

# A Case of COVID-19 and Tuberculous Meningitis Coinfection



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## ABSTRACT

Neurological symptoms like headache have been reported in patients infected with tuberculosis (TB) and COVID-19 infection [1]. A high index of suspicions is necessary for diagnosing of COVID-19 and neurologic tuberculous coinfection, particularly in the communities at high risk for TB or in an endemic region. Herein, we report a case of a 60-year-old man diagnosed with acute COVID-19 and tuberculous meningitis coinfection, to emphasize challenges about this coinfection, because underlying lung diseases like latent TB will affect the clinical categorization (for severity) of COVID-19, and then active TB disease may severe illness.

## Introduction

Coronavirus disease (COVID-19) has infected millions of people worldwide. Immunomodulatory in moderate-severe COVID-19 may reactivate latent tuberculosis (TB) in the high endemic districts. Recently, there is a limited described literature on the co-infection of COVID-19 in patients with TB [1-6]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mainly involves the pulmonary system. Although, in concomitant pulmonary tuberculosis patients, it can be a kind of challenge. In addition, both tuberculosis and COVID-19 can have atypical and extrapulmonary

manifestations, which increase the diagnostic challenges. Herein, we report a case of a 60-year-old man admitted with persistent headache to highlights the diagnostic difficulties in such cases.

## Case Presentation

A 60-year-old Afghan man, living in Iran, was admitted to hospital on April 6 with persistent headache for five days associated with myalgia, fever, and chills. His headache was located in temporal regions and pulsatile, of moderate-severe intensity, associated with photophobia and phonophobia. His headaches were not accompanied by nausea, vomiting, and blurred vision. He did not have a history of cough,

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weight loss or night sweats. There was no exact history of exposure to patients infected or suspected of coinfection with COVID-19 or tuberculosis. He hasn't received Bacillus Calmette-Guérin (BCG) vaccination. Past medical history and drug history were negative. The habitual history was remarkable for opium addiction. On arrival at the hospital, he was awake and oriented, and neurologically intact. His vital signs were as follows: blood pressure of 150/90 mmHg, heart rate of 100 /min, temperature 37 degrees Celsius and respiratory rate of 20 /min. Oximetry showed a 96% saturation on room air. On physical examination, the patient looked cachectic. Neurological examination was normal. Neck redness and Brudzinski signs were negative and cranial neuropathies were not seen. Initial lab test showed: a white blood cell ( $4 \times 10^3$  / $\mu$ l with lymphocyte count 20/8%), c-reactive protein (CRP) 7.8 mg/l, hemoglobin(HB) 12.8 g/dl, platelets  $225 \times 10^3$  / $\mu$ l, erythrocyte sedimentation rate (ESR) 27 mm/hr., creatinine 0.7 mg/dl and normal liver function test (LFT). CNS infection was proposed as the most likely diagnosis. Due to a history of flu-like symptoms in our case and following global COVID-19 crisis, a spiral computed tomography scan (CT scan) of the chest and polymerase chain reaction (PCR) for COVID-19 were performed. His pharyngeal PCR test was positive, and a chest CT scan was reported micro nodular and nodular pattern in both lungs (Figure 1).

He underwent lumbar puncture (LP), and analysis of cerebrospinal fluid (CSF) revealed colorless and

transparent fluid, white blood cell count (WBC) 0-1 cells/ $\mu$ L, protein level 132 mg/dl, glucose level 25 mg/dl, Red blood cell (RBC) count 0-1 cells/ $\mu$ L, and CSF bacillus Koch (BK) PCR positive. An acid-fast bacillus in CSF was found. CSF culture was assessed as positive for tuberculosis too. Therefore, the diagnosis of tuberculosis meningitis was given. Brain magnetic resonance imaging (MRI) with contrast was requested. It showed tiny ring enhancing mass lesions in both cerebral hemispheres, and patchy meningeal enhancement in sylvian fissure (Figure 2). MRI and CXR were mostly indicative for miliary TB with meningitis and Cerebritis. Due to positive PCR for the COVID-19, the patient was treated with hydroxychloroquine 400 mg BD. For initial treatment of TB, a two months daily anti-tuberculosis regimen (isoniazid, rifampin, pyrazinamide and ethambutol) was used followed by ten months of isoniazid and rifampin [7]. His headache during hospitalization was not controlled by oral acetaminophen at first. He was prescribed dexamethasone 8 mg twice daily. His headaches resolved entirely in 4th days, and he has not seen any other neurological symptoms and was discharged with stable vital signs.

