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Acute Systolic Heart Failure as the only Risk Factor for Cardioembolic Cerebrovascular Accident in the Setting of Nonischemic Cardiomyopathy and Normal Sinus Rhythm: A Case Report with Literature Review

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Abstract The association between atrial fibrillation and stroke is well-known by use of the CHA_2DS_2VASc risk assessment. However, little is known about the thromboembolic risk in patients who have isolated systolic heart failure (HF) with sinus rhythm. Despite growing literature which shows how HF in the setting of normal sinus rhythm is a risk factor for thromboembolic disease, the recommendation for use of anticoagulation, whether warfarin or direct oral anticoagulation (DOAC) in this setting, is not yet reflected in cardiology guidelines. To reduce the risk of thromboembolism, anticoagulation trials have been done but have not conclusively shown benefit over risk. We present a case of left middle cerebral artery (MCA) stroke after de novo HF in a patient with sinus rhythm, who was previously not on anticoagulation. Case: A 57-year-old male presented to our hospital with worsening shortness of breath for 3 days. He had signs of hypervolemia consistent with an acute heart failure exacerbation. Pertinent physical exam findings included lower extremity edema, rales, and jugular venous distension. He also had fatigue and exertional dyspnea. During his hospital course, he underwent imaging studies that revealed cardiomegaly, absence of pulmonary embolism, and a severely reduced ejection fraction. During his acute heart failure admission, he developed a left MCA stroke suspected to be of cardioembolic etiology and was successfully treated with tissue plasminogen activator (tPA). Conclusion: According to the most recent AHA/ACC cardiovascular disease guidelines, anticoagulation is not indicated in systolic heart failure patients with sinus rhythm. However, our case is rare because the patient had no underlying risk factors for thromboembolism and significant past medical history. He developed new-onset nonischemic cardiomyopathy complicated by a stroke. Therefore, we suggest the need for prophylactic anticoagulation should be assessed on an individual basis, with the assistance of shared decision making, especially when the ejection fraction is acutely and severely reduced.

Keywords: *heart failure, normal sinus rhythm, atrial fibrillation, cardioembolic stroke*

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1. Introduction

Heart failure (HF) is an emerging epidemic that affects 26 million people worldwide. [1] HF is an important contributor to both morbidity and mortality. [1] Current estimates of the HF burden in the US indicate that from 2009 to 2012, 5.7 million American adults have heart failure, and projections show that the prevalence will increase 46% from 2012 to 2030. [1]

In patients with systolic dysfunction and idiopathic dilated cardiomyopathy, incidence of LV thrombus ranges from 11% to 44%. [2] Thromboembolization occurs at a rate of 1.4% to 12% in these patients. [2] As more time passes after a CHF exacerbation, the risk of thromboembolism decreases, but can remain elevated for up to 5 years after the initial HF diagnosis, compared to the general

population. [2] Stroke prevention with anticoagulation is needed in HF patients with or without atrial fibrillation. To date, studies conflict on the risks versus benefits of anticoagulation in this patient population. The growing body of literature appears to support individualized risk assessment regarding anticoagulation. [3]

2. Case Presentation

A 57-year-old male patient without any significant past medical history presented with a 3-day history of worsening dyspnea and orthopnea. He had no significant past medical history and was not on any home medications. His examination was significant for signs of *de novo* heart failure; this included jugular venous distension, lung crackles, and lower extremity edema. Lab values revealed a pro-BNP of 2495, serum creatinine 1.2, and potassium of 5.4. Troponin level was 0.08. His EKG showed sinus tachycardia and nonspecific T-wave abnormalities. Chest X ray on arrival showed interstitial edema. Echocardiography revealed severely reduced left ventricular ejection fraction (LVEF) at 10-15% and grade III diastolic dysfunction (Figure 1). The transthoracic echocardiogram did not reveal any LV thrombus. CT angiography of the chest was negative for PE but showed dilated cardiomyopathy concerning for CHF and moderate pleural effusions. He was treated with intravenous furosemide, which alleviated the patient's symptoms and restored euvolemia. During his hospitalization, he underwent a cardiac catheterization (Figure 2) which did not reveal significant coronary artery disease (CAD). The patient was stable thereafter and was medically managed. On day three of his hospital course, he suddenly developed right-sided body weakness, dysarthria and aphasia. He was immediately taken for a head cat scan with angiography, which showed occlusion of the left middle cerebral artery (MCA) (Figure 3). He received tissue plasminogen activator (tPA) and had successful resolution of the stroke with no residual focal neurologic deficits. He returned to his baseline, and repeat echocardiography showed persistently low EF.

