

Case Reports and Series

Aortic thrombosis in COVID-19

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ABSTRACT

Background: Venous thrombo-embolism is now well-recognised as a common complication of severe COVID-19 disease. Arterial thrombosis has been less well recognised, although it is increasingly reported, mostly in the context of myocardial infarction and stroke.

Case report: A 63-year-old man developed a pale, cold foot with an absent dorsalis pedis pulse 7 days into his admission with COVID-19. A CT angiogram demonstrated a large thrombus in the lower thoracic aorta, which had not been present on CT pulmonary angiogram the preceding week, along with occlusion of both popliteal arteries. He was managed with therapeutic dose of low molecular weight heparin (LMWH) for 6 weeks.

Results: This case adds to the growing list of potential sites and consequences of thrombosis in COVID-19.

Conclusion: This case underscores the urgent need for pathophysiological studies and clinical trials to target treatments and guidelines for thromboprophylaxis in COVID-19.

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Case presentation

A 63-year-old man with a background of chronic obstructive pulmonary disease (COPD) presented to the Emergency Department with a 3-day history of exertional dyspnoea, left-sided chest pain, and a cough productive of white sputum. He had been discharged 8 days earlier from another hospital, where he had been treated for a secondary pneumothorax with a surgical chest drain. During that admission he had developed subcutaneous emphysema from which he had recovered. His most recent COVID-19 PCR test from seven days into his admission at the previous hospital, and 15 days prior to his presentation at our hospital, had been negative.

He was an ex-smoker (30–40 pack year history), having stopped 15 years ago, with no past medical history of cardiovascular disease or peripheral vascular disease. He did not drink alcohol. He was obese, with a body mass index (BMI) of 30.92 kg/m². At baseline, he was slightly breathless on exertion, but had unlimited exercise tolerance, with no previous admissions for COPD. Radio-

logically, confluent centrilobular and limited paraseptal emphysema was noted on CT imaging from his previous hospital admission. He lived alone and was fully independent, running his own business.

On admission, he was breathless, with a respiratory rate of 20 breaths per minute. His oxygen saturation level was 82% on room air and 95% on 3 L of oxygen/minute. He was afebrile, with a heart rate of 90 beats per minute and blood pressure of 122/65 mmHg. He had a large haematoma over the site of his recent chest drain and there was reduced air entry bibasally on auscultation of his chest. He had no leg swelling, nor any clinical suspicion of a deep vein thrombosis.

Initial investigations (Fig. 1) included a raised C-reactive protein (CRP) of 151 mg/L, an elevated D-dimer of 3390 µg/L, a normal prothrombin time (PT) of 11.3 s and a normal activated partial thromboplastin time (APTT) of 33 s. Ferritin was 1484 µg/L. A chest radiograph showed increased opacification in the left hemithorax, left-sided subcutaneous emphysema, but no obvious infiltrates. He had a CT pulmonary angiogram (Fig. 2a) on the day of admission which showed no pulmonary emboli, a small left pleural effusion, a resolving pneumomediastinum, and non-specific inflammatory signs on a background of emphysema. A nasopharyngeal swab for SARS-CoV-2 was PCR positive. The timing suggests possible nosocomial infection from the first hospital admission.

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He was started on standard prophylactic dosing of low molecular weight heparin (LMWH) (40 mg enoxaparin once a day, given his body weight of 90.7 kg) and oxygen therapy was continued. He was also treated for possible bacterial superinfection, initially with intravenous amoxicillin/clavulanic acid and clarithromycin. This was escalated to intravenous cefuroxime 2 days later, due to persistent oxygen requirements, rising inflammatory markers (see Fig. 1), and worsening consolidation on chest radiograph.

He was transferred to the high dependency respiratory unit on day 7 of admission (day 10 on onset of symptoms) as there was concern that he might require non-invasive ventilation. That day, he reported that his left foot had suddenly become cold and complained of pins and needles in the same foot. On examination, the left foot was pale and cool to touch, with an absent dorsalis pedis pulse. Movement in both feet was intact.

Haematological investigations showed a further increase in white cell count, neutrophilia, and stably elevated CRP (see Fig. 1). D-dimer had risen further to 6470 $\mu\text{g/L}$, but the coagulation screen remained normal (PT 12.1 s, APTT 33 s).

