

Primary multidrug-resistant pulmonary tuberculosis with a concomitant COVID-19 infection in an Indian female- World's first case of its type in this current pandemic

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ABSTRACT

The world is plagued by the historic pandemic of coronavirus disease. The situation is gruesome in developing countries with a large burden of other infectious diseases like tuberculosis (TB), and HIV-AIDS. Globally the chaos due to the ever-growing cases of coronavirus disease-2019 (COVID-19) has overwhelmed the health systems. The condition of healthcare in some of the underprivileged countries is grave. In this current scenario, the attention is mostly towards the COVID-19 and the efforts for the control of other diseases like TB have taken a back step. We herein, present the world's first case of primary multidrug-resistant pulmonary TB with COVID-19 in an Indian female. To the best of our knowledge, there is no such case ever reported in the medical literature to date.

Keywords: Co-infection, COVID-19, SARS-CoV-2, tuberculosis

Introduction

The never seen before pandemic of coronavirus disease-2019 (COVID-19) due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has put life at a standstill.^[1] The sudden and global impact of this pandemic has resulted in large-scale morbidity and mortality.^[1] The situation is spine-chilling in some of the developed countries which had the best healthcare facilities around the globe.^[2] Besides, the situation in the poor and underprivileged countries is extremely woeful and alarming.^[2]

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The impact of COVID-19 on other diseases is a hot topic and is reported in the medical literature.^[3] However, there is a paucity of literature on the impact of this pandemic on diseases like TB which are known to mankind for a long.^[1] Also, the reports of the co-infection of COVID-19 with drug-resistant TB are not available except for a case report with many variations and no clear history from Haiti.^[4] We herein, present the world's first case of primary multidrug-resistant (MDR) pulmonary TB with COVID-19 in an Indian female. To the best of our knowledge, there is no such case ever reported in the medical literature to date. The author's aim was to create awareness in this pandemic as a high degree of suspicion is required to rule out COVID-19 in TB cases and a very detailed clinical examination along with numerous lab investigations is essential to diagnose and treat the MDR-TB with a concomitant SARS-CoV-2 infection.

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Case Report

A 26-year-old Indian female reported to our OPD with chief complaints of fever with chills, chest pain, cough with expectoration, and generalized weakness with loss of appetite and weight loss.

On detailed history, she told us that the fever was high grade (100–101°C) with chills and was off and on for the last 4 days and was relieved after taking tablet Paracetamol. She had a cough with expectoration which was mostly green in color, non-foul smelling and the coughing increased on lying supine, there was not much improvement in cough after taking cough syrup. She also noted that the sputum was blood-tinged on around four occasions. She had breathlessness on exertion and on lying supine which was partially relieved by sitting. There was a loss of appetite with generalized weakness and she also reported that she had lost around six kilograms of her body weight in the last month. The chest pain was mostly in the upper chest, localized to the right side of the chest, and was aggravated on exertion.

She was a worker in a private company but due to lockdown due to COVID-19 in the country, she was staying at home for the last 2 months. There was no history of any substance abuse or any contact of TB or COVID-19 case in the family or close contacts. And there was no history of foreign travel or a visit to a containment zone of COVID-19 in the recent past. There was no history of similar complaints or any other major illness in the past to her or any other member of her family.

On examination, her vitals were pulse-106/minute, arterial BP 130/70 mm of Hg, respiratory rate of 35 breaths/minute, Sp_o₂ 86% on room air, temperature 101°C. Her Sp_o₂ fell by 60% on room air after waking. Dyspnea on exertion was noted which subsided when the patient took a rest. On auscultation, there was crepitation on the upper, middle, and lower lobes of the right lung and upper lobe of the left lung. The rest of the systemic examination was unremarkable.

With the present scenario of COVID-19 pandemic, she was diagnosed as a probable case of TB with COVID-19 and was advised sputum microscopy (Ziehl Neelsen (ZN) staining for acid-fast bacilli), Cartridge-based nucleic acid amplification test (CBNAAT) of the sputum, and a chest radiograph with other routine investigations. To check for the COVID-19 she was advised qualitative polymerase chain reaction (PCR) test from the oropharyngeal swab.

These tests revealed that she was a case of TB with *Mycobacterium tuberculosis* (MTB) detected on sputum fluorescent microscopy. The results of CBNAAT confirmed the findings of sputum smear microscopy and showed MTB detected as medium and was resistant to Rifampicin. Simultaneously a sample of sputum was sent for Line Probe Assay and culture for drug susceptibility testing for first and second-line antitubercular drugs to the

Intermediate Reference Laboratory (IRL). And other relevant investigations as a part of her pre-treatment evaluation to start the shorter MDR regimen were advised.