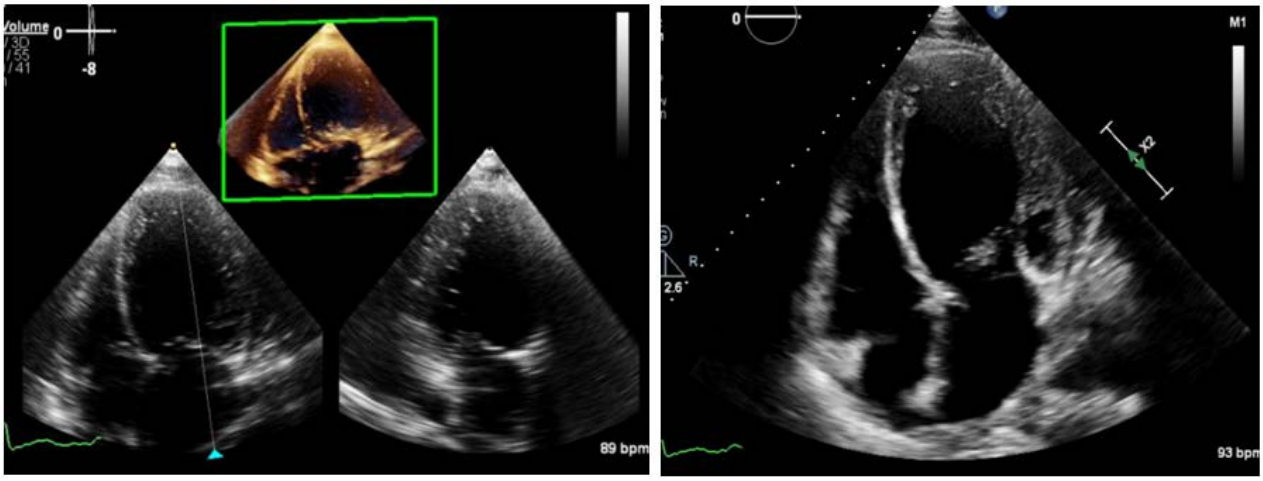

Figure 1. Transthoracic echo showing normal left ventricular wall thickness, LVEF 10-15%. Severe global hypokinesis, biventricular dilatation. Grade III diastolic dysfunction with elevated left atrial pressure. The left atrium is severely dilated. The pulmonary artery systolic pressure estimation is 40-45 mmHg

