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5-5-2022

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Left ventricular outflow tract thrombus in a patient with COVID-19—a ticking time bomb: a case report

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Received 27 July 2021; first decision 28 September 2021; accepted 29 April 2022; online publish-ahead-of-print 5 May 2022

Background

Coronavirus disease 2019 (COVID-19) is a manifestation of severe acute respiratory syndrome coronavirus 2, which results in many different complications including left ventricular (LV) thrombi.

Case summary

We present a 30-year-old female presenting with chest pain and shortness of breath. Patient had an extensive history including heart failure with an ejection fraction 15–20% and COVID-19 2 months ago. Echocardiogram revealed a 3.3 cm × 1.7 cm LV thrombus which was not present 4 months ago before her diagnosis of COVID-19. The LV thrombus embolized resulting in an embolus extending from the distal infrarenal abdominal aorta to the common iliac arteries bilaterally. Repeat COVID pre-procedure was positive. She underwent bilateral femoral artery cutdown, bilateral iliac artery embolectomy, superficial femoral artery embolectomy, and bilateral lower extremity fasciotomy. An extensive workup for the aetiology of the LV thrombus turned out to be negative and COVID-19 was deemed to be the aetiology of the thrombus. The patient was bridged from apixaban to warfarin and was successfully discharged within a few weeks.

Discussion

Hypercoagulability is a known complication of COVID-19 causing thrombi in various parts of the body including the LV. Early recognition with echocardiography, especially in patients with heart failure, and prompt treatment is key to avoid further complications such as embolization.

Keywords

Heart failure • COVID-19 • Left ventricular thrombus • Embolization • Hypercoagulability • Case report

ESC Curriculum

6.2 Heart failure with reduced ejection fraction • 6.5 Cardiomyopathy • 5.10 Implantable cardioverter defibrillators • 9.4 Thromboembolic venous disease

Learning points

- Coagulation abnormalities leading to a pro-coagulant state have been noted extensively in literature as one of the manifestations of Coronavirus disease 2019 (COVID-19), including the formation of left ventricular (LV) thrombus.
- Early initiation of anticoagulation in patients with LV thrombus, exacerbated by heart failure, is key to the prevention of further clots. Patients with LV thrombi must be closely observed for signs and symptoms of embolization of LV thrombus.
- Thromboembolism should still be on the differential diagnosis, especially in COVID-19, even if patients are on anticoagulant therapy.

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Handling Editor: Erike Holy/Marta Cvijic

Peer-reviewers: Roberto Lorusso; Andreas Mitsis and Pruthvi C. Revaiah

Compliance Editor: Abdelsalam Bensaoud

Supplementary Material Editor: Damien Farhad Nur Salekin

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Introduction

Since its emergence in late 2019, Coronavirus disease 2019 (COVID-19) has resulted in almost 490 million cases and over 6.1 million deaths worldwide as of April 2022.¹ COVID-19 can involve multiple organs including the respiratory, cardiac, and immune systems.² The most dreaded complication is acute respiratory distress syndrome, but it also leads to a hypercoagulable state causing multiple thrombi, including in the left ventricle. We present a case of left ventricular (LV) thrombus due to COVID-19 infection.

Timeline

Timing	Events
4 years before presentation	<ul style="list-style-type: none"> Diagnosed with heart failure. Left heart catheterization revealing normal coronaries
4 months before presentation	<ul style="list-style-type: none"> Echo ejection fraction 15–20%, right ventricular normal size and function. No left ventricular thrombus
1 month before presentation	<ul style="list-style-type: none"> COVID-19: treated with 5 days of remdesivir
Initial presentation	<ul style="list-style-type: none"> Patient presented with chest pain and shortness of breath
Day 1	<ul style="list-style-type: none"> Transthoracic echocardiogram (TTE) showing left ventricular ejection fraction (LVEF) 10–15% and a new 3.3 × 1.7 cm thrombus in the left ventricular outflow tract at mitral valve base, not present previously Heparin infusion was started. Apixaban was discontinued
Day 2	<ul style="list-style-type: none"> Patient has absent pulses in lower extremity bilaterally Cardiothoracic angiogram aorta with run-off revealed a near-occlusive embolus within the distal infrarenal abdominal aorta extending into the common iliac arteries bilaterally She underwent a bilateral femoral artery cutdown with embolectomy and bilateral lower extremity fasciotomy
Day 3	<ul style="list-style-type: none"> Repeat TTE with original LV thrombus not being present but showing two new mobile, echogenic structures in the LV apex and at the basal antero-lateral wall suggestive of further LV thrombus
Day 5	<ul style="list-style-type: none"> Hypercoagulable workup including antineutrophilic antibodies, beta-2-glycoprotein, anticardiolipin antibody was conducted, however, all were negative

