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A 28-Year-Old Man from India with SARS-Cov-2 and Pulmonary Tuberculosis Co-Infection with Central Nervous System Involvement

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Male, 28-year-old
Final Diagnosis: COVID-19 • tuberculosis
Symptoms: Dizziness • headache • vomiting
Medication: —
Clinical Procedure: Craniectomy
Specialty: Infectious Diseases • Neurology • Pathology

Objective: Rare co-existance of disease or pathology

Background: Tuberculosis (TB) is a great mimic of central nervous system (CNS) tumors. This mimicry may pose a challenge, as the management of both diseases is quite different. Furthermore, the temporal association of initiating treatment affects prognosis. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mainly infects the pulmonary system. However, in a patient with concomitant pulmonary tuberculosis, it can be a diagnostic challenge.

Case Report: A 28-year-old man of Indian origin presented with headache and vomiting. He had a brain mass on imaging suggestive of a glioma. He also had lung infiltrates and was diagnosed with a co-infection by SARS-CoV-2, by a reverse-transcription polymerase chain reaction (RT-PCR) using the GeneXpert system. The mass was excised and was found to be a tuberculoma, diagnosed by Xpert MTB. He received first-line anti-TB and treatment for COVID-19 pneumonia based on local guidelines.

Conclusions: This report highlights that COVID-19 can co-exist with other infectious diseases, such as TB. A high degree of clinical suspicion is required to detect TB with atypical presentation. A co-infection of pulmonary and CNS TB with COVID-19 can present a diagnostic challenge, and appropriate patient management relies on an accurate and rapid diagnosis. Surgery may be necessary if there are compressive signs and symptoms secondary to CNS TB. A diagnosis of COVID-19 should not delay urgent surgeries. Further studies are needed to understand the effects of COVID-19 on the clinical course of TB.

MeSH Keywords: COVID-19 • Glioma • Mycobacterium Infections • Tuberculosis, Central Nervous System

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/926034

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Background

TB is an extensively studied disease [1]. Occasionally, a diagnostically challenging case presents atypically. The prevalence of TB is higher in patients infected with human immunodeficiency virus (HIV) [2]. The co-infection of active pulmonary TB with COVID-19 has recently been described [3]. As of 10 July 2020, COVID-19 has infected more than 12 million people globally [4]. Indirectly, it has affected society's entire fabric, with psychological, social, and economic repercussions [5]. There are concerns about a possible increase in TB-related mortality and morbidity if the disease diagnosis is delayed or missed. Changes in clinical practice due to the COVID-19 pandemic may negatively affect clinical outcomes in such patients [6]. Any critical procedures, including neurosurgery, must not be delayed due to SARS-CoV-2 co-infection.

Case Report

A 28-year-old, previously healthy, Indian man presented with a one-day history of severe non-remitting headache, vomiting, and dizziness. He was a non-smoker and non-alcohol user. He had stable vital signs, and the physical examination was unremarkable. There were no meningeal signs on examination. Because of the possibility of a CNS pathology, an urgent CT scan of the head was done, which unveiled a ring-enhancing lesion in the left cerebellar hemisphere with surrounding edema causing effacement of the 4th ventricle, midbrain, and pons, leading to obstructing hydrocephalus with supratentorial ventricular dilatation (Figure 1). The lesion raised the possibility of an infective pathology or a malignancy. Considering the findings in the CT scan (ring enhancement) and that the patient came from an endemic region, TB was one of the differentials. The QuantiFERON Gold test for Tb (QFT) was positive, indicating possible latent TB infection. Lumbar puncture was not performed due to the risk of herniation of the CNS mass. Initial chemistry showed lymphopenia (0.7, normal range 1–3×10^3/uL) with a normal white cell count, kidney, and liver function (Table 1).

The patient's chest X-ray, which was done as part of the initial diagnostic workup, showed patchy bilateral opacities (Figure 2). Due to the pandemic, a SARS-Cov-2 reverse-transcription-polymerase chain reaction (RT-PCR) via the GeneXpert system from a nasopharyngeal swab was done, which was positive. Considering the pneumonia to be possibly secondary to COVID-19 infection, the infectious disease team started the patient on oral Azithromycin 500 mg once daily and oral Hydroxychloroquine 400 mg daily, as per the local guidelines at that time.

On day 3, MRI (perfusion and spectroscopy) revealed an irregular-shaped left cerebellar mass with ill-defined margins and

