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Case Report

A Rare Case of Biventricular Mural Thrombus Causing Cardio Embolic Stroke Associated with Hyperhomocysteinemia

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Abstract

Ventricular thrombus is a potentially life-threatening condition following acute myocardial infarction. Although detection of ventricular mural thrombi is not rare after acute myocardial infarction with lv dysfunction during routine echocardiography, presence of biventricular thrombi is very rare and less documented condition. Biventricular thrombi are generally seen in patients with a pro thrombotic state like anti-phospholipid antibody syndrome, heparin induced thrombocytopenia induced thrombosis, hypereosinophilic syndrome etc. Biventricular thrombi in presence of hyperhomocysteinemia is not a documented entity in the literature. In our case we have reported presence of apical thrombus in both left ventricle and right ventricle in a patient of hyperhomocysteinemia who was presented with acute myocardial infarction and cerebrovascular event.

Keywords: *Biventricular Mural Thrombus; Cardio Embolic Stroke; Hyperhomocysteinemia*

Introduction

The development of biventricular mural thrombi is rare, and it mainly increases the risk of embolization in the systemic and pulmonary circulations. The detection of biventricular mural thrombi is rare during routine echocardiography, although this imaging modality is a valuable tool for their diagnosis. We report a case of cardio embolic stroke in a young male patient with both arterial and venous thrombosis with biventricular thrombi secondary to hyperhomocysteinemia.

Case Presentation

A 31-year-old man presented with symptoms of breathlessness on exertion (New York Heart Association [NYHA] class III) with paroxysmal nocturnal dyspnea of one week duration. He also had swelling of left lower limb since 3 weeks. He was chronic smoker and quit smoking since 8 months. He had suffered extensive anterior wall myocardial infarction eight months before, for which he was administered thrombolytic therapy in the form of injection of 1.5 million units of streptokinase. Upon admission, he was started on anti-failure treatment, including intravenous diuretics, angiotensin-converting enzyme inhibitors, statins, and beta blockers, which relieved his symptoms (NYHA class II). Doppler venogram of left lower limb revealed deep venous thrombosis involving left common iliac, femoral and popliteal veins. Two days later patient developed right side hemiparesis.

To our surprise, two-dimensional echocardiography showed a large mural thrombus in the left ventricle (LV) extending from the mid and distal septal segments into the LV apex and then to the apical anterior and apical inferior segments (Figure 1). The LV was dilated with

akinetic and scarred segments supplied by the left anterior descending artery (LV ejection fraction = 35% by modified Simpsons' method). The other segments were contracting normally. There was mild mitral regurgitation and moderate pulmonary hypertension (PASP = 42 mmHg), there was no septal defects. The right ventricle also showed thrombus attached to the mid to distal part of the interventricular septum into apex (Figure 2). The right atrium and ventricle were normal in size. CT brain done showed acute infarct involving left temporoparietal area.

