Talaromyces (*Penicillium)* marneffei and Mycobacterium tuberculosis coinfection in a HIV negative patient in Amritsar Punjab, India

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Abstract

A 54-year-old, male patient with a history of Pulmonary Tuberculosis and Diabetes mellitus for the past 20 years was admitted to a tertiary care hospital with chief complaints of high-grade fever with chills, productive cough and a one month history of loss of appetite and generalized malaise. On FNAC of cervical lymph nodes; impression of tubercular pathology (AFB positive) was reported. Talaromyces (*Penicillium)* marneffei and Mycobacterium tuberculosis co-infection was confirmed. *Talaromyces marneffei* (*Penicillium marneffei*) is a thermally dimorphic fungus that can cause severe infections particularly in immunocompromised patients was first discovered in 1956 in the regions of Southeast Asia. It exists as mycelia form at 25 °C and yeast like form at 37 °C. A large number of *T. marneffei* infected patients who are HIV negative have been reported in recent years.

Key words: Talaromyces (*Penicillium)* marneffei, Mycobacterium tuberculosis, co infection

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Introduction

Talaromyces marneffei (*Penicillium marneffei*) is a thermally dimorphic fungus that can cause severe infections particularly in immunocompromised patients was first discovered in 1956 in the regions of Southeast Asia [1,2]. The first report of human infection was reported by G. Segretain who accidentally pricked his finger with a needle containing the yeast cells of *P. marneffei*. A small nodule appeared at the site of infection followed by lymphangitis and lymphadenopathy 9 days after the accident [3]. There is no other species of this genus which is dimorphic in nature [4]. It exists as mycelia form at 25 °C and yeast like form at 37 °C. Patients with HIV/AIDS have been reported to be vulnerable to *T. marneffei*. [5,6]. However, a large number of *T. marneffei* infected patients who are HIV negative have been reported in recent years [7,8,9]. 55 to 77% of cases may have other concurrent opportunistic infections such as tuberculosis, disseminated herpes zoster, *Pneumocystis jiroveci* pneumonia, cryptococcosis, toxoplasmosis and should be watched out for [10,11,12].

Case History

A 54-year-old, male patient with a history of Pulmonary Tuberculosis and Diabetes mellitus for the past 20 years was admitted to a tertiary care hospital with chief complaints of high-grade fever with chills, productive cough and a one-month history of loss of appetite and generalized malaise. He had lost approximately 10 kg body weight in 2 months. He had a history of Pulmonary Tuberculosis infection diagnosed in 1999 but was not on treatment until 2013. Antitubercular therapy was subsequently initiated, but the patient had discontinued his medication 8 months prior. The patient was a known case of Diabetes Mellitus type2 since the last 20 years and is on regular medication. His body temperature was 101.5°F; blood pressure was 142/88 mmHg; pulse rate 86/minute; respiratory rate, 22/minute; and oxygen saturation,95% in ambient air. On examination multiple cervical enlarged lymph nodes were palpated and hepatosplenomegaly was noted. The patient's laboratory test results were as follows: Total leucocyte count of 5,730/mm^3; Differential leucocyte count of 61/35/02/02/0 (neutrophils/ lymphocytes/monocytes/eosinophils/basophils); hemoglobin concentration 8.2 g/dL; platelet count 1.5 lakh/mm^3. The glycosylated hemoglobin levels (HbA1C) was 0.9% indicating a fair to poor control of diabetes. The serum urea levels were 45mg/dl; serum creatinine levels were 1mg/dl, serum uric acid level was 6.5 mg/dl; total serum bilirubin 0.73mg/dl,

Manuscript received: 26th October 2019
Reviewed: 4th November 2019
Author Corrected: 10th November 2019
Accepted for Publication: 14th November 2019