A CT angiogram was performed (Fig. 2b and c). This showed a large aortic thrombus in the lower thoracic/upper abdominal aorta, above the level of the coeliac trunk and renal arteries, with occlusion of both popliteal arteries, possibly due to emboli from the proximal thrombus. Collateral flow allowed for filling of the right lower limb vessels but there was no evidence of arterial perfusion below the left knee. The aortic thrombus had not been present on the CTPA of 7 days earlier, nor was there aortic wall atheroma visible on these images. There was no evidence of intracardiac thrombus on transthoracic echocardiogram.

The patient's dose of LMWH was increased to a therapeutic level (1.5 mg/kg enoxaparin once a day). After further review by the vascular surgery team, it was felt that no surgical intervention was required. Handheld doppler ultrasound demonstrated biphasic flow of peripheral pulses bilaterally and symptoms resolved. It was agreed to continue the therapeutic dose LMWH for 6 weeks, with vascular and anticoagulation follow-up as an outpatient once the patient's respiratory symptoms, oxygen requirements, and mobility permitted discharge. He was discharged 3 days later (10 days

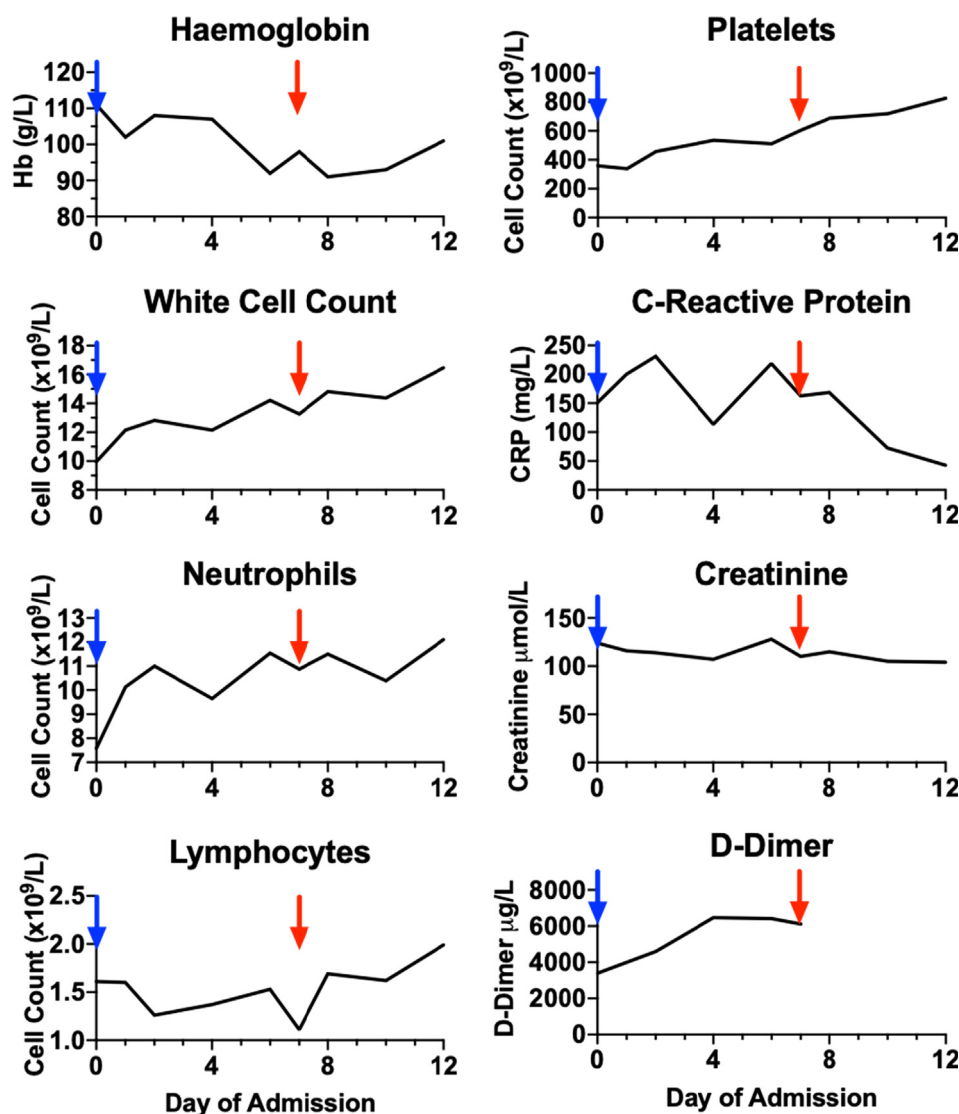


Fig. 1. Haematological parameters during the 12 days of admission. Blue arrows indicate day of admission, correlating with initial imaging; with red arrows indicating day 7, when thrombus was first noted clinically and radiologically. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

