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Pulmonary arterial hypertension confirmed by right heart catheterization following COVID-19 pneumonia: A case report and review of literature

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Abstract

BACKGROUND

¹ Pulmonary arterial hypertension (PAH) is a disease of the arterioles resulting in an increased resistance in pulmonary circulation with associated high pressures in the pulmonary arteries, causing irreversible remodeling of the pulmonary arterial walls. Coronavirus disease 2019 (COVID-19) has been associated with development of new onset PAH in the literature leading to symptoms of dyspnea, cough and fatigue that persist in spite of resolution of acute COVID-19 infection. However, the majority of these cases of COVID related PAH were diagnosed using echocardiographic data or *via* right heart catheterization in mechanically ventilated patients.

CASE SUMMARY

Our case is the first reported case of COVID related PAH diagnosed by right heart catheterization in a non-mechanically ventilated ⁶ patient. Right heart catheterization has been the gold standard for diagnosis of pulmonary hypertension. Our patient had right heart catheterization four months after her initial COVID-19 infection due to persistent dyspnea.

CONCLUSION

This revealed new onset PAH that developed following her infection with COVID-19, an emerging sequela of the infection

INTRODUCTION

This case highlights pulmonary arterial hypertension (PAH) as a potential pulmonary-vascular complication of coronavirus disease 2019 (COVID-19).

CASE PRESENTATION

Chief complaints

A 71-year-old African American woman ³ with a history of hypertension, chronic renal impairment and hyperlipidemia presented to the emergency department (ED) with fatigue, non-productive cough and mild dyspnea for a few days. She denied fever, myalgias, headaches, vomiting or diarrhea.

History of present illness

She worked at a medical facility and reported possible exposure to COVID-19 while at work.

History of past illness

She had no history of pulmonary disease, cardiac problems, venous thromboembolism, or sleep apnea. She denied smoking or use of illicit drugs.

Personal and family history

She also reported no family history of dyspnea.

Physical examination

On examination, her temperature was 98.4 F, pulse 73/min, blood pressure (BP) 118/74, respiratory rate 17/min and oxygen saturation 96% on room air. She had bibasilar crackles on chest auscultation with otherwise normal exam findings.

Laboratory examinations

Labs revealed a normal blood cell count, creatinine 2.08 mg/dL, N-terminal fragment of B-type natriuretic peptides 57 pg/mL, Troponin-T < 0.01 ng/mL and normal urinalysis.

Imaging examinations

Electrocardiographic showed normal sinus rhythm with no abnormalities. Her chest X-ray showed patchy opacities in the right lung with no pleural effusions.

FINAL DIAGNOSIS

She was COVID-19 tested, and initially discharged home on azithromycin with a subsequent positive test result two days later.

Seven days after her initial ED visit, she experienced worsening shortness of breath (SOB) and called 911. Emergency medical personnel, noting an oxygen saturation of 80%, placed her on supplemental oxygen at 2 L/min and transported her to the ED. There she reported severe SOB, a non-productive cough, loss of taste, and diarrhea. She denied fever, chest pain, or leg swelling.

Vitals revealed temperature 97.6 F, pulse 85/min, BP 94/71, respiratory rate 21/min with oxygen saturation 91% on 2 L/min *via* nasal cannula. On examination she had crackles bilaterally over the lung fields with an otherwise unremarkable exam.

Her labs revealed white blood cell $9.47 \times 10^9/L$, creatinine 1.23 mg/dL, lactic acid 1.5 mmol/L, procalcitonin 0.13 ng/mL, C-reactive protein 8.4 mg/dL, D-dimer 521 ng/mL with D-Dimer 392 ng/mL, ferritin 1585 ng/mL. Repeat CXR found increased patchy opacities in both lungs. Renal impairment prevented use of chest computed tomography (CT) angiography to assess for an acute pulmonary embolism and a lung scan was not pursued given her lung opacities which rendered that form of testing unreliable.

TREATMENT

She was admitted and placed on Levaquin for possible superimposed bacterial community-acquired pneumonia, vitamin C, and thiamine. Blood cultures showed no growth of any bacterial organisms, so antibiotics were discontinued. She improved clinically, was weaned off oxygen, and discharged home six days after admission.

OUTCOME AND FOLLOW-UP

Two weeks post-discharge, during out-patient follow-up with pulmonary medicine she reported persistence of fatigue, a predominantly nocturnal non-productive cough, and SOB episodes.

Pulmonary function test (PFT) revealed mild restrictive changes with no evidence of airway obstruction. The diffusing capacity was normal after adjusting for alveolar volume.

