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DIAGNOSTIC DILEMMA
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A Left Atrial Mass in the Time of COVID

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PRESENTATION

A 60-year-old woman presented to the emergency department with chest pain and worsening dyspnea. On initial vital signs, she was afebrile with a blood pressure of 160/107 mmHg, a heart rate of 89 beats/min, a respiratory rate of 30 breaths/min, and an oxygen saturation of 95% on 4 liters oxygen via nasal cannula (an increase from her home requirement of 2 liters oxygen via nasal cannula). Her weight on presentation was 10.9 kg above her baseline. Her exam was notable for elevated jugular venous pressure to 14 cm of water, rales in bilateral lung bases without wheezes, and significant bilateral lower extremity edema to her thighs. She was admitted for management of her heart failure.

Her past medical history included systolic heart failure secondary to non-ischemic cardiomyopathy diagnosed 3 years ago, tobacco use, hypertension, hypothyroidism, and SARS-CoV-2 infection requiring hospitalizations at an outside hospital 11 months prior to presentation. Three months prior to this admission, she completed the Pfizer/BioNTech (BNT162b2) SARS-CoV-2 mRNA vaccinations but reported worsening heart failure symptoms with dyspnea, orthopnea, lower extremity swelling after each dose. She required hospitalization following the second dose for acute on chronic systolic heart failure. A transthoracic echocardiogram (TTE) was performed then, which demonstrated left ventricular ejection fraction (LVEF) of 20%-24%. She had no prior history of atrial arrhythmias, stroke, deep vein thrombosis, pulmonary embolism, or pregnancy loss.

ASSESSMENT

Initial labs were notable for white blood cell of 7.5 K/uL, hemoglobin of 12.7 g/dL, platelets of 177 K/uL, creatinine of 1.4 mg/dL, troponin I of 0.10 ng/mL, brain natriuretic peptide of 4,387 pg/mL. Electrocardiogram showed sinus rhythm with first degree atrioventricular block with occasional premature ventricular complexes, left axis deviation, left atrial enlargement, and intraventricular conduction delay. A TTE showed a dilated left ventricle with normal wall thickness, LVEF less than 15%, and a mildly dilated left atrium with a new 2.6 cm x 2.4 cm well-circumscribed retro-aortic left atrium mass close to the interatrial septum that was not clearly attached by a stalk (Figure 1). There were no significant valvular abnormalities.

A transesophageal echocardiogram (TEE) was performed next, showing a 2.4 cm x 2.2 cm well-circumscribed left atrium mass with an echolucent core and a broad-based attachment to the superior retro-aortic LA wall (Figures 2 and 3). Although there was spontaneous echo contrast seen in the left atrium, there was no thrombus visualized in the left atrial appendage or the 4 pulmonary veins.

Cardiac magnetic resonance (CMR) demonstrated a 1.9-cm low-signal intensity left atrium mass near the right upper pulmonary vein with evidence of severe slow flow throughout the left atrium body surrounding the mass (Figure 4). The left atrium mass had no uptake on late gadolinium enhancement imaging. The left ventricle was moderately enlarged with severely decreased systolic function (LVEF of 8.5%) and severe global hypokinesis. No left ventricular thrombus was present. There was also mild interstitial fibrosis in the mid-interventricular septum, likely related to long-standing non-ischemic dilated cardiomyopathy, but similar findings could also be seen in post-SARS-CoV-2 infection.[1]

DIAGNOSIS

The echocardiographic findings were highly suspicious for a thrombus versus a tumor, although tumor was less likely given the rapid growth since the last TTE 3 months prior