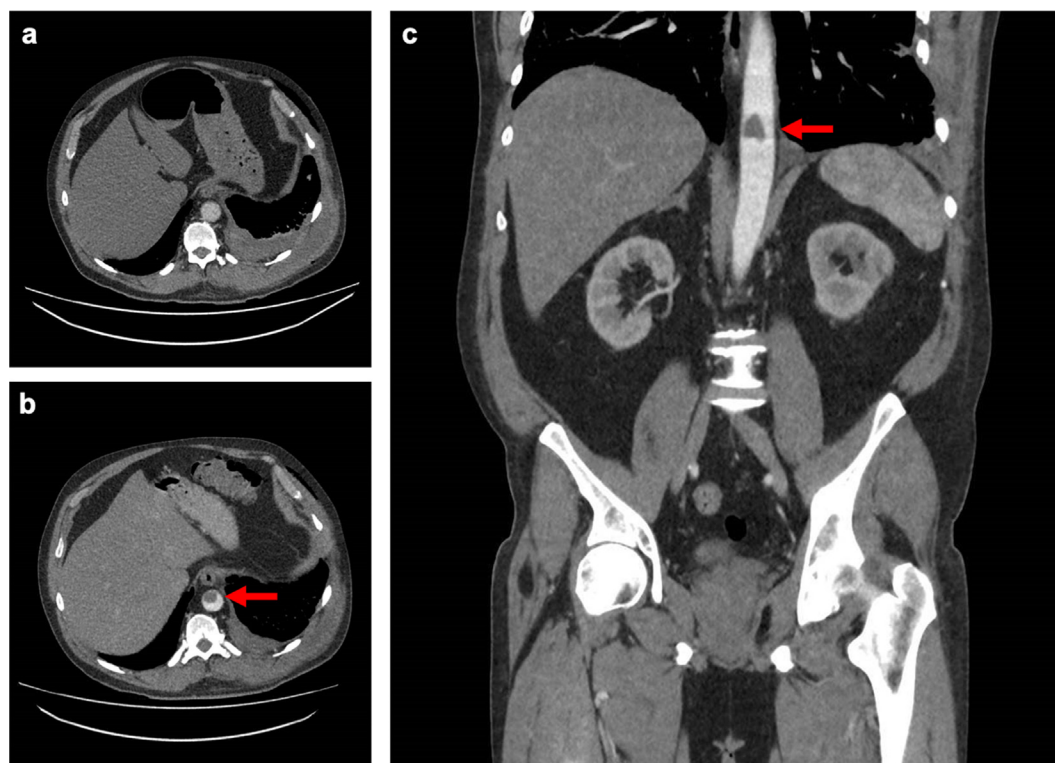


Fig. 2. Computerised tomography (CT) at the level of T11 vertebrae – a) on admission, taken in pulmonary arterial phase as part of CT Pulmonary Angiogram and b) & c) axial and coronal planes of a CT Lower Limb Angiogram taken in arterial phase, 7 days into admission, showing a large filling defect in the aortic lumen (red arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

following admission). Follow-up imaging has since shown resolution of the thrombus.

Discussion

Venous thrombo-embolism is now well-recognised as a common complication of severe COVID-19 disease (Ferner et al., 2020). Arterial thrombosis has been less well recognised, although it is increasingly reported, typically in the context of myocardial infarction and stroke (Klok, 2020; Mao, 2020). This case adds to the growing list of potential sites and consequences of thrombosis in COVID-19. Together, these varied consequences add to our understanding of the pathophysiology of thromboembolism in COVID-19 disease.

