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Case Report

Multiple biventricular thrombi in a patient with alcoholic cardiomyopathy and COVID-19: A tragic association in a deadly pandemic

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ABSTRACT

As a primary cause, intracardiac thrombi are seen in a variety of cardiac conditions such as acute anterior myocardial infarctions and dilated cardiomyopathy. However, there are secondary predisposing conditions that increase the risk of clot formation in normally functioning ventricles. Migration or embolization of thrombus produced elsewhere, such as pulmonary thrombo-embolism, may occur at times. However, the current coronavirus disease 2019 (COVID-19) pandemic has resulted in a variety of intracardiac or extracardiac thrombi formations due to systemic inflammation and activation of the clotting system. We present a unique and rare case in association with alcoholic dilated cardiomyopathy and COVID-19, which resulted in the development of multiple biventricular thrombi.

Learning objectives:

- Significant systolic dysfunction is unusual, especially in people with prolonged alcoholism.
- The hypercoagulable condition of coronavirus disease 2019 (COVID-19), combined with myocardial damage secondary to alcohol, can result in extensive intracardiac thrombosis.
- Thrombotic manifestations in COVID-19 are associated with a high mortality rate.

Introduction

Biventricular thrombi (BVT) are an uncommon thromboembolic complication that can occur in both ischemic and non-ischemic cardiomyopathies and can lead to embolization. The majority of BVT management in the twenty-first century is focused on studies conducted before the widespread use of powerful pharmacological and interventional therapies. Despite advancements in diagnostic technologies, clinicians still face several challenges in managing BVT in everyday practice [1].

Alcoholic cardiomyopathy (ACMP) is one of a variety of diseases caused solely by prolonged alcohol consumption. It induces left ventricular (LV) dilation and dysfunction, which leads to heart failure with a reduced ejection fraction (HFrEF) [2]. Coronavirus disease-19 (COVID-19) infection is a prothrombotic state that predisposes the formation of thrombosis in different vascular territories, including the intracardiac chambers [3]. We present a case in which multiple BVT developed as a result of the COVID-19 infection in patients with underlying ACMP.

Case report

A 48-year-old male labourer, a known chronic alcoholic was admitted with recent onset of breathlessness on exertion, New York Heart Association class III, and a 2-week history of paroxysmal nocturnal dyspnoea (PND). There were no risk factors, such as hypertension or diabetes, and there was no history of dilated cardiomyopathy or sudden cardiac death in the family. He has consumed 14–16 standard drinks (2–3 oz) of illicit liquor per week for the past 15 years. On examination, his vital parameters recorded heart rate of 112/beats per minutes, blood pressure of 100/58 mm Hg, respiratory rate of 16/min, and temperature of 37.2 °C. Also, there were increased jugular venous pulsations with prominent v-waves. The cardiac examination demonstrated increased parasternal pulsations with downward and laterally displaced cardiac apex to the 6th intercostal space. There was a gallop rhythm with no

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Table 1
Laboratory values during COVID-19 and hospitalization for heart failure.

Parameters	Results		Normal range
	During COVID-19 infection	During hospitalization for heart failure	
Hemoglobin	14.3	14.1	13–17 g/dL
Erythrocyte sedimentation rate	90	74	0–20 mm at 1-h
White blood cells	13,400	8300	4000–10,000 cells/mm^3
Platelet count	170,000	150,000	150,000–450,000 cells/mm^3
Creatinine	1.1	1.2	0.8–1.2 mg/dL
D-dimer	2230	523	0–500 pg/dL
C-reactive protein	16.8	18.7	0–11 mg/dL
Interleukin-6	18.6	10.2	0–6.4 pg/mL
Ferritin levels	632	ND	17.90–464 ng/mL
N-terminal prohormone B-type natriuretic peptide	4503	22,430	<450 pg/mL for age <50 years
High sensitivity troponin I	ND	15	0–0.12 ng/mL
Creatine kinase	ND	220	50–170 U/L
Alanine transaminase	69	68	0–50 U/L
Aspartate transaminase	147	150	17–60 U/L

COVID-19, coronavirus disease 2019; ND, not done.

murmur. Per abdominal examination demonstrated tender hepatomegaly with normal bowel sounds.