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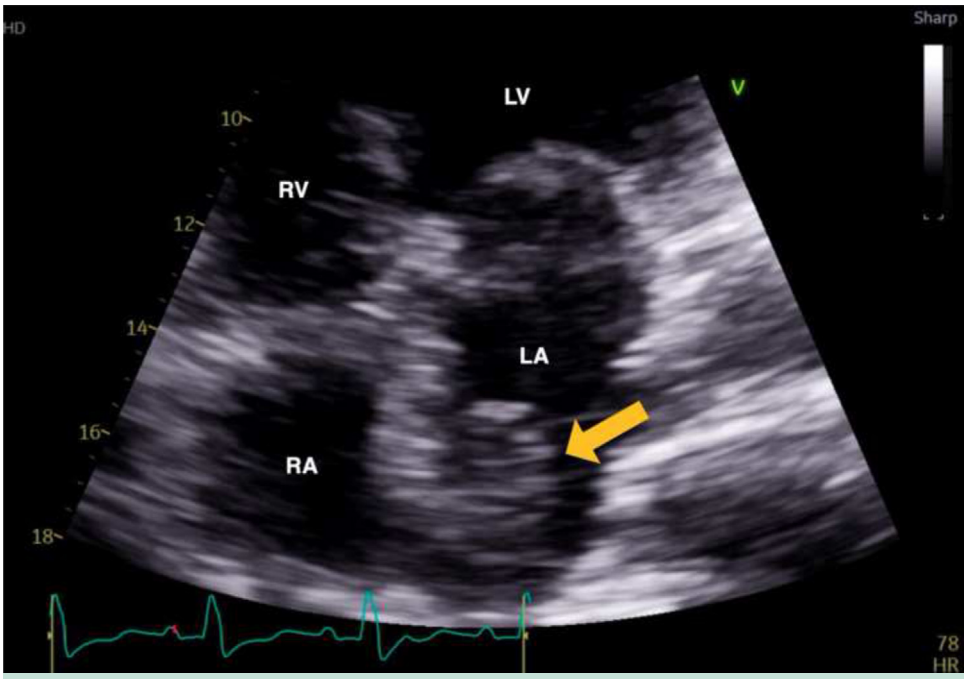

Figure 1 Apical 4-chamber view on transthoracic echocardiogram demonstrating a 2.6 cm x 2.4 cm well-circumscribed left atrial mass (arrow). LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

