COVID-19 and Pulmonary Mycobacterium Tuberculosis Co-infection-Report of Two Cases

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Abstract

The Corona virus disease-2019 (COVID-19) outbreak classified as a global pandemic by the World Health Organization (WHO) on March 11, 2020, is caused by a novel corona virus called “severe acute respiratory syndrome coronavirus 2” (SARS-CoV-2). The virus affects mainly the human respiratory system. Mycobacterium Tuberculosis (TB) is another respiratory infection known to affect human for centuries and may share common clinical presentation and risk factors with COVID-19 infection. Clinicians must have a high index of suspicion that the two infections might co-exist so there is no delay in the diagnosis and starting the appropriate treatment. There are few case reports about TB and COVID-19 co-infection, the first case report ever was from china, and few others around the world. Here we report two cases of co-existing COVID-19 and newly diagnosed pulmonary TB infections in Oman.

Introduction

The Corona virus disease-2019 (COVID-19 is caused by a novel corona virus called “severe acute respiratory syndrome coronavirus 2” (SARS-CoV-2), that targets the respiratory

system. COVID-19 started in China in December 2019; it was declared as pandemic by World Health Organization (WHO) on March 11, 2020 [1]. The incubation period is around 5-6 days and the symptoms are mainly fever, cough, shortness of breath or loss of smell sensation. The main reported risk factors include age above 65 years or having comorbid conditions such as diabetes mellites, ischemic heart disease, hypertension, chronic lung disease and immunosuppression [2, 3].

On the other hand, Pulmonary Tuberculosis (TB) is one of the oldest diseases that affected human long time ago [4]. Mycobacterium tuberculosis is the most common cause of tuberculosis (TB) worldwide. TB is a contagious disease and 90% of individuals after infection will develop latent TB [5]. Diabetes mellites, immunosuppression, underlying chronic lung diseases and Human Immunodeficiency Virus (HIV) are among the risk factors to develop active TB disease [6].

During the pandemic of COVID-19, several respiratory pathogens co-infection with COVID-19 were reported, including bacterial and fungal pathogens. About 50% of the patients who died from COVID-19 had secondary respiratory infections [7]. A multination study found that 49 patients had TB and COVID-19 co-infection, 85% of the patients had active TB, and 18% of the cohort had diagnosis of TB and COVID-19 in the same period [8]. Another report was from Italy, they had 20 cases of TB and COVID-19 co-infection, 95% of them were having pulmonary tuberculosis, and one patient had disseminated TB [9]. A recent report from Qatar of 6 cases with co-infection of COVID-19 and tuberculosis, all of them were middle aged men, none of the patients had a known history of direct exposure to TB; however, all of them were south-Asian descents where TB is endemic. All of them had pulmonary TB and one of them had pulmonary and pleural TB [10]. Since there is only one published case report in the Middle East and North Africa region as per our knowledge [10], hereby, we report two cases of Pulmonary TB and COVID-19 co-infection in Oman.

Case 1

56 years old Omani man who is an active smoker and known to have Hypertension and diabetes mellitus on treatment, presented with a 3-months history of productive cough with whitish sputum, for which he did not seek any medical attention. Patient developed high-grade fever associated with sore throat, flu-like symptoms and headache three days prior to

his admission to our hospital. He had no hemoptysis, shortness of breath, chest discomfort, weight loss or night sweats and no history of travel or contact with sick patients.

On physical examination, the patient was febrile with temperature of 39.2 ºC and tachypneic with a respiratory rate of 26 breath per minute. His heart rate was ranging between 80-90 beats per minute and his blood pressure was normal. He did not have any palpable cervical or axillary lymphadenopathy. His chest examination revealed bilateral equal air entry with bronchial breathing in the right upper lung.

The chest X-Ray showed a right upper lung zone thick wall cavitary lesion associated with surrounding innumerable nodular opacities. In addition, there was a right lower lung zone ill-defined airspace opacity with a subtle nodularity. Findings were highly suggestive of pulmonary TB. (Figure 1).

