International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

*Case Report .*

# Disseminated Tuberculosis and Candidiasis in an Immunocompetent Individual: A Case Report

**Shalini M[1], Vazhavandal G[2*], Madhan Mohan K[3], Vallab Ganesh B[4], Thirumalaikolundusubramanian P[5], Uma A[6]**

**[1]Post Graduate, [2*]Associate Professor, [6]Professor, Department of Microbiology,**
**Chennai Medical College Hospital and Research Centre (SRM Group), Tiruchirapalli, India**
**[Affiliated to The Tamilnadu Dr. M.G.R. Medical University, Chennai]**
**[3]Assistant Professor, Department of Chest & TB,**
**Chennai Medical College Hospital and Research Centre (SRM Group), Tiruchirapalli, India**
**[Affiliated to The Tamilnadu Dr. M.G.R. Medical University, Chennai]**
**[5]Professor, Department of General Medicine,**
**Chennai Medical College Hospital and Research Centre (SRM Group), Tiruchirapalli, India**
**[Affiliated to The Tamilnadu Dr. M.G.R. Medical University, Chennai]**
**[4]Scientist, Department of Microbiology, Manipal University, Manipal, Karnataka, India.**

## ABSTRACT

Immunosuppressive individuals are very much prone to various opportunistic infections including tuberculosis and candidiasis. However, immunocompetent patients may have these co-infections very rarely. In this case study, we report a case of an immunocompetent female patient diagnosed with *Mycobacterium tuberculosis* and *Candida* co-infections. The patient presented with the diarrhea, low grade fever, dyspnea, anorexia and hemoptysis with the weight loss of 10kgs within 5 months. She had history of exposure to tuberculosis with her father who died of the disease. She was unmarried. On clinical examination, she was tachypnic, normotensive, non-icteric and white patches were seen over the tongue and palate. Chest auscultation revealed normal vesicular breath sounds with scattered bilateral course crepitations. Laboratory investigations revealed hemoglobin (6.1g%) and other biochemical parameters were normal; Chest x-rays revealed bilateral infiltrations; Sputum was positive for acid fast bacilli and *Candida tropicalis* was isolated from throat swab, urine and oesophagal biopsy. Stool sample was negative for Pneumocystis, Cryptosporidiosis, Isosporiasis and Cyclosporiasis. The $CD_4$ count was less than 150; but serological tests for HIV, hepatitis B and C were non-reactive. After months of Anti- tuberculous therapy (ATT) and fluconozole, Chest x-ray, sputum microscopy and *Candida* screening was negative. Pulmonary tuberculosis and fungal co-infections are not common in immunocompetent patients; thus this study is a rare case presentation.

**Keywords:** Pulmonary Tuberculosis, Candidiasis, Immunocompetent, $CD_4$

***Correspondence to:**

**Dr. G. Vazhavandal,**
Associate Professor of Microbiology,
Chennai Medical College Hosptial and Research Centre,
(SRM Group), Tiruchirapalli.

**Article History:**

**Received:** 12-03-2017, **Revised:** 24-03-2017, **Accepted:** 30-03-2017

| Access this article online | |
|---|---|
| Website: www.ijmrp.com | Quick Response code |
| DOI: 10.21276/ijmrp.2017.3.2.074 | |

## INTRODUCTION

Tuberculosis (TB) remains an infectious disease causing significant morbidity and mortality on a global scale. India is the country with the highest burden of TB. The World Health Organization (WHO) statistics for 2015 reported an estimated incidence figure of 2.2 million cases of TB in India out of a global incidence of 9.6 million. Every second a person gets infected by the tuberculus bacillus in the world, not all infected individuals have clinical disease.[1] The bacillus causes the disease when the immune system is weakened. The predisposing conditions include human immunodeficiency virus infection (46% of patients), immunosuppressive therapy (21%), alcoholism (12%), diabetes mellitus (12%), and hematologic disorders (8%). Out of them, 17% did not have any immunological disorders.[1] By means of hematogenous or lymphatic dissemination or contiguity, tuberculosis affects various internal organs.[2]