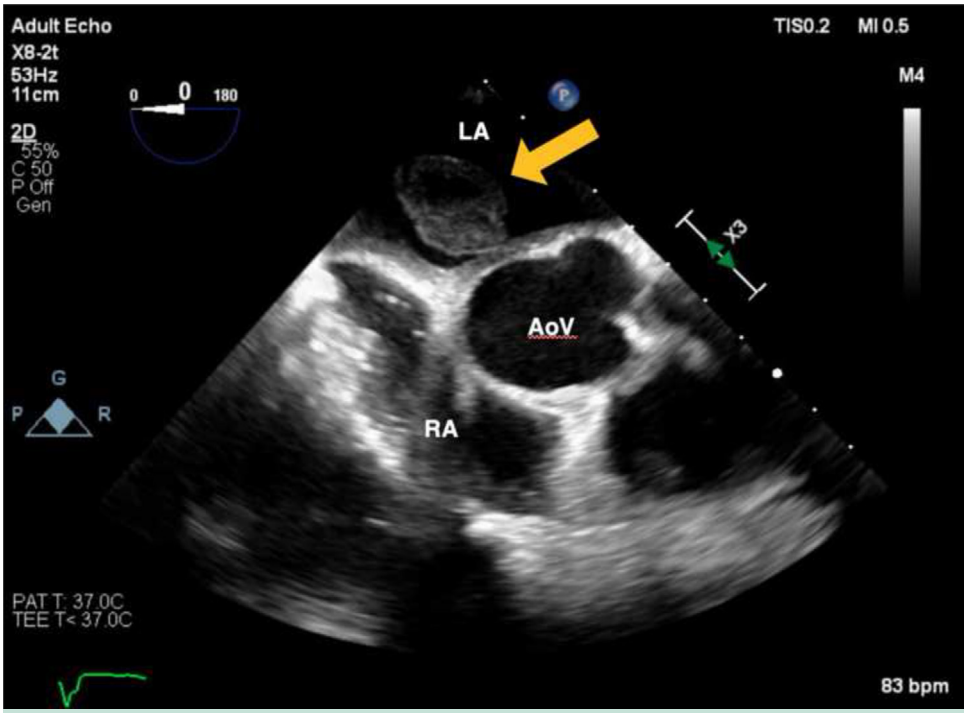

Figure 2 Short axis view on transesophageal echocardiogram shows a 2.4 cm x 2.2 cm well-circumscribed LA mass (arrow) with an echolucent core and a broad-based attachment to the retro-aortic left atrial wall, most consistent with a thrombus. AoV = aortic valve; LA = left atrium; RA = right atrium.

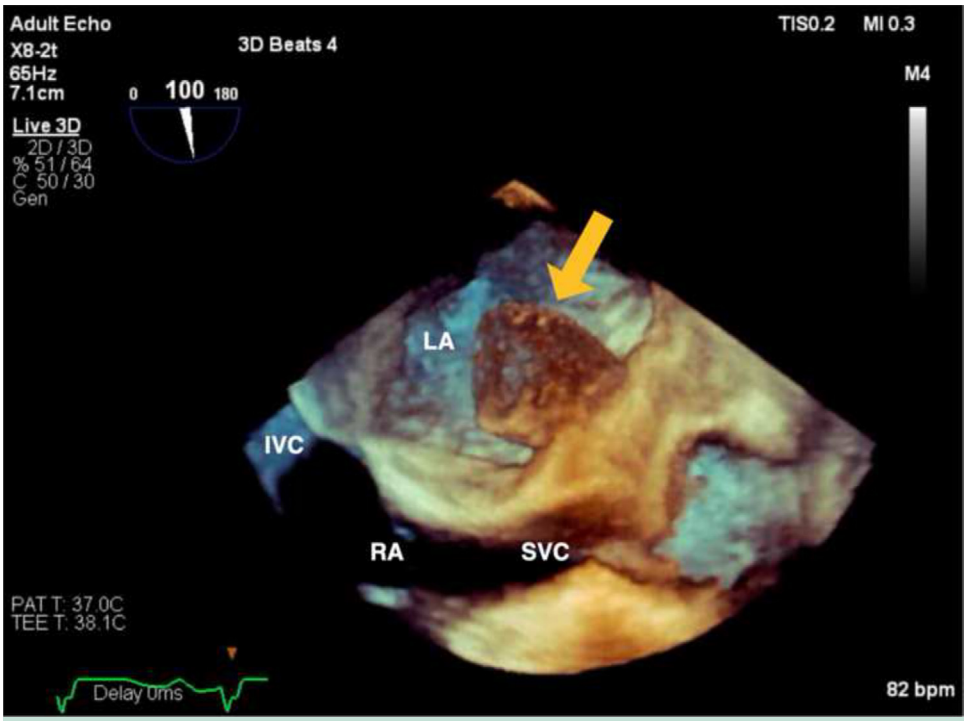

Figure 3 Bicaval view on 3-dimensional transesophageal echocardiogram demonstrates the echolucent mass (arrow) is attached to the superior retro-aortic left atrial wall and not the interatrial septum. IVC = inferior vena cava; LA = left atrium; RA = right atrium; SVC = superior vena cava.

that did not demonstrate the mass. The low-intensity signal of the mass and lack of contrast enhancement on CMR were also consistent with a thrombus.

