International Journal of Medical Science in Clinical Research and Review
Online ISSN: 2581-8945
Available Online at http://www.ijmscrr.in Volume 05|Issue 05 (September-October)|2022|Page: 890-895

Case Report

A battle against Covid -19 and tuberculosis – a case series of six post Covid tuberculosis

Authors:
Dr. Anitha S Menon[1*], Dr. S Praveen Raj[2], Dr. N Nalini Jayanthi[3], Dr.Syed Akram C[4]
[1,2,3,4]*Department of Respiratory Medicine, SRM Medical College Hospital and Research Centre, Chennai, India*
Corresponding Author: Dr. N Nalini Jayanthi, Professor and Hod department of respiratory medicine,SRM medical college and research centre.

Article Received: 25-08-2022 **Revised:** 14-09-2022 **Accepted:** 04-10-2022

ABSTRACT:
Severe Acute Respiratory Syndrome – Coronavirus 2 (SARS Cov-2) disease, the so-called Covid-19 pandemic, has been one of the most spread diseases in medical history. However, it did not end with just the infection. It had taken away millions of lives through the post-Covid-19 Sequel. Preventive measures against COVID-19 such as self-quarantine, social distancing and use of facemasks is likely to reduce the spread of *Mycobacterium tuberculosis (MTB)*. However, there is an anticipated net negative effect of COVID-19 on TB control, including an increase in the number of TB cases, death and the proportion of drug- resistant TB. Here, we present six cases of *Mycobacterium tuberculosis* infection out of which five patients never had history or exposure to TB bacteria. This raises a concern to the TB syndemic since the activation and pathogenesis of the bacteria after Covid -19 exposure could be due to CD4+ T-cell depletion associated with Covid-19 which resulted in progression of latent tuberculosis into active tuberculosis.[1] This study is presented to increase awareness of the suspicion of infection, early diagnosis and meticulous contact tracing is undertaken to treat the infection.

Keywords: Mycobacterium tuberculosis, Covid-19, Global TB burden, post-Covid TB

INTRODUCTION:

Severe acute respiratory syndrome – coronavirus 2 (SARS- COV-2, referred to as Covid or Covid - 19 in this series) pandemic has been the significant interest of clinicians and researchers since its onset in 2020. On the other hand, it is well known that India has been one of the leading hubs for tuberculosis (TB) as called pulmonary tuberculosis (PTB) disease caused by *Mycobacterium tuberculosis (MTB)*. Connecting the situations, though options are provided for prevention, treatment and support for TB patients and hygienic measures, social distancing and quarantine options for Covid patients, several comorbidities and post-Covid tuberculosis has been observed in various patients. Several cases have been presented on the concomitant Covid -19 and TB [1–4], presenting one of the crucial areas of study in addition to the TB/HIV, TB/Diabetes studies prevalent in the country. Most cases focus on the latent tuberculosis which explains the reactivation of the bacterial cells after exposure to Covid-19 due to depletion of CD4+ T-Cells and CD8+ T-Cells in Covid-19 patients [5]. Here, we present the case series with six patients with or without previous tuberculosis history and an attack of Covid with or without hospital-based treatment. Overall, this paper could be a preliminary resource for decoding the progression and the symptoms of post-Covid tuberculosis patients.

Case Series:

The investigation and clinical characteristics of the cases are presented in Table 1, and the Computed Tomography (CT) chest has been presented for each case in Fig 1. (a-f), respectively. The cases were addressed through preliminary blood investigation, CT imaging, Sputum Acid-fast bacillus (AFB) test, and either a TRUNAT test or a cartridge-based nucleic acid amplification test (CBNAAT) test was recommended.

Case 1:

A 57-year-old male, has had diabetes and has been undertaking treatment for the past two years; he presented with complaints of cough with expectoration for three weeks. He has a week-long history of worsening breathlessness, with loss of weight and

appetite for a month. Intermittent low-grade fever has been observed for ten days. The patient had no past Pulmonary tuberculosis history or had never been in contact with PTB. However, he was diagnosed with Covid -19 6- months back and was managed with a minimal oxygen requirement of 2L via nasal cannula and ten days course of IV methylprednisolone and one dose of bevacizumab. The patient had clinically improved during discharge with a saturation rate of 96% on room air without external support. On the current admission, patient was advised for a Chest CT, which showed areas of consolidation with the cavity communicating with sub-segmental bronchus and adjacent multiple centrilobular nodules. Most areas showcased tree in bud opacities in bilateral lung fields. Simultaneously, the sputum AFB revealed AFB 1 – 2+ and AFB 2 - 2+ with *MTB* detection in the TRUNAT test. However, no traces of fungal growth were detected with nil culture sensitivity. Considering the investigations performed, the patient was advised for antitubercular therapy.