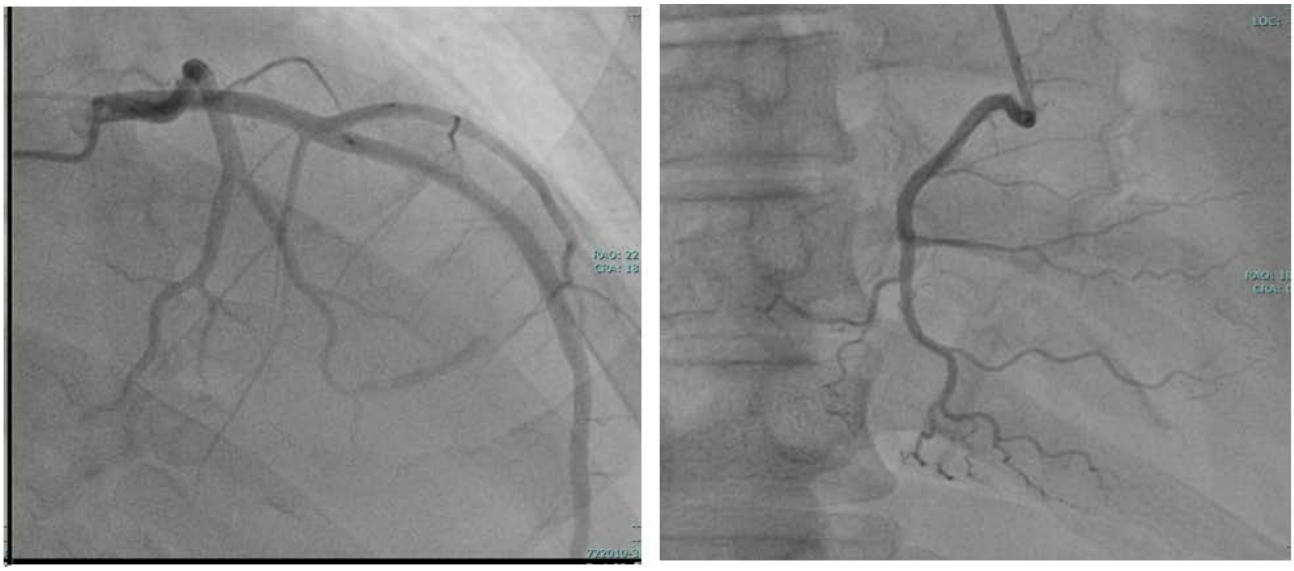

Figure 2. Cardiac catheterization showed no obstructive coronary artery disease, normal right atrial pressure (5 mmHg), mildly elevated pulmonary capillary wedge pressure of 18 mmHg, reduced cardiac output (Cardiac Index 1.5), consistent with a non-ischemic cardiomyopathy with mildly elevated left-sided filling pressures

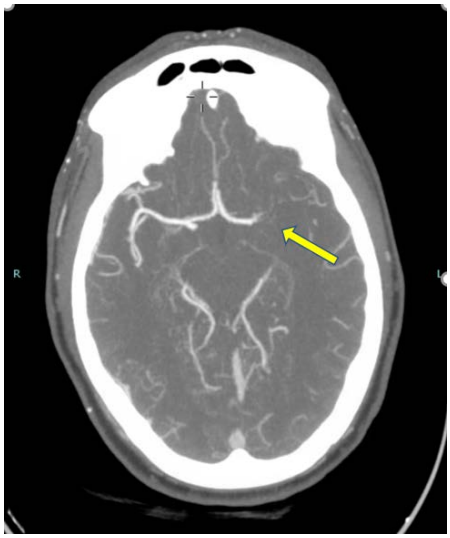

Figure 3. CT angiography of the head showed proximal left M1 cut off with subtly diminished attenuation in the left basal ganglia and insula suggesting early evolving infarct. No other cutoff

Due to suspicion for myocarditis, he underwent cardiac MRI which showed a severely dilated cardiomyopathy with ejection fraction of 13%; there was no focal wall motion abnormality. His CHA_2DS_2VASc score was 0. After the cerebrovascular event, the patient was started on warfarin to prevent any further thromboembolic events. He was discharged with goal directed medical therapy for his heart failure, with plans for repeat echocardiography in three months to determine candidacy for an implantable cardioverter defibrillator.

3. Discussion

HF with accompanying thromboembolic events are expected to increase in prevalence in the aging population. [6] Patients with HF, without AF, had remarkably higher rates of ischemic stroke compared to patients with neither HF nor AF during follow-up; the incidence rate ratio was statistically significant at 1.91. [6] Heart failure with normal sinus rhythm represents 70%-85% of all cases of heart failure. [6] These patients also had incremental increase in risk of ischemic stroke during 3 years of follow-up, and the highest incremental risk was observed within 12 months. [6] In looking at HF patients who appear to be in sinus rhythm, they may carry a burden of subclinical atrial fibrillation contributing to thromboembolic events. [7]

Thromboembolism occurs in systolic heart failure patients because of the reduction of LVEF and left ventricular end-diastolic pressure (LVEDP), as well as Virchow's triad. This triad consists of blood stasis, endothelial disruption, and hypercoagulability. [4,5] In looking at HF patients who appear to be in sinus rhythm, they may carry a burden of subclinical atrial fibrillation contributing to thromboembolic events. [7]

Thromboembolic risk stratification is important in HF with normal sinus rhythm. Hai et al. found that CHA_2DS_2VASc can be used for this purpose in Asian patients, but this scoring system had stronger predictive value when chronic kidney disease (CKD) and chronic ischemic heart disease were included as risk factors. [8] The study also cited a Danish registry, which predicted thromboembolism in HF patients with sinus rhythm, where the CHA_2DS_2VASc score was also concomitantly used. [8,9] Even if patients were placed on dual-antiplatelet therapy (DAPT) and heart failure medications, the risk of thromboembolism remained elevated. [8] A third study conducted in Spain used the Redinscor registry to show that despite reduction in adverse cardiovascular outcomes, anticoagulation did not reduce incidence of mortality or stroke. [10] These three studies are limited by the lack of external validity.

