Case Series

Presentations of pulmonary embolism in COVID-19: An Indian case series

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ABSTRACT

The prevalence of pulmonary embolism (PE) among COVID-19 infections is significantly high. However, in resource-limited settings, appropriate computed tomography (CT) imaging is not possible for all COVID-19 patients. Very sick patients suspected of a PE may not be fit to be shifted to the CT room. Hence, it is likely that PE is underdiagnosed in Indian COVID-19 patients. Coexisting PE should be considered in all patients with influenza-like illnesses who have a Type 1 respiratory failure out of proportion to the severity of COVID-19 radiology. In this case series, we discuss the different presentations of PE in patients with COVID-19.

Key words: Coagulopathy, COVID-19, Pulmonary embolism, Pulmonary thrombosis

The association between COVID-19 and pulmonary embolism (PE) is well known. About 20% of the COVID population and 50% of those who had a COVID-related death have some form of coagulopathy [1-3]. A recently published study that screened consecutive COVID-19 patients reported the prevalence of PE to be 14.2% [4]. Studies report a 21–24% prevalence of acute PE among COVID-19 patients despite prophylactic anticoagulation [5,6]. Mortality rate as high as 45.1% has been reported in cases of COVID-19 with a PE [7]. With the fall in the first wave of the COVID pandemic in India, there is a rise in patients visiting respiratory clinics with post-COVID complications, and PE is among them [8]. In resource-limited settings and centers where computed tomography pulmonary angiogram (CTPA) or contrast-enhanced computed tomography (CT) thorax is not routinely done for COVID-19 care, PE may not always be picked up.

Here, we report a series of patients who presented with PEs associated with COVID-19.

CASE SERIES

Cases 1 and 2 presented with PE or deep vein thrombosis (DVT) and were later found to have COVID-19. Case 3 was diagnosed to have COVID-19 and PE concurrently. Cases 4 and 5 presented with PE after recovery from COVID-19. The characteristics of the cases are shown in Table 1.

Access this article online	
Received - 12 October 2022 Initial Review - 26 October 2022 Accepted - 02 January 2023	Quick Response code
DOI: 10.32677/ijcr.v9i1.3656	

Case 1

A 51-year-old lady was referred from a peripheral clinic to the emergency room with complaints of chest pain and breathlessness for 2 days. She was briefly managed in the peripheral clinic, where her oxygen requirement constantly increased. She was found to have a possible DVT of her left lower limb, and her blood pressure gradually dropped. The local doctors clinically diagnosed her to have a PE and performed thrombolysis with alteplase. Since she further deteriorated, she was referred here for further care. When she presented to us, her Glasgow coma scale was 7/15, and her blood pressure was not recordable. She was stabilized, intubated, and mechanical ventilation was initiated. Her D-dimer was 6015 ng/mL, electrocardiogram showed sinus tachycardia, and CTPA showed bilateral filling defects in all the lobar branches of the pulmonary artery along with patchy peripheral consolidations in the lung parenchyma. Despite best treatment efforts, she succumbed to refractory hypoxia the next day. Her pre-admission SARS-CoV2 polymerase chain reaction (PCR) test was positive and positive radiology for COVID-19. Although a prothrombotic workup could not be done, she had no history suggestive of alternative causes for PE.

Case 2

A 62-year-old female presented with the left lower limb swelling and breathlessness for 1 day at our outpatient clinic. Her vitals

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Table 1: Characteristics of the cases (n=5)

Case	Age	Sex	Diagnosis	Days from COVID 19 to PE diagnosis	Comorbidities	Other Risk factors for PE	D Dimer ng/mL	Ferritin µ/L	ECG	ECHO	CT scan (location, severity)	COVID 19 management	Outcome
Pulmonary embolism with concurrent asymptomatic COVID-19													
1	51	F	PCR+ve	-2	Diabetes	None	6015	281	Sinus Tachycardia	N/A	B/L Lobar, Massive	Invasive Ventilation, Thrombolysis, Therapeutic anticoagulation.	Dead
2	62	F	PCR+ve	-1	None	None	3780	134	Normal	N/A	U/L segmental, low risk	Therapeutic anticoagulation	Discharged Alive
Pulmonary embolism diagnosed during hospitalization for symptomatic COVID-19													
3	52	F	PCR+ve	10	Asthma, Idiopathic Pulmonary Fibrosis – Mild stable	None	6875	759	T wave inversions	N/A	Right Main, Submassive	Non-invasive ventilation, Remdesivir, Dexamethasone, Therapeutic anticoagulation.	Discharged Alive
Pulmonary embolism diagnosed in the post-COVID period													
4	58	F	PCR+ve	33	Hypertension	None	16819	376	Sinus Tachycardia	Mild PHTN	Left main, Submassive	Invasive ventilation, Remdesivir, Dexamethasone, Therapeutic anticoagulation.	Discharged Alive
5	73	M	PCR+ve	80	Idiopathic ILD stable, Psoriasis, Hypertension	None	256	62	Normal	N/A	B/L segmental, low risk	Therapeutic anticoagulation	Discharged Alive

were stable, but the color Doppler scan to evaluate her tender and swollen left lower limb confirmed the presence of DVT. Her SARS-CoV2 PCR test was found to be positive. CTPA, done later, confirmed subsegmental PE with typical COVID-19 radiological changes. She was initiated on oral anticoagulation and was managed conservatively for COVID-19. Subsequently, her prothrombotic workup was negative. She remained healthy at her 6-month follow-up.

