

FROM SILENCE TO RESURGENCE: TUBERCULOSIS REACTIVATION FOLLOWING COVID-19 – A SINGULAR CASE ANALYSIS

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Abstract: Tuberculosis (TB) stands as a prominent global health threat, persisting as a leading cause of mortality on a worldwide scale (World Health Organization, 2022a). Caused by the infectious agent *Mycobacterium tuberculosis*, TB spreads through respiratory droplets when an infected individual coughs or sneezes. While primarily affecting the lungs, TB can extend its impact to various organs and systems within the body (Centers for Disease Control and Prevention, 2022).

This research aims to shed light on the diverse facets of TB, focusing on its two principal manifestations: latent TB infection and active TB disease. Latent TB infection characterizes individuals who carry the TB bacteria but remain asymptomatic and do not transmit the disease. However, the latent form poses a risk of progressing into active TB disease, particularly in cases where the individual's immune system becomes compromised (Centers for Disease Control and Prevention).

The urgency of addressing TB is underscored by its potential to transition from latent to active, thereby elevating the risk of transmission and severe health consequences. The study delves into the dynamics of TB infection, emphasizing the critical importance of early detection and intervention to mitigate the escalation from latent to active TB. Furthermore, it explores factors contributing to the weakening of the immune system, which serves as a pivotal link between latent TB and the development of active disease.

By elucidating the intricate interplay between latent and active TB, this research not only contributes to a deeper understanding of the disease but also provides insights crucial for public health strategies and interventions. The overarching goal is to inform targeted measures that can effectively curb the spread of TB and reduce its impact on global health.

Keywords: Tuberculosis (TB), Latent TB Infection, Active TB Disease, *Mycobacterium tuberculosis*, Immune System Compromise

INTRODUCTION

Tuberculosis (TB) is a significant global health concern and remains one of the leading causes of death worldwide (World Health Organization, 2022a). It is an infectious disease caused by the *Mycobacterium tuberculosis*. TB is spread through the air when an infected person coughs or sneezes. It primarily affects the lungs, but can also affect other parts of the body (Centers for Disease Control and Prevention, 2022).

TB can present in two main forms: latent TB infection and active TB disease. Latent TB infection occurs when a person has been infected with the TB bacteria but does not yet have active disease or symptoms. In this case, the bacteria are dormant and cannot be spread to others. However, people with latent TB infection are at risk of developing active TB disease if their immune system becomes weakened (Centers for Disease Control and 2 Med. Case Stud.

Prevention, 2022). COVID-19 infection can increase the risk of TB reactivation due to a combination of factors. These factors include immune system suppression, as well as disruptions to TB diagnosis, treatment, and prevention services (World Health Organization, 2022b).

Tuberculous meningitis (TBM) is one of the most severe manifestations of extrapulmonary TB. CNS-TB represented the 13.91% of all cases of meningitis and 4.55% of all cases of TB (Navarro-Flores et al., 2022). The pathophysiology is primarily driven by three components, which also explain the clinical symptoms (Rich and McCordock, 1933; Dastur et al., 1995). Thick gelatinous exudate, which is especially apparent at the basal region of the brain, eventually produces a fibrous mass that encases nearby structures. As a result, periventricular infarcts and cranial nerve palsies are developed. Spasm, constriction, thrombosis, and occlusion of intracerebral arteries are all possible effects of tuberculous vasculitis and the concomitant inflammatory vascular changes (Chan et al., 2005). The intracranial vasculitis is expected to have a major impact on the remaining neurologic deficits (Poltera, 1977).

Clinical approach and diagnostic tools, including CSF analysis and radiographic imaging, are equally important to diagnose TB meningitis (Lewinsohn et al., 2017). The treatment for tuberculous meningitis is very complex. Commonly, the combination of Isoniazid, Rifampin, Pyrazinamide and Ethambutol/Streptomycin/Fluoroquinolone is given for an extended period of time. However, sometimes drug resistance is found which leads to adjustments in treatment (Donald, 2010; World Health Organization, 2017). This case describes the development of tuberculous meningitis in a patient with COVID-19.

CASE PRESENTATION

39-year-old male presented to the emergency department on June 4, 2022, with fatigue, fever, shortness of breath, nausea, and vomiting. He tested positive for COVID-19. A cardiopulmonary examination showed clear lung fields and normal heart sounds. Neurological assessment showed signs of ataxia, vertigo, and horizontal nystagmus; however, a head CT scan has not shown any pathological features. Two days later, the patient developed new clinical signs, including facial asymmetry with loss of the left nasolabial fold, right-sided ptosis, spontaneous rotatory nystagmus, dysphagia, dysarthria, and trouble coordinating. Jaw jerk and gag reflexes were both diminished. Reduced deep tendon reflexes were present in all extremities, more so on the left. He also suffered from neck rigidity.