Four weeks previously, he had a fever with chills and rigors, a dry cough, generalized weakness, and a lack of appetite, and was diagnosed with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (COVID-19 PCR test positive – cycle threshold of 24). He did not experience any breathlessness, orthopnea, or PND episodes. He sought advice from a local general practitioner and stayed in quarantine at home. Laboratory parameters showed elevated levels of D-dimer, C-reactive protein, interleukin-6, ferritin, and N-terminal prohormone B-type natriuretic peptide (Table 1). Since his D-dimer levels were initially elevated, he was placed on rivaroxaban 10 mg once daily for thromboprophylaxis by a local practitioner. He also was prescribed oral medications such as dexamethasone (6 mg once a day) for 1 week, doxycycline 100 mg twice daily for 5 days, ivermectin 12 mg once daily for 3 days, vitamin C, and zinc. Mild cardiomegaly and bilateral interstitial infiltrates were seen on a chest X-ray. Computed tomography (CT) of the chest revealed bilateral peripheral ground glass opacities (CORADS -4).

During hospitalization, electrocardiogram demonstrated sinus tachycardia with poor 'R-wave' progression with nonspecific ST-T changes (Fig. 1). 2D trans-thoracic echocardiography (TTE) revealed dilated LV (end-diastolic diameter/volume – 60.4 mm/182.8 mL, end-systolic diameter/volume – 55.8 mm/152.4 mL) with severe LV dysfunction (ejection fraction-16.6%). Furthermore, the right ventricle (RV), right atrium, and inferior vena cava (no respiratory collapse) were dilated, associated with severe RV dysfunction (tricuspid annular plane systolic excursion – 8 mm). In addition, there was mild mitral regurgitation and severe tricuspid regurgitation with increased LV end-diastolic pressure (Grade-III diastolic dysfunction) and moderate pulmonary hypertension (pulmonary artery systolic pressure – 54.3 mm Hg) The appearance of two large echo-dense sessile well-circumscribed masses connected to the interventricular septum (IVS) in parasternal long-axis and short-axis views was notable (Fig. 2A–D). A first thrombus, measuring 46.3 × 28.1 mm, originated from the LV apex, mid and distal portions of the IVS, and extended upwards toward the mitral valve, while a second thrombus, measuring 49.4 × 22.5 mm, was adhered to the inferolateral wall. There was also a small, mobile thrombus measuring 15.9 × 11.4 mm in the RV apex. All the thrombi had a hypoechoic core with a hyperechoic border at the periphery, indicating recent thrombi (Fig. 2E–H; Videos 1–4).

In-hospital laboratory parameters revealed elevated acute phase reactants such as C-reactive protein and erythrocyte sedimentation rate. Serum high-sensitivity troponin-I and creatine kinase levels were raised, as were alanine transaminase and aspartate transaminase but bilirubin levels were normal. His complete hemogram and renal function were normal (Table 1). The coagulation profile revealed a normal prothrombin time/international normalized ratio (13 s/1.1), activated partial thromboplastin clotting time (30 s), homocysteine levels (16 μmol/L), negative antinuclear antibody, anti-double strand DNA antibody, and anti-phospholipid antibody (IgM and IgG) tests.

