Coinfection of SARS-CoV-2 and MTB: how not to miss the wood for the trees

Jeny Jacob [1], Rajesh Venkataram [2], Giridhar Belur Hosmane[3]

[1]General Medicine, KS Hegde Medical Academy, Mangalore, Karnataka, India
[2]Department of Pulmonary Medicine, KS Hegde Medical Academy, Mangalore, Karnataka, India
[3]Pulmonary Medicine, KS Hegde Medical Academy, Mangalore, Karnataka, India

Correspondence to
Dr Rajesh Venkataram;
rajdocmmc@gmail.com

Accepted 24 June 2021

To cite: Jacob J, Venkataram R, Hosmane GB. *BMJ Case Rep* 2021;**14**:e240581. doi:10.1136/bcr-2020-240581

SUMMARY

Scarce data exist about the coinfection of SARS-CoV-2 and *Mycobacterium tuberculosis* (MTB). A young woman who was undergoing treatment for multiple sclerosis was brought to our hospital with a COVID-19 positive status. On further evaluation, her chest X-ray showed right upper and mid-zone opacity, which lead to the suspicion of MTB. Her sputum came positive for acid-fast bacilli (AFB) staining and cartridge-based nucleic acid amplification test (CBNAAT) confirmed it, and rifampicin resistance was not detected. She was started on an antitubercular regimen. She was discharged, and by the end of the intensive phase of treatment, her symptoms subsided, but her sputum CBNAAT still showed the presence of TB bacillus.

BACKGROUND

The WHO declared the outbreak of novel COVID-19 a Public Health Emergency of International on 30 January 2020 and as a pandemic on 11 March 2020.[1] In India, country wide lockdown was enforced on 24 March 2020. Subsequently, akin to the situation in most parts of the world, tuberculosis (TB) services provided under National Tuberculosis Elimination Programme got affected badly. Certain viral infections have been known to aggravate Pulmonary TB (PTB), presumably as a result of depressed cellular immunity.[2 3] We present a case of coinfection of SARS-CoV-2 with TB in a patient who had the risk factor for both the diseases.

CASE PRESENTATION

A young woman aged 20 years, who was on immunosuppressant treatment for multiple sclerosis with dimethyl fumarate 240 mg two times per day for the last 1 year, presented with a history of fever, productive cough of 1 month duration, weight loss, fatigue. There was no history suggestive of contact with patients with COVID-19 positive. She was already diagnosed with COVID-19 by real time-PCR (RT-PCR) assay of the nasopharyngeal swab, done on the same day at another hospital. Physical examination showed peripheral oxygen saturation of 95% on room air, blood pressure of 70/56 mm Hg, respiratory rate of 20 cycles/min. Chest examination revealed crepitations in the right mammary area. Chest X-ray showed right upper and mid-zone nonhomogenous opacity (figure 1). Relevant laboratory investigations are given in table 1. She was negative for HIV.

INVESTIGATIONS

TREATMENT

In COVID ICU, she was started on intravenous dexamethasone along with inotropes, antibiotics and other supportive care as per the state health agency protocol. However, the history of weight loss, location of the opacity in chest X-ray and background medication history prompted us to consider PTB as a possibility. Matching our expectations, sputum was positive for acid-fast bacilli (AFB). Cartridge-based nucleic acid amplification test (CBNAAT) confirmed the presence of mycobacterium TB. Resistance to rifampicin was not detected. She was started on standard 4 drug antitubercular regimen containing rifampicin, isoniazid, ethambutol and pyrazinamide as per her body weight. Dimethyl fumarate was continued. During the hospital stay of 10 days, she did not show any features of adverse effects to treatment. Inotropes were tapered and stopped. She required supplemental oxygen via face mask as her Arterial Blood Gas analysis (ABG) in the ICU showed PaO2 of 7 kPa. We were able to taper and stop it over next 12 hours as her saturation gradually improved to 95%. She was not treated with drugs like remdesivir, tocilizumab.

