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Case Report

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When Tuberculosis Co-Presenting with COVID-19 Becomes a Challenge, Case Report and Short Review

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ABSTRACT

With current SARS-CoV-2 pandemic, patients with respiratory symptoms are diagnosed with SARS-CoV-2 more readily, but we may oversee some prevalent infective diseases that may co-exist. We report a case of SARS-CoV-2/tuberculosis co-infection and the importance of considering tuberculosis amidst SARS-CoV-2 pandemic.

Introduction

Concurrent tuberculosis and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection poses a unique challenge in the midst of current pandemic. We illustrate a case of miliary tuberculosis manifesting after the diagnosis of SARS-CoV-2 infection and briefly review this scenario of clinical 'double jeopardy'.

Case presentation

A 27-year-old South Asian migrant worker residing in a dormitory with no prior SARS-CoV-2 contact, presented to the emergency department with a 3-week history of fever. He has no acute respiratory infection symptoms. On examination, he was febrile with 38°C, not in respiratory distress. Lung examination was normal. Chest X-ray showed no evidence of infiltrates (Fig. 1A). SARS-CoV-2 PCR (nasopharyngeal swab) was positive. He was given symptomatic treatment and did not require anti-viral agent.

Over the next two weeks, patient continued to experience daily unremitting fever. New finding of bilateral nodular densities was noted on repeat chest X-ray (Fig. 1B). Further CT imaging revealed diffuse

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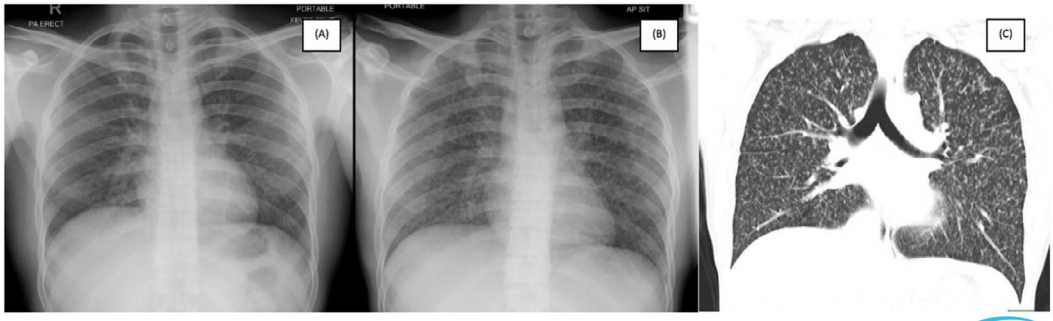

Fig. 1A. Chest X-Ray at initial presentation shows clear lung fields.
Fig. 1B. Subsequent chest X-Ray demonstrates extensive miliary opacities in both lungs.
Fig. 1C. Coronal image in lung window from CT scan performed two weeks later demonstrates extensive tiny (0.1-0.3 cm), randomly distributed nodules with no lobar sparing or predominance in keeping with miliary nodules.

miliary nodules in both lungs (Fig. 1C) with systemic dissemination involving spleen, liver and kidney. Sputum smear for acid-fast bacilli was negative, but sputum analysis for Mycobacterium tuberculosis PCR (Xpert MTB/RIF assay) was positive. He was then started on anti-tuberculosis therapy. A follow-up swab for SARS-CoV-2 PCR became negative.

The remainder of the investigations: respiratory virus multiplex PCR, Rickettsia/ Orientia serology, Bartonella serology, Malaria parasite, leptospirosis IgM, Brucella antibody, Burkholderia pseudomallei serology, Coxiella burnetii and human immunodeficiency virus serology were all negative. Blood culture for Mycobacterium tuberculosis was negative. Following treatment, patient was discharged well.

Discussion

Tuberculosis and SARS-CoV-2 infection are two conditions with overlapping clinical features: fever and cough. Both conditions find themselves thriving in ideal situations of transmissibility: close contact, cramped living quarters with inadequate ventilation, amongst migrant workers as depicted in this case. In the middle of a pandemic storm, it is easy to overlook another concurrent infection such as tuberculosis. Typically, tuberculosis has an insidious onset as compared to the more rapid presentation of SARS-CoV-2 infection, thus an early tuberculosis infection may not be apparent initially. As a result, presence of SARS-CoV-2 infection may prompt early medical consultation thus unmasking underlying tuberculosis infection.

In our patient with SARS-CoV-2 infection, tuberculosis was not considered initially as he had a normal chest X-ray. He was from South Asian country, which is highly endemic for tuberculosis and had a protracted history of fever, beyond what would be expected in a patient with SARS-CoV-2 infection. With persistence of symptoms, repeated evaluation revealed new changes on chest imaging which prompted a cascade of further investigations. He could have developed tuberculosis during the course of SARS-CoV-2 infection or the diagnosis of tuberculosis may be delayed as we did not perform early CT imaging that would have revealed subtle pulmonary changes not evident on chest X-ray.

Miliary tuberculosis usually has classical X-ray appearance compared to viral pneumonia. If the changes are subtle, CT imaging can help us better characterise the pulmonary changes. While ground-glass opacities are the predominant CT findings in SARS-CoV-2 infection [1], the presence of 1 to 3mm miliary nodules with random distribution on CT thorax as in our patient's CXR and CT is more suggestive of tuberculosis instead of viral pneumonia [2]. The diagnosis was further supported by positive microbiology testing of sputum.

SARS-CoV-2/tuberculosis co-infection is not uncommon. Tadolini *et al* recently reported a series of 49 cases of SARS-CoV-2/tuberculosis co-infection [3]. From their observation, they were unable to conclude a causal relationship between SARS-CoV-2/ tuberculosis infections, but noted higher mortality in older patients diagnosed of SARS-CoV-2 infection with TB sequelae. From a prognostic point of view, Stochino *et al* found that patients with SARS-CoV-2 /tuberculosis co-infection did not necessarily do worse clinically and radiologically although the study population was younger and had less comorbidities [4].

Nevertheless, there is still a paucity of data regarding pathophysiologic association between SARS-CoV-2/ tuberculosis infections. Reports from previous respiratory virus and tuberculosis co-infections,

particularly influenza and SARS, suggested that viral infection may alter host cellular immunity leading to tuberculosis infection [5] and affect its disease severity [6]. More data is needed to understand how SARS-CoV-2 affect our host immunity and how/whether this alteration influences one's susceptibility to other infection. Furthermore, the link between SARS-CoV-2 and the severity of underlying tuberculosis infection is uncertain. In this case, the delay in diagnosis may be contributed by diagnostic challenges with SARS-CoV-2 co-infection instead of a direct effect of SARS-CoV-2 pathogenicity.

In Singapore, we witnessed outbreaks of SARS-CoV-2 infection among the migrant worker population who reside in dormitories. Given the crowded living conditions with vast majority of the migrant workers originating from South Asian countries that are highly endemic for tuberculosis, the clustering of SARS-CoV-2 and pulmonary tuberculosis cases among this group is not all that surprising [7].

Tuberculosis is an important consideration in patients with chronic fever and respiratory symptoms particularly in countries with high disease prevalence. One must always have a high index of suspicion for tuberculosis in the appropriate clinical setting. The outbreak of a pandemic should not preclude the possibility of an already prevalent disease like tuberculosis. As such, we should avoid the trap of "tunnel vision" and consider tuberculosis as a primary differential in high-risk patients with relevant clinical features.

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 declare that there is no conflict of interest regarding the publication of this article.

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