The patient was empirically treated per national clinical management for COVID-19 guideline with ceftriaxone, clarithromycin and oseltamivir. Nasopharyngeal SARSCoV-2 PCR test, sputum for Mycobacterium Tuberculosis Polymerase Chain Reaction (MTB/RIF GeneXpert Cepheid-PCR) and sputum for TB cultures were all performed and tested positive. The patients white blood cells count was $7.2*10^9$/L (2.2-10), absolute neutrophils count was $4.3*10^9$/L (1-5) and absolute lymphocytes count was $1.8*10^9$/L (1.2-4). C-Reactive Protein was 63.5 mg/L (<30) and ESR was >130 mm/hr (2-25), lactate dehydrogenase level was 128 iU/L (120-246), ferritin level was 514 ug/L (48-708), cross linked D-Dimer level was 0.44 mg/L (0.1-0.5). He was started on Hydroxychloroquine and lopinavir/ritonavir and anti TB treatment with isoniazid, rifampicin, ethambutol and pyrazinamide. The patient improved and he was discharged home to continue anti-TB treatment.

Case 2

A 42-years-old non-smoker expatriate man, not known to have any medical background, presented with cough, chest pain and shortness of breath for three months associated with 4-kilogram weight loss for which he did not seek any medical treatment. The patient developed a high-grade fever of 39 ºC three days prior to admission. He had no sick contact or recent travel outside the country. On presentation to the emergency department, he was desaturating on room air with an oxygen saturation (SpO2) of less than 90%, that increased to > 95% with 2L of oxygen. He was hypotensive with BP of 85/50 mmHg. He had dry mucous membranes and his capillary refill was > 3 seconds. His chest examination revealed bilateral course

crackles; however, it was more in the right side. The patient had a negative SARS-CoV-2 PCR test done in local health center. The patient was started on ceftriaxone, clarithromycin and oseltamivir empirically due to high suspicious of COVID-19 infection.

His Chest X-Ray showed diffuse nodular pattern along with airspace opacities involving all the right lung zone. In addition, there was a left upper lung zone airspace opacity along with subtle nodularity involving the left mid lung zone, finding suggestive of pulmonary TB along with co-exiting infection. (Figure 2).

The patient's white blood cells count was $8.1*10^9$/L (2.2-10), absolute neutrophils count was $6.5*10^9$/L (1-5) initially. He had lymphopenia of $0.5*10^9$/L (1.2-4), C-Reactive Protein was 194 mg/L (<30) and ESR was >85 mm/h (2-25). A repeat nasopharyngeal SARS-CoV-2 PCR was performed as well as sputum was collected for MTB/RIF GeneXpert Cepheid-PCR and TB cultures, and all were positive. His Ferritin level was high around 1170 ug/L (48-708) along with lactate dehydrogenase of 352 iU/L (120-246) and D-Dimer of 11.44 mg/L (0.1-0.5). Patient was treated with hydroxychloroquine and anti TB medications. The patient improved and discharged home to continue anti-TB treatment.

Discussion

COVID-19 is caused by a novel corona virus, belongs to the genus Betacoronavirus, called "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2), and can transmit through human-to-human contact [(11)]. In human, corona viruses can cause a variety of respiratory illnesses ranging from common cold to severe pneumonia such as severe acute respiratory syndrome (SARS-CoV) and Middle East respiratory syndrome (MERS). There are few case reports that reported co-infections between SARS- CoV and MERS-CoV infections [(12-14)], and regarding COVID-19, a report from Islamic Republic of Iran of Influenza A virus co-infection [(15)].

We are reporting two cases of COVID-19 and pulmonary TB co-infection, to our knowledge there are very few reports worldwide, the first reported cases were from China, 2 of their patients were treated for active TB years before having COVID-19 and now they presented with re-activation of TB, the other one was not treated for TB for more than 50 years [(16)]. In Philippines, 1% of the patients who were infected with COVID-19 had co-infection with TB, and it was found that patients with TB had 2.17 times higher risk of death

when compared to those without TB. Additionally, those with TB and COVID-19 co-infection had 25% less risk of recovery than patients without TB [17]. In South Africa around 2128 patients had TB and COVID 19 co-infection out of 22308 studied and they found that having TB have worse outcome compared to non-TB patients [18].

In this case report, the first patient is a chronic smoker, and he is hypertensive and diabetic, all of those could increase the risk of TB and since his symptoms started in the period were COVID-19 infection started in Oman, his findings are more likely to be co-infection rather than co-incidence. The other patient despite being free of medical background, however, he is from an area that has high TB burden; hence, it is more likely that he had reactivation and co-infection.

