminated Penicillium marneffei infection with multiple cavitatory lesions of the lung.

Keyword: Penicillium marneffei, HIV sero positive, lung cavity

BACKGROUND
Penicillium marneffei is an AIDS defining illness in South East Asian countries including North eastern states of India. Though the typical presentation of the disease is that of a prolonged febrile illness with respiratory and cutaneous involvement and organomegaly, atypical pulmonary manifestations in the form of lung cavi ties and masses have been described. Knowledge of the atypical pulmonary presentations is vital for diagnosis and early institution of anti fungal therapy thereby preventing poorer outcomes in the immuno compromised host.

CASE PRESENTATION
Mrs M, a 30 year old housewife from Assam presented with a 3 month history of low grade fever, mildly productive cough with loss of appetite and significant loss of weight. Her past history is significant for recurrent painful genital ulcers over the past 6 months. Her husband was diagnosed to have acquired immunodeficiency syndrome one year back and had been initiated on anti retroviral therapy.

INVESTIGATION
Oral Ulcers
Laboratory investigations revealed her HIV sero positive status with a CD4+ T lymphocyte count of 35 cells / ml. There was no serological evidence of any other sexually transmitted infections. On examination, she was emaciated, grossly underweight (weight : 22 kg) and had pallor, glossitis and angularcheilitis with no significant lymphadenopathy.

Examination of the oral cavity revealed candidiasis and painless 1cm X 1cm clean based oval ulcers over the hard palate and left buccal mucosa. Examination of the abdomen showed hepatosplenomegaly and multiple superficial painful ulcers over the labia minora. The rest of the systemic examination was unremarkable.

Work up also showed a microcytic hypochromic anemia (Hb:6.9 gmv/dL), peripheral leucocytosis with left shift (Total Count: 10,200 cells/ml, Differential count: Band forms: 2,Neutrophils: 90, Monocytes: 5, Lymphocytes: 3), and hypoalbuminemia (albumin: 2.8gm/dl) with elevated alkaline phosphatase (alkaline phosphatase: 211 IU/ml). Multiple blood cultures drawn were sterile and bone marrow biopsy, cultures and biopsy from the oral ulcers taken were non contributory to the cause of fever. Ultrasound imaging of the abdomen showed necrotic mesenteric adenopathy with a diffuse infiltrative pathology involving the liver. A chest X ray was done and was further corroborated by CT imaging of the chest which showed a thin walled cavitary lesion measuring 5.6 X 3.7 cm in the anterior segment of the right upper lobe and multiple small thin smooth walled cavitary lesions scattered in both the lungs without lobarpredominance.

Chest X Ray CT Thorax
Sputum cultures for Ziel Neisson stains and mycobacterium cultures were negative for Mycobacterium tuberculosis. Sputum samples sent for fungal cultures were however found to be positive for growth of Penicillium marneffei with cultures growing characteristic granular colonies with red diffusible pigment on Sabaraud’s agar at 25 C.

**Sputum Cultures on Sabaraud’s Agar**

**TREATMENT**

Patient was treated for a disseminated Penicillium infection with an induction phase of two weeks of parenteral Amphotericin B at 0.6 mg/kg/day followed by a 10 week course of oral Itraconazole (200 mg twice daily) and advised continuation of a prophylactic dose of Itraconazole (200 mg per day) till CD4+ T lymphocyte counts were above 100 cells/ml for more than 6 months. She was advised initiation of Anti Retroviral Therapy in her home town, under the national programme, after the induction phase of Amphotericin B therapy.

**DISCUSSION**

*Penicillium marneffei* is a dimorphic fungus presenting as an opportunistic infection in endemic regions of South East Asia, with infections in India reported from North Eastern states of Assam and Manipur. *Penicillium* infections are seen mostly in late HIV infections with CD4+ T lymphocyte counts less than 200 cells/ml and are an AIDS defining illness in endemic regions. Patients typically present with systemic complaints like fever, weight loss and malaise. The typical clinical presentation of disseminated penicilliosis includes respiratory complaints, skin lesions, anaemia, lymphadenopathy and hepatosplenomegaly. The most common pulmonary manifestation is cough with chest Xrays of most patients showing diffuse reticulonodular, localised alveolar or diffuse alveolar infiltrates. Cavitary lung lesions as in our patient are an atypical pulmonary presentation and case reports with *Penicillium marneffei* infections presenting as lung cavities in HIV sero positive patients are few with 3 case reports published in 1998. Identification of the organism is crucial as there is good therapeutic response with early institution of treatment while any delay in initiation of antifungal therapy is associated with poor outcome.

The diagnosis of penicilliosis is made through examination of cytology or biopsy specimens with Periodic Acid Schiff and Silver Methanamine stains showing non budding yeast cells with characteristic central transverse septum. Isolation of the organism remains the gold standard for diagnosis with cultures on Sabaraud’s dextrose agar after 7 days of incubation at 25 C showing characteristic granular colonies with red diffusible pigment. The recommended treatment is 2 weeks of intravenous Amphotericin B (0.6 mg/kg) followed by oral Itraconazole (400 mg per day) for 10 weeks to be continued with secondary prophylaxis with Itraconazole 200 mg per day till CD4+ T Lymphocyte counts are more than 100 cells/ml for more than 6 months.

Patients should be initiated on anti retro viral therapy simultaneously or at the end of two weeks of induction therapy with Amphotericin B. In view of data from pharmacokinetic studies suggesting Nevirapine induced metabolism of Itraconazole, patient’s clinical response to therapy needs to be closely monitored.

**LEARNING POINTS**

1. Cavitary lung lesions are an atypical pulmonary presentation of *Penicillium marneffei* infections in the immunocompromised host.
2. Isolation of the organism in fungal cultures is vital for early institution of appropriate anti fungal therapy.

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