## Discussion

Neurological presentations like headache have been described in patients infected with the COVID-19 infection [8], and tuberculosis (TB) is also an excellent mimic of central nervous system (CNS)

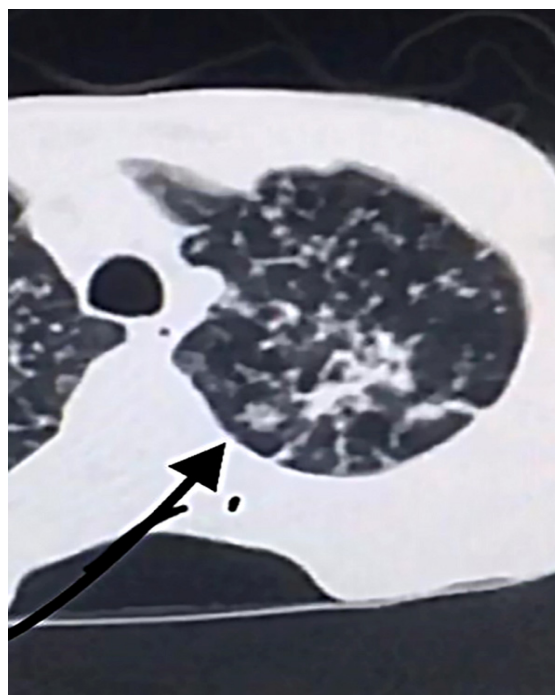
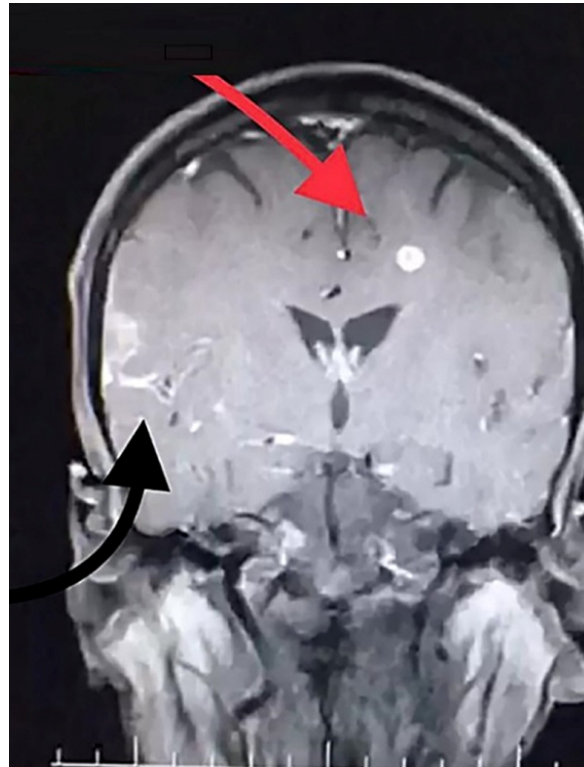


Fig. 1. Patient's chest CT-scan shows miliary tuberculosis



**Fig. 2.** Patient's brain MRI with contrast shows multiple enhancing nodular lesions in both cerebral hemispheres and leptomeningeal enhancement

lesions [1]. A high index of suspicions is necessary for diagnosing COVID-19 and neurologic tuberculous coinfection, particularly in the communities at high risk for TB or in an endemic region. It may not relate to the worse consequences if diagnosed early [2]. Delayed diagnosis can result in fast progression of neurological problems and poor prognosis. Wan-Mei song et al. evaluated 36 studies for an overview of COVID-TB cases. They discovered COVID-TB patients are more probably to suffer intense disease or mortality than COVID-19 patients [4]. In more than half of the cases of coinfection with COVID-19 and mycobacterium tuberculosis, evidence of an old miliary pattern is seen on CXR. In our case, miliary tuberculosis was reported. There are scarce case reports of TBM and COVID-19 coinfection; Nadershabbaz et al. [5] reported a young Afghan woman with TB meningitis and COVID-19 too; their patient had anxiety and depression. Tuberculous meningitis and depression as risk factors increased the risk of COVID-19 infection that causes psychological disorders like conversion disorder that did not answer to treatment. Their patient, as our case, was Afghan; As D P Spence et al. showed, the historical link between tuberculosis and poverty still exists [9]. Ata et al. [1] reported an Indian 28-year-old man who admitted with headache and vomiting.

