CASE REPORT e-ISSN: 2349-0659 p-ISSN; 2350-0964

Coronavirus Disease-19 Pneumonia or *Pneumocystis carinii* Pneumonia in a Patient with Diabetes: A Diagnostic Dilemma

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Abstract

Coronavirus disease 2019 (COVID-19) and pneumocystis pneumonia share many overlapping features and may be clinically indistinguishable on initial presentation in people living with human immunodeficiency virus severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) belongs to the subfamily of beta-coronavirus, which are responsible for respiratory, enteric, hepatic, and neurologic diseases, due to their broad tissue tropism. In the present patient, the course was acute with dyspnea being one of the major symptoms and lung involvement was seen to be peripheral. The two negative reverse transcription polymerase chain reaction (RT-PCR) reports for SARS-CoV-2 along with the differences in the interpretation of the computed tomography scans led to the diagnosis difficulty in the present case. COVID-19 pneumonia may have similar presentation like that of *Pneumocystis carinii* pneumonia. The low sensitivity of RT-PCR which is considered the gold standard of diagnosis of SARS-CoV-2 and the similarities in presentation between the two types of pneumonia, along with increased prevalence of both the types of pneumonia amongst diabetics, may give rise to diagnostic difficulties.

Keywords: Coronavirus disease 2019, Coronavirus disease-19 pneumonia, High-resolution computed tomography of thorax, *Pneumocystis carinii* pneumonia, Reverse transcription polymerase chain reaction, Severe acute respiratory syndrome-coronavirus 2, Type 2 diabetes mellitus

Asian Pac. J. Health Sci., (2021); DOI: 10.21276/apjhs.2021.8.3.03

Case Report

A 75-year-old male with a history of type 2 diabetes mellitus for the past 10 years on oral hypoglycemic agents along with a history of ischemic heart disease presented to the emergency department with complaints of dyspnea on exertion and shortness of breath for the past 7 days, decreased urine output for the past 2 days and pain in the left lower limb. The patient had been admitted at his local hospital where a reverse transcription polymerase chain reaction (RT-PCR) test for severe acute respiratory syndrome-coronavirus 2 (SARS-CoV2) was found to be negative and he was given treatment with bronchodilators, diuretics, and antibiotics for 2 days without any improvement in symptoms. On examination, he was conscious and oriented. He had tachycardia (140/min), was normotensive (140/80 mmHg). There was bilateral crepitation on chest examination. Examination of all the other systems was found to be normal.

Investigations

Following are the results of the investigations done:

- Hypoxia in arterial blood gas analysis with oxygen saturation of 93% without oxygen
- Total leukocyte count was raised (18,000/mm^3) with a left shift (neutrophil count: 93%, lymphocyte count: 7%)
- Random blood sugar at admission: 260 mg/dL
- Glycosylated hemoglobin: 9.5%
- Creatinine: 1.5 mg/dL
- Blood urea: 65 mg/dL.

Inflammatory parameters were as follows:

- C-reactive protein: 20.8 mg/dL
- Lactate dehydrogenase (LDH): 638 U/L
- D-dimer: 2231 DDU
- Ferritin: 586 ng/mL
- Procalcitonin: 0.4 ng/mL
- Interleukin-6: 6.2 pg/mL
- Troponin I: Negative
- Liver function test was normal
- Urine and blood culture/sensitivity were not suggestive of any infections, were sterile
- Left lower limb venous Doppler revealed complete obstruction of the venous system
- Multiplex polymerase chain reaction (BioFire) from nasopharyngeal swab was negative.

High-resolution computed tomography (HRCT) of thorax was done twice 3 days apart which had entirely different interpretations from two different radiologists:

The first HRCT of thorax revealed multiple areas of ground-glass opacity with small patches of consolidation and inter/intraseptal thickening in all segments of both lungs, more predominant in the peripheral lung and multiple rounded air cysts with a computed tomography (CT) severity index of 23/25, suggestive of coronavirus disease (COVID)-19 pneumonia [Figure 1a]. A second RT-PCR for

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How to cite this article: Banerjee A, Bhattacharya P, Roy H, Sen S. Coronavirus Disease-19 Pneumonia or *Pneumocystis carinii* Pneumonia in a Patient with Diabetes: A Diagnostic Dilemma. Asian Pac. J. Health Sci., 2021; 8(3):15-17

Source of support: Nil

Conflicts of interest: None.