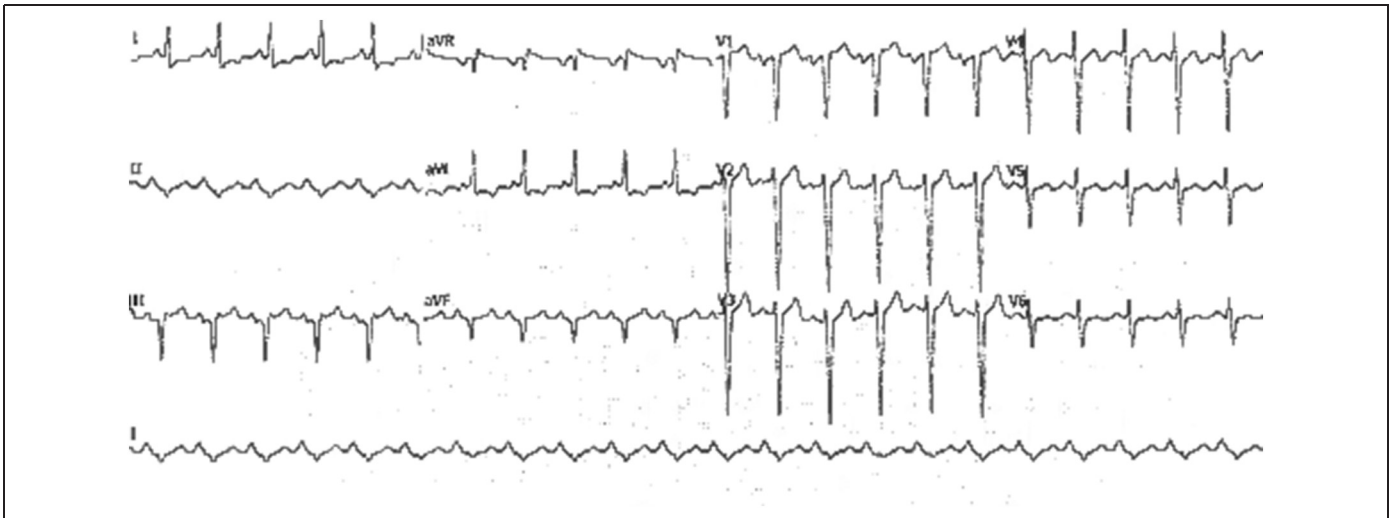

Fig. 1. Electrocardiogram showing sinus tachycardia with poor 'R-wave' progression suggestive of left ventricular dilatation. There were also abnormal Q-waves in the inferior leads, which might be attributed to regional myocardial scarring.

