

Simultaneous arterial and venous thromboembolic events associated with COVID-19. A case report

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Abstract

Infections with COVID-19 can induce thrombophilia and increase the risk of thrombotic events. We describe a case of a 64-years-old male who presents with intermediate-risk pulmonary embolism and brachial artery thrombosis secondary to an undiagnosed patent foramen ovale and COVID-19 infection. The patient was successfully treated with thrombolysis and heparin infusions and was discharged home with long-term anticoagulation. Managing patients with multiple pathologies occurring concurrently requires effective inter-speciality working in order to take a holistic approach to managing the patient opposed to managing the conditions in isolation. This case report highlights how clinical guidelines can support decision making of the individual pathologies but working as a team will enable the best care.

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Key words: Pulmonary embolism; COVID-19; arterial embolism; patent foramen ovale; venous embolism; case report.

Contributions: AR, MB, AN: Managed the patient, devised the manuscript and the revisions; CH: Input into the manuscript and revisions

Conflict of interest: None. This work was not supported by any grant.

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate: Ethics approval is not required at our institution to publish an anonymous case report. Informed consent was obtained from the patient included in this study.

Consent for publication: Informed consent gained from the patient.

Received for publication: 1 March 2021.

Revision received: 14 April 2021.

Accepted for publication: 20 April 2021.

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Emergency Care Journal 2021; 17:9718

doi:10.4081/ecj.2021.9718

Case Report

A 64-years-old black African male had been complaining of left arm pain for three days. He had been prescribed naproxen and lansoprazole by his General Practitioner (GP) on day two for suspected musculoskeletal pain or diabetic neuropathy given that reduced sensation to C5/C6 dermatome was noted. On the third day of symptoms, he suddenly became short of breath then collapsed, when walking from his car to the GP surgery. An emergency ambulance was called, they provided 15 litres per minute of oxygen and pre-alerted him to the Emergency Department (ED).

At our evaluation in the ED the patient was alert, dyspnoeic with tachypnoea (respiratory rate of 28), oxygen saturation was unrecordable, pulse rate of 128bpm and blood pressure of 154/96mmHg. The observations made him score 10 on the National Early Warning Score. He was recently diagnosed with type two diabetes and had a blood glucose of 13.4mmol/L. He was prescribed and compliant with naproxen, lansoprazole and metformin.

On examination, his left upper limb was cold and pale with slight reduction in the sensation of the hand. The axillary pulse was palpable, but nil further was palpable distally. The patient's chest was clear.

Given this history and clinical findings suggestive of a Pulmonary Embolism (PE) and potential left upper limb arterial thrombosis an arterial blood gas was obtained from his right radial artery and a Computed Tomography Pulmonary Angiogram (CTPA) and left upper limb angiogram was requested (Figure 1 and 2). The intensive care team and vascular surgeon were alerted for their specialist input.

The ABG demonstrated a significant type one respiratory failure (PaO₂ of 6.36, FiO₂ of 0.85), a compensatory respiratory alkalosis (pH 7.42, PaCO₂ of 4.17) secondary to a metabolic lactic acidosis (HCO₃⁻ 20.1, Lactate 2.28).

The electrocardiogram showed a sinus tachycardia which is the most common rhythm seen in acute PE.¹

Blood tests including full blood count, urea and electrolytes, coagulation studies and a blood culture were obtained. D-dimer test was requested only for its prognostic role in COVID-19 patients, as its use in the diagnostic algorithm of PE was not indicated (pre-test probability of 4.5 using the Wells' Criteria for PE).² The result did not affect the treatment decision and it was elevated at 9526mcg/L. Some evidence is emerging regarding thresholds for d-dimer that are strongly indicative of PE in COVID-19 patients (>2660mcg/L having 100% sensitivity and 67% specificity).³ The renal function had declined [creatinine 155 (baseline 95), urea 13.0 (baseline 5.7)], demonstrating an Acute Kidney Injury (AKI) stage one.