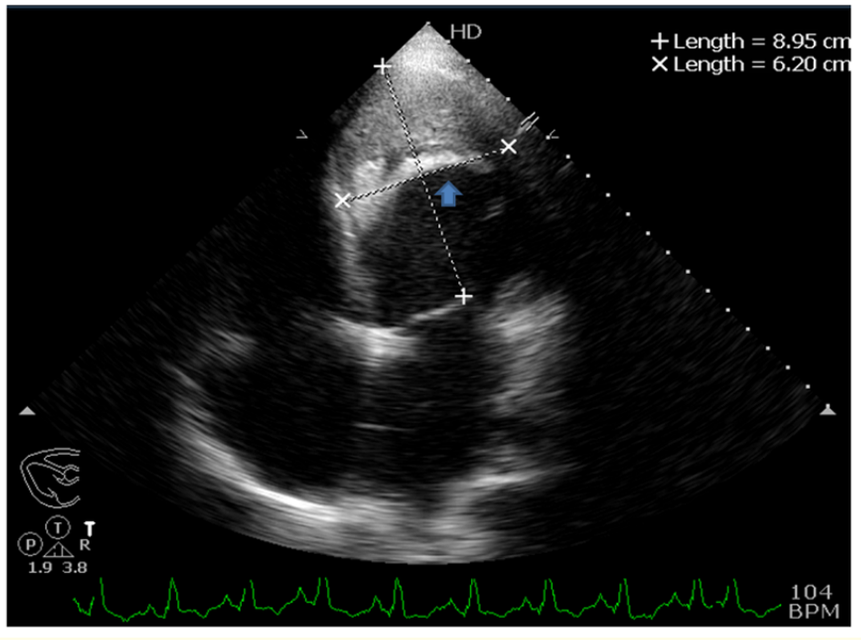

Figure 1: *TTE showing LV thrombus extending from mid septum to apex.*

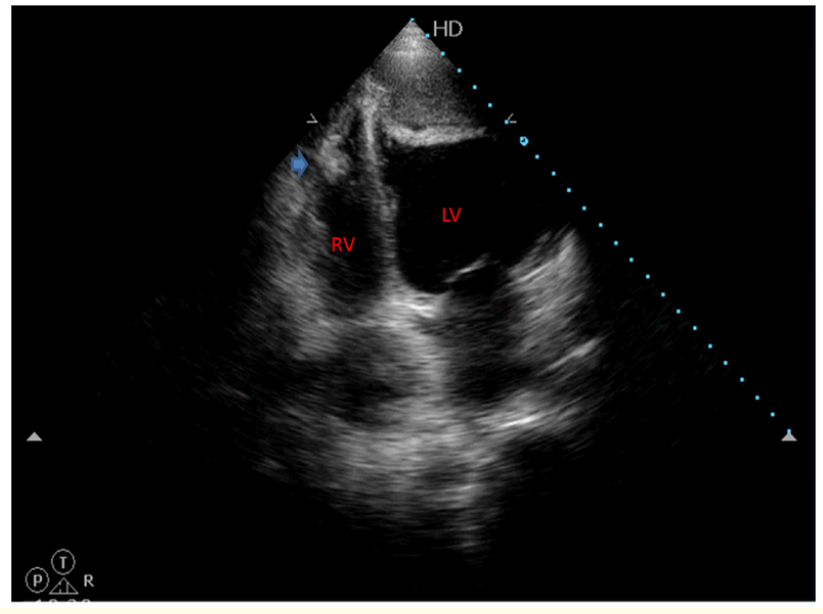

Figure 2: *TTE showing biventricular thrombus with RV thrombus extending from mid septum to apex.*

The patient was started on low-molecular-weight Heparin (1 mg/kg/dose) twice a day. Routine blood counts, renal and liver function tests were normal. Lipid profile showed low density cholesterol (LDL) of 144 mg/dl and normal triglycerides. His peripheral blood eosinophil counts were normal. His coagulation profile showed significantly elevated homocysteine levels and was positive for 677C→T MTHFR gene mutation. Hence, he was started on 5 mg per day of oral folic acid and vitamin B12. The patient was discharged on oral anticoagulation (Warfarin 5 mg) with the advice of bed rest and close follow-ups, with a plan of surgical intervention if the thrombi did not dissolve.

Discussion

The LV thrombi usually occur in the setting of acute myocardial infarction, LV aneurysms, or dilated cardiomyopathy [1]. The LV thrombi occur in at least 5% of patients after acute myocardial infarction, which increases the morbidity and mortality of patients [2]. As such, any etiology which causes transient or permanent insult/damage to the myocardium leading to dilated cardiomyopathy (ischemic/non-ischemic) can cause the formation of thrombi because of the akinesia/dyskinesia of the apical segments of the LV wall. Mobile, larger thrombi extending up to the LV outflow tract are at higher risk of embolization [3]. The risk of systemic embolization is between 5% and 50%, particularly cardio-embolic stroke and acute limb ischemia [1]. The embolization of a right ventricular thrombus can lead to pulmonary embolism and infarction [4].

Echocardiography is valuable for the diagnosis and characterization of the LV thrombi [5]. Cardiac magnetic resonance imaging (MRI) has an approximate sensitivity of 90% in detecting ventricular thrombi using gadolinium contrast. Delayed enhancement cardiac MRI is the gold-standard test for detecting the complications of ventricular dysfunction and also studying the viability of the myocardium. Though contrast echocardiography also can be used for the diagnosis of ventricular thrombi, it has a sensitivity of 60%. In our case, the diagnosis of biventricular thrombi was evident on two-dimensional echocardiography, precluding the need for other imaging modalities.