OUTCOME AND FOLLOW-UP

Even after discharge, she was closely monitored for adverse effects (particularly the neurological and ophthalmic-keeping in mind her pre-existing neurological disease) through frequent telephonic enquiries. By the end of intensive phase of 2 months, she had put on 6 kg of weight and all symptoms had subsided. However, her sputum CBNAAT still showed presence of TB bacillus but resistance to rifampicin was not detected. Further testing with Line Probe Assay (LPA) confirmed the absence of resistance to both rifampicin and isoniazid. Now, at the end of 6 months of therapy, her sputum is negative for AFB, she has put on 8 kg of weight in total and all chest reports have subsided.

DISCUSSION

Several authors across the globe have reported the effect of ongoing COVID-19 pandemic on TB services. These include transfer of TB services for COVID-19 use,[4] significant reduction in TB notification rates with the surge of COVID-19[5] and considerable disruption in TB services both in primary care settings in the field as well as hospital settings.[6] The overwhelming nature of the pandemic has rendered many hospitals busy in handling

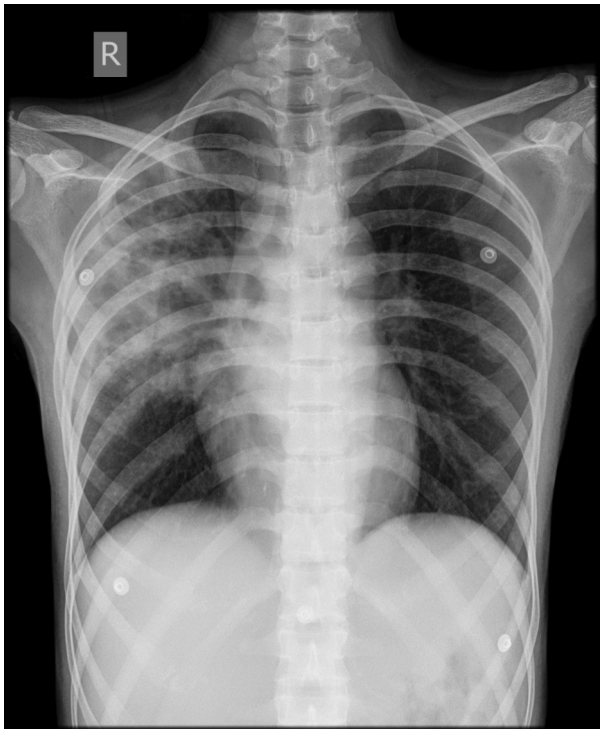

Figure 1 Chest X-ray showing right upper and middle zone opacities.

COVID-19 cases and the focus on non-COVID-19 diseases has taken a hit. In our own experience, it has not become surprising to see the history taking being curtailed to match the definition of severe acute respiratory infections, which has been defined by WHO as an acute respiratory infection with a history of fever or measured fever of ≥38 C° and cough with onset within the last 10 days and requiring hospitalisation.[1] This is being done from a triage point of view, and once the patient fits into these criteria, the next step invariably becomes looking for COVID-19. Once COVID-19 is established, there is less emphasis on relooking at the remaining part of the history and correlating it with imaging features.

This case report underscores the value of being rooted in the basics. The patient presented with features of severe acute respiratory illness coupled with hypotension and a COVID-19-positive RT-PCR report. But careful attention to the history of weight loss in the background of ongoing immunosuppressive medications gave a different perspective to the chest X-ray findings of right upper and mid-zone opacities. Since long, TB is known to present mostly as unilateral disease with a particular predilection to right upper lobe, whereas COVID-19 is usaually a bilateral disease without predilection to any lobe. Hence, it was imperative to investigate for PTB as well.