⁷ Transthoracic echocardiogram revealed normal left ventricular systolic function with mild diastolic dysfunction and normal left atrial pressure. Right ventricular systolic function was normal, but there was moderate tricuspid regurgitation and moderate pulmonary hypertension (PH), with an estimated right ventricular systolic pressure of 50 to 55 mmHg.

A six-minute walk test (6MWT) revealed no evidence of exercise desaturation on room air and she ambulated 708 feet during the test.

Right heart catheterization (RHC) was scheduled to further evaluate her PH, but was initially postponed due to a positive repeat COVID-19 test done prior to the procedure (2.5 mo after her initial COVID-19 diagnosis).

This was finally performed four months after initial COVID-19 positive test and revealed mild PAH Table 1.

A lung perfusion scan, to assess chronic thromboembolic pulmonary hypertension, revealed no evidence of acute or chronic pulmonary embolism. CT chest, to assess for interstitial pulmonary parenchymal abnormalities, showed clear lung fields with complete resolution of previous COVID-related lung opacities.

Patient was given the option to start Sildenafil however, given the fact that her pulmonary hypertension was mild at the time, the patient opted for watchful waiting and declined initiation of therapy. Patient was then referred to pulmonary rehabilitation following which her functional capacity improved slightly. She made the decision to retire early due to concerns of being re-exposed to COVID in the workplace.

DISCUSSION

5 COVID-19 has been associated with a number of cardiovascular complications including dysrhythmias, myocarditis, acute myocardial infarction, and venous thromboembolic events^[1]. Several cases of PH related to COVID-19 have now been reported^[2-5], however, in the majority of cases, the diagnosis was based on echocardiography data without confirmation via RHC which is the gold standard. Data on hemodynamics in COVID-19 patients on mechanical ventilation has also been published^[6].

To our knowledge, this is the first case of PAH confirmed by RHC in non-mechanically ventilated patient following infection with COVID-19.

2 PAH is defined as a mean pulmonary artery pressure > 20 mmHg measured via RHC with a pulmonary artery wedge pressure < 15 mmHg and pulmonary vascular resistance > 3 units^[3,7].

Mechanisms in which new onset PAH develop in the setting of COVID-19 could be multifactorial. Interstitial and alveolar inflammation can lead to extensive pulmonary damage (group 3)^[8]. COVID-19 induced endothelial injury^[9], microvascular pulmonary thrombosis^[10] and hypoxic vasoconstriction^[11] could also lead to alterations in pulmonary vasculature (group 4). SARS-COV-2 spike protein has been associated with pulmonary vascular remodeling seen in development of new PAH after COVID-19 infection^[12-14].

In addition, positive end-expiratory pressure used in mechanical ventilation increases pulmonary vascular resistance^[15], leading to changes in right ventricular function^[16,17]. Therefore, the measurement of pulmonary pressures *via* right heart catheterization in mechanically ventilated patients may be falsely elevated^[6].

Risk factors for COVID-19 patients developing new onset PAH include a history of cardiac disease^[5,18].

Like in our patient, symptoms of COVID-19 induced PAH include persistent dyspnea, cough and fatigue^[3]. Our patient continued to experience exertional dyspnea after resolution of her acute COVID-19 illness. This was in spite of resolution of her bilateral lung opacities on imaging and normal PFT and 6MWT studies. Prior to diagnosis with COVID-19, our patient was employed full-time and was very active with no dyspnea.

PAH development after COVID-19 infection can lead to a more severe course of illness^[19] and increased mortality^[5]. It has been hypothesized that it can be managed with medications such as endothelin receptor antagonists, phosphodiesterase five (PDE-5) inhibitors and prostacyclin, all of which have been used to treat persons with group 1 PH (PAH)^[8,19,20]. However, none of these drugs have been studied in sufficiently powered randomized clinical trials in this specific PAH population^[8]. It is also currently unknown whether treatment could reverse the course of this form of PAH.

PAH related to infections is not an uncommon phenomenon. Worldwide, the most common cause of PAH is schistosomiasis^[21], and the prevalence of PAH in the human immunodeficiency virus population is 100 to 1000 times greater than in the general population^[22-31].

CONCLUSION

Development of PAH following infection with COVID-19 is an emerging area that deserves more investigation. Physicians and healthcare providers should have a reasonable level of suspicion for new onset PAH following COVID-19 and subsequently investigate patients presenting with persisting dyspnea following resolution of acute COVID-19 infection.

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