ESC European Society of Cardiology

European Heart Journal - Case Reports (2020) **4**, 1–6
doi:10.1093/ehjcr/ytaa437

GRAND ROUND
Other

Saddle pulmonary embolism and clot in transit in COVID-19 infection: a case report of catastrophic venous thromboembolism

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Received 5 June 2020; first decision 21 July 2020; accepted 28 October 2020; online publish-ahead-of-print 7 December 2020

Background Coronavirus disease 2019 (COVID-19) is associated with a coagulopathy favouring thrombosis over bleeding that imparts a poor prognosis. Clot in transit (CIT) is considered a rare entity and the most severe form of venous thromboembolism (VTE), carrying a higher mortality than isolated pulmonary embolism (PE). The incidence of this phenomenon in patients with COVID-19 infection is unknown and likely under-recognized.

Case summary During the peak of the COVID-19 pandemic in New York City, a 70-year-old Hispanic female presented with syncope due to a saddle PE further complicated by a highly mobile CIT. Polymerase chain reaction was positive for COVID-19 infection, however, there was no evidence of lung parenchymal involvement or hyper-inflammation. Based on consensus from a multidisciplinary team, aspiration thrombectomy was attempted to treat this extreme case of VTE, however, the patient died during the procedure.

Discussion This case raises awareness to the most catastrophic form of VTE, presenting in an early phase of COVID-19 infection without the typical hyper-inflammation and severe lung injury associated with development of COVID-related coagulopathy. It also serves to inform on the critical role echocardiography has in the comprehensive evaluation and re-evaluation of hospitalized patients with COVID-19, and the importance of a multidisciplinary organized approach in clinical decision-making for this complex and poorly understood disease and its sequelae.

Keywords COVID-19 • Pulmonary embolism • Clot in transit • Case report

Learning points

- To recognize the confounding and varying presentations of venous thromboembolism in all stages of coronavirus disease 2019 (COVID-19) illness even in the absence of lung parenchymal involvement and hyper-inflammation.
- To recognize that mobile clot in transit is associated with a high mortality and likely under-recognized in COVID-19 patients.
- To highlight the importance of a multidisciplinary team approach to pulmonary embolism and COVID-19.

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Handling Editor: Yuichi Tamura
Peer-reviewers: Giulia Ferrannini and Amardeep Ghosh Dastidar
Compliance Editor: Linh Ngo
Supplementary Material Editor: Ross Thomson
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Primary specialties involved other than cardiology

Pulmonary critical care, Hematology, Infectious diseases, Interventional radiology, Internal medicine.

Introduction

The novel coronavirus disease 2019 (COVID-19) pandemic has significantly impacted the healthcare system across the world. Other than its primary pathology of severe respiratory disease, COVID-19 is also associated with a coagulopathy favouring thrombosis over bleeding, which imparts a poor prognosis.[1,2] Clot in transit (CIT) is considered a rare entity, a most severe form of venous thromboembolism (VTE), and is a medical emergency carrying a higher mortality than isolated pulmonary embolism (PE).[3,4] The incidence of this phenomenon in COVID-19 is unknown and likely under-recognized, and if significant would influence the diagnostic and therapeutic approaches to these patients.

Timeline

	Events
2 days prior	Symptom onset of weakness, polyuria, and elevated blood glucose
Day 0	Syncope and patient presentation to the emergency department.
	Negative RT–PCR swab for coronavirus disease 2019 (COVID-19).
	Prophylactic anticoagulation started.
Day 1	Transthoratic echocardiogram showing dilated right ventricle
Day 2	Computed tomography pulmonary angiogram and repeat echocardiogram showing pulmonary embolism and clot in transit.
	Therapeutic anticoagulation started.
	Repeat RT–PCR swab for COVID-19 returns positive.
	Transferred for percutaneous aspiration thrombectomy with AngioVac.
	Patient died during the procedure.