Miliary TB results from massive lymphohaematogeneous dissemination from a *Mycobacterium tuberculosis* laden focus. It is often a puzzling disease due to a myriad of clinical presentations and atypical radiologic findings. The cases of disseminated TB have recently been increasingly recognized in adults; hence

mortality remains high despite available effective therapy. In immunocompetent adults, miliary TB accounts for less than 2% of all TB cases and up to 20% of all extra-pulmonary TB cases.[3] The control of TB has been challenging because of the natural history of the disease and numerous manifestations.

Respiratory candidiasis secondary to pulmonary tuberculosis has been reported in the past has gained more relevance recently due to increased use of broad spectrum antibiotics and immunosuppressive drugs. The synergistic growth promoting association of *Candida* and *M. tuberculosis* has also been documented experimentally.[4] A correlation of *Candida* positivity with duration of illness was found, higher the duration of illness more was the percentage of positivity.[5]

Although *Candida albicans* continues to be the most predominant species in pulmonary candidiasis, several non albicans *Candida* species are also reported increasingly.[6] We report a young woman who developed active pulmonary and intestinal tuberculosis with esophageal candidiasis due to poor nutrition and anemia.

## CASE REPORT

A 30-year-old woman presented to the chest physician in rural teaching hospital with chief complaints of diarrhea, low grade fever and dyspnoea of seven days duration. She also complained with anorexia and productive cough for the past one month which was not associated with haemoptysis. Weight loss was present (approximately of 10kgs within 5 months). She had a past history of exposure to an active case of tuberculosis, from which her father died twenty years back**.** Her menstrual history recorded that she had complaints of irregular menstrual cycles with oligomenorrhoea. There was no history of any hospitalization, previous surgical exposure or any exanthematous illness in the last one year. She is unmarried and no history of any sexual activity. On clinical examination, she was febrile with core temperature of 101$^{o}$C, pallor and tachypnic with respiratory rate of 22/min, pulse rate of 80 beats/min. She was normotensive and the pulse oxymetric reading was 96% on air. Her height was 153cm, weight (on admission) was 42kg, and body mass index was 17.9kg /m2 (underweight). No icterus, clubbing, pedal edema and generalized lymphadenopathy. Oral examination revealed whitish patches on tongue and palate suggesting oral candidiasis. Chest auscultation revealed normal vesicular breath sounds with scattered bilateral coarse crepitations. On abdominal examination, abdomen was soft and there was no organomegaly. There was neither distension nor tenderness. Cardiovascular, neurological and genital examinations were normal.

Her laboratory investigation revealed microcytic hypochromic anaemia with relative leukocytosis. Haemoglobin 6.1 g%, RBC 3,000,000/ mm$^3$, MCV 60fl, MCHC 300g / l, WBC 15,000 cells/ mm$^3$, differential count – neutrophils 45%, lymphocytes 45%, monocytes 10%, platelets 2,50,000/cu mm with high Erythrocyte sedimentation rate (ESR) of 120mm/hr. Her serum iron level and serum ferritin levels were low (5.1 µg/l and 20 ng/l respectively) and iron binding capacity was high (33.1 µmol/l). The blood picture revealed microcytic hypochromic anaemia with toxic granules and vacuolations in neutrophils indicating severe bacterial infection. The peripheral smear was negative for malarial parasite. Her renal and liver functions were normal. Her fasting blood sugar and lipid profile were normal. Chest X-ray showed bilateral infiltrations in upper and mid zone and a cavitatory lesion on the right upper zone with right sided pleural effusion. Ultrasound scan of abdomen and pelvis showed mild ascites, no organomegaly and lymphadenopathy.

