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**Case Report**

# Pulmonary penicilliosis in HIV negative child simulating pulmonary tuberculosis

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## ABSTRACT

Penicillium marneffei (*P. marneffei*) is a rare human pathogen, unique among species of penicillium by its thermal dimorphism and its propensity to infect the lungs and reticulo endothelial system and to proliferate within histiocytes either in healthy or immunocompromised hosts. Penicillium marneffei is a rare in HIV negative child. Clinical characteristics of study were 9 years old male presented with fever, cough and loss of appetite for 6 months that persisted despite ante tuberculosis treatment. Broncho alveolar lavage showed typical elements and culture yielded the growth of penicillium marneffei. Outcome of this study was child responded to amphotericin and did not relapse on itraconozole prophylaxis. Penicilliosis mimics pulmonary tuberculosis.

**Keywords:** Fungal infection, Nonresponse to antitubercular drugs, Opportunistic infection, Penicilliosis

## INTRODUCTION

Penicillium marneffei (*P. marneffei*) is a rare human pathogen, unique among species of penicillium by its thermal dimorphism and its propensity to infect the lungs and reticulo endothelial system and to proliferate within histiocytes either in healthy or immunocompromised hosts.[1,2] This infection has been seen in north eastern India.[3] However, none has been reported in who has HIV negative from south India to the best of our knowledge. We are reporting *P. marneffei* infection in HIV negative child with symptoms mimicking tuberculosis, as early diagnosis and treatment improves the outcome.

## CASE REPORT

9 years old male, only child of non-consanguineous parentage hailing from low socioeconomic status presented with fever cough and loss of appetite for 6 months. Fever was on and off, low grade, intermittent, more during night time. Cough was associated with expectoration of greenish, copious sputum without having postural variations. Child has been treated as sputum negative pulmonary tuberculosis as per RNTCP. But there was no response to anti tubercular treatment. Perinatal and developmental history was normal. Child has been immunized up to date. Child was sick looking with: temperature 102 F, pulse rate 120/minute, respiratory rate 50/minute, blood pressure 106/70 mmHg Spo2 of 96 in room air. Child has weight of 24 kgs, height of 1.24 meter, body mass index- 13 kg/m, pallor, grade 3 clubbing. There was decreased chest expansion in right side with no mediastinal shift. Impaired note and bronchial breath sounds were heard in infra scapular, mammary, infra mammary and infra axillary regions on right side.

Other systems were normal clinically. Investigations revealed: Haemoglobin- 9.6 g/dl, total counts- 6,800/micro L, lymphocytes-24%, neutrophils-65%, eosinophils-5%, monocytes 6% and platelets- 7.72 lakhs/microL. ESR-50 mm/hr. Chest x-ray was

suggestive of right middle and lower lobe consolidation (Figure 1A). There was a reversal of albumin/globulin ratio (3.7/4.4). Liver enzymes, renal function test and serum electrolytes were within normal limits. Computed tomography of thorax suggested right middle and lower lobe consolidation (Figure 2A and B). Broncho alveolar lavage, wright stained microscopic examination revealed intracellular and extra cellular basophilic, spherical, oval and epithelial yeast like organism with few central septations suggestive of *P. marneffei* infection. Same was confirmed by culture. ELISA for HIV was negative, IgA-188 mg/dl (17-318), IgG- 2430 mg/dl (350-1620 mg/dl) IgE - 269.6 IU/ml (up to 90 IU/ml) C4 was 41 mg/dl (14-44 mg/dl); C3 was 146 mg/dl (70-170 mg/dl). CD3 cells were 76% of total lymphocyte count, CD4 - 36%, NK cells 8% and CD 19 - 14% of lymphocyte count. NBT test was negative. Child was treated with amphotericin B (1 mg/kg) 25 mg in 30 ml 10% dextrose slow infusion over 4 hours for 2 weeks.

Renal functions and serum electrolytes were normal during treatment. Clinical and radiological improvement was observed in 2 weeks (Figure 1B and 2B) subsequently, Itraconazole 100 mg (4 mg/kg) was given once daily for 2 weeks with monitoring QT prolongation and arrhythmias followed by fluconazole 6 mg/kg orally once a week as parents insisted discharge in view of difficulty in monitoring in remote place. However, there was a recurrence of symptoms and radiological signs while on fluconazole prophylaxis. Symptoms and signs disappeared with itraconazole 4 mg/kg once a day. Child is asymptomatic at latest follows up. Long term continuation of itraconazole was advised.