Received: 23/03/2021 **Revised:** 25/04/2021 **Accepted:** 13/05/2021

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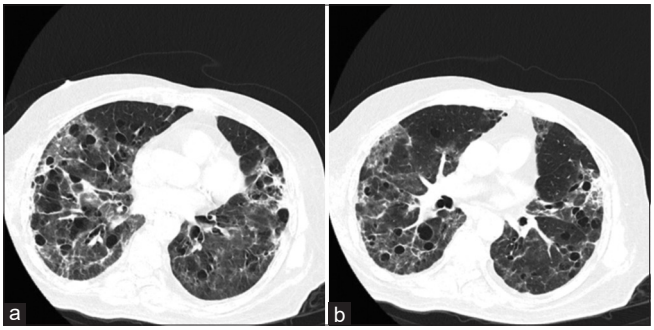

Figure 1: (b) Multiple areas of ground-glass opacity with small patches of consolidation and inter/intraseptal thickening in all segments of both lungs multiple. (b) Diffuse ground-glass opacities of bilateral lungs with multiple pneumatoceles suggestive of *P. carinii* pneumonia

SARS-CoV-2 was sent which was again negative. The second HRCT of thorax was reported as diffuse ground-glass opacities of bilateral lungs with multiple pneumatoceles suggestive of *Pneumocystis carinii* pneumonia [Figure 1b]. Human immunodeficiency virus (HIV) serology was negative. CD4 count was sent and was found to be low at 150.

Management Approach

In view of the present pandemic situation, though RT-PCR was negative, taking into consideration of the clinical presentation and first CT findings, treatment was started in the line of moderate COVID-19 pneumonia with remdesivir, methylprednisolone, anticoagulants, and awake proning and rebreather mask. Hyperglycemia was managed with intravenous insulin pump.

After the second CT report, the possibility of *P. carinii* pneumonia given the background of diabetes mellitus was also taken into consideration. The low CD4 count propelled the possibility of *P. carinii* pneumonia and the patient was started on trimethoprim sulfamethoxazole. Bronchioalveolar lavage was attempted which was not successful because of severe shortness of breath. However, in the next 2 days, the oxygen status deteriorated and the patient was put on mechanical ventilation (continuous positive airway pressure-non-invasive ventilation). Keeping in mind the high chances of false negativity of RT-PCR for SARS-CoV-2, a third RT-PCR for SARS CoV2 was sent which was positive. The patient gradually improved on the treatment protocol for COVID-19 pneumonia and was weaned and extubated after 4 days. The leg swelling improved. Glycemic control was maintained with subcutaneous basal-bolus therapy. All the clinical and biochemical parameters improved over a period of 1 month. Before discharge, the RT-PCR for SARS-CoV-2 was negative. He was discharged on rivaroxaban, basal-bolus insulin, statins, antiplatelets, and antioxidants.

Discussion

The present case has been presented with an aim to highlight the diagnostic difficulty that may arise in differentiating between *P. carinii* pneumonia and COVID-19 pneumonia. Both the types of pneumonia may occur more commonly in diabetics and share some similarities in their presentation.

P. carinii is an opportunistic eukaryotic pathogen, which is a cause of pneumonia most often in persons with HIV infection though it can also occur in patients without HIV infection, in conditions associated with certain diseases and immunocompromised states.[1] *P. carinii* pneumonia has been reported to have a higher incidence among patients of diabetes mellitus also. A study from Iran had reported a prevalence rate of *P. carinii* pneumonia to be around 20% among patients of type 2 diabetes.[2]