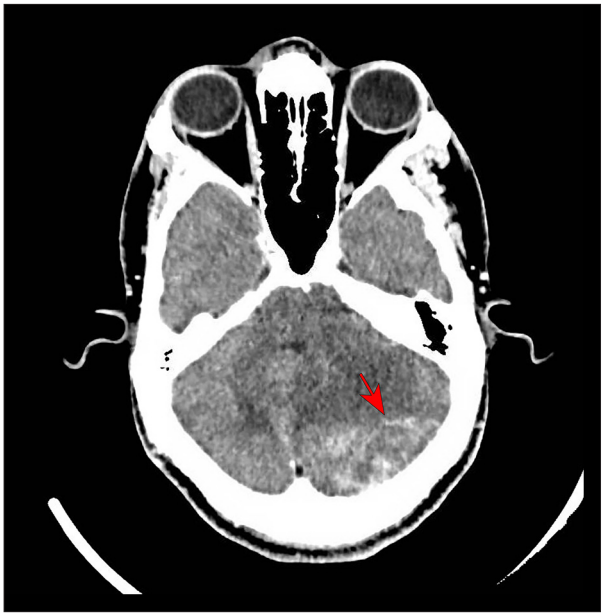

Figure 1. CT scan head (red arrow: ring-enhancing lesion (post-contrast images) seen in left the cerebellar folia measuring approximately 3.6×3.0 cm close to the left tentorium, with marked surrounding edema causing effacement of the fourth ventricle, pons, and part of the midbrain.

Table 1. Relevant Lab investigations.

Investigation	Result	Normal range
WBC count	4.80	4–10×10^3/uL
Hb	12.2	13–17 gm/dL
Lymphocyte count	0.7	1–3×10^3/uL
Creatinine	82	62–106 umol/L
Alanine aminotransferase	21	0–41 U/L
Sputum AFB	Negative	–
Quantiferon TB	Positive	–
SARS-Cov 2 PCR	Positive	–
HIV	Non-reactive	–

lobulated surface (Figure 3). The perfusion scan showed increased peripheral cerebellar blood volume (CBV). The spectroscopy showed an increased choline/N-acetyl aspartate (NAA) ratio, with a high lactate/lipid peak suggestive of CNS glioma. The compressive nature of the mass necessitated neurosurgical intervention on day 5, and a left suboccipital craniotomy with resection of the left cerebellar mass was performed. The biopsy report revealed necrotizing granulomatous inflammation with multiple acid-fast bacilli (AFB). A subsequently TB PCR (Xpert MTB nucleic acid amplification) was positive, and

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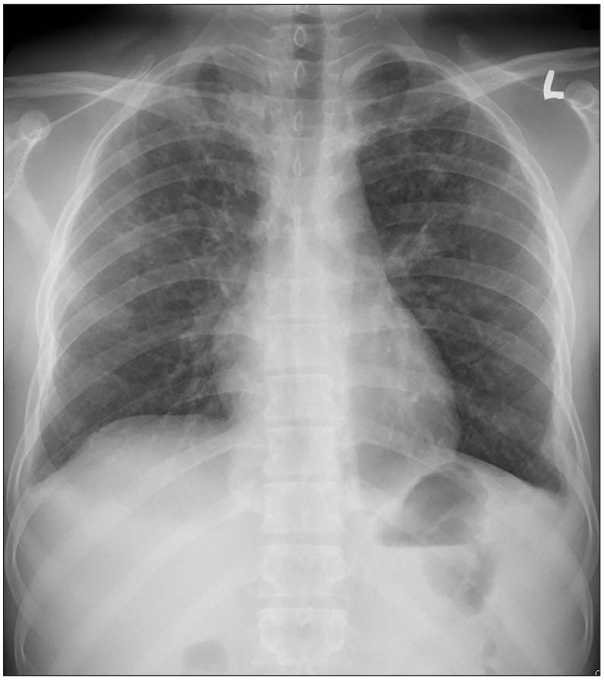

Figure 2. Chest X-ray showing bilateral infiltrates, mainly in the upper zones.

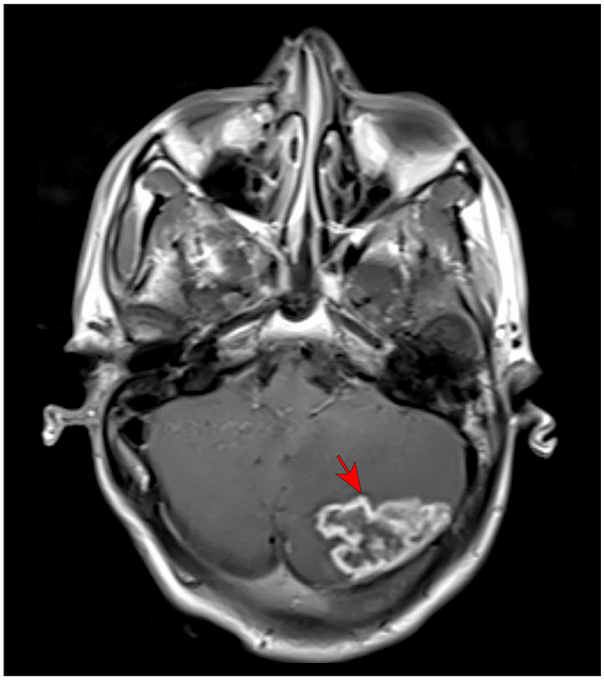

Figure 3. MRI head (red arrow: irregular intra-axial mass (3×4×2.7 cm) in the posterosuperior aspect of the left cerebellar hemisphere abutting the inferior surface of the left tentorial leaflet.

the patient was diagnosed with pulmonary TB with CNS involvement. A combined HIV antibody/p24 antigen test was non-reactive.

