Case Report

Hoarseness due to penicillium marneffei infection – an unusual presentation

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ABSTRACT

Penicillium marneffei is a dimorphic fungus causing infection mainly in immunocompromised individuals, especially those with HIV infection. Penicillium marneffei is an important opportunistic pathogen of HIV infection in South East Asia including Manipur. Common clinical manifestations are fever, cough, weight loss, generalised lymphadenopathy, and papulonodular eruptions. We report an unusual case of HIV patient with Penicillium marneffei infection presenting as hoarseness.

Key words: *ART, HIV, Manipur, penicillium marneffei, vocal cord*

Introduction

Penicillium marneffei, a dimorphic fungus that is endemic in South East Asia, causes disease in both immunocompetent and immune-compromised hosts. The fungus was first isolated from the bamboo rats (Rhizomys sinensis) in Vietnam in 1956. [1] It was identified as a new species by Segratain, who named the fungus Penicillium marneffei. [2] The first spontaneous infection in a human was reported in 1973 in a 61 years old American minister with Hodgkin's disiease, who had travelled to South East Asia one year before. [3] Disseminated infection usually presents with fever, weight loss, anaemia, generalised lymphadenopathy, hepato-splenomegaly, cough and may rapidly progress to death if not treated. [4] Skin lesions commonly occur on the face, upper trunk and extremities. Papular skin lesions with central necrotic umbilication occur more commonly in HIV infected patients and tend to involve the palatal, pharyngeal regions and other organs like bone marrow, intestine, kidney, pericardium and meninges. [5] Intravenous Amphotericin B followed by oral Itraconazole is the treatment of choice for P. marneffei infection.

Case Report

A 33 years-old male on Antiretroviral Therapy (ART) since 2012 presented with two months history of progressive hoarseness, fever and cough with expectorations at ART Centre, Regional Institute of Medical Sciences (RIMS), Imphal. Hoarseness was gradual in onset, slowly progressive aggravated by repeated use of voice which was associated with mild difficulty and pain on swallowing, more with solid than liquids. There was no associated stridor or wheezing. Fever was low grade and intermittent in nature, not associated with chills, headache or convulsions and subsided on taking Paracetamol tablet. There was cough with whitish scanty sputum in the morning without associated haemoptysis, chest pain. He also had 2 months history of painless, non pruritic skin eruptions on his face, chest, back and proximal extremities. He had a history of multiple blood transfusion for surgical operation of bullet injury of left shoulder

with exit wound in the right infra-axillary region in 2001. He was also treated for Pulmonary tuberculosis 5 years back. ART was initiated in 2012 with Stavudine, Lamivudine and Efavirenz. Since August 2015 the regimen had been changed to second line ART (Stavudine, Lamivudine, Lopinavir and Ritonavir) due to treatment failure with CD4 count 5 and HIV viral load of 73600 copies/ml. The patient had no other significant past history of illness. He is a non smoker and non-alcoholic and non- vegetarian.

On physical examination, he was conscious, co-operative and oriented to time, place and person. His body temperature was 98.8˚F, Blood Pressure of 110/70 mmHg and pulse rate of 72/minute. His respiratory rate was 18/minute and SPO2 of 97% at room air. His weight was 58 kgs and BMI was 21.30 kg/m². Pallor and oral candidiasis were present; there was no lymphadenopathy. Multiple discrete papules and nodules with central umbilication of varying size (5-20mm) situated over the face, chest, abdomen, shoulders, back and proximal thigh were present (Fig.1). There was no hepatosplenomegaly and other systemic examinations were normal.

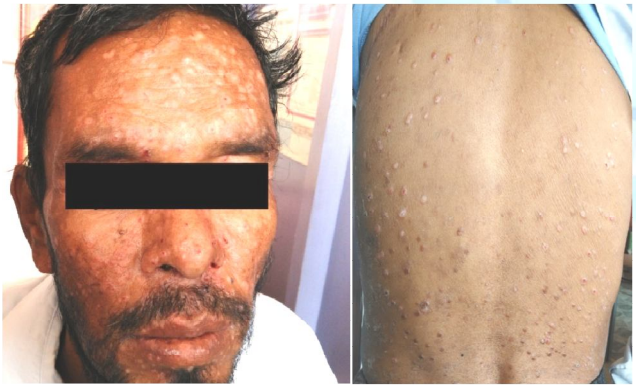

Fig.1 Papulonodular skin lesions with central necrotic umbilications on the face and back

His haemoglobin was 6.3gm/dl, total leukocyte count (TLC) 7700/µl, differential leukocyte count (DLC) was Neutrophils 70%, Lymphocytes 28%, Monocytes 1%, Eosinophils 1%. RBC count of 1.75million/cmm with normocytic, normochromic blood picture. His platelet count was 3.15 lakhs/cmm. The LFT and KFT were normal. TSH was 1.85 mIU/L. Hepatitis B Surface antigen, Hepatitis C Virus antibody and VDRL test were negative. His initial CD4+T lymphocyte count was 32 c/mm3 and latest was 156/mm3 and last HIV RNA level was 73600 copies/ml. Skin biopsy taken from the back and face revealed dermis displaying foamy lymphocytes in sheets with numerous yeast forms of a fungus dividing by binary fission morphologically resembling Penicillium marneffei and stroma showed minimal lymphocytic infiltrations. (Fig.2) Diagnosis was confirmed by culture of skin samples on Saboraud's Dextrose Agar (SDA) with antibiotics and incubated at 25˚C and 37˚C. Culture revealed flat, moist, radially folded colonies with characteristic red pigment diffusing into the agar and mould to yeast conversion at 37˚C.