Continued

Continued

Timing	Events
Day 38	<ul style="list-style-type: none"> COVID-19 induced hypercoagulability was deemed the aetiology Repeat echocardiogram before discharge —resolution of LV thrombus. LVEF 15%
Day 40	<ul style="list-style-type: none"> Patient was discharged on warfarin, after medical and surgical management/pain management of bilateral lower extremity wounds
2 months post-discharge	<ul style="list-style-type: none"> Repeat TTE showed an LVEF of 25% with no recurrence of LV thrombus

Case presentation

A 30-year-old female presented with chest pain and shortness of breath. The patient denies any complaints of palpitations or fevers. Her medical history was significant for non-ischemic cardiomyopathy, diagnosed 4 years ago, requiring an automatic implantable cardioverter-defibrillator, hypertension, diabetes mellitus, obstructive sleep apnoea, paroxysmal atrial fibrillation on apixaban, and recent COVID-19 infection. Her heart failure had been evaluated by her primary cardiologist and heart failure doctor by doing a cardiac catheterization showing normal coronary arteries, ever since her diagnosis 4 years ago. Previous transthoracic echocardiogram (TTE) done 4 months prior to admission showed a left ventricular ejection fraction (LVEF) of 15–20% with Grade 2 diastolic dysfunction and severe global hypokinesis of the LV, along with elevated right ventricular systolic pressure of 45–50 mmHg. Her medication history included carvedilol 37.5 mg/day twice a day (b.i.d.), sacubitril-valsartan 97–103 mg/day b.i.d., spironolactone 25 mg daily, hydralazine 25 mg three times a day (t.i.d.), isosorbide-dinitrate 10 mg t.i.d., torsemide 20 mg b.i.d., apixaban 5 mg b.i.d., and glipizide 5 mg b.i.d. She was admitted to an outside hospital a month prior with COVID-19, not requiring mechanical ventilation, where she was treated with remdesivir and dexamethasone, which lead to her recovery, and continued her Eliquis due to normal renal function. She denies any smoking, or illicit drugs and drinks alcohol socially. She also has had multiple past admissions for heart failure.

Vital signs showed tachycardia to 117 b.p.m. and elevated blood pressure at 181/136 mmHg; rest of the vitals including temperature were within normal limits. Physical examination was significant for a regular, tachycardic pulse but diminished breath sounds at the bases but no crackles. Cardiovascular examination was unremarkable, including no peripheral signs of endocarditis, including Roth spots, Osler nodes, Janeway lesions, and splinter haemorrhages. SpO₂ was 102 mmHg on arterial blood gas and patient was not requiring supplemental oxygen.

Initial workup was significant for brain natriuretic peptide of 1599 pg/mL (0–99 pg/mL), troponin I high sensitivity of 34 ng/L (<16ng/L), serum creatinine of 1.15 mg/dL (baseline 0.7 mg/dL) (0–1.11 mg/dL), D-dimer of 2442 ng/mL (0–230 ng/mL), ferritin 1852 ng/mL (5–204 ng/mL), fibrinogen 925 mg/dL (194–450 mg/

