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Original Research Article

Pulmonary Thrombus in Covid 19: A Case Series

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Abstract

Coronavirus disease 19 (COVID-19) increases the risk of thromboembolism by creating a prothrombotic state. COVID-19 and pulmonary embolism, both are associated with tachypnoea, hypoxemia, dyspnoea and increased D- dimer. Diagnosing pulmonary embolism in a patient with COVID-19 compared to a patient without it using conventional clinical and biochemical evidence is challenging. In this study, we report 8 cases affected by COVID-19 admitted to Medical Intensive Care Unit of a tertiary care centre in Udaipur. All the patients presented with fever, cough, shortness of breath. All the patients were hypoxic at the time of admission. Computed Tomographic Pulmonary Angiography (CTPA) was done in all of them when their hypoxia worsened, and D-dimer levels increased. All the patients were on therapeutic or prophylactic anticoagulation, yet they all developed pulmonary thrombus. Further studies are required to define the role of prophylactic and therapeutic anticoagulants in patients with COVID-19 infection.

Keywords: Acute pulmonary thrombus, COVID-19, D-dimer, anticoagulation, Computed Tomographic Pulmonary Angiography

Introduction

COVID 19 is a respiratory illness caused by the SARS COV-2 virus. In its severe form the COVID-19 illness is characterized by cytokine outburst and hyper inflammation, platelet activation, endothelial dysfunction and sepsis related coagulopathy. [1] COVID 19 patients with high D- dimer levels are more likely to need ICU admission and are more likely to die. [2] There have been observational studies done which suggest that venous thrombo embolic events are common among patients with COVID19 hospitalised in the ICU, thrombosis prevalence ranging from 0% [3] to 69% [4]. Many studies have also reported a low prevalence of DVT [4] indicating that the mechanisms responsible for pulmonary

thrombi are different [3]. It has been suggested that vascular Endothelitis due to an activated immune response or an infection of the vascular endothelium with COVID19 may lead to blood clotting [5]. Though some international experts have suggested early therapeutic anticoagulation for these patients [6,7], the relevant estimates of the occurrence of pulmonary thromboembolism are lacking to inform on the best therapeutic approach in these patients. In this article we report 8 cases of coronavirus infections who were diagnosed to be having pulmonary artery thrombi by CT pulmonary angiography.

Case 1

A 67 year old male was admitted with c/o cough and shortness of breath since 6-7 days.He earlier got admitted in our hospital 12 days back with similar complaints when he tested positive for Covid-19.He was not put on anticoagulant therapy post discharge. He was a known case of Type II Diabetes Mellitus. On admission, he was conscious, oriented with no sensorimotor deficit and had mild hypoxia; SpO_2 85% on room air and 92% with O_2 2 l/min.

Within 72 hours of admission, patient's O_2 requirement increased upto 6 L/min O_2 to maintain target saturation of >91% . In view of worsening hypoxia and rise in D-dimer levels a CTPA was done which was showed hypodense filling defects in the segmental branches of pulmonary arteries. The patient was commenced on iv antibiotics on Day 3 to cover the chest sepsis and an urgent CTPA was arranged. Blood examination showed increased inflammatory markers. CTPA s/o hypodense filling defects in the segmental branches of B/L descending pulmonary arteries s/o thrombosis.

Patient was initially managed with therapeutic dose of anticoagulants in the form of LMWH 0.6 ml s/c BD. After 3 days, he was put on oral anticoagulants T. Dabigatran 110 mg BD. The respiratory status of the patient gradually improved and after 5 days of starting T. Dabigatran, he no longer required any supplemental O_2. He was discharged on day 11 post admission and was advised to continue Tab. Dabigatran 110 mg BD and came for follow up in OPD.