MANAGEMENT

During her hospitalization, she was given intravenous diuretics until she was euvolemic. For the left atrium thrombus, she was started on therapeutic subcutaneous enoxaparin for anticoagulation and on discharge was transitioned to apixaban 10 mg twice a day for 1 week then 5 mg twice a day indefinitely. Inpatient telemetry did not show any evidence of atrial fibrillation or flutter; she remained in normal sinus rhythm with occasional runs of non-sustained ventricular tachycardia. Hematology was consulted, and hypercoagulable lab studies for beta-2 glycoprotein and anticardiolipin antibodies were sent and came back negative. The etiology of the left atrium thrombus was thought to be due to the low-flow state in the setting of severe left ventricular systolic dysfunction. Therefore, long-term anticoagulation was recommended.

A follow-up TTE 2 months later showed LVEF of less than 20% and resolution of the left atrium thrombus. She had a biventricular pacemaker-implantable cardiac defibrillator placed, and subsequent device monitoring has not shown any episodes of atrial arrhythmias. She currently remains on apixaban.

DISCUSSION

Virchow's triad comprises of 3 physiological processes that contribute to the formation of thromboses: venous stasis, endothelial damage, and hypercoagulability. The etiology and pathophysiology for intracardiac thrombi is multifactorial and, as in this case, all 3 components of Virchow's triad likely contributed to the formation of a left atrium thrombus.

Left atrium and left atrial appendage thrombi are usually associated with atrial arrhythmias due to the low-flow state that subsequently induces stagnation and therefore coagulation to occur. However, in cases of atrial thrombi in normal sinus rhythm, there are certain high-risk features associated with increased risk of intracardiac thrombi formation, such as severe systolic dysfunction (as with this patient), severe diastolic dysfunction, and valvular disease.[2] As seen on this patient's CMR, her severe systolic dysfunction caused a low-flow state in her left atrium, likely resulting in stasis and subsequent thrombus formation. On echocardiography, left atrium spontaneous echo contrast (LASEC) is a finding that shows increased echogenicity from ultrasonic backscatter from red blood cell aggregates, a result of non-covalent binding between red cells and plasma proteins in low-flow and low-shear conditions.[3] In cases of patients with LASEC while in sinus rhythm, significant left atrium dilation and decreased left atrial appendage emptying velocity are additional findings.[2] The combination of increased left atrium