The outbreak of SARS-CoV-2 that causes an atypical form of pneumonia started in Wuhan, China, in December 2019 and has affected 29,459,649 people till the time writing of this case study. Studies have shown that patients with diabetes who are infected with SARS-CoV-2 virus are at a higher risk for severe pneumonia associated with dysregulation of glucose metabolism when compared with patients without diabetes.[3,4] Although, nasopharyngeal RT-PCR remains the gold standard for diagnosing COVID-19, the rate of false negatives is also quite high with reports of up to 54% initial false-negative RT-PCR which subsequently turned to be positive.[5] Chest CT has a high degree of sensitivity for diagnosis of COVID-19 pneumonia. In a report of 1014 cases, 60–93% had initial positive CT scans consistent with COVID-19 before the initial positive RT-PCR results.[6,7] It has been suggested that patients with typical CT findings but negative RT-PCR results should be treated as COVID-19 pneumonia and RT-PCR should be repeated to avoid misdiagnosis.[7]

The similarities between the two types of pneumonia caused by SARS-CoV-2 and *P. carinii* include: [8,9]

- Fever, fatigue, dry cough, and dyspnea are the shared common clinical features in both *P. carinii* pneumonia and COVID-19
- Lyphopenia is a common presentation in patients with both *P. carinii* pneumonia and COVID-19, although leukocytosis has also been reported in COVID-19 pneumonia
- Symmetrical bilateral ground-glass opacities are common findings in the chest CT scans in both types of pneumonia
- Elevations of LDH as a prognostic marker that has also been reported in both COVID-19 pneumonia and *P. carinii* pneumonia.

However, in spite of these similarities, there are certain points which help to differentiate between the two: [10,11]

- The course of *P. carinii* pneumonia is generally more subacute as compared to COVID-19 pneumonia with majority of patients having symptoms for at least 2–4 weeks in the former as compared to 8–9 days in the later.[10] In the present, the patient symptoms were present about a week before presentation
- Dyspnea is also a more prominent symptom in *P. carinii* pneumonia with one series showing presence of dyspnea in 95% compared to 30% in COVID-19
- Oral thrush, which has a strong association with *P. carinii* pneumonia, has not been seen in COVID-19. This was not present in the present patient
- Peripheral involvement of the lungs occurs in COVID-19 pneumonia while *P. carinii* pneumonia-related ground-glass opacities tend to spare the lung peripheries and may be associated with cyst formation and spontaneous pneumothorax.[11]

Broadhurst *et al*.[12] also reported a case of coinfection with COVID-19 and pneumocystis pneumonia (PCP) in a patient with progressive respiratory failure admitted to our intensive care unit where the dominant disease was uncertain. That case highlights the

difficulty in differentiating between the two diseases, especially in a high HIV prevalence setting where PCP is frequently diagnosed using case definitions and clinical experience due to limited access to bronchoscopy, appropriate laboratory testing, and CT scans. In addition, diagnostic testing may yield false-negative results in both diseases, and clinician awareness to the overlap and pitfalls is essential if COVID-19 becomes endemic in such settings.[12]

In the present patient, the course was acute with dyspnea being one of the major symptoms and lung involvement was seen to be peripheral. The two negative RT-PCR reports for SARS-CoV-2 along with the differences in the interpretation of the CT scans led to the diagnosis difficulty in the present case.

Case Clinical Pearls

- COVID-19 pneumonia may have similar presentation like that of *P. carinii* pneumonia
- The low sensitivity of RT-PCR which is considered the gold standard of diagnosis of SARS-CoV-2 and the similarities in presentation between the two types of pneumonia, along with increased prevalence of both the types of pneumonia amongst diabetics, may give rise to diagnostic difficulties.

Conclusion

In the present patient, the course was acute with dyspnea being one of the major symptoms and lung involvement was seen to be peripheral. The two negative RT-PCR reports for SARS-CoV-2 along with the differences in the interpretation of the CT scans led to the diagnosis difficulty in the present case. Clinicians working with increased prevalence of both the types of pneumonia amongst diabetics in populations need to consider PCP as a differential in a patient with COVID-19 pneumonia and consider empiric treatment while awaiting a definitive diagnosis. Pitfalls remain around imaging and definitive diagnostic testing.

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