His brain Magnetic resonance imaging (MRI) showed a brain mass, and glioma was suspected. His CXR also had infiltration and was diagnosed with a coinfection by SARS-CoV-2, by RT-PCR. The mass was found to be a tuberculoma when it was excised. Tuberculous meningitis (TBM) is usually subacute. In TBM, symptoms were present for an average of 7-10 days prior to diagnosis. A prodromal phase of malaise, fever, headache, dizziness, nausea, and personality changes may appear for a few weeks; after that, patients can then show more intense headaches, cranial neuropathies, and altered mental status [10]. In general, CSF analysis in TBM reveals a high leukocyte count (up to 1000 $\mu$ /l), usually a predominance of lymphocytes, a protein level of 1-8 g/l (100-800mg/dl), and low glucose content. However, any of these three items can be within the normal range. CSF culture is diagnostic up to 80% of cases and remains the gold standard [11]. In our patient, CSF result analysis showed increased CSF protein and decreased CSF glucose.

The definite mechanism underlying the coinfection of COVID-19 and TB is not known. Various interleukins (IL) interplay and are stimulated by the inflammatory response to the virus, and they cause a T-cell immune response. Type-I interferon (INF) has an antiviral part,

but improper Type-I INF response in viral infections also may promote sensitivity to TB infection. Dysregulated glucose metabolism, prompts patients to an uninhibited inflammatory response, that causes a higher risk of severe pneumonia in COVID-19 cases and fast disease development [12]. Coinfection with TB and COVID-19 is a particular concern due to several reasons like non-specific clinical patterns in both (TB & COVID-19), so, the major obstacle to exact diagnosis and treatment of tuberculous meningitis is a lack of clinical suspicion and radiological finding specific to TB. However, headache as the symptom of COVID-19 has been reported, but this case alerts clinicians to suspect meningitis in patients with TBM and COVID-19 coinfection, which is potentially life-threatening but treatable. Our case presented to the emergency department with persistent headaches associated with myalgia, fever and chills. Due to CSF culture, CSF analysis, and Clinico-radiological evidence, the diagnosis of tuberculosis meningitis was given for him. Another challenge for the clinicians in TBM and COVID-19 coinfection is the possibility of drug-drug interaction in patients prescribed remdesivir and anti-tubercular drugs as additive hepatotoxicity. However, due to lack of the remdesivir in our hospital, antiviral drugs like remdesivir were not prescribed for this patient. The recommended treatment regimen for TBM is two months of daily rifampin (RIF), Isoniazid (INH), pyrazinamide (PZA), and either ethambutol (EMB) or streptomycin (SM), followed by 7–10 months of RIF and INH [7]. His headache during hospitalization was not controlled by oral acetaminophen at first. He was prescribed dexamethasone 8 mg twice daily. WHO recommends that glucocorticoid as adjuvant therapy with either prednisolone or dexamethasone, tapered gradually over 6-8 weeks, should be given in tuberculous meningitis [7]. Clinical trials have proved that patients prescribed glucocorticoids as adjunctive, may have faster resolution and even lower rates of relapse, severe illness and, mortality [11]. Eventually, routine screening for TB may be helpful in cases of COVID-19 in populations with high TB outbreaks. In the current report, there are concerns if TB diagnosis is delayed or missed, TB-related mortality and morbidity will increase.

## Conclusion

TB meningitis remains a significant problem worldwide. Coinfection COVID-19 and mycobacterium tuberculosis can change the management and course of the disease. A high index of suspicions is necessary to diagnose, and despite recent progress, more studies are required to detect early disease and optimize

therapy. Delay in the treatment of TBM results in, either death or considerable neurological morbidity.

## Ethical Considerations

### Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

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### Conflict of Interests

The authors have no conflict of interest to declare.

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