Case presentation

A 70-year-old Hispanic female was brought to the emergency department after a syncopal episode, following 2 days of progressive weakness, polyuria, and elevated blood glucose. Syncope occurred upon standing and was witnessed by her family. The patient regained consciousness immediately. She denied fever, chills, sore throat, cough, chest pain, or dyspnoea. Initial blood pressure was 84/55 mmHg, pulse 72 b.p.m., oxygen saturation 88% on room air, respiratory rate 16/min, and temperature 36.6°C. Physical exam was unremarkable, including no jugular venous distension (JVD), normal heart and lung sounds, and no peripheral oedema.

The patient had a history of hypertension, hyperlipidaemia, diabetes, and supraventricular tachycardia treated successfully with ablation. She denied recent travel or contact with a known COVID-19 patient.

Blood pressure and oxygenation improved rapidly with intravenous fluids and supplemental oxygen. She was admitted to telemetry and treated with hydration, insulin, antibiotics, and prophylactic dose anticoagulation. Droplet precautions and contact isolation were ordered for suspected COVID-19 infection.

The differential diagnosis included hypovolaemia due to diabetic ketoacidosis and sepsis. Syncope and hypoxaemia in a patient with a normal lung exam raised the suspicion for acute PE. Other causes of syncope and transient hypotension such as myocardial infarction, arrhythmia, and heart failure were also considered. Underlying COVID-19 was also suspected, given it was the peak of the COVID-19 pandemic in New York City (NYC), when the clinical behaviour of the virus was still mostly unknown.

Chest X-ray (*Figure 1*) and head computed tomography were unremarkable. Electrocardiogram showed sinus rhythm at 80 b.p.m. with an S1, Q3, T3 pattern, prolonged QTc, and T-wave inversions across the precordium (*Figure 2*). Initial laboratory testing revealed hyperglycaemia (580 mg/dL), elevated anion gap, serum creatinine (1.6 mg/dL), lactate (7.5 mml/L), D-dimer (2,153 ng/mL), C-reactive protein (8.6 mg/L), and pro-BNP (14 042 pg/mL). INR was 1.2. Serial troponin *T*-tests were negative. Urine was positive for ketones and white cells. Initial nasopharyngeal swab for COVID-19 was negative. Other findings are presented in *Table 1*.

Bedside echocardiogram revealed a moderately dilated right ventricle with mild hypokinesis, without thrombus, and elevated right ventricular systolic pressure (67 mmHg). Patient remained comfortable and haemodynamically stable with a saturation of 98% on 3 L of oxygen. The next morning dyspnoea and desaturation ensued (93% on 3 L). Pulse was 80 b.p.m. and blood pressure 132/78 mmHg. Computed tomography pulmonary angiogram showed a saddle PE

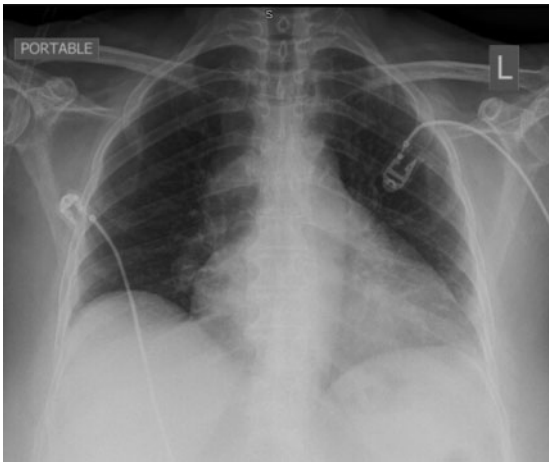


Figure 1 Initial presentation chest X-ray with normal lung fields.