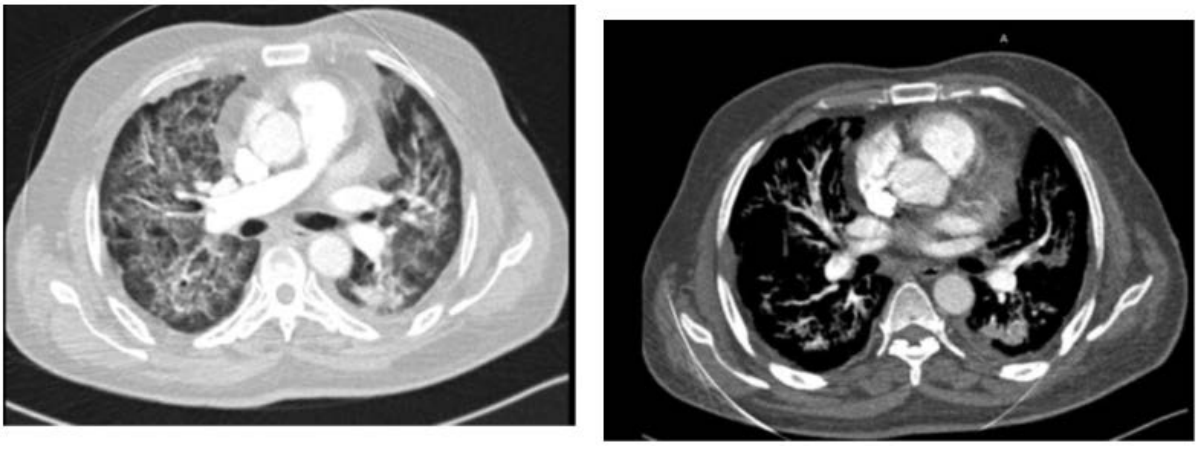

Figure 1: Lung window of case 1 showing features of COVID 19 infection. CT pulmonary angiography shows thrombus in segmental branches of bilateral descending pulmonary arteries

Case 2

A 60-year-old male admitted in April,2021 with c/o cough, fever and shortness of breath since 7 days. He was a known case of Type II DM. He tested positive for Covid-19 RTPCR. Initially, he maintained saturation of 89% with 10 L/min O_2 with NRBM. His O_2 requirement gradually

increased to 15 L/min via NRBM and his D-dimer levels also increased. A CTPA was done which showed subtle non enhancing filling defect in segmental branch of left ascending pulmonary artery possibly a thrombus. He was put on therapeutic anticoagulants. His inflammatory markers gradually decreased. Supportive care was given. His O_2 requirement gradually decreased and was discharged after 29 days of hospitalization.

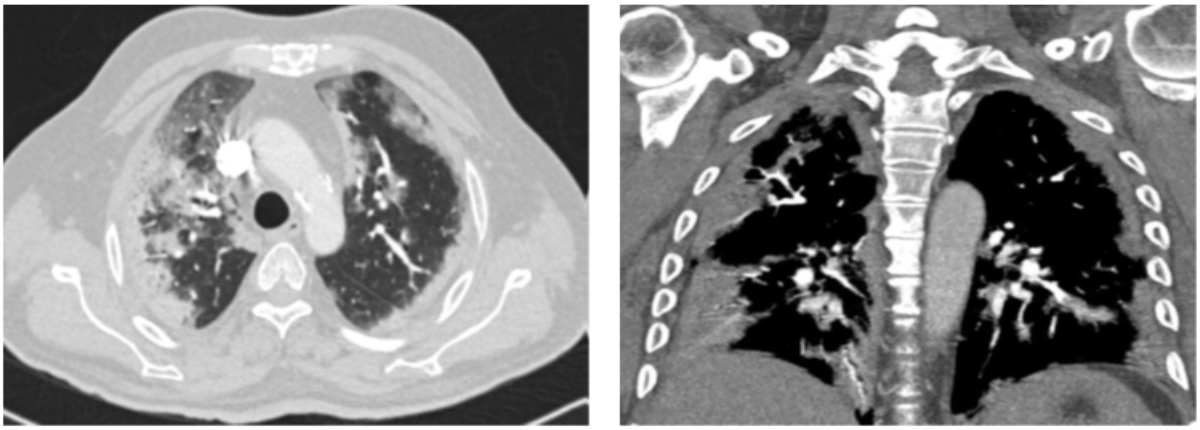

Figure 2: Lung window of case 2 showing features of atypical pneumonia with CT severity score 15/25. CT pulmonary angiography non enhancing filling defect is seen in segmental branch of right ascending and left descending pulmonary artery