SGOT/SGPT OF 36/ 39 IU/L. The serum sodium concentration 129 mmol/L; and potassium concentration 3.7 mmol/L. The fasting blood sugar level was 270mg/dl. On FNAC of cervical lymph nodes; impression of tubercular pathology (AFB positive) was reported. The HRCT chest revealed diffuse miliary nodules in both the lungs along with multiple patchy exudative shadows in the superior lobes and right inferior lobe, consolidation of the right superior lobe with multiple hilar and mediastinal lymphadenopathies .Sputum sample was collected in a clean wide mouth container under aspetic precautions for the isolation of respiratory pathogens, including mycobacteria and fungi. It was subjected for direct examination and for the culture. On KOH mount, no fungal elements were seen. Gram's stain shows yeast cells as gram positive oval cells. The sputum sample was inoculated on Sabouraud's dextrose agar (SDA) at 37°C and 22°C. After ten days of incubation, SDA at 37°C showed no growth but SDA at 22°C showed yellowish green velvety colonies with brick red-coloured pigment on the reverse. Wet mount with Lactophenol cotton blue showed brush-like structures typical of the genus *Penicillium*, i.e., hyaline, septate hyphae with conidiophores with four to five short, broad metulae, each bearing four to six phialides with oval conidia. Subculture was done to demonstrate dimorphism. The fungus was inoculated on to Sabouraud's dextrose agar plate at 22°C and at 37°C. Mycelial forms were seen at 22°C and yeast forms were seen at 37°C. The isolate was identified as *T. marneffei*. The patient was started on Itraconazole200mg twice daily.

Discussion

Talaromyces marneffei (formally *Penicillium marneffei*) is a thermally dimorphic and pathogenic fungus that is a major cause of morbidity and mortality among HIV positive and other immunocompromised patients who reside in, or travel to, regions where this fungus is endemic. *T. marneffei* is endemic to southern China, Taiwan, Hong Kong, and other parts of southeast Asia, particularly Northern Thailand, Vietnam, Cambodia, and northeastern India [13,14]. Prior to 2015, *T. marneffei* was known as *Penicillium marneffei*.

The disease caused by *T. marneffei* was referred to as penicilliosis but is now called talaromycosis [15]. In recent years, it has been increasingly seen both in AIDS patients and in HIV-negative individuals. Among HIV negative patients with a history of pulmonary tuberculosis [16] or chronic obstructive pulmonary disease (COPD), T. marneffei infection has been reported [17].

The main route of transmission of T. marneffei is by inhalation; rarely is by direct animal contact. The typical clinical features are fever, weight loss, skin lesions, generalized lymphadenopathy, hepatosplenomegaly but the severity of the disease depends on the immune status of the patient.[18] The patient in this case was a male and non-HIV-infected patient but his lung immunity was probably impaired due to long-standing pulmonary tuberculosis.

The isolation of *T. marneffei* in HIV negative Patient is in consonance with a large multi-centric study done in Nanfang Hospital, Southern Medical University, Guangzhou, China for understanding of this disease and contribute to an appropriate regime of therapy.[19] A study conducted in Chiba University, Chiba, Japan showed a Disseminated Talaromyces (Penicillium) marneffei and Mycobacterium tuberculosis coinfection in a Japanese Patient with Acquired Immunodeficiency Syndrome [20]. Diagnosis of *T. marneffei* infection is made by visualization of the organism in clinical specimens by microscopy or by isolation of the organism on culture. The gold standard in diagnosis of talaromycosis is positive culture from appropriate clinical specimen. *T. marneffei* is a biohazard to laboratory staff [13] Slide cultures should not be performed; specimens and cultures should be handled in a biosafety level 3 containment or above [21].

Although methods have been developed for the detection of *T. marneffei*-specific antibodies and antigens, no standardized commercial serological assays are available.

Therefore, serology is not widely used for the diagnosis of *T. marneffei* infection [13,14]. Treatment with itraconazole alone has also been shown to be effective but is associated with higher relapse rate.

It has been suggested that itraconazole alone 400 mg/day for 8 weeks could be considered for mild disease, followed by maintenance therapy with 200 mg per day to prevent relapse [22].

Conclusion

In summary, our study reports a case of *T. marneffei* and M. tuberculosis coinfection in a HIV negative patient. This study invites clinicians to consider *T. marneffei* infection in non-HIV-infected patients with underlying diseases because early diagnosis and timely treatment can lead to reduction in the mortality associated with *T. marneffei*.

Funding: No funding sources
Conflict of interest: None declared

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How to cite this article?

Chalana M, Oberoi L. Talaromyces (*Penicillium)* marneffei and Mycobacterium tuberculosis coinfection in a HIV negative patient in Amritsar Punjab, India. Trop J Path Micro 2019;5(11): 959-961.doi:10.17511/jopm.2019.i11.20