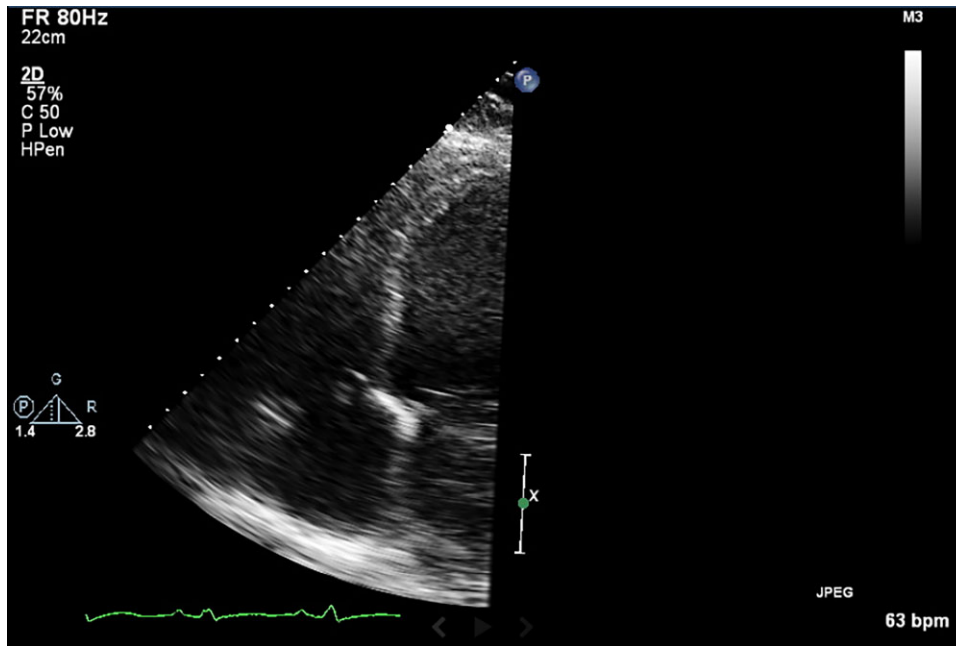


Figure 1 Transthoracic echocardiogram from 4 months prior to patient current presentation not showing any left ventricular thrombus.

dL), lactate dehydrogenase 1738 U/L (100–220 U/L), WBC 6.1 K/ μ L (4.0–12.0 K/ μ L), and thrombocytopenia at 103 000/mcL (150 000–400 000/mcL). Electrocardiogram showed sinus tachycardia, tall P- and QRS-waves suggestive of left atrial enlargement (with bifid P waves in lead II with >40 ms between the two peaks) and LV hypertrophy (R wave in aVL > 11 mm). Chest X-ray revealed cardiomegaly and central vascular prominence. A repeat COVID test was positive. The previous echo from 4 months prior to the current presentation did not show any LV thrombus (*Figure 1*). TTE during current admission showed decreased LVEF to 10–15%, and a new mobile mass in the LV outflow tract at the base of the mitral valve which measured 3.3 cm by 1.7 cm suggestive of a thrombus; however, vegetation could not be excluded (*Figure 2*, *Supplemental data*). LV internal dimension in systole and diastole were 7.1 cm and 7.3 cm, respectively.

The patient was admitted, and a heparin infusion was started for the LV thrombus. Patient continued to be afebrile and blood cultures were drawn for concerns for the possibility of endocarditis. Apixaban was discontinued. Cardiothoracic (CT) surgery was consulted for evaluation for a LV embolectomy; however, medical management was favoured. On Day 2, the patient felt heaviness in her lower extremities and physical examination revealed absent pulses bilaterally. Cardiothoracic angiogram aorta with bilateral run-off (*Figure 3*) revealed a near-occlusive embolus within the distal infrarenal abdominal aorta extending into the common iliac arteries bilaterally. She underwent a bilateral femoral artery cutdown, bilateral iliac artery embolectomy, superficial femoral artery embolectomy, and bilateral lower extremity fasciotomy. A repeat TTE, on Day 3, did not reveal the original LV thrombus. However, there were two new mobile, echogenic structures in the LV apex and at the basal antero-lateral wall suggestive of further LV thrombus.

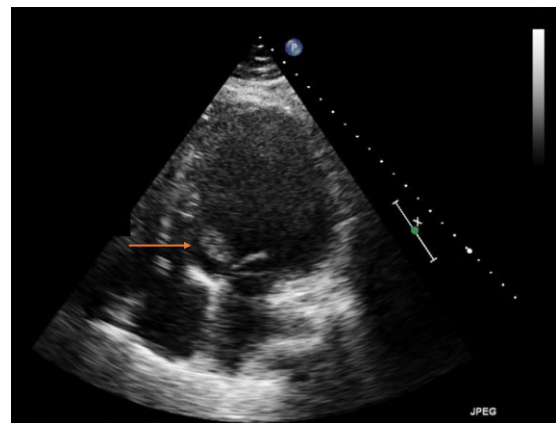


Figure 2 Apical four-chamber view on echocardiogram showing a 3.3 × 1.7 cm mobile mass concerning for thrombus during the current presentation.