The sputum smear was positive for Acid fast bacilli (AFB) with 3+ grading as per RNTCP guidelines and stool smear was also positive for AFB. Her sputum was also examined for the presence of opportunistic pathogen like *Pneumocystis jiroveci* and found to be negative. Stool sample was negative for opportunistic parasites (*Cryptosporidium, Isospora* and *Cyclospora*). Upper endoscopy was done as she complained of dyspagia on the second day of admission, further revealed yellowish white plaque like lesions of the oesophageal mucosa. A provisional diagnosis of esophageal candidiasis was made, based on the endoscopic findings and a biopsy was performed. Grams staining, culture and histological examination of the endoscopy biopsy specimen revealed the presence of *Candida*.

Two throat swabs were taken for microbiological examinations; one throat swab was used for direct microscopic examination which revealed the presence of 3-4 pus cell/HPF, pseudohyphae and Gram positive budding yeast cells. And the other swab was used for culture which showed the presence of small curdy white colonies on 24hrs of incubation and was confirmed to be *Candida*. Urine routine examination by wet mount preparations, there was plenty of pus cells/HPF and budding yeast cells was found and urine culture revealed the *Candida*. Stool culture also had budding yeast cells. All these *Candida* isolates when subjected to speciation by the conventional methods like Germ tube test, *Candida* CHROM agar, Dalmau technique, sugar fermentation and sugar assimilation and was confirmed as *Candida tropicalis,* whereas *Candida parapsilosis* was isolated from the stool sample. The antifungal susceptibility pattern was also the same for all the isolates. Her $CD_4$ count was 150, whereas her HIV serology and PCR were negative. Serological tests for Hepatitis B and C viruses were also negative.

The patient was started with anti-tuberculus treatment (ATT), DOTS regimen under category 1 of Revised National Tuberculosis Control Programme (RNTCP) of India, comprising of isoniazid, rifampicin, pyrazinamide and ethambutol for two months (intensive phase) followed by isoniazid and rifampicin for four months (continuation phase) along with full course of fluconazole (150mg once daily for 30 days) for candidiasis. She was given supportive therapy in the form of fluids, packed cells transfusion and other symptomatic management. After 3 weeks, $CD_4$ count was done again which has increased to 700 cells/cu.mm of blood and the other fractions were normal.

She was discharged after counseling and advised for regular follow up visits. She was reviewed at the medical clinic after 2 months. Stool AFB was done showed negative but sputum AFB was 1+, since the smear reversion has not occurred even after 2 months of intensive phase, so she was advised to continue the intensive phase for one more month. After a month, the sputum AFB was found to be negative. The reversal of AFB negativity was prolonged, this may be due to her poor nutritional status and anemia. After 3 months of intensive phase she was advised for 6 months of continuation phase. The chest X-ray was taken at three months, it shows resolving infiltration and pleural effusion. The patient completed 9 months of anti-tuberculosis treatment. An USG abdomen was done and there was no ascites. The clinical

course, outcome and follow up were uneventful. She regained her weight (after ATT – 55 kgs).

Two months after completion of ATT course, she visited chest physician clinic with complaints of productive cough and dyspnoea. Sputum AFB was done and was found to negative. The chest radiograph showed chronic obstructive pulmonary disease changes, she was treated with appropriate antibiotics. Her health condition improved and is on regular follow up.

## DISCUSSION

Humans acquire infection with *Mycobacterium tuberculosis* by inhaling the bacterium. In order to establish an infection only a small number of bacilli are needed to enter distal alveoli of the human lungs. The alveolar macrophages are the first line of defense against the inhaled droplets. The Cell-mediated immunity plays a major role thereby the mechanism involves rapid onset of Th1 cytokine response comprising interferon (IFN)-γ and tumour necrosis factor (TNF)-α. Induction of Th17 cells leads to production of IL-17 and IL-23. These cytokines cause inflammation and recruitment of Th1 cytokine producing cells.[1,2] In most healthy adults, adaptive immunity mediated by T-cells controls the TB infection but do not eradicate it.[2]