Case 3

A 47-year-old female admitted in April 2021, with c/o shortness of breath for 2 days. Initial physical and clinical examination of the patient were normal, and she had no comorbidity. Her SpO_2 was 84-94% with O_2 @ 10 l/min via NRBM. PCR on the nasopharyngeal swab was performed on the day of hospitalization, which confirmed the diagnosis of COVID-19. On the next day, patient became more hypoxic, and her D-dimer levels also increased hence a CTPA was done which showed non-enhancing filling defect in segmental branches of left descending pulmonary artery s/o thrombosis. She was given Inj. Clexane 0.6 ml s/c BD for three days and then put on Tab. Dabigatran 110 mg BD. Her O_2 requirement gradually decreased and then she was shifted out of the ICU after 4 days maintaining O_2 saturation 97% on room air.

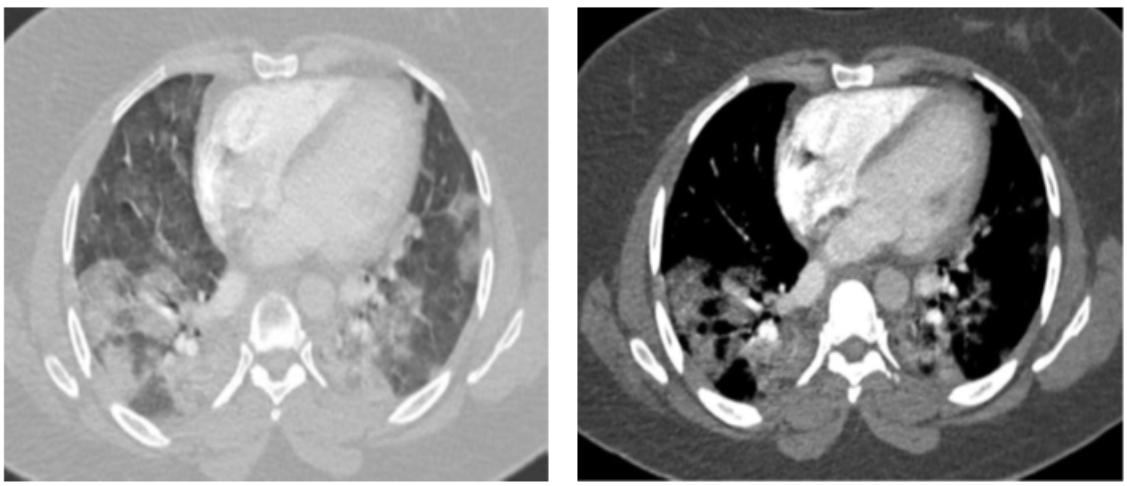

Figure 3: Lung window of case 3 showing features of atypical pneumonia. CT

pulmonary angiography hypodense filling defects in the segmental branches of left pulmonary arteries

Case 4

A 71 year old male admitted in Oct 2020, with c/o fever 3 days before admission. His COVID-19 RTPCR tested positive two days before admission. He had hypoxemia with SpO_2 level of 89-94% with 10 L O_2 with NRBM.

His initial total leukocyte count and D-Dimer were raised. Supportive care, antibiotics were used to treat the patient. His O_2 level did not improve even after 8 days of admission and his D-dimer levels also increased so a CTPA was performed which showed non-enhancing filling defects in segmental branches of B/L ascending and descending pulmonary arteries s/o thrombosis.

He was put on Tab. Dabigatran 110 mg BD. His O_2 requirement gradually decreased to 3L/min maintaining SpO_2 94-99%. He was shifted to ward from ICU on day 12 from admission with O_2 requirement of 2 L/min and was discharged after 25 days of hospitalization.