To identify the aetiology of the thrombi, a hypercoagulable work-up including antinuclear antibodies, beta-2-glycoprotein, and anticardiolipin antibody was conducted; however, all were negative. Blood cultures that were previously drawn on admission, continued to be negative for any pathogen making endocarditis and a septic embolus unlikely. COVID-19 was deemed the aetiology for the LV thrombus. Heparin was bridged to warfarin. Repeat echocardiogram before discharge did not show any apical thrombus with a LVEF of 15%. After concerns for surgical wound healing, pain management due to bilateral fasciotomies, successful bridging from heparin to warfarin and

titration of her heart failure therapy were addressed, the patient was successfully discharged after 6 weeks. Patient was discharged on carvedilol 25 mg b.i.d., Entresto 49–51 mg b.i.d., spironolactone 25 mg daily, torsemide 20 mg daily, and warfarin 9 mg daily, until the next follow-up with her cardiologist. A follow-up echocardiogram, 2

months later post-discharge, showed an ejection fraction of 25% with no recurrence of the LV thrombi (Figure 4).

Discussion

The virus SARS-CoV-2 belongs to the coronavirus family, which is enveloped positive-stranded RNA viruses. This virus is presumed to act via viral structural spike (S) protein by binding with the angiotensin-converting enzyme (ACE) II receptor, which is present in many organs of the body including the pulmonary, cardiac, and endothelial cells of the blood vessels.² Of the clinical manifestations of COVID-19, coagulation abnormalities leading to a hypercoagulable state have been noted extensively in evolving literature. The exact mechanism for the hypercoagulability is not completely understood. However, *in vitro* studies of SARS-CoV-1 and data collected regarding COVID-19 suggests that SARS-CoV-2, due to its near-similarity in its genome with SARS-CoV-1, acts by causing hyperinflammation due to increased pro-inflammatory cytokines, reducing innate and adaptive responses to the virus, and interfering with the renin-angiotensin-aldosterone system by decreasing ACE II activity and hence increasing Ang II, resulting in vasoconstriction and pro-inflammatory and pro-oxidative state.³

Endothelial injury is a hallmark of the SARS-CoV-2. Inflammatory cells attached to the endothelial cells of the blood vessels in different organs including the lungs and heart as well as the elevated levels of von Willebrand factor and P-selectin, that are released by endothelial cells when they are compromised, in patients with COVID-19, lead to hypercoagulability.⁴ COVID-19 also leads to a hypercoagulable state by increasing pro-thrombotic factors such as fibrinogen, D-dimer, Factor VIII, and many others as seen in our patient as

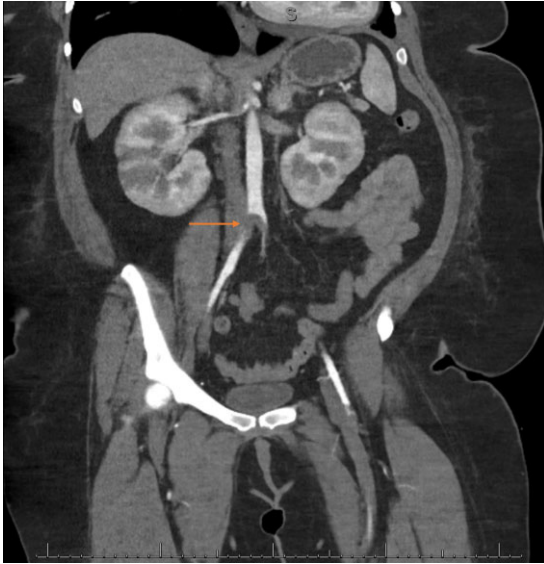


Figure 3 Cardiothoracic angiogram showing a near-occlusive thrombus within the distal infrarenal abdominal aorta extending into the common iliac arteries bilaterally.