A head MRI revealed hyperintensity in the brainstem and left cerebellum (Figures 1 and 2). CSF analysis revealed lymphocytosis, decreased glucose, and elevated protein. Adenosine deaminase levels and CSF PCR for tuberculosis were both positive as well.

Following the lumbar puncture, treatment with Dexamethasone, Vancomycin, and Ceftriaxone was started immediately due to an increased suspicion of meningitis. After the patient's cerebrospinal fluid results confirmed TB meningitis, the treatment regimen was adjusted to Streptomycin, Rifampicin, Isoniazid, Pyrazinamide and Dexamethasone.

The following day, the patient was diagnosed with purulent endobronchitis based on an X-ray and bronchoalveolar lavage. Soon after, he developed a cytokine storm and was taken to the intensive care unit, where he was intubated, sedated, and mechanically ventilated. Due to a protracted need for breathing support, he underwent tracheostomy placement. The patient was taken off the ventilator on July 9th, 2022, but continued to receive oxygen through a tracheostomy.

On August 1, 2022, the patient was discharged with stable vital signs. Oropharyngeal and cardiopulmonary examinations revealed no abnormalities. During neurological examination, the patient was spatially and temporally oriented and was able to follow simple commands. Pupils were equally round and lightresponsive. However, he still displayed dysmetria and Babinski reflex on the left side, along with horizontal nystagmus, as residual neurological deficit. The patient was advised to take Rifampicin and Isoniazid for 9 months.

Ethics section

Informed consent was obtained from the patient prior to data collection, ensuring their comprehensive understanding of the study's objectives, potential implications, and the confidentiality of their sensitive medical information. The patient was provided with detailed information about the case report, including its purpose, methodology, and the intended use of medical records and clinical details. It was explicitly communicated that participation in the study was entirely voluntary, and the patient could opt out at any stage without affecting their medical care or rights. Emphasis was placed on the de-identification of all data, ensuring the anonymity of the patient. The patient was reassured that the patient's personal and medical information would be treated with the utmost confidentiality and solely utilized for the purpose of this case report.

DISCUSSION

Based on this case, it is apparent that even a benign case of COVID-19 may eventually lead to severe consequences, such as TB reactivation. The timely identification of early neurological manifestations allowed for prompt evaluation and diagnosis of TB meningitis,



Figure 1. MRI revealed hyperintensity in the brainstem.

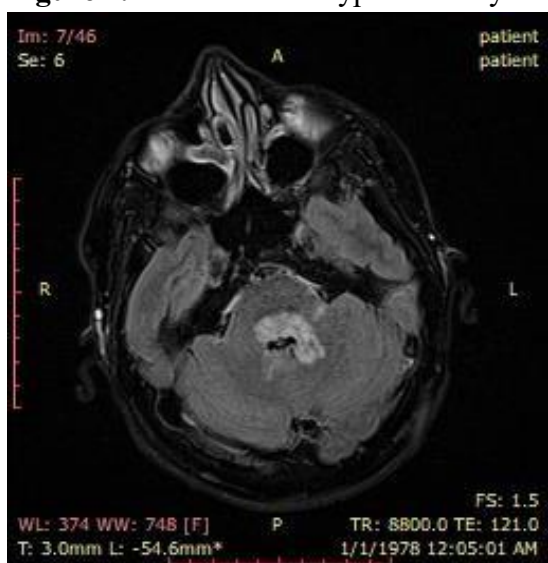


Figure 2. MRI revealed hyperintensity in the left cerebellum.

Which prevented further delays in treatment. So, despite the severity and complexity of the presented case, the overall outcome was positive. However, it should be mentioned that the patient still developed a residual neurological deficit.

Conclusion

In conclusion, this case highlights that the potential complications and challenges associated with COVID-19 infection extend beyond the impact of a single infectious Megrelishvili et al.3

Agent. The combined effects of multiple factors can significantly affect various organ systems, including the nervous system. COVID-19 affects several organ systems, thus any symptom could be attributed to it and underlying pathology may go unnoticed. The immune system suppression induced by COVID-19 can increase the risk of TB reactivation, thereby complicating diagnosis and treatment. Therefore, it is crucial to consider the possibility of TB reactivation in COVID-19 patients, particularly those from regions with high TB prevalence. Therefore, timely detection and prompt treatment of TB are essential to prevent severe complications and improve clinical outcomes in these patients.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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