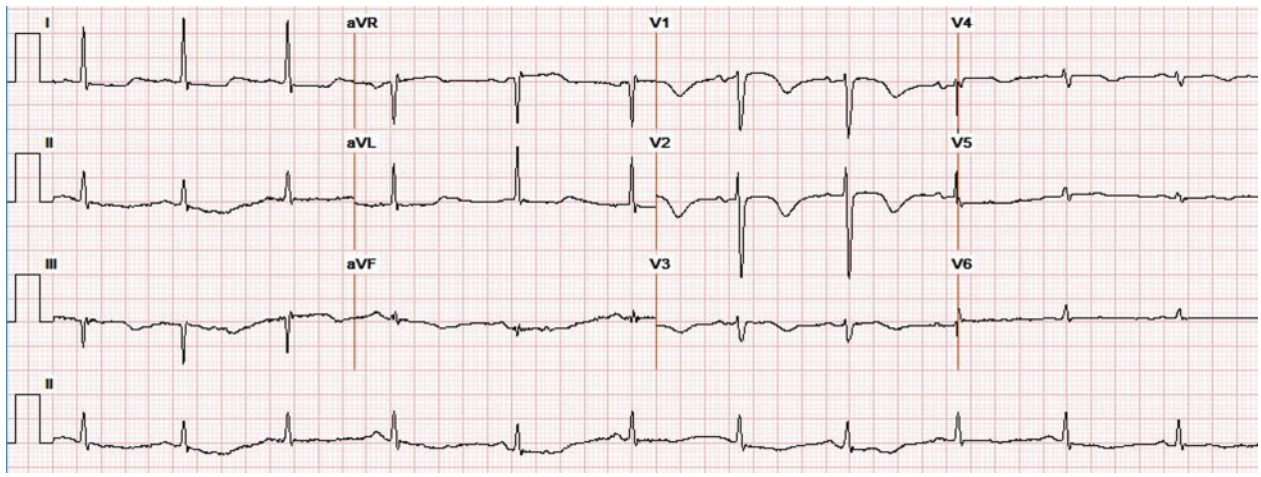


Figure 2 Initial electrocardiogram.

Table 1 Demographic, clinical, and laboratory data

	Reference range	
Date of admission		21 April 2020
Age		70
Sex		Female
Body mass index (kg/m^2)		31.8
Hypertension		Yes
Diabetes mellitus		Yes
Hyperlipidaemia		Yes
Smoking		No
History of thromboembolic disease		No
Anticoagulation on admission		Heparin prophylaxis
Time from symptom to hospitalization (day)		2
Time to diagnosis of clot in transit (day)		2
Condition at the time of diagnosis		Stable on the floor, not intubated, not on vasopressors
Laboratory values		
White-cell count, admission (per nL)	3.5–11.0	14.3
Haemoglobin, admission (g/dL)	12.0–16.0	13.7
Platelet count, admission (per nL)	150–440	210
Creatinine, admission (mg/dL)	0.5–1.5	1.6
Troponin T, admission (ug/L)	0.000–0.090	0.042
Troponin T, at diagnosis		0.022
Pro B-type natriuretic peptide, admission (pg/mL)	1.0–125.0	14 042.0
Pro B-type natriuretic peptide, at diagnosis		5830.0
D-dimer, admission (ng/mL)	0–230	2153
D-dimer, at diagnosis		2985
Fibrinogen, at diagnosis (mg/dL)	200–400	182
C-reactive protein, admission (mg/L)	0.0–5.0	8.6
C-reactive protein, at diagnosis		NA
Ferritin, at diagnosis (μg/L)	12–150	61
Procalcitonin, at diagnosis (ng/mL)	0.02–0.08	NA
Blood gas (venous), at diagnosis		pH 7.41, pCO_2 35.6 mmHg, pO_2 30.5 mmHg, HCO_3 22 mmol/L, sO_2 59.3%

Continued

Table 1 *Continued*

	Reference range	
Transthoracic echocardiographic findings		
RV dilatation		Yes
Septal flattening		Yes
RV systolic pressure (mmHg)		67
RV Fractional Area Change (%)	>35	24.2
RV Free Wall Strain (%)	≥-23	-10
Left Ventricular Ejection Fraction (%)	≥55	65
Repeat transthoracic echocardiogram		Highly mobile clot in transit in RA/RV
CT diagnosis of pulmonary embolism		Yes
DVT on lower extremity venous Duplex		NA
Thrombolysis		Yes
Survival (in-hospital)		No (Day 2)

CT, computed tomography; RV, right ventricular.