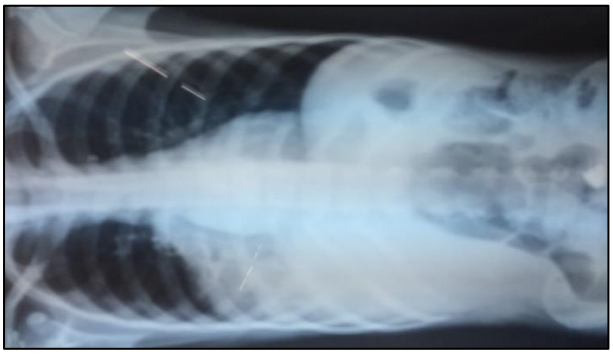

**Figure 1 (A): Chest X-ray of right middle and lower lobe consolidation.**

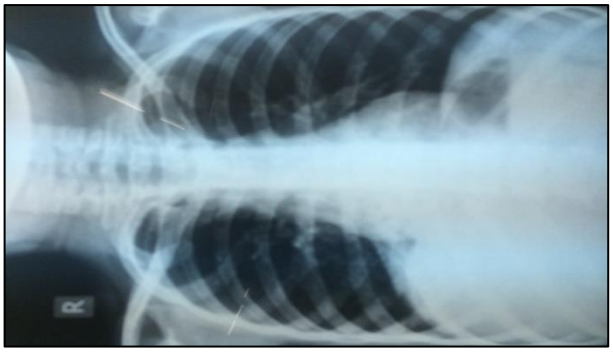

**Figure 1 (B): Chest X-ray of resolution of consolidation with amphotericin treatment.**

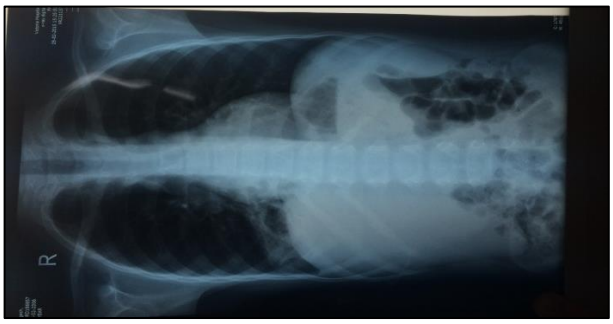

**Figure 1 (C): Chest X-ray of recurrence of consolidation while on fluconazole prophylaxis.**

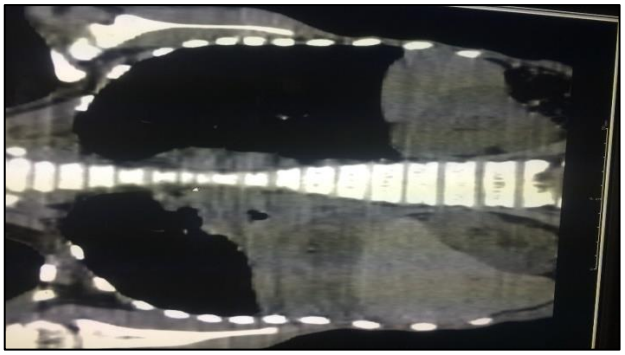

**Figure 2 (A): CT thorax of right middle consolidation.**

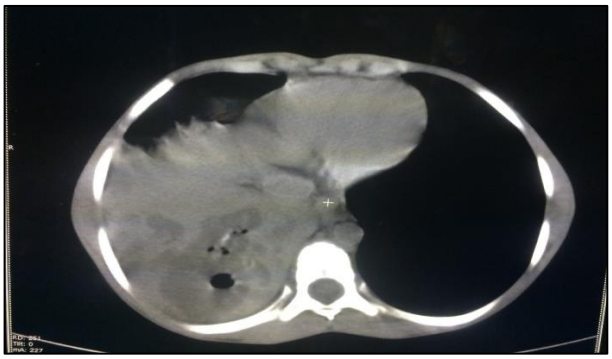

**Figure 2 (B): CT thorax of and lower lobe consolidation.**

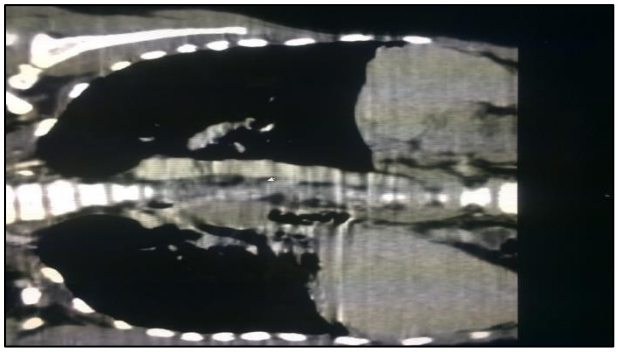

**Figure 2 (C): CT thorax of resolution of right middle lobe consolidation with treatment.**

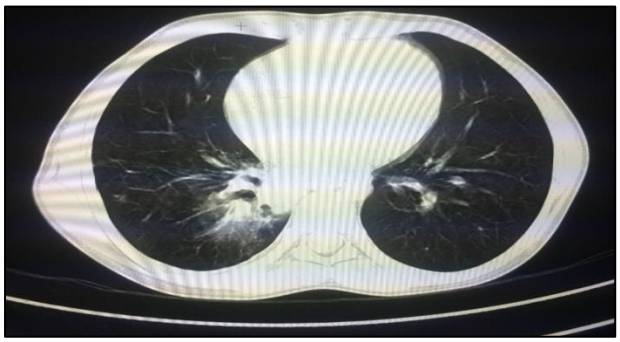

**Figure 2 (D): CT thorax of resolution of lower lobe consolidation with treatment.**

## DISCUSSION

Most *P. marneffei* infections occur in immunodeficiency patients. Only 32 (6.2%) of 509 patients, all aged less than 16 years, with penicilliosis were being HIV negative in one report.[4] In these 32 patients, 8 had primary immunodeficiency or blood disorder and 4 had abnormal immune functions and unknown in rest.[4] Non HIV infected patients may contribute for 6.2 - 20% of all penicilliosis.[4-6] To best of our knowledge, ours is the first HIV negative penicilliosis in child from south India who was initially misdiagnosed as pulmonary tuberculosis. In fact, this was diagnosed while working for non-responsiveness to standard antitubercular treatment.

Lymphopenia with low NK cell count and phagocyte defect, hyper IgE syndrome and functional defect in interleukin-12/ interferon-gamma axis has observed in these cases.[4,7] Chronic granulomatous disease, severe combined immunodeficiency, myeloperoxidase deficiency, leukocyte adhesion deficiency, hyper IgM syndrome, and common variable immunodeficiency have also been implicated. Increased total white cell count, CD4/CD8 > 0.5, positive blood culture than HIV positive group.[8] CD4, CD8, CD4/CD8 ratio, NK cells, immunoglobulin, and complements were within normal limits in our case. Body reaction to infection is dependent on level of immunity. Granulomatous and suppurative reaction seen in normal immunity and allergic and necrotizing pneumonia in immunodeficiency.[1]