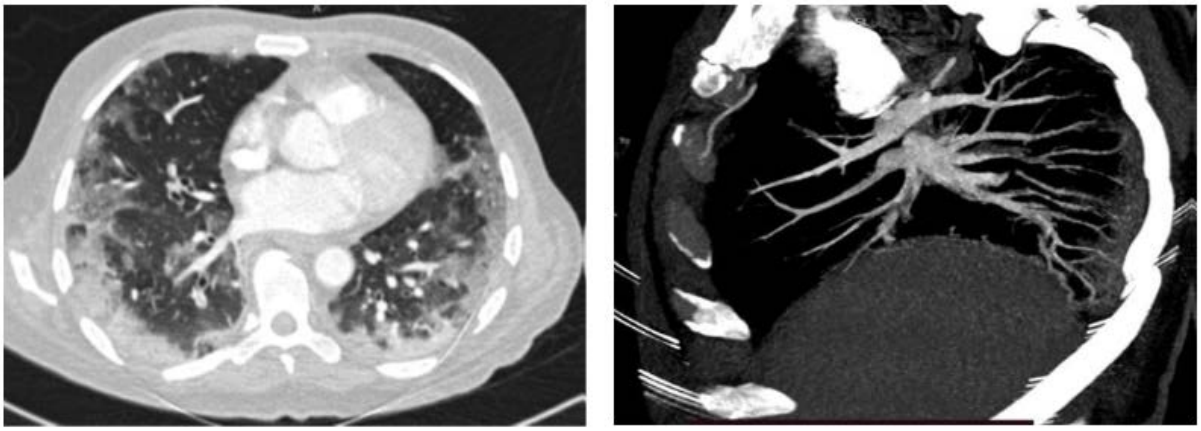

Fig. 4 Lung window of case 4 showing features of COVID 19 infection CT severity score of oblique sagittal MPR CT pulmonary angiography shows partial and complete filling defects in left lower segmental and subsegmental branches

Case 5

An 82-year-old gentleman who was a known case of hypertension and hyperthyroidism was admitted with chief complaints of fever and cough for 2-3 days. His RTPCR for COVID 19 was positive. On the day of admission, he was slightly tachypneic but was maintaining $SpO_2\infty$ 92% on O_2 via face mask @ 8L/min. On the day of admission his IL-6 levels were high for which he was given Inj. Dexona 4 mg iv BD and was put on prophylactic anticoagulation with Inj. Clexane 0.6 ml s/c OD as his D dimer was only slightly high. Patient responded well to the treatment and started maintaining SpO_2 of 96% on O_2 @ 3 L/min. Eight days after his admission to the ICU the patient suddenly became dyspneic, tachypneic and hypotensive. D dimer levels rose to 3370. A CTPA was done which revealed non enhancing filling defects in Rt. Descending pulmonary artery and its segmental branches. ECHO was done which was suggestive of severe pulmonary hypertension and dilated right ventricle. His blood investigations were suggestive of thrombocytopenia and deranged coagulation profile (INR 2.97) suggestive of DIC. Cardiology and pulmonology consultation was taken and a decision to not thrombolyse the patient was taken in view of deranged INR and thrombocytopenia. The condition of the patient kept on worsening, and he eventually succumbed.

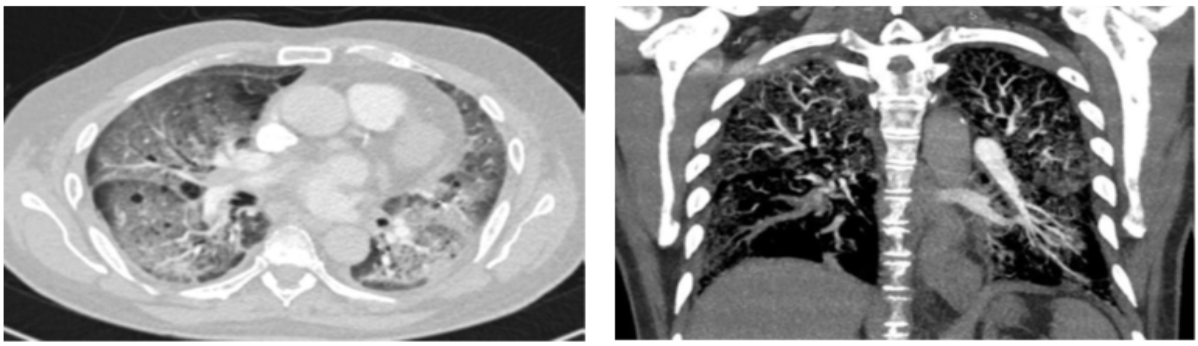

Figure 5: Lung window of case 5 showing features of COVID 19 infection. Coronal MPR CT pulmonary angiography shows thrombus in right descending pulmonary artery and its

