CASE REPORT

# Pulmonary Tuberculosis in Coronavirus Disease-19 Patients: Report of Cases

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**ABSTRACT**

The coronavirus disease 2019 (COVID-19) is known to cause severe respiratory illness manifesting in a spectrum of related disorders. Amidst the continuous evolution of this pandemic which has caused vast devastation globally, it is crucial to note that tuberculosis (TB), which also causes respiratory diseases, has and still affects over a quarter of the world's population. Coinfection of both diseases have severe health implications. Therefore, it is vital to understand the effects of this novel virus on the immune system and coinfection with a bacterial infection, like TB. Based on peer-reviewed cases, there seems to be an associational relationship between COVID-19 and TB; research suggests both weaken the immune system and further complicate clinical outcomes, which was further explored in this paper.

**Key words:** Coronavirus disease-19, Coronavirus, Severe acute respiratory syndrome coronavirus 2, *Mycobacterium tuberculosis*

## INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus which caused the 2019 coronavirus disease (COVID-19), is a respiratory tract infection that was first reported in Wuhan, China. It has spread globally, signifying a pandemic with over 70 million cases and 1.6 million deaths as of December 13, 2020.[1] Clinical features consist of a wide spectrum of manifestations that include, but are not limited to flu-like symptoms, pneumonia, gastrointestinal disorders, or may present asymptomatically.[2,3] Furthermore, the current pandemic threatens to impede countries' efforts to overcome various diseases, such as tuberculosis (TB), a communicable disease that is one of the top 10 causes of death worldwide.[4,5] TB, caused by the bacterium *Mycobacterium tuberculosis,*[5] currently affects over a quarter of the world's population,[6] and in 2019, 7.1 million newly diagnosed individuals with TB were reported globally, up from the 7.0 million in 2018, and the 6.4 million in 2017.[4] The bacterium is distinctive because its cell surface is waxy making it impermeable to Gram staining used for identifying other bacteria; therefore, acid-fast staining techniques are used for the identification.[6] The causative agent is spread from one person to another through minuscule droplets released into the air through talking, laughing, sneezing, and/or coughing.[4] TB is, therefore, a potentially serious infectious disease that mainly affects the lungs (pulmonary TB), further weakens a person's immune system, and can also affect other sites (extrapulmonary TB).[4,5] Furthermore, bacterial infections are prevalent in patients with viral pneumonia and have been noted in case reports with COVID-19 pneumonia, further increasing the severity of the illness.[7] This paper aims to present and explore the health implication of coinfection with COVID-19 and TB.

## CASE REPORTS

### Case one

A 32-year-old female who had been vaccinated at the age of one with Bacille Calmette-Guérin (BCG) was diagnosed with

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COVID-19 pneumonia and apical tuberculous pneumonia of the right lung simultaneously.[8]

- Hospitalized on March 29, 2020, due to a 3-week long fever and muscle pain.
- History of travel to high-risk country: Milan, Italy.
- Initially treated with amoxicillin/clavulanic acid 1000 mg twice a day (BID) and paracetamol 1000 mg/day.
- Day 1 of hospitalization: RNA test for SARS-CoV-2 by nasopharyngeal swab was undetermined.
  - High-resolution chest computer tomography scan showed parenchymal consolidation of 54 × 25 mm, with air bronchogram, at the apical segment of the right upper lobe; consolidation of the posterior segment of the same lobe at the para-scissural site, middle lobe para-mediastinal site, and contralaterally to the anterior segment of the left upper lobe in the subpleural area. Large right pleural effusion leading to atelectasis of the right lower lobe (RLL) was also detected.
  - Blood tests: Lymphopenia, increase in highly sensitive C-reactive protein (CRP), procalcitonin, fibrinogen, and d-dimer.
  - Treatment: Clarithromycin 500 mg/BID and piperacillin/tazobactam 4.5 g 3 times a day.
- Day 2 of hospitalization: RNA test for SARS-CoV-2 was negative by nasopharyngeal swab.
- Day 3 of hospitalization: RNA test for SARS-CoV-2 was negative by nasopharyngeal swab.
- Day 4 of hospitalization: RNA test for SARS-CoV-2 positive, IgG and IgM antibodies assays negative.
  - Treatment: Hydroxychloroquine and lopinavir/ritonavir.
  - Testing: QuantiFERON indeterminate and human immunodeficiency virus test negative.
- Day 7 of hospitalization:
  - Treatment: Linezolid 500 mg/BID replaced previous antibiotic therapies.
  - Testing: Thoracentesis to remove 1 L of citrine yellow liquid → culture tests for common germs and real-time polymerase chain reaction (RT-PCR) assay of Bacillus of Koch (KB) both negative; QuantiFERON indeterminate; chest computed tomography (CT) undetermined, lung CT biopsy showed multiple areas of caseous necrosis delimited by a fibrous wall and giant multinucleated cells suggestive for TB infection; and RT-PCR performed on histological samples resulted positive for KB.
- Day 9–12 of hospitalization: Three RNA tests for SARS-CoV-2 negative, while clinical conditions improved.
- Day 12 of hospitalization: Antiviral therapy stopped first then hydroxychloroquine; discharged and self-quarantined for an additional 14 days; and treated with rifampicin, isoniazid, pyrazinamide, and ethambutol (RIPE) therapy.