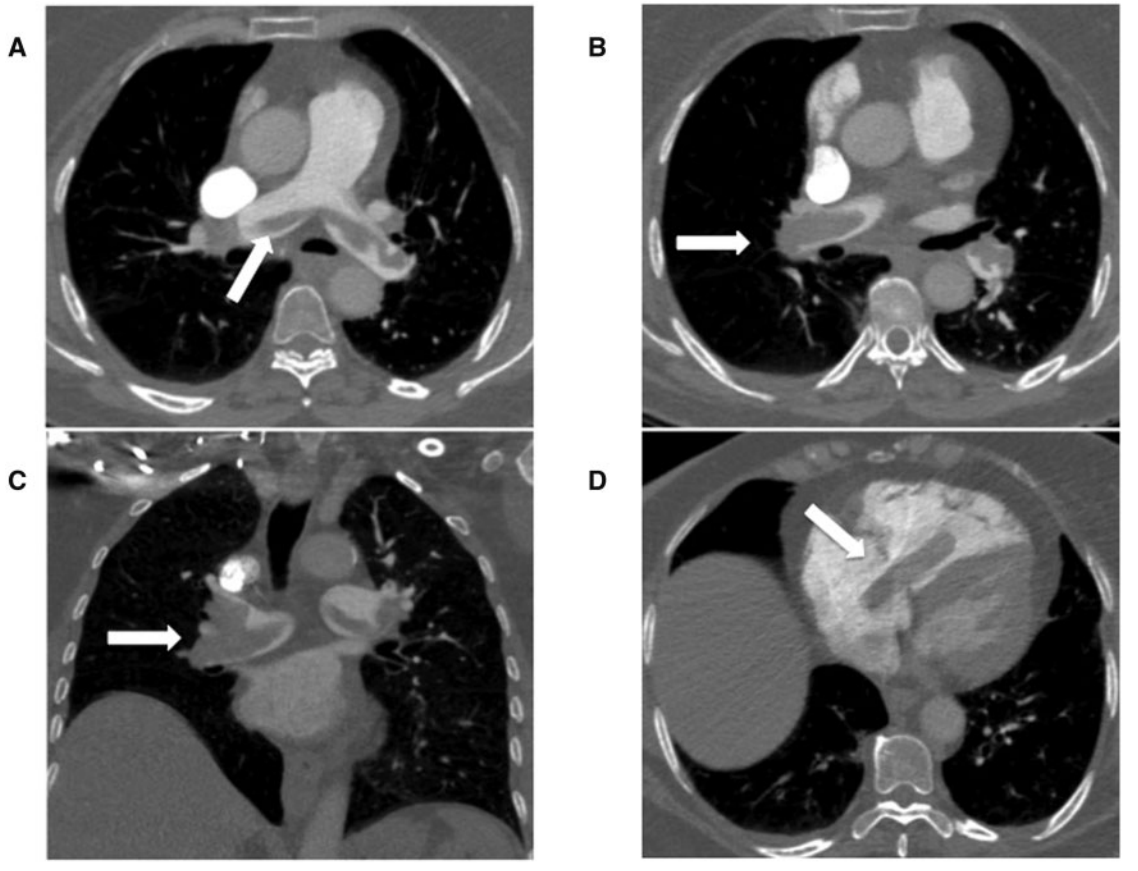


Figure 3 Initial computed tomography angiography. (*A–C*) Extensive pulmonary emboli (arrow), saddle embolus and multiple filling defects in bilateral pulmonary arteries. (*D*) Clot in transit (arrow).

and bilateral filling defects involving all lobes with notable thrombus in the right atrium extending into the right ventricle (*Figure 3*). Repeat echo revealed a highly mobile CIT (*Figure 4*, *Video 1*). Repeat nasopharyngeal swab for COVID-19 was positive.