Another study found that CHF was correlated with a 4-fold increased risk of ischemic stroke. [11] Stroke risk with CHF is comparable to risk with atrial fibrillation when patients are stratified by CHA_2DS_2VASc. [11] Among a Danish cohort, a high CHA_2DS_2VASc score greater than 4 was associated with greater risk of thromboembolism in patients without AF compared with those with AF. [12] The highest risk of stroke and systemic embolism (SSE) occurred during the first year after hospitalization for heart failure. [12] Instead of the CHA_2DS_2VASc, Ferreira et al. reported the use of a Stroke Risk Score (SRS) that incorporates multiple factors such as age (65-74 years), estimated glomerular filtration rate (eGFR), hypertension, myocardial infarction with ejection fraction <35% without atrial fibrillation, and previous stroke, to assess stroke risk in heart failure patients. [13] An SRS >3 caused the stroke risk to be comparable to the risk in patients with atrial fibrillation. [13]

A different study that evaluated patients with heart failure, irrespective of ejection fraction, found that atrial fibrillation was correlated with a higher stroke risk compared to patients without atrial fibrillation, but the stroke risk is greater than the risk in the general population. [14] However, Hung et al. reported that stroke risk is high among HF patients with high CHA_2DS_2VASc score, regardless of atrial fibrillation. The risk of thromboembolism in HF was higher in patients without atrial fibrillation compared to those with atrial fibrillation. [15] The inconsistency between these two studies brings into question whether heart failure may contribute to thromboembolism risk more than previously thought. Furthermore, data from secondary analyses of the Studies of Left Ventricular Dysfunction (SOLVD) and the Survival and Ventricular Enlargement (SAVE) trials support the view that patients with low EF are at an elevated risk of thromboembolism when compared to patients with higher EF. Ultimately, anticoagulation can decrease the risk. [16]

In looking at agents of anticoagulation, warfarin and rivaroxaban were evaluated in the literature. The WARCEF (Warfarin versus aspirin in reduced cardiac ejection fraction) trial showed benefit in thromboembolism prevention that was offset by increased bleeding risk compared to aspirin in HF patients in sinus rhythm. [1,8] By contrast, the trial entitled "A Study to Assess the Effectiveness and Safety of Rivaroxaban in Reducing the Risk of Death, Myocardial Infarction, or Stroke in Participants with Heart Failure and Coronary Artery Disease Following an Episode of Decompensated Heart Failure" (COMMANDER-HF) demonstrated that

rivaroxaban resulted in fewer thromboembolic events without an increased risk of critical or fatal bleeding, over a period of approximately two years. [17] Compared to placebo, rivaroxaban reduced the rate of thromboembolic events by 17%. [17] Individual risk stratification was useful, and there is data favoring use of NOACs over warfarin. [3]

Lastly, stroke in HF patients is associated with a mortality rate that is 2-2.5 times higher than the rate in patients who have a stroke in the absence of HF. [18] Despite this increased risk of mortality, a systematic review demonstrated that there was no statistically significant difference in rehospitalization, nonfatal MI, or all-cause mortality between patients given anticoagulation and those given placebo. [5] However, a reduced incidence of nonfatal stroke was attributed to anticoagulation. [5] The conflicting statements between these two studies necessitates the need for individualized risk assessment as well as further studies to demonstrate the benefit of using anticoagulation in patients with heart failure and normal sinus rhythm.

4. Conclusion

In this review, we highlight that patients with acute systolic heart failure, in the absence of significant coronary artery disease, and no risk factors, are still at risk of a cerebrovascular accident of likely cardioembolic etiology. Heart failure represents a possible indication for prophylactic anticoagulation. The current guidelines do not incorporate this patient population into consideration for anticoagulation. We think that the benefit of starting anticoagulation in this patient population to prevent stroke may outweigh bleeding risk, but this assessment needs to be done on an individual basis, with shared decision making between the patient and clinician. Both warfarin and novel oral anticoagulation were trialed in these patients, but further studies are needed to validate their utility for stroke prevention.

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