### Case two

A 44-year-old male was simultaneously diagnosed with severe COVID-19 and reactivation TB.[9]

- History of hypertension, diabetes, and atrial fibrillation.
- March 24, 2020: Presented with a 5-day history of cough and fever.
  - Positive coronavirus PCR.
  - Physical examination: febrile, temperature 101.8°F, and tachycardic.
  - Laboratories: Leukocytosis 16.9 K/ul and elevated inflammatory markers including CRP: 328 mg/dl, lactic acid dehydrogenase: 570 U/L, ferritin: 2043 ng/ml, fibrinogen 1216 mg/dl, and interleukin 6:21.
  - Testing: Chest X-ray bilateral patchy ground-glass opacities.
  - Treatment: Plaquenil, ceftriaxone, azithromycin, and anticoagulation were continued for atrial fibrillation.
- March 27, 2020: Worsening hypoxia requiring intubation.
  - Treatment: Dexamethasone 20 mg intravenous (IV) daily for severe acute respiratory distress syndrome; high inflammatory markers, tocilizumab 800 mg IV was given for cytokine release syndrome, after a negative QuantiFERON.
- April 8, 2020: Extubated.
- April 18, 2020: New fevers and leukocytosis to 20.6 K/uL.
  - Chest CT: 9.5 cm RLL consolidation with multiple air spaces, for which vancomycin and zosyn were given with no response.
  - Sputum testing: Positive for acid-fast bacilli and grew *M. tuberculosis*; started on RIPE with an appropriate response.
- May 13, 2020: Discharged after 51 days of hospitalization.

## DISCUSSION

COVID-19 and TB have many clinical and epidemiological characteristics in common. Both are transmitted by respiratory droplets, spread through close contact, attack the lungs primarily, and share clinical symptoms such as cough, fever, and difficulty breathing.[10,11] Furthermore, comorbidities and risk factors such as diabetes, immunosuppression, and old age are among the shared characteristics.[12] Risk stratification models propose that the COVID-19 pandemic threatens to reverse recent progress in mitigating the global burden of TB disease; as it is a disease of poverty, vulnerability, economic distress, stigma, marginalization, and discrimination.[4,13,14] For instance, essential TB services have been reallocated to combat COVID-19; diagnostic equipment previously used for TB has been reassigned to COVID-19 in many countries, staff in the national TB programs has been reallocated to COVID-19-related duties, and financial budgets have been similarly redirected.[4] Furthermore, in many countries, data collection of TB and disease reporting have been affected; therefore, threatening the health-care systems and affecting the delivery

of essential TB services. It has been suggested that within the next 5 years, 1.4 million TB-related deaths may be registered as a repercussion for the actions, or lack thereof, taken this year.[10]

The 100-year-old BCG vaccine is the only licensed vaccine for the prevention of TB disease, predominately in severe forms of TB among children.[4] At present, there is no vaccine effective in preventing TB disease among adults, either before or after exposure.[4] BCG is effective in eliciting an antigen-specific immune response against TB, though it also exhibits non-specific effects against certain viral infections.[15] The two mechanisms that explain the non-specific effects of BCG are its trained immunity (i.e., macrophages that develop a pro-inflammatory response protecting the host from non-mycobacterial, fungal, or viral pathogens) and heterologous immunity (i.e., vaccine antigen that elicits a cross-reactive host response and antibody production against non-mycobacterial pathogens).[15] However, BCG only confers immunity against *M. tuberculosis* bacteria for about 10–20 years.[8] Unfortunately, the non-specific immune response elicited by BCG in correlation with COVID-19 is not fully understood;[4] therefore, extensive scientific efforts to evaluate the effects of BCG on SARS-CoV-2 infection and COVID-19 through research studies are essential.[15]

## CONCLUSION

The COVID-19 pandemic has and continues to challenge society to swiftly adapt. The most valuable lessons have been learned by studying the successes and failures along the way and highlighting the need for continued research. As seen in the case reports listed above, additional attention should be given to other diseases and disorders such as TB while combating the COVID-19 pandemic, as severe consequences may occur if proper care is not taken. The ideal course of action for TB patients to prevent COVID-19 is to avoid being exposed to the virus. This may be achieved, non-pharmacologically, by wearing a facial mask appropriately, routinely keeping good hand hygiene with frequent washes, and maintaining social distance. Furthermore, pharmacological agents, as well as the recently approved and the up-and-coming vaccines, may effectively prevent symptomatic infection, reduce hospitalizations, and minimize mortality rates.

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