Case 6

A 54-year-old gentleman presented with c/o severe dry cough and breathlessness for 5 days. The patient was a known case of DVT and was not on any medication. At the time of admission, the patient was hemodynamically stable but was severely hypoxic (~ 86% on O_2 @15 L/min via NRBM). On the day of admission nasal swab RT-PCR was sent which came as positive. His blood investigations were suggestive of very high D-Dimer levels. He was given therapeutic Inj. Enoxaparin 0.6ml S/C in view of his past history of DVT and raised D-Dimer. He was also given Inj. Dexamethasone 4mg BD as his IL-6 levels were raised. He was also given broad-spectrum antibiotics and Inj. Remdesivir. After being on the same treatment for 7 days the condition of the patient didn't improve. A decision to get a CTPA was taken which revealed B/L filling defects in both main pulmonary arteries. ECHO was suggestive of severe TR & grossly dilated RA & RV. His condition worsened, he was intubated and put on mechanical ventilatory support but he could not survive.

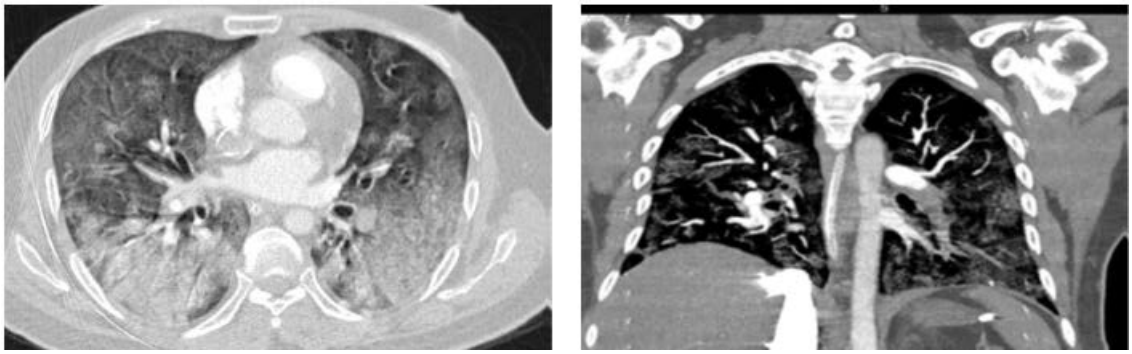

Figure 6: Lung window of case 6 showing features of COVID 19 infection with CT severity score of 23. CT pulmonary angiography shows a large thrombus in the left descending pulmonary artery and its segmental branches

Case 7

A 69-year-old male presented with complaints of cough for 10 days, dyspnoea for 3 days. He had been diagnosed with COVID-19 by RT-PCR test and he was in home quarantine. On the day of admission patient was dyspnoeic and hypoxic and maintaining SpO_2 around 88% On O_2 @ 4L /min via face mask. His lab reports were unremarkable. His D-Dimer was 430. He was put on Antibiotics, prophylactic anticoagulants and Inj. Dexamethasone 4mg BD. 5 Days after his admission patient suddenly became extremely dyspnoeic, tachypnoeic and severely

hypoxic. His D-Dimer rose to 3790. A CTPA was done which showed hypodense filling defects in the segmental branches of B/L pulmonary arteries; suggestive of thrombosis. His ECHO was within normal limits. Patient was thrombolysed with Inj. Alteplase in view of severe hypoxia, In spite of thrombolysation the condition of the patient did not improve and he was put on mechanical ventilation and eventually died.