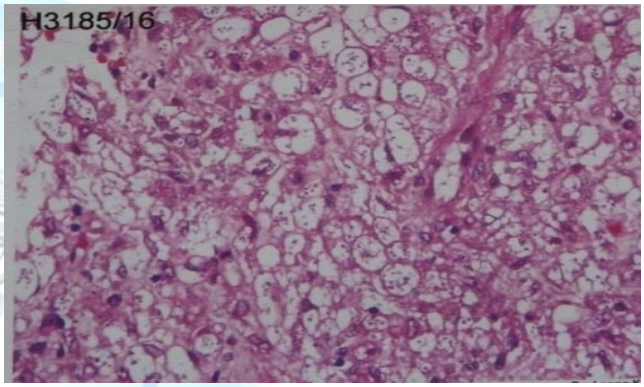

Fig. 2 Skin biopsy showing numerous yeast forms of a fungus

Video laryngoscopy revealed thick epiglottis with widespread pale nodules over the pharyngeal wall. There was congestion of laryngeal inlet, thickened right vocal cord with nodular mass and retarded mobility. (Fig.3A) Left vocal cord and pyriform sinuses were normal. The patient was initiated on Inj. Amphotericin B 0.6mg/kg IV daily after a test dose for 14 days followed by oral Itraconazole 200mg twice daily for 10 weeks and he was advised to continue oral Itraconazole 200mg once daily as maintenance dose till his next CD4 report is available. After 10 weeks of treatment, the patient got symptomatic improvements in the hoarseness and the skin lesions have healed. Laryngoscopy repeated after 10 weeks of treatment revealed normal vocal cord and recession of the nodules. (Fig.3B)

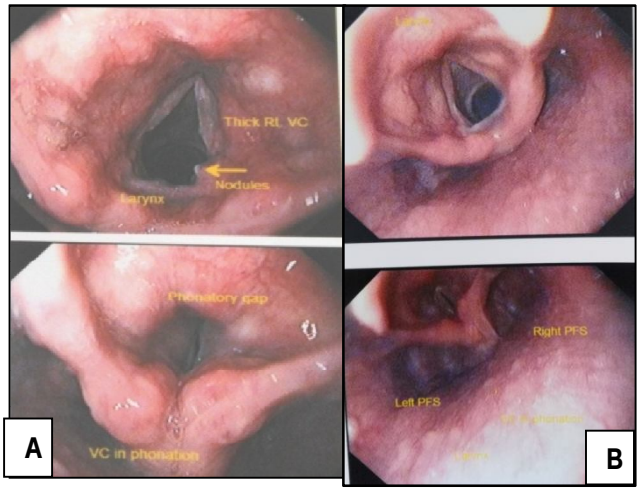

Fig.3 (A) Video laryngoscope showing thick right vocal cord with nodular mass
(B) Recession of the nodular mass after 10 weeks of treatment

Discussion

Penicillium marneffei is classified under the class, Ascomycetes, genus Penicillium and subgenus Beverticillium. It is the only penicillium species to cause significant human disease. [1] Penicillium marneffei, an important opportunistic infection in Southeast Asia including Manipur and is classified as an AIDS defining illness. It can be said that Manipur, a north-eastern state of India is bordering Myanmar, a country with a high incidence of HIV/AIDS and also known to be endemic for Penicillium marneffei infection. Manipur has cultural and ecological similarities to Myanmar and neighbouring countries of South East Asia. Bamboo groves which are the habitat of bamboo rats are found in eastern India. [5] It is the second commonest opportunistic fungal infection following oropharyngeal candidiasis in early part of 21st century.[6] P. marneffei infection occurs late in the course of HIV infection, when CD4 lymphocyte counts is <100 cells/cmm. [5]

P. marneffei infection was first reported in HIV infected patients in 1988. [7] The number has increased markedly over the past 15 years as this fungus has emerged as an important cause of fever, anemia, weight loss, generalized lymphadenopathy and skin rash in patients with AIDS. It is considered as an AIDS defining illness in those parts of the world where it occurs. The mode of infection is considered to be due to inhalation of conidia reaching lungs and subsequent disseminations to the reticuloendothelial system when the host experiences immunosuppression. Some patients with only hepatic penicilliosis had marked increase in serum alkaline phosphatase levels. [8]

The skin lesions of P. marneffei, which occur on the face, upper trunk and extremities, may manifest as papules, pustules, abscesses, nodules, or ulcers. The lesions typically are umbilicated papules mimicking molluscum contagiosum. [9] Diagnosis is by identification of the organism from smear, histopathologic sections and confirmed by culture. Treatment with Amphotericin B (0.6 mg/kg) for 2 weeks followed by oral Itraconazole 400 mg daily for 10 weeks has resulted in excellent response rates. [10] Voriconazole can be used as alternative as it has been found to be highly active in vitro against P. marneffei and may thus provide another option for treatment or prophylaxis. [11] All patients who successfully complete treatment for penicilliosis should receive secondary prophylaxis (chronic maintenance therapy) with oral Itraconazole 200 mg/day and should be started on ART if that was not done during acute disease. Secondary prophylaxis for penicilliosis can be discontinued in AIDS patients who receive combination ART and have CD4 cell counts >100 cells/mm3 for at least 6 months. Secondary prophylaxis should be reintroduced if the CD4 cell count decreases to <100 cells/mm3. [12] HIV patients with Penicilliosis involving different systems of the body have been reported in literatures. However, Penicilliosis with involvement of vocal cord has not been reported so far in literatures to the best of our knowledge and our case is the first reported case of Penicilliosis involving vocal cord. Therefore, clinicians need to maintain a high index of suspicion for making an early diagnosis of Penicilliosis when HIV infected person presents with hoarseness and papulonodular eruptions.

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