Case 2:

A 52-year-old male, known smoker with complaints of dyspnoea periodically for the past six months, with expectoration cough in the last two months, came to emergency. The patient also got a high-grade fever at intervals for the past two weeks. The patient had no prior history of pulmonary tuberculosis or any primary contact with PTB. The patient had Covid 6months back and was managed with two weeks of Methylprednisolone, intra-venous antibiotics and 10 litres of O2 in the non-rebreather mask (NRBM). CT Chest showed diffuse ground glass opacities in the right, middle and lower lobes of the right lung and upper and lower lobes of the left lung, suggesting atypical viral pneumonia. The CT reported COVID-19 Reporting and Data System 5 (CORADS-5) with CT scan Severity Score **(**CTSS) - 22/25. However, at discharge patient did not require Oxygen and improved with the saturation of 95% Oxygen on room air. The current admission reported symptoms of tuberculosis and was advised to CT Chest again. In the present admission, the CT chest showed severe traction bronchiectasis with adjacent fibrosis, thick-walled cavities, alveolar consolidation with air bronchogram and partial break down, centrilobular nodules in tree in bud appearance with endo bronchial spread are noted in diffusely in bilateral lung fields, more pronounced in upper lobe of left lung. On the other hand, sputum AFB, gram strain, and culture sensitivity showed no positive results. However, the Sputum cartridge-based nucleic acid amplification test **(**CBNAAT) detected the *MTB* strain and was sensitive to rifampicin (RIF). Hence, the patient was prone to antitubercular therapy.

Case 3:

A 74 year old female patient was rushed to the emergency department for breathlessness and decreased urine output. The patient has a known history of Chronic obstructive pulmonary disease **(**COPD), Paroxysmal atrial fibrillation (PAF), seizures, diabetes. The patient was intubated in view of tachypnoea, tachycardia, and desaturation. She had been on treatment for tuberculosis 20 years back and was diagnosed with Covid -19 8 months back. She was managed with 15 litres of O2 via NRBM, IV antibiotics and IV methylprednisolone for two weeks and was discharged on domiciliary oxygen support. Her current CT chest showed bilateral lower lobe bronchiectasis and bilateral lower lobe patchy consolidation, AFB not seen and *MTB* was detected in the tracheal aspirate CBNAAT with RIF sensitivity. Patient was started on antitubercular therapy.

Case 4:

This 45-year-old lady with diabetes was presented to the emergency. The patient was having symptoms of cough with expectoration, breathlessness, weight loss, and loss of appetite for the past 3-month period. The patient on arrival at the hospital was dyspnoeic and tachypnoeic; the saturation was 70% on room air and 95% with 5 litres of Oxygen. The patient had a previous diagnosis of Covid-19 6 months back and was hospitalized for treatment, during the time received supplemental Oxygen, non-invasive ventilation, intravenous antibiotics, and intravenous Methylprednisolone for two weeks. A chest CT was performed. During the patient's prior admission, large confluent areas of fibrotic bands and septal thickening associated with ground glass density were observed with predominant peripheral or subpleural distribution, involving approximately one hundred percent of the lung parenchyma. This condition was likely due to post viral pneumonitis sequelae with parenchymal and interstitial fibrosis. The patient was discharged with domiciliary oxygen support. On current admission CT chest was done showed few thick-walled cavitating lesions with patchy areas of consolidation scattered in bilateral lung parenchyma. Fibro-bronchiectatic changes with subpleural bands scattered in bilateral lung parenchyma. Diffuse ground glassing with fibro-atelectatic changes in bilateral lung fields. Sputum investigation were performed sputum AFB 1-1+ 2 -3+ seen and MTB detected in sputum CBNAAT. Patient started on antitubercular therapy.