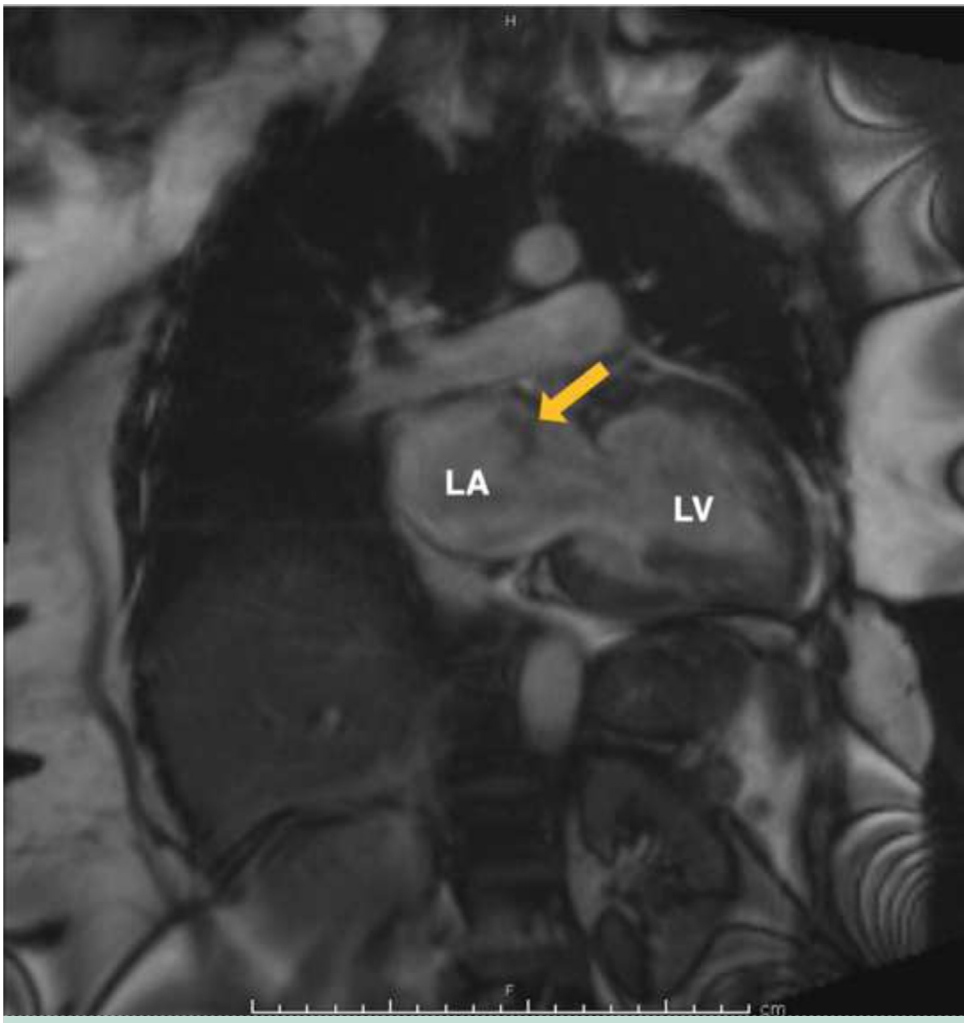

Figure 4 On cardiac magnetic resonance, balanced steady-state free precession 2-chamber long-axis cine view demonstrates a 1.9-cm left atrial thrombus (arrow) near the right upper pulmonary vein with evidence of severe slow flow throughout the left atrial body surrounding the thrombus. LA = left atrium; LV = left ventricle.

size along with decreased left atrium contractility likely are predisposing factors for LASEC and thrombus formation.[3]

Furthermore, the presence of cardiomyopathy itself can lead to inflammation and endothelial dysfunction, which, in conjunction with left atrium enlargement, place these patients at higher risk of thrombus formation and may necessitate longer anticoagulation for thrombus resolution.[4-5] Tobacco use is also known to cause endothelial damage and dysfunction through pro-inflammatory pathway activation and induction of oxidative stress.[6] Another potential cause of left atrium thrombus in the absence of atrial fibrillation is cardiac amyloidosis through atrial electromechanical dissociation resulting from extensive amyloid infiltration of the atria and ventricles.[7] However, the findings of left ventricular dilation and absence of wall thickening on this patient's TTE coupled with her CMR findings were not consistent with an infiltrative cardiomyopathy.

Lastly, there remains a possibility that thrombus formation can be a late sequela of SARS-CoV-2 infection or the mRNA vaccination given the relative timing of the onset of symptoms compared with our patient's previous infection and vaccinations. SARS-CoV-2 infection can lead to thrombotic complications, such as pulmonary emboli, strokes, and intracardiac thrombi; however, the exact etiology is not well understood but involves the interplay between inflammation and hypercoagulability.[8] Although most of the intracardiac thrombi reported in SARS-CoV-2 infections have occurred during the acute period, the pro-thrombotic state may persist for months after the resolution of the infection.[8] There have been adverse events reported of thromboembolism occurring after SARCoV-2 mRNA vaccinations, although is far less common in patients who received the Pfizer/BioNTech (BNT162b2) SARS-CoV-2 mRNA vaccine compared with those who received the AstraZeneca ChAdOx1 vaccine based on the EudraVigilance European database.[9]

In patients who are in sinus rhythm with no history of atrial arrhythmias or other hypercoagulable disorders, new findings of an intracardiac thrombus should prompt extended telemetry monitoring and hypercoagulability workup. Currently, no guidelines exist on the anticoagulation treatment and duration for left atrium thrombi in patients with sinus rhythm. This patient warrants long-term anticoagulation, which could be revisited if left ventricular systolic function recovers.

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