A small number of case reports have hypothesized that the presence of the hypercoagulable state may be an important causative mechanism for the formation of the LV thrombi. Laboratory tests like fibrinogen, protein S, protein C, antithrombin III, Factor V Leiden, lupus antibody, and homocysteine should be performed in all cases to rule out the hypercoagulable state [7]. The correction of the underlying factors such as hyper eosinophilia and hypercoagulable states may help resolve ventricular thrombi [8].

The hyper eosinophilia syndrome with Loffler's endocarditis one of close differential diagnosis can present with biventricular mural thrombi. Usually diagnosis is confirmed by blood picture, which reveals peripheral blood eosinophilia more than 1500 cells/mm^3 for at least a 6-month period after ruling out other secondary causes of hypereosinophilia and respond to steroid therapy with the resolution of the symptoms and biventricular thrombi. In our case we ruled out as peripheral blood eosinophil count was 340 cells/cumm.

We evaluated patient for coagulation profile and had hyperhomocysteinemia (93micromoles) with positive for gene 677C→T MTHFR mutation. Hyperhomocysteinemia (HHcy) is a pathological condition characterized by an increase in plasma concentration of total homocysteine [9]. Numerous clinical and epidemiological studies have indicated that HHcy is an independent risk factor for atherothrombotic disease. Up to 40% of patients diagnosed with premature coronary artery disease, peripheral vascular disease, or recurrent venous thrombosis present with HHcy [10]. Recent studies have now demonstrated that homocysteine causes endothelial cell dysfunction and induces apoptotic cell death in cell types relevant to atherothrombotic disease, including endothelial cells and smooth muscle cells.

The mechanisms by which HHcy induces endothelial dysfunction are incompletely defined. However, one consistent finding from studies of experimental HHcy is impairment of vasodilation mediated by endothelium-derived nitric oxide.

In the studies where an increased risk was shown, it was generally in the range of the other modifiable risk factors for arterial disease: smoking, hypertension, hyperlipidemia , obesity, sedentary lifestyle . As a result, modification of the above risk factors in addition

to control of hyperhomocysteinemia will have a more significant impact on lowering one's risk of arterial disease than controlling the hyperhomocysteinemia alone.

Kang and co-workers have classified hyperhomocysteinemia as follows: 1. Moderate Risk: 15 - 30 μmol/L 2. Intermediate Risk: 30 - 100 μmol/L 3. Severe Risk: > 100 μmol/L.

When one has a venous clot, regardless of what thrombophilic states one may have, that person will receive anticoagulation. This is accomplished by several different medications like heparin, warfarin and or low-molecular-weight heparins. These medications are generally used for 3 - 6 months. Further continuation is generally not indicated in hyperhomocysteinemia after a single thromboembolic episode given the risk of bleeding associated with anticoagulation. Patients that have had multiple thromboembolic episodes or are at high risk of further episodes are likely started on long-term anticoagulation. Accordingly, we patient was then treated with low molecular weight heparin-Enoxaparin at a dose of 1 mg/kg subcutaneously twice a day for 3 days along with complete bed rest and graded compression stockings. Oral anticoagulant in form of warfarin (5 mg) was started along with folic acid and vitamin B12 suggested oral anticoagulation with one antiplatelet agent at least for our patient lifelong therapy or therapy until improvement in the LV function.

Larger thrombi which are at the risk of embolization need aggressive management. Fibrinolysis should not be advocated as it carries risk of embolization at the time of the lysis of the thrombus [11]. Additionally, it carries higher risk of hemorrhagic complications In patients who already have major disease, reducing homocysteine levels may in fact have no effect on stroke risk, the risk of a heart attack, or thromboembolic events [12].

No case reports of association of biventricular mural thrombus with hyperhomocysteinemia were reported in the literature. We report first case of biventricular mural thrombus associated with hyperhomocysteinemia resulting in cardioembolic stroke and both arterial and venous thrombosis.

Conclusion

Echocardiography is the gold-standard technique for the diagnosis of ventricular thrombi. Anticoagulation is the accepted therapy to resolve thrombi and to prevent embolization. There are, however, no specific scientifically validated guidelines as to the best therapeutic approach. More randomized clinical trials or observational retrospective data will delineate the future course of patients presenting with biventricular thrombi formation secondary to dilated cardiomyopathy.

A young patient presenting with both arterial and venous thrombosis should undergo evaluation of hypercoagulable states and correction of underlying factors may resolve the biventricular mural thrombus. Echocardiography is the gold-standard technique for the diagnosis of ventricular thrombi.

Disclosure

There is no conflict of interest.

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