Case 5:

Having a history of diabetes for four years and undergoing treatment for the same, this 31-year-old male patient came up with symptoms of on-and-off fever for two weeks with cough expectoration and complained about loss of weight and appetite for the past two months. Following the case, it was observed that patient had been affected by Covid-19 six months ago and suggested having home isolation due to less severe symptoms. Chest CT, which revealed the presence of consolidation with air bronchogram and centrilobular nodules in both lung fields, most prominently in the bilateral upper lobe. In addition, there was a slight pleural effusion on the left side, accompanied by a passive collapse of the underlying basal regions of the left lower lobe. Patient was started on antitubercular therapy based on MTB detected on sputum TRU-NAT testing.

Case 6:

Recently diagnosed with diabetes, aged 35, this male patient came to the outpatient department (OPD) complaining of fever with chills and the cough for two weeks. However, he did not have any history of PTB or any primary contact with PTB. Since the patient showed a history of COVID-19 half a year ago, he had been recommended for home isolation as the symptoms were not severe.

The patient was instructed to undergo a chest CT, indicating a thick wall in the apical region of the right upper lobe. Centrilobular nodules bordered this wall. The kidneys and liver function were normal, and no AFB seen on sputum. Fibreoptic bronchoscopy was done along with bronchial wash, which proved the presence of *MTB* in bronchial wash TRU-NAT and patient started on antitubercular therapy.

DISCUSSION:

This paper presents the series of cases in multiple combinations, including the age and the sample history. However, considering the previously presented reports, case studies and research letters on TB/Covid-19 shown that COVID-19 infection affect the innate immune system and T cells,which are essiential to prevent LTBI reactivation. Similarly, studies claim that exposure to Covid-19 can lead to T cell dysfunction, cytokine storm and reduction in the lymphocytes especially depleting CD4+ T-Cells and CD8+ T-Cells[5]. However, the blood tests of these patients showed a normal or increased count of WBCs in general. This could be due to the treatment taken after the disease onset or restoration of the cells since the time of exposure is equal to or more than six months in each of them. On the other hand, this pushes to question on the severity of the disease in the patients, the cause for the onset of TB and the implications which have to be explored in detail. The epidemiological study by Ryckman T et al. (2022)[6] showed similar yet expanded sampling, setting the base for the age groups, mortality, gender, demographics and comorbidity fatalities. Our results are consistent with their findings; however, we exempt the part of fatalities since all six patients were discharged safely and with or without domiciliary oxygen support. Several research letters reporting individual cases and cohorts were found to be communicated, including Tadolini M et al., (2020)[7], Dahanayake C, et. al., (2021)[2], Noori M, et. al., (2022)[8] are consistent with the age range, symptoms and the treatment strategies. An alternative perspective to the diagnosis was added through histopathology by Zahid A et al. (2021)[9], which was not needed in our cases since the CT-Chest showed a clear understanding of the lung fields and the spread of pneumonia on the lobes. Overall, it is evident from the WHO report[10] and the current trends published by Khatri U et. al., (2022)[11] that TB after Covid-19 will likely increase the burden of treatment strategies and achieving the SDGs on eradicating TB by 2030. Hence, every clinical understanding, prognosis and diagnosis in effectuating specific treatments for TB, TB/disease comorbidities, and drug-resistant TB has to be considered.

CONCLUSION:

Covid -19 plays a major role in reactivation of LTBI through T cell dysfunction and cytokine storms, leading to immunosuppression,the risk was higher in patients receiving corticosteroids.Also, the impact of CD4+ T-Cells, other cytokines and interleukins on the cause of these two diseases have to be explored in detail. This paper presents the investigation profile of six treated patients and their complications, the disease, its onset and treatment strategies. Early identification of patients with TB and subsequent contact tracing is essential to help control the spread of TB.