Failure of the adaptive immunity results in clinical tuberculosis. Similar to our case report, recent study also depicted the $CD_4$ lymphopenia in patients with tuberculosis, with reversibility of the counts towards normality after treatment. In another study it was also found that extra-pulmonary especially miliary tuberculosis have lower $CD_4$ counts.[7] The $CD_4$ cell count is depressed in approximately one-half of hospitalized HIV-negative patients with tuberculosis and can be as low as that found in HIV-positive patients. However, the $CD_4$:$CD_8$ ratio remains normal in 90% of patients with tuberculosis. Alternatively, underlying malnutrition in patients who develop tuberculosis may result in low serum albumin levels, low hematocrit, and low body-mass index as well as low total lymphocyte and $CD_4$ cell counts and this in turn predisposes to the development of more-severe pulmonary disease.[3,7]

Disseminated TB is a major health problem in many underdeveloped countries and there is significant increase in disseminated tuberculosis has noticed in developed countries recently.[1,3] Disseminated disease can occur within weeks of the primary infection. Sometimes, it does not occur until years after the person become infected. Intestinal tuberculosis can occur either primarily or secondary to a tuberculous focus at a different site.[2] Intestinal involvement was observed in 55 – 90% of autopsies in patients with fatal pulmonary TB before the era of effective treatment. However, approximately 20-25% of patients with Gastrointestinal TB have pulmonary TB. An association between intestinal tuberculosis and esophageal candidiasis is possible, as both may occur spontaneously even in individuals with normal nutritional and immune status, their occurrence is more common among patients with predisposing conditions that impair host defenses, including poor nutritional or immunocompromised status.[1,2]

TB cannot be fought by drugs alone but requires comprehensive approach to address all factors related to the disease including many social issues such as alleviation of poverty, overcoming illiteracy and universal access to primary health care. There is a need for the Indian TB programme to engage with private health providers and change their traditional, empirical approach by ordering a chest X-ray early, a greater use of sputum TB tests like GeneXpert and referrals to the public sector to dealing with TB.

## REFERENCES

1. John AC, Barth RL. Two decades of disseminated tuberculosis at a University Medical Center: The expanding role of Mycobacterial blood culture. Clin Infect Dis. 2003; 37:1037-43.
2. Sharma DP, Sharma DN, Sharma DN, Motiwale DS, Gautam DB, Sharma DD. A case report of Abdominal Tuberculosis. SEAJCRR. 2014; 3: 670-4.
3. Caliskan T, Ozkisa T, Aribal S. High resolution computed tomography findings in smear- negative pulmonary tuberculosis patients according to their culture status. J Thorac Dis. 2014; 6: 706-12.
4. Chen X, Gao Y, Zhang Y. Tuberculosis infection might increase the risk of invasive candidiasis in an immunocompetent patient. Rev Inst Med Trop Sao Paulo. 2015; 57: 273-5.
5. Dilia MF, Gustavo JB, Doris GC, Neylor CJ, Javier BR, Bernarda CC, et al. Tuberculosis and pulmonary candidiasis co-infection present in a previously healthy patient. Colomb Med. 2016; 47: 105-8.
6. Kali A, Charles MP, Noyal MJ, Sivaraman U, Kumar S, Easow JM. Prevalence of *Candida* co-infection in patients with pulmonary tuberculosis. Australas Med J. 2013; 6: 387-91.
7. Rishi KG, Stephen DL, Linda GB, Judy C, Rishard K, Robin W. Impact of HIV and CD4 count on tuberculosis diagnosis: analysis of citywide data from Cape town, South Africa. Int J Tuberc Lung Dis. 2013; 17: 1014-22.

**Source of Support:** Nil.

**Conflict of Interest:** None Declared.



**Cite this article as:** Shalini M, Vazhavandal G, Madhan Mohan K, Vallab Ganesh B, Thirumalaikolundusubramanian P, Uma A. Disseminated Tuberculosis and Candidiasis in an Immunocompetent Individual: A Case Report. Int J Med Res Prof. 2017; 3(2):357-59. DOI:10.21276/ijmrp.2017.3.2.074