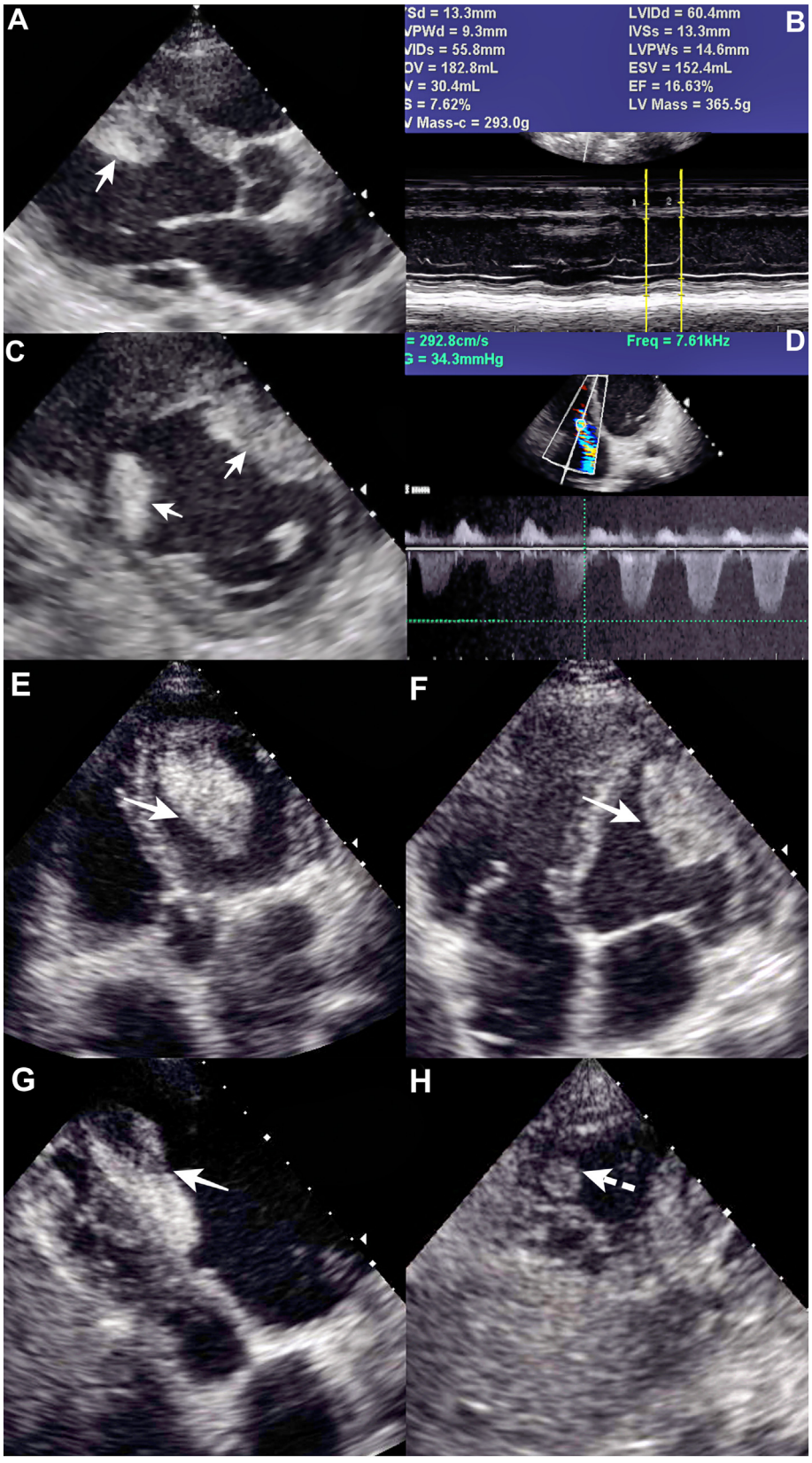

Fig. 2. (A–H) 2D-trans-thoracic echocardiography in parasternal and short-axis views demonstrated two echo-dense masses attached to the infero-septal and antero-lateral segments of the left ventricle and grossly dilated left ventricle (LV) (A, C; white solid arrows). M-mode echocardiographic measurement of the LV revealed global hypokinesia with severe LV dysfunction (ejection fraction – 16.6%) (B). The continuous wave Doppler interrogation of severe tricuspid regurgitation in a 4-chamber view measured moderate pulmonary hypertension (right ventricular systolic pressure – 34.3 + 20 = 54.3 mm Hg) (D). 2D-transthoracic echocardiography in two dimensions in modified views for better delineation of LV thrombi in 4-chamber views exhibited: a thrombus attached to the distal interventricular septum and LV apex, extending through the LV cavity, and dangling above the mitral valve (E), another thrombus attached to the infero-lateral segment with a small region of echolucency (F, G). There was an enlargement of the right ventricle (RV) and atrium (G) with a round, mobile thrombus seen in a modified apical view of the RV apex (H).

Except for mild hepatomegaly with altered echotexture (liver span of 16 cm), ultrasound findings were normal. Coronary angiography showed insignificant, non-obstructive lesions of the left anterior descending and right coronary arteries. CT pulmonary angiography did not reveal any evidence of pulmonary thrombo-embolism. A clinical diagnosis of HFrEF secondary to alcoholic cardiomyopathy with the post-COVID prothrombotic state was made.

Intravenous furosemide and heparin infusions were initiated in the intensive care unit. A broad-spectrum antibiotic along with optimal guideline-directed medical therapy for HFrEF was started. An urgent cardiothoracic surgeon consultation was taken and a surgical LV thrombectomy was scheduled for the same day. Unfortunately, while being prepared for surgery, he developed refractory ventricular tachycardia and fibrillation within 6 h of admission, resulting in cardiac arrest, and despite continued cardiopulmonary resuscitation, he failed to respond and was declared dead.

Discussion

HFrEF, whether caused by ischemic or non-ischemic dilated cardiomyopathy, is a major cause of intracardiac LV thrombus, rarely BVT. Multiple LV thrombi have been documented sporadically in patients with LV noncompaction, arrhythmogenic RV cardiomyopathy, and dilated cardiomyopathy [4,5]. BVT are unusual findings in a variety of dilated cardiomyopathies, including peripartum cardiomyopathy, hypereosinophilic syndrome with Loeffler endocarditis, toxin-induced cardiomyopathy (alcohol, adriamycin, selenium); hypercoagulable states, like protein C and S deficiency, antiphospholipid antibody syndrome (APS), Factor-V Leiden mutation, and, inflammatory disorders such as ulcerative colitis, salmonella septicaemia, COVID-19 [6].