Table 1. Clinical characteristics of the six patients

Case/ Criteria	**Case 1**	**Case 2**	**Case 3**	**Case 4**	**Case 5**	**Case 6**
Age/ Gender	57 M	52 M	74 F	45 F	31 M	35 M
History of TB*	No	No	Yes	No	No	No
History of Covid*	6months before diagnosis – Hospitalized	6months before diagnosis - Hospitalized	8 months before diagnosis - Hospitalized	6months before diagnosis - Hospitalized	6 months before diagnosis – Home Isolation	6 months before diagnosis – Home Isolation
History of other co-morbidities	Diabetes		Diabetes COPD AF Seizure disorder	Diabetes	Diabetes	Diabetes
Blood Test						
Hemoglobin (grams per deciliter)	10.1	11.6	10	7.5	9.2	13
WBC (per microliter)	8,590	13,910	20,300	15,760	9,510	1,000
Platelets (per cumm)	2,71,000	4,87,100	-	1,50,000	1,50,000	1,00,000
Renal Function Test	Normal	-	Normal	Normal	Normal	Normal
Liver Function Test	Normal	-	Normal	Normal	Normal	Normal
Sputum AFB	AFB 1 - 2+, AFB 2 – 2+	No AFB	-	AFB 1-1+, AFB 2 - 3+	No AFB	No AFB
Sputum TRUNAT/ CBNAAT	MTB detected	MTB detected	-	MTB detected	MTB detected	-
Tracheal aspirate	-	-	MTB detected	-	-	-
Bronchial wash TRUNAT	-	-	-	-	-	MTB detected

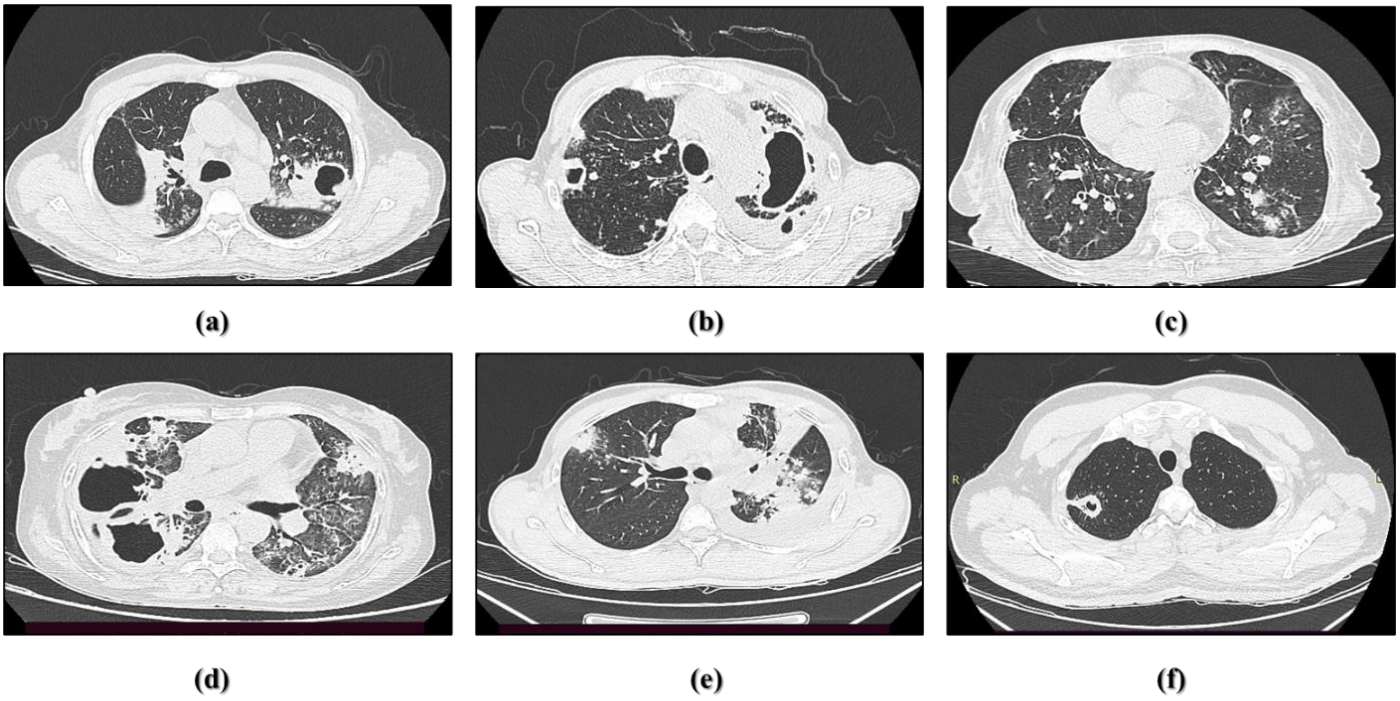

Fig 1. CT Chest of the six patients from a-f respectively. The images are presented to represent the consolidation of the axial lung window