CTPA, completed after 126 minutes in the ED due to departmental radiology delays, confirmed left and right main pulmonary artery emboli extending into the segmental branches of all lobes and a dilated

right atrium and flattening of the interventricular septum consistent with right heart strain. There was a bulging at the left side of the interatrial septum, which raised the suspicion of a patent foramen ovale. The CTPA also highlighted peripheral ground glass opacities consistent with moderate/severe COVID-19 infection.

Left upper limb angiogram confirmed a brachial artery embolus extending into the radial artery.

A polymerase chain reaction swab later confirmed the suspicion of COVID-19 infection.

The initial treatment for the type one respiratory failure was oxygen, which was provided at 15 litres per minute through a tight-fitting mask with reservoir. This achieved arterial oxygen saturations of only 80%. Given the fluid losses through the increased ventilatory rate and AKI, sodium chloride was administered.

Risk stratification and guidance on treatment for PE with COVID-19 infection do not exist. However, factors such as patient location, disease severity, d-dimer thresholds and clinical features of venous thromboembolism should all be considered to make decisions regarding treatment as suggested by the British Thoracic Society.⁴ We judged the disease state as severe due to the high oxygen requirements (PaO₂ of 6.36, FiO₂ of 0.85), the signs of right heart strain and the concomitant arterial thrombosis. This patient's Pulmonary Embolism Severity Index (PESI) score was 134 which is classed as very high risk and has an associated 30-day mortality of 10-24.5%.⁵

Considering the acutely ischaemic left upper limb as an isolated pathology, the most definitive treatment option would have been open or endovascular embolectomy. However, including the more challenging pathology, PE and COVID-19, the benefit of medical management overrode the surgical approach. Therefore, the patient was treated with systemic thrombolysis (alteplase in this case) for both the PE and arterial thrombus, after 189 minutes in the ED. The dose of alteplase was 0.9mg/kg, which was 81mg of alteplase given as 10% (8mg bolus over 2 minutes) followed by 90% (73mg) infusion over 1 hour. Thirty minutes after the alteplase infusion a maintenance dose intravenous unfractionated heparin at 1mL/hr (1000 units/hour) was administered.



Figure 1. Computed tomography pulmonary angiogram demonstrating pulmonary emboli and appearances suggestive of COVID-19 infection.

One hour after the thrombolytic infusion had finished the patient was titrated off oxygen and maintained oxygen saturations of 98%. He reported his limb was starting to feel normal again and clinically had a better capillary refill time.

The patient was managed on an acute respiratory ward and discharged home on day 5 with rivaroxaban for long term anticoagulation. He was followed up with the respiratory team as an outpatient. An echocardiogram performed two months after discharge highlighted a shunt across the atrial septum (Figure 3).



Figure 2. Upper limb angiogram demonstrating embolus in brachial artery

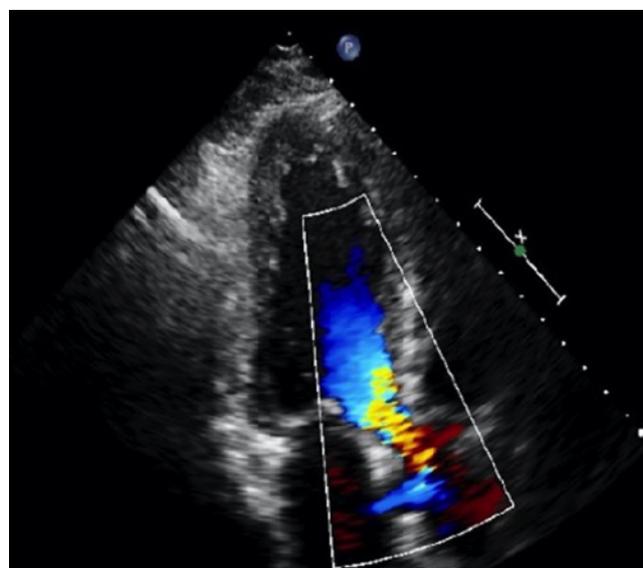


Figure 3. Echocardiogram demonstrating shunt across atrial septum.