Fever, multiple organ dysfunction and poor prognosis are common clinical characteristics. Non HIV infected patients do have longer duration of Illness, intermittent fever, subcutaneous nodules, abscess while cutaneous manifestations and disseminated infection predominate (4 of 5 non HIV infected patients) in one report.[4] Single or multiple cavities lung mimic tuberculosis or malignancy.[9] These lesions heal by interstitial fibrosis with successful treatment.[9]

Presumptive diagnosis was made by microscopy examination of wright's stained or meth enamine silver stained preparations of Broncho alveolar lavage.[2,10] Intracellular and extracellular basophilic, spherical, oval, and elliptical yeast like organism with or without clear central septaion is characteristic of P marneffei.[2,5,10] Diagnosis was confirmed by culture of the organism.[2]

Treatment involves amphotericin B (1 mg/kg) intravenous once a day for 14 days, voriconazole in those unresponsive to amphotericin B followed by itraconazole. Our patient responded very well to amphotericin B alone. Fluconazole prophylaxis at dose of 6 mg/kg once a week for one year to protect relapse has been advised.[7]

However, there was relapse in our patient when itraconazole was switched over to fluconazole. Itraconazole is available in capsule formulation, administered orally at 4-5 mg/kg once or twice a day. Itraconazole solution is preferred because of better bioavailability. Patients are monitored for QT prolongation and arrhythmias and are contraindicated in ventricular arrhythmias, left ventricular dysfunction, prolonged QT intervals. During prolonging QT interval should be avoided. Nearly 13% relapse within 6 months of stopping treatment. Long term prophylaxis with itraconazole than fluconazole is advised to prevent relapse.

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