Table 1 Laboratory investigation results are summarised

Lowest leucocyte count	5000
Lowest PaO_2, kPa	70
Highest serum alanine aminotransferase, U/L	18
Highest C reactive protein, mg/L	23.59
Highest *erythrocyte sedimentation rate*, mm/h	70
Ferritin, ng/mL (reference range 13–150)	145.1
Total bilirubin, mg/dL	0.28

PaO2, Partial pressure of arterial oxygen, expressed in kilopascal unit .

Tadolini M and colleagues have published the first cohort of 49 TB and COVID-19 coinfection cases from eight countries. They have observed higher percentage of multidrug-resistant TB in their cohort.[7] Hence, this patient was closely monitored for emergence of resistance with appropriate molecular tests like CBNAAT and LPA, as, at the end of second month of treatment, the sputum smear was positive for AFB. This is generally attributed to the presence of nonviable bacilli in the sputum. As the molecular tests showed absence of resistance, she was continued on same first-line medications. Now, at the end of 6 months treatment, sputum smear is negative for AFB.

Our patient contracted COVID-19 at a time when community transmission was rampant in the region as evidenced by overwhelming number of cases being detected without history of contact with a known case. Hence, we agree with the observations of Saunders and Evans[8] who have opined that COVID-19 maybe a superimposition on underlying TB. In the initial days of pandemic when the transmission of the virus was happening among the contacts of the index case, people with subtle symptoms were scared of visiting hospitals because of the fear of contracting infection from COVID-19 cases in the hospital premises. The subsequent stage of community transmission of the virus is probably unmasking such subtle but probable cases of active TB, as they are now actively seeking medical help to get tested for COVID-19.

Learning points

- COVID 19 pandemic has caused a remarkable dent in the ongoing TB control activities across the country adversely affecting the routine programmatic activities like case finding, initiation of treatment, follow-up to ensure adherence and to check for adverse reactions and contact tracing.
- Any delay diagnosis and treatment can lead to progressive disease requiring extensive management, and some may develop multidrug resistance and super infection by coronavirus.
- Though there is considerable overlap between the clinical features, TB has a subacute natural history, whereas that of COVID is acute one and differentiating between the two holds the key for what is known as 'not missing the wood for the trees'.

Contributors JJ contributed to the patient management, data collection and writing of the manuscript. RV contributed to the diagnosis and management of the patient, designing the manuscript and approval of the final version of the manuscript. GB-H contributed to the diagnosis and management of the patient, designing the manuscript and approval of the final version of the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Jeny Jacob http://orcid.org/0000-0002-4386-2095
Rajesh Venkataram http://orcid.org/0000-0002-4474-6117

REFERENCES

1 World Health Organization. Statement on the second meeting of the International health regulations (2005) emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). Available: https://www.who.int/news-room/detail/30-01-2020-statement-on-the-secondmeeting-of-the-international-health-regulations-(2005)-emergencycommittee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov)
2 Griffin DE, Bellini WJ. Measles virus. In: Fields BN, Knipe DM, Howley PM, eds. *Virology*. Philadelphia, PA: Lippincott-Raven, 1996: 1267–312.
3 Kempe CH, Fulginiti VA. The pathogenesis of measles virus infection. *Arch Gesamte Virusforsch* 1965;16:103–28.
4 Cronin AM, Railey S, Fortune D, *et al*. Notes from the Field: Effects of the COVID-19 Response on Tuberculosis Prevention and Control Efforts - United States, March-April 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:971–2.
5 Kwak N, Hwang S-S, Yim J-J. Effect of COVID-19 on tuberculosis notification, South Korea. *Emerg Infect Dis* 2020;26:2506–8.
6 Jain VK, Iyengar KP, Samy DA, *et al*. Tuberculosis in the era of COVID-19 in India. *Diabetes Metab Syndr* 2020;14:1439–43.
7 Tadolini M, Codecasa LR, García-García J-M, *et al*. Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases. *Eur Respir J* 2020;56:2001398.
8 Saunders MJ, Evans CA. COVID-19, tuberculosis and poverty: preventing a perfect storm. *Eur Respir J* 2020;56:2001348.