(a) Areas of consolidation with the cavity communicating with sub-segmental bronchus and adjacent multiple centrilobular nodules and areas of tree in bud opacities in bilateral lung fields
(b) Severe traction bronchiectasis with adjacent fibrosis, thick walled cavities, alveolar consolidation with air bronchogram and partial break down, centrilobular nodules in tree in bud appearance with endo bronchial spread are noted in diffusely in bilateral lung fields, more pronounced in upper lobe of left lung
(c) Bilateral lower lobe bronchiectasis and bilateral lower lobe patchy consolidation.
(d) Few thick-walled cavitating lesions with patchy areas of consolidation scattered in bilateral lung parenchyma. Fibrobronchiectatic changes with subpleural bands scattered in bilateral lung parenchyma. Diffuse ground glassing with fibroatelectatic changes in bilateral lung fields
(e) Presence of an air bronchogram with centrilobular nodules in both lung fields, most prominently in the bilateral upper lobe; slight pleural effusion on the left side, accompanied by a passive collapse of the underlying basal regions of the left lower lobe
(f) A thick wall in the apical region of the right upper lobe; centrilobular nodules bordered this wall.

Funding: Nil

Competing Interests:

Authors declare that they have no competing interests

REFERENCES:

1. Khayat, M.; Fan, H.; Vali, Y. COVID-19 Promoting the Development of Active Tuberculosis in a Patient with Latent Tuberculosis Infection: A Case Report. *Respir Med Case Rep* **2021**, *32*, doi: 10.1016/j.rmcr.2021.101344.
2. Dahanayake, C.; Malinda, S.; Nanayakkara, M.; Silva, S.; Peera, E. A Post Covid Activation of Latent Tuberculosis. In Proceedings of the Respirology; 2021.
3. Fatima, R.; Akhtar, N.; Yaqoob, A.; Harries, A.D.; Khan, M.S. Building Better Tuberculosis Control Systems in a Post-COVID World: Learning from Pakistan during the COVID-19 Pandemic. *International Journal of Infectious Diseases* **2021**, *113*, S88–S90, doi:10.1016/j.ijid.2021.03.026.

4. Stochino, C.; Villa, S.; Zucchi, P.; Parravicini, P.; Gori, A.; Raviglione, M.C. Clinical Characteristics of COVID-19 and Active Tuberculosis Co-Infection in an Italian Reference Hospital. *European Respiratory Journal* 2020, *56*.
5. Dass, S.A.; Balakrishnan, V.; Arifin, N.; Lim, C.S.Y.; Nordin, F.; Tye, G.J. The COVID-19/Tuberculosis Syndemic and Potential Antibody Therapy for TB Based on the Lessons Learnt From the Pandemic. *Front Immunol* 2022, *13*.
6. Migliori, G.B.; Casco, N.; Jorge, A.L.; Palmero, D.J.; Alffenaar, J.W.; Denholm, J.; Fox, G.J.; Ezz, W.; Cho, J.G.; Skrahina, A.; et al. Tuberculosis and COVID-19 Co-Infection: Description of the Global Cohort. *European Respiratory Journal* **2022**, *59*, doi:10.1183/13993003.02538-2021.
7. Tadolini, M.; Codecasa, L.R.; García-García, J.M.; Blanc, F.X.; Borisov, S.; Alffenaar, J.W.; Andréjak, C.; Bachez, P.; Bart, P.A.; Belilovski, E.; et al. Active Tuberculosis, Sequelae and COVID-19 Co-Infection: First Cohort of 49 Cases. *European Respiratory Journal* 2020, *56*.
8. Noori, M.A.M.; Younes, I.; Latif, A.; Fichadiya, H.; Elkattawy, S.; Khandait, H.; Nawachukwu, O.; Garg, V. Reactivation of Tuberculosis in the Setting of COVID-19 Infection. *Cureus* **2022**, doi:10.7759/cureus.23417.
9. Zahid, A.; Iqbal, N.; Moeen, S.; Irfan, M. Post COVID-19 Tuberculosis: An Emerging Threat of Pandemic. *Monaldi Arch Chest Dis* **2021**, *91*, doi:10.4081/monaldi.2021.1749.
10. World Health Organization *GLOBAL TUBERCULOSIS REPORT 2021*; 2021;
11. Khatri, U.G.; Winkelman, T.N.A. Strengthening the Medicaid Reentry Act — Supporting the Health of People Who Are Incarcerated. *New England Journal of Medicine* **2022**, *386*, 1488–1490, doi:10.1056/nejmp2119571.