Therapeutic dose anticoagulation with intravenous heparin (5000 unit bolus followed by 1260 units per hour) was started and the patient was transferred to the intensive care unit (ICU). She was evaluated by the multidisciplinary institutional Pulmonary

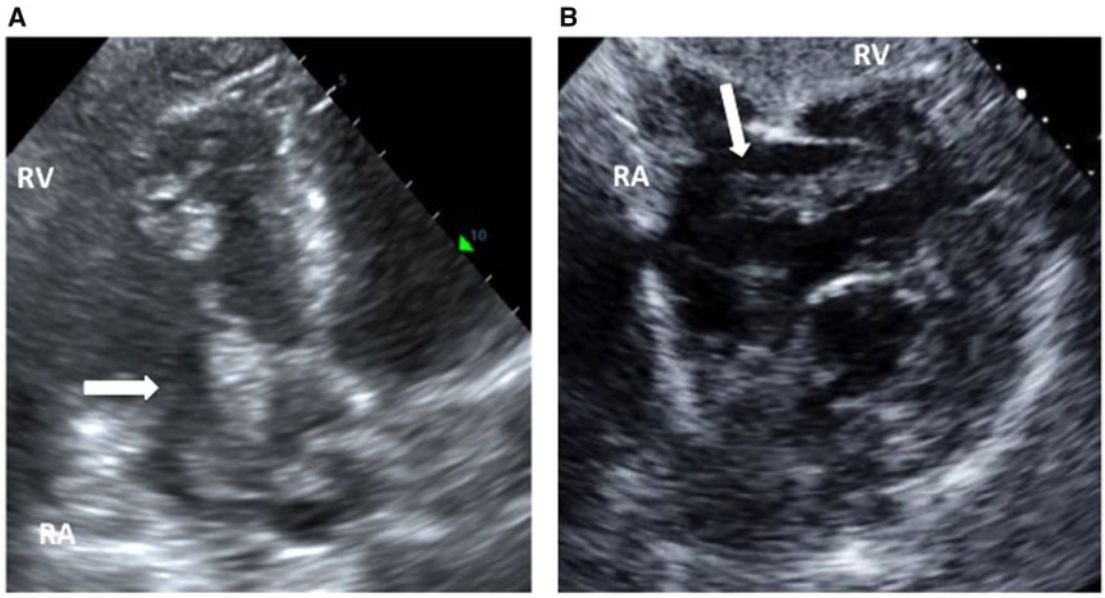
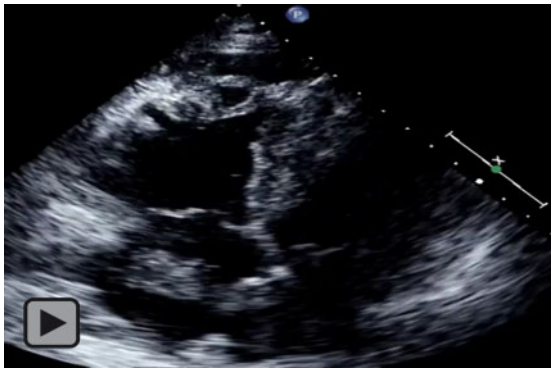


Figure 4 Echocardiogram (*A*) four-chamber view showing dilated right ventricle, and clot in transit (arrow), (*B*) subcostal view with clot in transit (arrow) through the right atrium to the right ventricle.



Video 1 Echocardiogram showing dilated right ventricle, McConnell sign and clot in transit.

Embolism Response Team (PERT) and given concurrent illness and comorbidities, percutaneous aspiration thrombectomy with adjunctive intra-pulmonary and catheter-directed thrombolysis was recommended. Foregoing general anaesthesia which has known risks in this setting, an AngioVac device (Angiodynamics, Latham, NY, USA) was advanced on suction from a femoral venous approach. The patient was given a total of 13 000 units of heparin intravenously to achieve an activated clotting time above 300. The patient decompensated after initial successful aspiration. Despite further rescue thrombectomy with the Inari FlowTriever device (Inari Medical, Irvine, CA, USA) and administration of intra-pulmonary and systemic thrombolysis the patient arrested and eventually died.