Discussion

The incidence of thrombosis in COVID-19 pneumonia patients has been highlighted to be 49% in three Dutch intensive care units, of which 87% were PEs.⁶ These thrombotic complications associated with COVID-19 are thought to be due to the cytokine storm that occurs with the infection which subsequently increases the clotting factors, notably fibrinogen.⁷ However, the patient's fibrinogen in this case was within the normal limits at 4.65 g/L at admission. Moreover, the other prognostic markers of COVID-19 infection, C-reactive protein (18mg/L where normal is <5), lymphopenia, ($1.05 \times 10^9/L$) and liver enzymes (only globulin 40 where normal is 20-35g/L) were not pronounced to indicate severe COVID-19 infection.

It has been found in a study of 183 patients with severe COVID-19 infections that d-dimers with a median level of 2,120mcg/L occurred in non survivors and 610mcg/L in survivors.⁸ This patient had a d-dimer of 9526mcg/L indicating that survival may be compromised by the inflammatory/thrombotic state. The d-dimer is non-specific, and it cannot differentiate between inflammation and thrombosis, and in this case the patient's other markers of inflammation were not significantly raised thus it may be that the elevated d-dimer in this case was secondary to thrombosis as opposed to systemic inflammation.

Surprisingly this patient did not present with cough, fever or myalgia preceding the limb ischaemia but had significant changes on CTPA to evidence moderate to severe COVID-19 infection. Therefore, the diagnosis of COVID-19 came after the thrombotic complications had manifested. It should also be noted that this was an otherwise unprovoked PE, as the patient otherwise had no risk factors for thromboembolism. In addition, the Sepsis Induced Coagulopathy (SIC) score was 2 meaning that SIC is unlikely yet still carries a mortality risk at 28 days of 20%.⁹ The low SIC score further supports a thromboembolic disease process rather than overt coagulopathy secondary to sepsis as a cause.

The use of thrombolysis for patients with high-risk PE defined as obstructive shock, sustained hypotension or cardiac arrest is supported by the evidence.¹⁰ However, evidence to support the use of thrombolysis in patients with intermediate-risk PE defined as PE with right ventricular dysfunction and/or raised cardiac biomarkers in the absence of shock, as in this case, is limited.¹¹ Intermediate-risk PEs are always based on a case-by-case basis, given the associated upper limb thrombus and high PESI score the collaborative decision was to thrombolys.

Conclusions

COVID-19 infections have been associated with thrombotic

events, this can include both PE and arterial thrombus as in this case. Management of such cases can be supported by clinical guidelines for the individual pathologies. However, when multiple pathologies exist as in this case the inter-speciality teams must work cohesively in order to manage the patient holistically for the best outcomes.

References

- Petruzzelli S, Palla A, Pieraccini F, et al. Routine electrocardiography in screening for pulmonary embolism. *Respiration* 1986;50:233-43.
- Zhang L, Yan X, Fan Q, et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. *J Thromb Haemost* 2020;18:1324-9.
- Leonard-Lorant I, Delabranche X, Severac F, et al. Acute pulmonary embolism in COVID-19 patients on CT angiography and relationship to D-dimer levels. *Radiology* 2020:201561.
- BTS Guidance on venous thromboembolic disease in patients with COVID-19. Updated 4 May 2020.
- Aujesky D, Obrosky DS, Stone RA, et al. Derivation and validation of a prognostic model for pulmonary embolism. *Am J Resp Critical Care Med* 2005;172:1041-6.
- Klok FA, Kruip MJ, Van Der Meer NJ, et al. Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID-19: an updated analysis. *Thromb Res* 2020;191:148-50.
- Wise J. Covid-19 and thrombosis: what do we know about the risks and treatment? *BMJ* 2020;369:m2058.
- Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost* 2020;18:844-7.
- Iba T, Di Nisio M, Levy JH, et al. New criteria for sepsis-induced coagulopathy (SIC) following the revised sepsis definition: a retrospective analysis of a nationwide survey. *BMJ Open* 2017;7:e017046.
- Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS) The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). *Eur Heart J* 2020;41:543-603.
- Meyer G, Vicaut E, Danays T, et al. Fibrinolysis for patients with intermediate-risk pulmonary embolism. *N Engl J Med* 2014;370:1402-11.