The patient received first-line anti-TB therapy with steroids. A CT scan of the thorax was done, which showed mosaic attenuation with multiple patchy areas of ground-glass attenuation in bilateral lungs. It also revealed reticulonodular shadowing, mainly in the upper lobe, with apical thickening more on the right side, and diffuse centrilobular, peribronchial, septal thickening, and patchy nodular opacities. A CT scan of the abdomen revealed multiple small lesions in the liver. Ground-glass opacities on the CT scan of the thorax was attributed to probably being due to COVID-19 and less likely to be due to TB. The upper-lobe involvement was more suggestive of being secondary to TB. However, due to both infections' overlapping features, a firm diagnosis for the pulmonary changes could not be established. The liver lesions were attributed to disseminated TB. Ten days after surgery, the patient was transferred to a TB treatment facility in an asymptomatic condition.

Follow-up

The patient was discharged from the TB facility 28 days after his initial presentation. On follow-up in the TB clinic after 2 weeks, he was asymptomatic. Ethambutol was stopped, and he was continued on Rifampicin, Isoniazid, and Pyridoxine, with a twice-a-monthly follow-up plan.

Discussion

Tuberculosis is one of the most extensively studied infectious diseases due to the mortality and morbidity burden since the stone age [7]. The most common organ system involved is the respiratory system, documented as far back as 1932 [8]. TB affects the CNS in 3 common patterns: meningitis, tuberculomas, or spinal arachnoiditis [9]. Patients with CNS involvement usually present with a headache and fever, which can progress to coma if left untreated or if diagnosis is delayed [10–12]. Atypical presentations of TB are relatively rare, but have been reported. CNS TB can mimic a malignant CNS tumor clinically and on radiography, which can pose a diagnostic challenge [13,14].

The diagnosis of CNS TB starts with a strong clinical suspicion followed by a cerebrospinal fluid (CSF) analysis, QuantiFERON TB test, or purified protein derivative test. The classical CSF picture shows a raised protein level and reduced glucose level, with a lymphocytic predominance. However, one-third of the cases have neutrophil predominance [15]. Additional tests from the CSF that can help include AFB smear, PCR, and culture. Although a spot AFB smear has a low yield, repeated samples can increase its yield to around 87% [12]. Adenosine deaminase from the CSF has a sensitivity and specificity of 79% and 91%, respectively [16]. Nucleic acid amplification can aid in rapid diagnosis, as results can be available within hours [17].

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Pulmonary TB should be considered if there are radiographic changes in the thoracic cavity in the presence of Tb involvement of any other system [18].

A treacherous situation arises when a patient has 2 menacing infections that are unrelated to each other. Our case report describes such a scenario of COVID-19 and TB co-infection. This is a diagnostic challenge because the presentation and radiological manifestations can be comparable. Fever is one of the most frequent clinical signs of TB. It is also the most common sign in COVID-19, irrespective of comorbidities [19]. Chest X-ray findings can be present in both. COVID-19 has a bilateral, diffuse, infiltrative pattern, and the most common X-ray finding seen in TB is unilateral upper-zone opacity [20].

In a high-resolution CT thorax, ground-glass opacities are seen mainly in COVID-19 infection, whereas disseminated TB usually manifests as multiple nodular opacities. However, 20% of TB patients have ground-glass opacities [21,22].

In a previous study describing TB and COVID-19 co-infection, ground-glass opacities were attributed to COVID-19 rather than TB, due to the higher prevalence of these findings in SARS-CoV-2 infection. However, as it can be due to both, it is difficult to confidently identify the cause [3].

A single ring-enhancing brain mass, with rapidly worsening clinical symptoms, can be seen in CNS tumors and TB. In addition to radiological similarities, the clinical presentation can be similar.

Upon initiation of ATT, an enhanced delayed-type hypersensitivity reaction leads to lymphocyte and macrophage chemotaxis to the site of TB infection. This chemotaxis in CNS TB can lead to a glioma-like aggravated lesion, causing a paradoxical worsening of symptoms despite being on appropriate anti-TB treatment [23].

A biopsy to diagnose TB is rarely the first step. With an initial suspicion of TB, the MRI described a glioma with a mass effect. In such a dilemma, a delay in surgical intervention could increase mortality and morbidity. Restrictions have been in place globally to mitigate the spread of SARS-CoV-2. These restrictions have negatively affected care for diseases other than COVID-19, including non-urgent surgeries. Prompt clinical diagnosis and careful clinical judgment are essential to assure performance of essential surgical interventions [6].

Conclusions

This report highlights that COVID-19 can co-exist with other infectious diseases, such as TB. A high degree of clinical suspicion is required to detect TB with atypical presentation. A co-infection of pulmonary and CNS TB with COVID-19 can present a diagnostic challenge, and appropriate patient management relies on an accurate and rapid diagnosis. Surgery may be necessary in the case of compressive signs and symptoms secondary to CNS TB. A diagnosis of COVID-19 should not delay urgent surgeries. Further studies are needed to understand the effects of COVID-19 on the clinical course of TB.

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