Meanwhile, her results of the PCR were positive for RNA specific to SARS-CoV-2. And the chest radiograph PA-view [Figure 1] was suggestive of consolidations on the upper, middle, and lower lobes of the right lung and upper lobe of the left lung with ill-defined borders. Other investigations revealed a low lymphocyte count ($1 \times 10^8/L$), a high ESR (80 mm in the 1st hour), increased levels of CRP (60 mg/L), and LDH (578 U/L).

Also, the sample which was sent to the IRL for liquid culture (MGIT BACTEC) revealed the growth of MTB. The reports of LPA were suggestive of Rifampicin resistance. Computed tomography was not performed as the diagnosis was established early by other cheaper and faster methods and also the patient was unwilling for the same. All the other routine investigations were within the reference range. She was referred to the nearest designated COVID-19 management center, where she was managed as per the national guidelines. There she was advised home quarantine for 15 days with symptomatic management. Post completion of the quarantine period she was tested negative on rapid antigen test (RAT) for COVID-19 and thus was started on an antitubercular treatment (ATT) involving the use of second-line ATT as per her body weight with drugs including high-dose Isoniazid, Kanamycin, high-dose Moxifloxacin, Clofazimine, Ethionamide, Ethambutol, and Pyrazinamide as per the Programmatic Management of Drug-resistant TB (PMDT) of the National Tuberculosis Elimination Program (NTEP) guidelines. Presently she is on treatment and doing well with no major complaints and is advised regular follow-ups in the OPD. Written informed consent was obtained from the patient for using images and other relevant data for publication in this study.



Figure 1: Chest radiograph PA-view suggestive of consolidations on the upper, middle, and lower lobes of the right lung and upper lobe of the left lung with ill-defined borders

Discussion

TB is a public health problem and with time it has grown into a bigger challenge with the development of drug resistance in the MTB strain due to mutations.^[5] The pandemic of COVID-19 has already crumbled the weak and fragile healthcare systems and thus in this situation the detection and management of a case with primary pulmonary MDR-TB with COVID-19 co-infection require great clinical skills and a high index of suspicion.^[1] To date, a case of primary pulmonary MDR-TB with COVID-19 co-infection has not been reported in the medical literature. A similar case in a Haitian male was published ahead of print but that case does not mention about the history of TB or any other infectious disease in their patient and our case differs from it as the present case is in an Indian female who had no history of TB in the past, and is from a different geographical location and belongs to different ethnicity, making it the first of its type case ever reported in the world.^[4] Besides, this case is remarkable as the primary MDR-TB constitutes only 3.5% of the total cases and is thus a very uncommon form of a very common infection due to MTB.^[6]

Another case similar to ours was published by Marwah *et al.*, in 2021, however, our case differs from their index case in the absence of hepatitis B, no derangement of liver function tests, no additional resistance to fluoroquinolone, patients gender, and in the management which was done as per the PMDT of NTEP guidelines with no significant delay.^[7] Their case was a Pre-XDR (extensively drug resistant) TB case with chronic hepatitis B and this case was managed with an all-oral WHO regimen involving Bedaquiline.^[7]

This case is an important addition to the medical literature as in the current pandemic other diseases have been given relatively lesser attention.^[3,8] It has been reported that the COVID-19 pandemic has resulted in the low notification of TB cases and thus it could adversely affect the set goals of TB elimination by 2035.^[3,8] The condition is noteworthy in the developed countries which have been affected tremendously by the COVID-19 and similarly, the situation in developing countries some of which had the highest burden of TB is appalling.^[8] The weak and crumbling healthcare systems, overburdened staff, depression among the healthcare workers, lack/improper management of funds, and fear are some of the problems which are evident in this pandemic.^[9] In such a situation the detection of an MDR-TB with a co-infection of SARS-CoV-2 and its management is a challenging task. Besides, the diagnosis of such a case in a patient with no previous history of either of the disease makes the task even more challenging.^[1] Also, the management involves the use of second-line ATT which has a greater number of adverse effects and requires continuous patient counseling for treatment adherence.^[10]

To conclude, the disease like TB is commonly seen in primary practice and in the current pandemic, a high index of suspicion

is required to diagnose the rare presentations as detailed in this index case. Primary pulmonary MDR-TB is very rare and that too with COVID-19 is never reported. The present case will help in creating awareness about these diseases in high TB burden settings where a majority of the population is underprivileged.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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