Modern interpretations of Virchow's triad describe three categories of pro-thrombotic factors: abnormalities of blood flow (stasis); abnormalities of the vessel wall (endothelial injury); and abnormalities in blood constituents (hypercoagulability) (Chung and Lip, 2003). Several explanations for the increased propensity to thrombi in COVID-19 disease have been proposed (Levi et al., 2020), including low-grade disseminated intravascular coagulation (DIC) and localised thrombotic microangiopathy, with inflammation, direct vascular damage by the virus, and immobilisation also contributing.

Our patient had an extensive descending aortic artery thrombus with a normal coagulation screen and no evidence of consumption of platelets/DIC or thrombotic microangiopathy. There are several other reported cases of aortic thrombosis in COVID-19 (Baeza

et al., 2020; Webster et al., 2020; Wengerter et al., 2020; Woehl et al., 2020). These cases share common features, including male sex, age over 50 years, smoking history, and obesity (Table 1). Some of these features may simply represent risk factors for severe COVID-19 whilst others may directly increase propensity to thrombosis. We speculate that these cases of aortic thrombosis were the result of direct COVID-19-induced vascular damage in the context of a hypercoagulable state. They represent the extreme end of a spectrum of vascular pathology seen in severe COVID-19. Further study is required to understand how to identify patients at most risk from these complications, and how best to prevent them. The World Health Organization recommends standard pharmacological thromboprophylaxis with low-molecular weight heparin for hospitalised patients with no contraindications (World Health Organization, 2020), in accordance with recommendations from the International Society on Thrombosis and Haemostasis (Thachil, 2020). The British Thoracic Society have suggested more intensive anticoagulation based on clinical risk, COVID-19 severity, and D-dimer thresholds (British Thoracic Society, 2020), however, this guidance needs confirmation in randomised controlled trials. These guidelines may need to be more targeted, as the specific characteristics of the coagulopathy in COVID-19, including laboratory abnormalities, are better understood (Webster et al., 2020).

The need for evidence-based anticoagulation and antiplatelet strategies specific to the prevention and management of thrombo-embolism in COVID-19 disease is becoming increasingly apparent. This case provides further illustration of the urgent need for pathophysiological studies and clinical trials in this area.

Table 1
Comparison with other reported cases of aortic thrombosis in COVID-19.

Publication		This study	Baeza et al. (2020)				Webster et al. (2020)	Wengerter et al. (2020)				Woehl et al. (2020)					
Location		London, UK	Madrid, Spain				Columbia, USA	New York, USA				France					
No. of Cases		1	3				1	4				4					
Age (years)		63	63				60	39	56	60	65	64	68	72	78		
Sex	M	X	X				X	X	X	X	X	X	X	X			
	F		X				X										
Day of COVID-19 illness		10	28				18	39	2 h	7	5	5	unclear	18	10	28	8
Treatments for COVID-19		None	Ritonavir-darunavir, Cyclosporin A, Hydroxychloroquine, Doxycycline;				Lopinavir-ritonavir, Azithromycin, Ceftriaxone, Prednisolone, Hydroxychloroquine	Tocilizumab	None recorded				None recorded				
Existing significant medical and social history	Smoking history	X	X				X	None	None				X	None	X		X
	Obesity	X	X				X							X	X	X	
	Hypertension		X				X		X					X	X		
	Diabetes		X				X		X					X	X		
	Dyslipidaemia		X				X		X					X	X		
	Other		HIV, Hepatitis C, Ischaemic stroke, atrial fibrillation (anticoagulated), rheumatic mitral stenosis;				Intermittent claudication	Atrial fibrillation (anticoagulated)					X	Previous deep vein thrombosis, Ischaemic Heart Disease	Ischaemic heart disease	Previous pulmonary embolism, cardiac hypertrophy	
Imaging for Thrombosis	Serial imaging Single scans	X	X				X		X				X				
Treatment for Thrombosis		Enoxaparin	Acenocoumarol				Bemiparin	Enoxaparin	Heparin	Heparin, then apixaban				"Therapeutic anticoagulation"			

Conflict of Interest Statement

The authors declare no conflicts of interest.

CRediT authorship contribution statement

Helena Wickham: Writing - original draft. **Jerry C.H. Tam:** Writing - original draft. **Xin Hui S. Chan:** Conceptualization, Supervision, Writing - review & editing. **Marc J. George:** Conceptualization, Supervision, Writing - review & editing. **Marcel Levi:** Writing - review & editing. **Michael Brown:** Writing - review & editing.

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