In 2018 the annual incident rate of TB in Oman was < 5.9 cases per 100000 population and 60% of the annual cases were from non-national citizens [19]. It was noted as well from previous MERS-CoV and SARS-CoV that TB and those infections may augment each other and cause immunosuppression [12, 20], which might be similar to what happens in SARS-CoV-2. There are few reports indicates that patients with pulmonary TB are more susceptible to develop SARS-CoV2 infection as both could impair the immune system and this synergism may cause a very severe clinical picture. The researchers claimed that pulmonary TB is a major risk factor for COVID-19 infection [21]. One of the pathophysiological mechanisms postulated for COVID-19 infection is cytokine storm, and these cytokines play an important role in TB host resistance [22]. Another pathophysiological mechanism is that lung damage caused by TB increases the body's susceptibility to get other airborne infection such as COVID-19 [23].

Future studies should aim at looking on the impact of TB and COVID-19 co-infection in terms of morbidity and mortality. Furthermore, studies are needed to develop strategies and plans on how to contain the co-infection and prevent further spread of both diseases.

Conclusion

In conclusion, COVID-19 is newly emerged infection that can co-exist with other pulmonary infections. Mycobacterium Tuberculosis is a pathogen that can co-exist with COVID-19 infection and requires a high clinical suspicion when the chest radiograph is very suggestive

of pulmonary TB. Early recognition of TB would result in initiating of appropriate infection control measures and anti TB therapy. Furthermore, screening all patients admitted with SARS-COV-2 infection for TB would be important to define the role of COVID-19 in reactivation of TB. Finally, clearly documented diagnostic and management algorithms should be implemented in order to improve the outcome from the co-infection.