Discussion

Early in the COVID-19 pandemic, NYC hospitals were inundated with COVID-19 infected patients, which in its most severe form progressed to acute respiratory distress syndrome, renal failure, and associated cardiovascular and neurologic sequelae.[5] Usually these complications were seen in the second phase of the illness (7–10 days after symptom onset), triggered by a hyper-immune response associated with a markedly elevated D-dimer.[6] Along with this was a newly described 'COVID associated coagulopathy' which led to increasingly observed thrombosis due to inflammation-induced coagulopathy and was associated with a poor prognosis.[1,2] Anticoagulation with heparin (mostly prophylactic dosing) appeared to confer a lower mortality in a subset of patients with very severe COVID-19 who had extreme elevations of D-dimer.[7] Others reported increased rates of VTE in patients with COVID-19 in the ICU, despite the use of prophylactic anticoagulation.[8–11] A recent report describing profound haemodynamic collapse due to acute cor pulmonale in five patients in an ICU over a 48-h period suggested that obstructive shock from thromboembolism may have been responsible for the sudden decline, but could not be confirmed in all patients. All were on prophylactic or full-dose anticoagulation, and two of the five patients had evidence of intracardiac thrombus on echo at the time of collapse.[12] Additionally, in another report, right ventricular dilatation identified by echocardiography in patients hospitalized with COVID-19 was independently associated with increased mortality.[13] A CIT, as seen in our case, in a patient already diagnosed with saddle PE and right ventricular dysfunction could rapidly lead to catastrophic shock and death, if undiagnosed and untreated. We also observed three additional cases at our institution of CIT in COVID-19 patients that presented in the later phases of the disease with profound haemodynamic and respiratory collapse.

Despite the high mortality rate associated with CIT, though, there are no recommendations on how best to treat CIT in the most up to date ESC guidelines. This likely reflects the paucity of evidence and consensus on management of this phenomenon. Involvement of a multidisciplinary team to manage PE is encouraged in the new guidelines to meet these types of concerns.[14] Combining the conundrums of COVID-19 infection with those of suspected or confirmed PE, especially with CIT, merges two clinical entities that lack robust data to guide decision-making. Pulmonary Embolism Response Teams are uniquely positioned to address this scenario as they can respond rapidly and bring a group of multidisciplinary experts together to provide consensus based and individualized recommendations. A modified PERT algorithm to address some of the unique challenges posed by VTE in the setting of COVID-19 was recently described.[15] Hence, we utilized our multidisciplinary PERT to improve our clinical decision-making and come to a rapid consensus on the best management approach for this patient.

We are unaware of any reports of the occurrence of such an extreme thrombotic venous event in the absence of severe lung injury and the hyper-inflammation typically linked to COVID-associated coagulopathy. Both VTE and CIT occurred in the first phase of disease when inflammation was modest, and D-dimer was only moderately elevated, raising the question of whether other mechanisms of thrombosis are more active in the early stages of the disease. Increasing number of reports of arterial macro-thrombosis in milder forms of COVID disease underscores the need to further understand the mechanisms related to COVID-associated coagulopathy.[16,17]

Conclusion

We report a rare case of COVID-19 presenting with saddle PE complicated by development of a highly mobile CIT in the absence of lung parenchymal involvement and hyper-inflammation associated with COVID coagulopathy. It is important to suspect and recognize the signs of VTE and CIT in COVID-19 patients, both in the early and later phases of the illness, and consider a lower threshold for diagnostic imaging and treatment. Our case further informs on the central role echocardiography plays in the comprehensive evaluation and re-evaluation of hospitalized patients with COVID-19, especially if we want to advance our understanding and management of the most severe forms of VTE in these patients. Finally, it highlights the importance of a multidisciplinary organized approach in meeting the challenges of clinical decision-making in complex diseases that suffer from a paucity of level 1 data such as PE, CIT, and COVID-19.

Lead author biography

Dr Shunsuke Aoi trained in Japan (Seirei Hamamatsu General Hospital) and in the USA (Mt Sinai Beth Israel) and is currently training as an interventional cardiology fellow at Jacobi Medical Center and Montefiore Medical Center (Bronx, NY, USA).

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The patient reported in this case is deceased. Despite the best efforts of the authors, they have been unable to contact the patient's next-of-kin to obtain consent for publication. Every effort has been made to anonymise the case. This situation has been discussed with the editors.

Conflict of interest: none declared.

Funding: none declared.

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