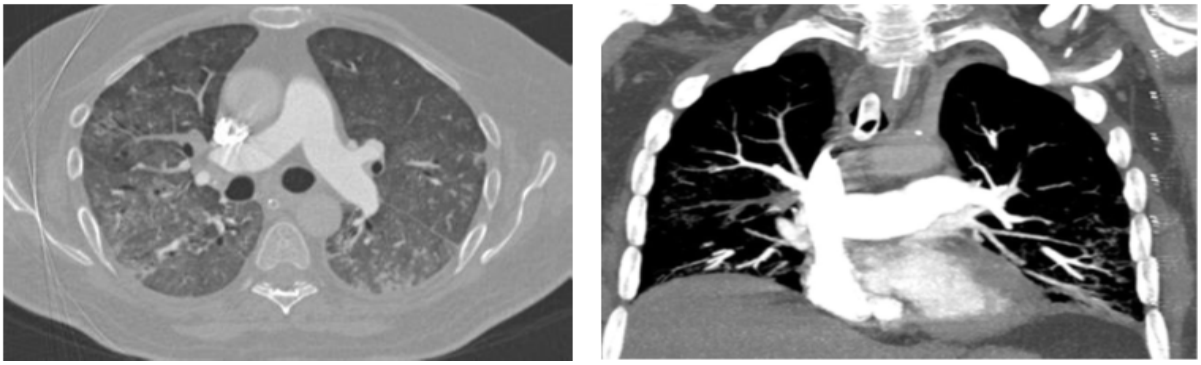

Figure 7 Lung window of case 7 showing features of atypical pneumonia. CT pulmonary angiography thrombus in middle segmental branch of right pulmonary artery

Case 8

58-year-old gentle man with no comorbidities was admitted with complaints of fever & shortness of breath since 4 days. He had been diagnosed with COVID – 19 infection3 days ago. At the time of admission, he was extremely dyspnoeic, tachypnoeic and severely hypoxic. Maintaining a SpO_2 of around 82% on room air and 91% on 15;/min O_2 supplement via NRBM mask. His D-Dimer was raised, and he was given therapeutic dose of Inj. Enoxaparin 6 ml S/C X BD. His IL-6 levels were also high, and he was given IV steroids and IV antibiotics& Inj. Remdesivir. The patient was put on non-invasive ventilation from the 2nd day of admission. The condition of the patient didn't improve, and he was intubated on the 15th day of the admission. His D-Dimer one the day of intubation was 3960. A CTPA was done which revealed hypodense filling defects in segmented branches of B/L pulmonary arteries. 2D echo revealed dilated RV & RA, hypokinetic basal and mid of RV free wall which was Normal with PAH. Patient was thrombolysed with Inj. Alteplase but the hypoxia didn't improve and he eventually succumbed to his illness 28 days after his admission.

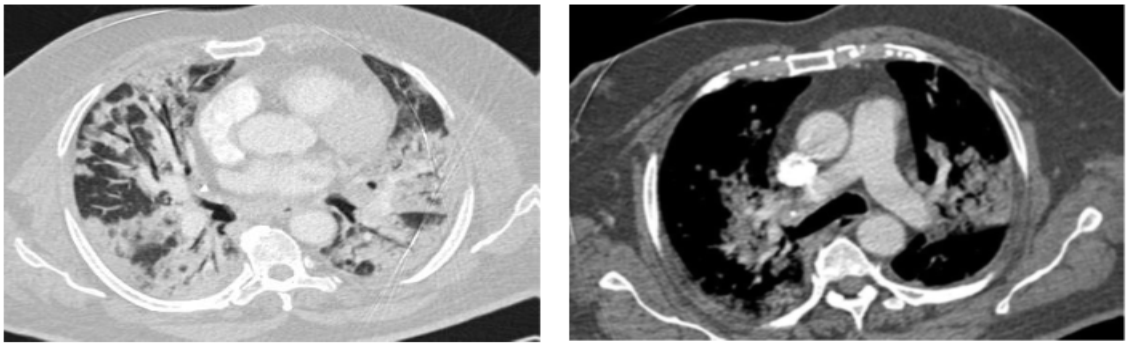

Figure 8: Lung window of case 8 showing features of atypical pneumonia. CT pulmonary angiography shows hypodense filling defects in the segmental branches of bilateral pulmonary arteries