The only way to diagnose ACMP is to look for a history of prolonged alcohol addiction (14 drinks per week of 1.5 oz of distilled spirit, 12-ounce bottle of beer, 5-ounce glass of wine) since there are no specific clinical or laboratory characteristics, including histological abnormalities, associated with the condition [2]. As a result, history of alcohol intake should be closely monitored in all the patients with non-ischemic dilated cardiomyopathy. Coagulation profiles, such as activated partial thromboplastin time, prothrombin time, clotting time, and bleeding time, were within normal ranges except for the increased D-dimer. APS is five-fold more prevalent in females, and the majority of patients are between the ages of 15 and 50 years, and may also be raised with COVID-19 infection [6–8]. In our instance, the patient was a nearly 50-year-old man, which is unusual for APS at this age, and the patient's anti-phospholipid antibody test was also negative.

Predisposing factors for the development of multiple intracardiac thrombi in our case, according to the Virchow triad, are 1) impaired ventricular wall motion - secondary to severe LV dysfunction, 2) local myocardial injury – alcohol functions as a toxin when consumed in large quantities for a prolonged period, 3) hypercoagulability/flow stasis – a prothrombotic state brought about by COVID-19 infection. Hypercoagulability and LV thrombi formation in COVID-19 has been demonstrated in a recently published case series [3]. In the literature, there are limited case reports of multiple LV thrombus or BVT in COVID-19 patients. COVID-19-induced LV or biventricular dysfunction may be caused by an anterior wall myocardial infarction, myocarditis, or a cytokine storm, predisposing to BVT or LV thrombi; however, intraventricular thrombus may also develop in patients with normal LV function [8,9].

A similar case where pre-existing alcoholic cardiomyopathy and multiple thrombi formation as a part of COVID-19 sequelae has not been reported until now.

COVID-19 infection also triggers an immune process that results in the activation of inflammatory markers. Proinflammatory cytokines may result in activation of coagulation pathway, complement activation, and endothelial inflammation. However, inflammation continues following COVID, leading to a hypercoagulable state and the formation of BVT, which precipitated heart failure in our patient with asymptomatic well-compensated LV dysfunction caused by ACMP [6]. Remarkably, distinctive coagulation activity is associated with multiorgan failure and enhances mortality [6,10].

An early referral for an echocardiography to rule out ACMP, as well as an early diagnosis of BVT based on the appearance of cardiomegaly on the chest X-ray after COVID-19 infection and a history of chronic alcoholism, might have saved our patient's life. Because the patient's D-dimer was high after his initial hospitalization for COVID-19 infection, he was put on rivaroxaban as thromboprophylaxis. However, the patient developed thrombosis while receiving rivaroxaban, which might have been caused by an inadequate rivaroxaban dosage.

As a consequence, we propose that all patients with known cardiac risk factors, prior cardiac ailments, or significantly raised D-dimer levels undergo regular echocardiographic screening in order to diagnose and manage such a dreaded complication at a much earlier stage.

Conclusion

Non-ischemic dilated cardiomyopathy is seldom caused by chronic alcoholism (ACMP). As the earliest clinical manifestation of COVID-19, we underline the necessity of being careful of serious and possibly fatal intraventricular thrombi formation leading to refractory heart failure and ventricular arrythmias, and hence efforts to prevent thrombosis are critical.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jccase.2022.03.019.

Consent from patient/patient's attender

Informed consent was obtained from the participant included in the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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CRediT authorship contribution statement

Pankaj V. Jariwala: Conception of the work, revising it critically for important intellectual content, final approval of the version and Agreement to be accountable for all aspects of the work ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Kartik Pandurang Jadhav: Design of the work, acquisition, analysis, interpretation of data, drafting of work, final approval of the version and Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy.

Saket Khetan: Design of the work, acquisition, analysis, interpretation of data, drafting of work, final approval of the version and Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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