Case 3

A 52-year-old lady presented to the fever clinic with a fever, cough, and breathlessness for 3 days. Her husband and children recently recovered from an acute febrile illness but did not have breathlessness. In the emergency room, she was found to have tachycardia, hypoxia, and tachypnea with the use of accessory muscles of respiration. Her chest X-ray showed bilateral peripheral consolidations, and her SARC-CoV2 PCR test was positive. She was initiated on non-invasive ventilation, but her oxygen requirement gradually increased. Since her D-dimer was 6875 ng/mL, a CTPA was done, which showed radiological features of COVID-19 and a right submassive PE. His prophylactic anticoagulation was escalated to therapeutic doses. Remdesivir and dexamethasone were also given. She eventually recovered was discharged in an improved condition. She did not have any other risk factor for PE and remained stable at the 6-month follow-up.

Case 4

A 58-year-old lady was discharged from our intensive care unit 1 month ago after recovering from a critical COVID-19 illness (confirmed by a positive SARS-CoV2 PCR). She received invasive ventilation, remdesivir, and dexamethasone during her stay. She was discharged in stable condition and was normal for 1 month before presenting to our emergency room with a new-onset fever, cough, and breathlessness for 2 days. She had tachycardia and hypoxia, but her blood pressure was normal. Her X-ray had bilateral peripheral consolidations, and D-dimer was 16819 ng/mL; hence, a CTPA was done, which showed an acute left submassive PE. She was managed conservatively with anticoagulation. She subsequently improved and remained healthy at a 6-month follow-up. Her prothrombotic workup was normal at 6 months. She had no other comorbidities other than systemic hypertension.

Case 5

A 73-year-old gentleman was diagnosed with a moderate COVID-19 illness based on a positive SARS-CoV2 PCR in our hospital and was managed with oxygen, remdesivir, and dexamethasone for 10 days. He was discharged and remained under follow-up for a stable early interstitial lung disease (ILD) he had. His baseline pulmonary function tests were normal, and he only had minimal subpleural fibrotic changes suggestive of non-specific interstitial pneumonia. He was not on any specific ILD treatment. Around 3 months after his COVID-19 admission, he presented to our outpatient department with a history of progressive breathlessness for 1 week. On examination, he had hypoxia; hence, an ILD exacerbation was considered. CT thorax showed stable ILD but had subacute filling defects in the bilateral segmental regions. He was initiated on anticoagulation therapy, with which he improved. A prothrombotic workup was done eventually, which was normal.

DISCUSSION

The prothrombotic state seen during COVID-19 infection is well documented. A rise in angiotensin II, reduced angiotensin-mediated vasodilation, and release of an array of pro-inflammatory cytokines make COVID-19 an hypercoagulable state by altering the hemodynamics and causing inflammation [9]. Adding to this, the SARS CoV2 virus induces endotheliitis causing impairment in blood microcirculation in the lungs, creating microthrombi and ventilation-perfusion mismatch [10]. PE could be the presenting complaint in a COVID patient; may be found incidentally in a COVID patient; may develop during admission; or can manifest in the post-discharge period.

The time of resolution of the procoagulant state in COVID-19 is unknown, leading to the possibility of developing venous thromboembolism even after discharge from the hospital [11,12]. A study from the UK has concluded that there is no increased risk for hospitalization-related PE post-discharge in COVID compared to other critical illnesses [13]. There have been a few case reports of the development of PE during the post-COVID recovery phase.

Benzakoun *et al.* reported three times higher PE-related unexplained deaths in the general population during this pandemic, compared to the previous year, in France [14]. The increased unexplained deaths could represent a population with mild symptoms of COVID or asymptomatic COVID who did not visit a health-care facility. We had two such patients who came with PE symptoms, and the COVID symptoms managed at home had abated by then. A recent meta-analysis concluded that the odds of developing venous thromboembolism in COVID-19 were lesser in those with therapeutic anticoagulation than those on prophylactic anticoagulation [15]. In our series, patients developed PE in the post-COVID period despite receiving therapeutic-range anticoagulation while in the hospital [14]. Therapeutic anticoagulation was stopped at discharge since most only had clinical suspicion of PE. Confirmation of PE was not possible if the patient's condition was unstable to undergo CTPA. In our cases, the average D-dimer value was 7186 ng/mL, which was higher than the average from other similar case series [16]. In our hospital, CTPA is not routinely performed to evaluate COVID-19. Hence, there is a good chance of missing patients who had PE during COVID-19.

There is a need for prospective studies in the post-COVID period to assess the true risk of PE and address the need for extended thromboprophylaxis. We feel that patients with no confirmed PE/DVT but whose clinical condition warranted a

therapeutic dose of anticoagulants should undergo CTPA to continue anticoagulation for the stipulated period if the presence of PE is demonstrated.

CONCLUSION

In the current COVID era, all patients presenting with PE should be evaluated for concomitant COVID. Similarly, there should be a high degree of suspicion of concomitant PE in all patients with symptomatic COVID.

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Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Daniel J, Isaac B, Balamugesh T, Nair AA, Christopher DJ. Presentations of pulmonary embolism in COVID-19: An Indian case series. Indian J Case Reports. 2023; 9(1):1-4.