Table 1: Showing the D Dimer levels on the day of admission and on day of CTPA

Case No.	D Dimer	
	Day of admission	Day of CTPA
1	2340	>4000
2	2340	3270
3	1500	2940
4	870	>4000
5	580	3370
6	2730	>4000
7	430	3790
8	3000	3960

Table 2: Showing demographic characteristics, comorbidities and TLC on the day of admission

CASE NO.	GENDER	AGE	COMORBIDITIES	TLC
1	MALE	67	TYPE II DM	12400
2	MALE	60	TYPE II DM	8300
3	FEMALE	47	NONE	4200
4	MALE	71	HYPERTENSION	20000
5	MALE	82	HYPERTENSION TYPE II DM	24200
6	MALE	54	HYPERTHYROIDISM PERIPHERAL VASCULAR DISEASE	15700
7	MALE	69	TYPE II DM HYPERTENSION	9900
8	MALE	58	NONE	20000

Table 3: Showing anticoagulant therapy, CRP levels and steroids given to the patient

CASE NO.	**ANTICOAGULANT AT TIME OF DIAGNOSIS**	**TREATMENT AFTER DIAGNOSIS**
1	INJ.CLEXANE 0.6 ml s/c OD	INJ. CLEXANE 0.6 ml s/c BD FOR 3 DAYS THEN TAB.DABIGATRAN 110 mg BD
2	INJ.CLEXANE 0.6 ml s/c OD	INJ. CLEXANE 0.6 ml s/c BD FOR 3DAYS THEN TAB.DABIGATRAN 110 mg BD
3	INJ.CLEXANE 0.4 ml s/c OD	INJ. CLEXANE 0.4 ml s/c BD FOR 3DAYS THEN TAB.DABIGATRAN 110 mg BD
4	INJ.CLEXANE 0.4 ml s/c OD	INJ. CLEXANE 0.4 ml s/c BD FOR 3DAYS THEN TAB.DABIGATRAN 110 mg BD
5	INJ.CLEXANE 0.4 ml s/c OD	NO ANTICOAGULANT GIVEN IN VIEW OF DIC
6	INJ.CLEXANE 0.6 ml s/c BD	INJ.ALTEPLASE
7	INJ.CLEXANE 0.6 ml s/c BD	INJ.ALTEPLASE
8	INJ.CLEXANE 0.6 ml s/c BD	INJ.ALTEPLASE

CASE NO.	CRP	STEROIDS
1	101	INJ.DEXONA 4 mg IV BD
2	20	INJ.DEXONA 4 mg IV BD
3	89	INJ.DEXONA 4 mg IV BD
4	78	INJ.DEXONA 4 mg IV BD
5	30	INJ.DEXONA 4 mg IV BD
6	85	INJ.DEXONA 4 mg IV BD
7	60	INJ.DEXONA 4 mg IV BD
8	65	INJ.DEXONA 4 mg IV BD

Table 4: showing the Oxygen requirement on the day of admission and on the day of CTPA

CASE NO.	SpO2 ON ADMISSION	O2 SUPPORT AT TIME OF DIAGNOSIS	TIME BETWEEN ADMISSION AND DIAGNOSIS OF PULMONARY THROMBUS
1	92% ON O2 @ 2 L/MIN	O2 VIA NRBM @12 L/MIN	7 DAYS
2	92% ON O2@10 L/MIN	O2 VIA FACE MASK @ 8 L/MIN	8 DAYS
3	94% ON O2 @ 10 L/MIN	O2 VIA NRBM @ 10 L/MIN	2 DAYS
4	92% ON O2 @ 10 L/MIN	O2 VIA NRBM @ 10 L/MIN	9 DAYS
5	92% ON O2 @ 2 L/MIN	INTUBATED AND ON VOLUME	15 DAYS
		CONTROL MODE WITH 100% FiO2	
6	89% ON O2 @ 15 L/MIN	INTUBATED AND ON PRESSURE	7 DAYS
		CONTROL MODE WITH 100% FiO2	
7	88% ON O2 @ 4 L/MIN	INTUBATED AND ON VOLUME	14 DAYS
		WITH 100% FiO2	
8	91% ON O2 @ 15 L/MIN	INTUBATED AND ON PRESSURE	25 DAYS
		CONTROL MODE WITH 100% FiO2	

Discussion

COVID-19 has been found to be associated with a higher risk of thrombotic complications than are other respiratory infections [8,9].