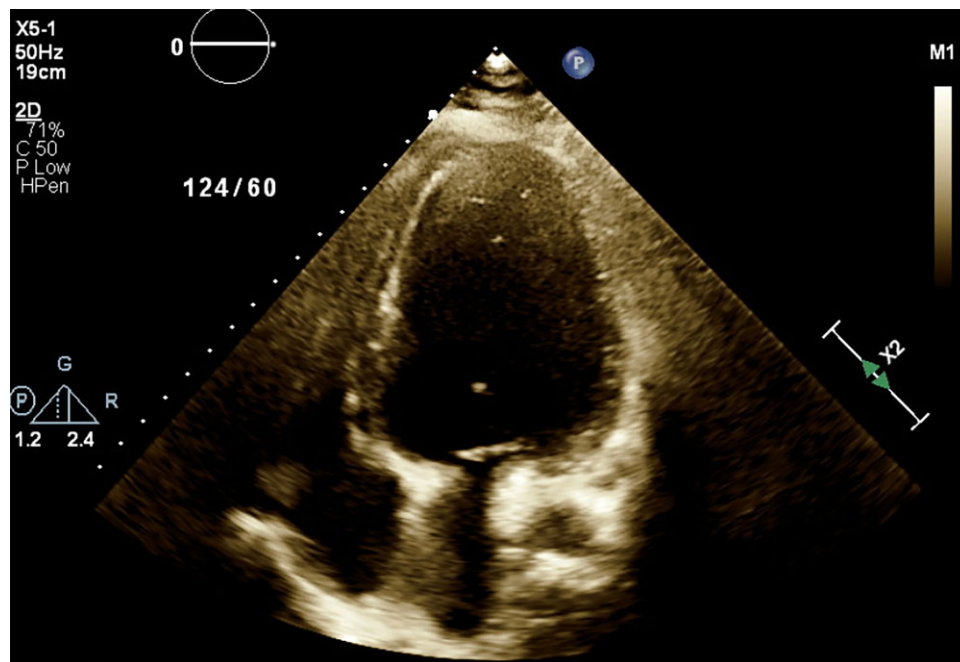


Figure 4 Echocardiogram 2 months post-discharge showing resolution of left ventricular thrombus.

well.⁵ Finally, our patient had several risk factors that could lead to stasis including heart failure.

Left ventricular thrombus is a dreaded complication arising from cardiac pathologies including myocardial infarction and heart failure. In a study at Brigham and Women's Hospital, heart failure was found to be the main cause of LV thrombi after evaluating over 140 000 echocardiograms.⁶ One of the many complications of LV thrombus is embolic events. A cohort study comparing patients with LV thrombus with patients without LV thrombus showed that the former had four times the long term incidence of embolic events.⁷

COVID-19 manifests in several haematologic complications including thrombotic complications in the venous system such as deep venous thrombosis, and the arterial system manifesting as myocardial infarction, stroke, and limb ischaemia.^{8,9} This patient had a severely depressed ejection fraction that led to stasis and had added risk factors of being hypercoagulable due to COVID-19, making her at risk for the formation of a LV thrombus and the subsequent embolization to the lower limbs.

There have been a few reports of patient developing intracardiac thrombi in patients with COVID-19.^{10,11} However, in medical literature, there has not been a reported incident of such LV intracardiac thrombi, resulting in subsequent embolization into the lower limb causing ischaemia. Since COVID-19 is a recent entity, there have been no studies to date regarding the incidence of LV thrombi or subsequent embolization in patients who have COVID-19.

Due to the lack of randomized trials showing the efficacy of direct oral anticoagulants (DOACs) in patients with LV thrombi, warfarin is the mainstay therapy to inhibit clot progression. American Heart Association guidelines recommend 3–6 months of therapy.¹² However, there have been case series and retrospective studies that have shown increased efficacy of DOACs in the resolution of LV thrombi^{13,14} including a quicker resolution of LV thrombi when comparing to warfarin.¹³ DOACs hold the advantage of having a safer profile in terms of bleeding risk¹³ and more infrequent monitoring.

Unfractionated heparin (UFH) or low molecular weight heparin (LMWH) are the most common methods for venous thromboembolism prophylaxis.¹⁴ In case of COVID-19, early reports suggest that UFH and LMWH have antiviral and anti-inflammatory properties as well as antithrombotic activities.¹⁵ Treatment failure with apixaban in our patient can be attributed to many factors, including medication non-compliance. Another reason for apixaban failure in our patient could be due to the ability of SARS-CoV-2 to alter the activity of multiple cytochrome P450 enzymes that also play a role in the metabolism of apixaban. However, the clinical significance of these interactions at this point is unknown. One of the many ways to transition to another anticoagulation in such patients is to transition to warfarin with parenteral anticoagulation, such as UFH, as bridging therapy.¹⁶ As in our patient, a heparin drip was started, and she was transitioned to warfarin. Echocardiogram done 2 months later after discharge (Figure 4) showed resolution of the LV thrombus.

Conclusion

Thromboembolism should be considered in the differential diagnosis of the patients with COVID-19 who develop new vascular or neurological symptoms. Early initiation of anticoagulation is key.

Lead author biography



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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 authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

Funding: None declared.

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