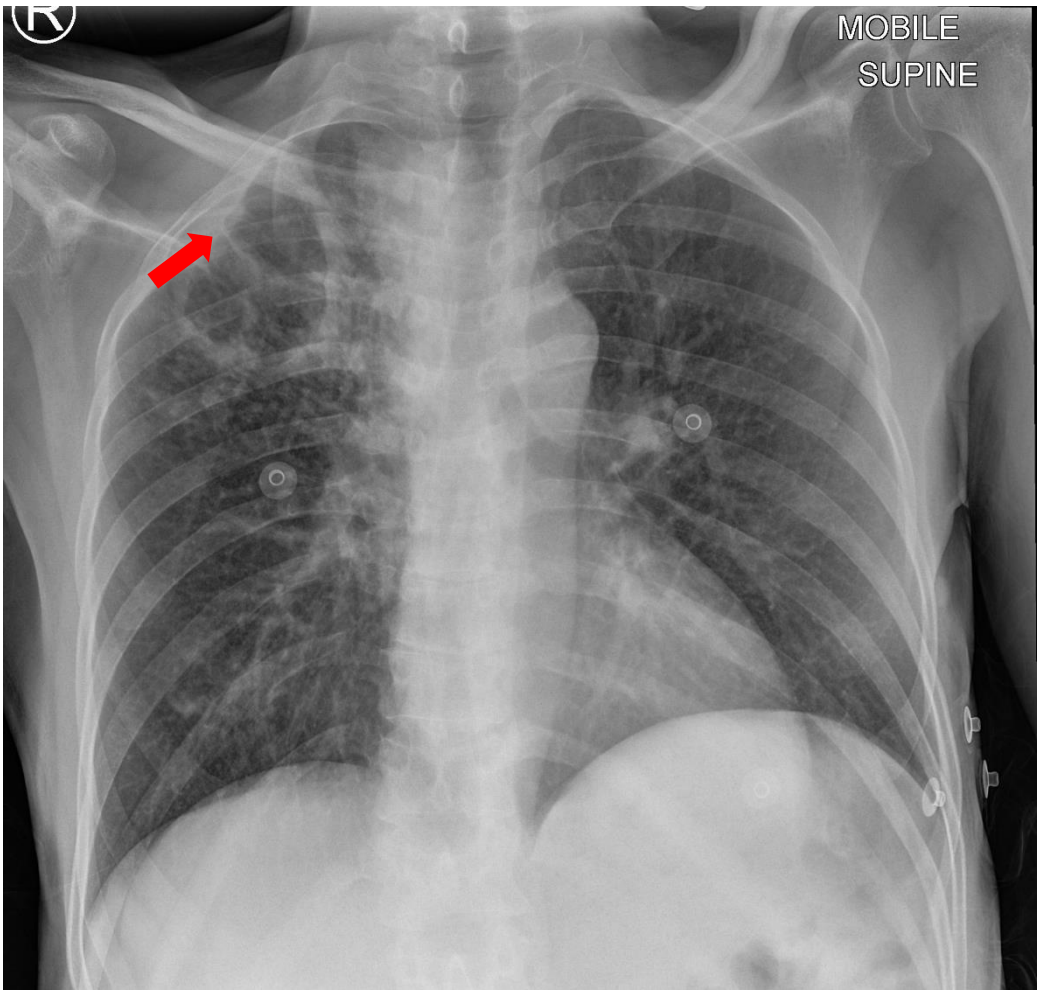

Figure 1. Frontal chest X-Ray showing a right upper lung zone thick wall cavitary lesion (Red arrow) associated with surrounding innumerable 1-2 mm. In addition, there is a right lower lung zone ill-defined airspace opacity with a subtle nodularity.

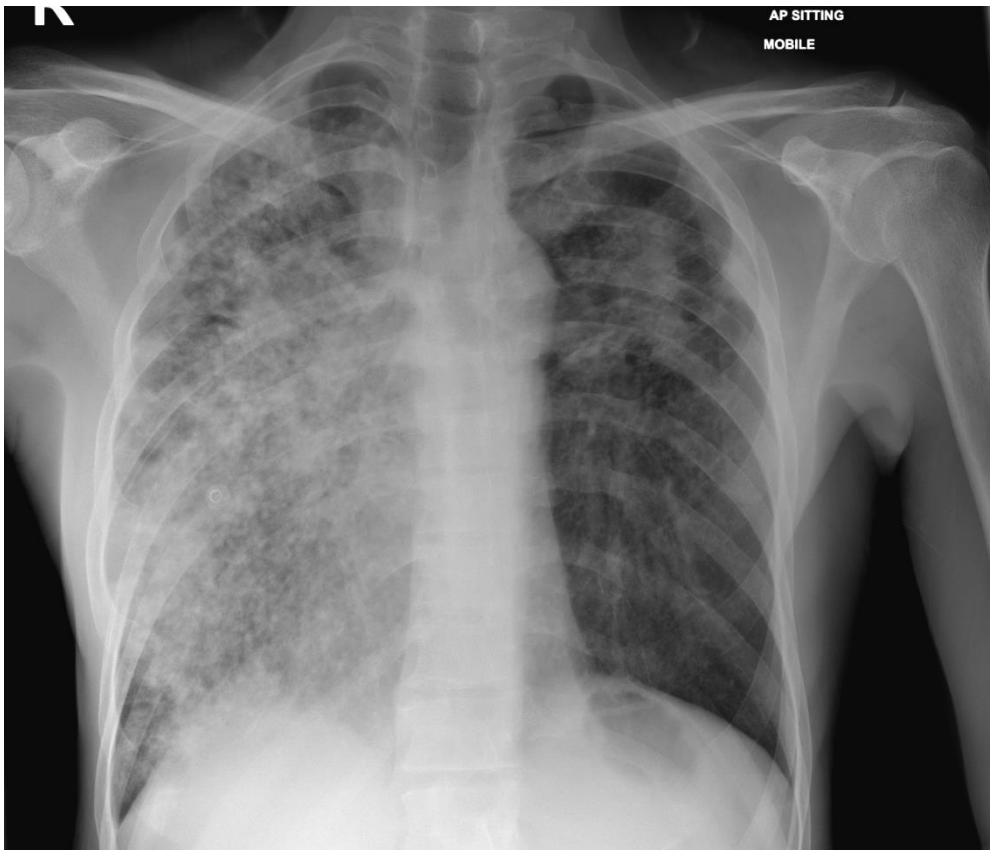

Figure 2. Frontal chest X-Ray showing a diffuse nodular pattern along with airspace opacities involving all the right lung. In addition, there is left upper lung zone airspace opacity along with subtle nodularity.

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