This is probably the first case series of pulmonary thrombi in COVID patients from Rajasthan , India. Our case series was observed in a single centre, catering to COVID-19 as well as non-covid patients from April 2021- July 2021.

Having seen 3 COVID waves worldwide it has become clear that infected patients may present in number of ways. Observational studies have suggested that almost all patients have parenchymal abnormalities on chest CT[10]. Pulmonary

vascular thickening has been observed more frequently in COVID-19 compared with non-COVID pneumonitis suggesting a potential tropism of the virus for the pulmonary vasculature[11]. This could be because SARS-CoV-2 interacts with its functional receptor from the host cells, the ACE-2 receptor[12], also present on the surface of endothelial cells of virtually all organs, but predominantly within the heart, lungs and kidneys [13].

Chen N et al and Zhou F et al studied the epidemiology of COVID-19 patients in Wuhan and found that 30% of inpatients with COVID-19 are dyspnoeic, 76% are hypoxemic and 29% are tachypneic[14,15]. Xu XW et al did a study on clinical findings in patients infected with Covid virus outside Wuhan and found that only 1-2% of inpatients with COVID-19 presented with hypotension (SBP <90), tachycardia, chest pain, haemoptysis [16]. Thus suspecting pulmonary embolism and distinguishing it from the typical features of COVID is difficult .

In a nationwide self-controlled case series and matched cohort study in Sweden the incidence ratios of pulmonary thrombi were higher in male participants than in female participants during the first 3 months after COVID and highest in age group 50-70 years [17]. In our case series also all patients except one are males. And all patients except the female are above the age of 50 years.

It has been shown that even in the absence of pulmonary embolism in patients with COVID -19 the level of D-Dimer increase [18]. An increase in the D-Dimer may indicate mortality in these patients. But D-dimer is not a reliable indicator in the diagnosis of venous thromboembolism [19,20]. In our case series all patients except one had high D-Dimer levels at admission and all had raised D-Dimer levels on the day they were diagnosed with Pulmonary thromboembolism. A rise in D-Dimer level with worsening hypoxia should prompt the clinician to rule out Pulmonary Thromboembolism.

A lower limb venous doppler was done in all patients and only one patient (Case 6) was found to have DVT.

None of the survivors had any abnormal findings on Echo and were haemodynamically stable. Three out of four non survivors were haemodynamically unstable and were on vasopressor support on the day of the diagnosis of pulmonary embolism. All the three haemodynamically unstable patients had findings of right ventricular failure and pulmonary artery hypertension on echocardiography. The CT severity index of all the patients who died was above 20. Two patients who were haemodynamically unstable were thrombolysed but didn't survive. One of the haemodynamically unstable patient couldn't be thromoblysed as he was suffering from thrombocytopaenia secondary to DIC. The other non-survivor was also thrombolysed with Injection Alteplase as his hypoxia was refractory.

All 4 patients who survived were on prophylactic dose of Injection Clexane for 3 days, then shifted to Tab Dabigatran 110mg X BD.

Three out of four non survivors were in fact on therapeutic dose of Injection Clexane and yet developed pulmonary thrombus. Our findings are similar to the findings of ACTION Trial which found that patient hospitalised with COVID-19 with increased D-Dimer initial in hospital therapeutic anticoagulation with Rivaroxaban for stable patients or Enoxaparin for unstable patients followed by Rivaroxaban didn't improve clinical outcomes. [21,22]

Conclusion

Patients admitted in ICU for COVID-19 appear to have high risk of VTE. Any increase in D-Dimer levels, especially in patient whose clinical condition has

worsened should prompt the clinician to search for the possibility of Pulmonary Thrombus. However, the occurrence of VTE in patients with COVID-19 infections remains to be defined. Further studies are required to define the role of prophylactic and therapeutic anticoagulants in patients with COVID-19 infection.

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