CASE REPORT

LARGE MOBILE LEFT VENTRICULAR THROMBUS IN A PATIENT WITH DILATED CARDIOMYOPATHY: A CASE REPORT AND REVIEW OF LITERATURE

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Abstract: Dilated cardiomyopathy (DCMP) and the resultant left ventricular (LV) dysfunction are risk factors for thrombus formation in the heart. Once formed, depending on their size, location, and mobility, LV thrombi have the tendency to embolise, sometimes with dire consequences. Early detection and treatment are important to reduce thromboembolic events and in resolution of LV thrombus. Two-dimensional (2D) echocardiography is the most commonly used technique for the diagnosis and follow-up of such cases. Here, we present a case of 30 years old female with DCMP with congestive heart failure (CHF) who developed a large mobile LV thrombus and was managed on anticoagulants to prevent distal embolisation. This case highlights that LV thrombi can even occur in patients in sinus rhythm who have reduced LV contractility.

Key Words: Left ventricular thrombus, dilated cardiomyopathy, thromboembolic events, 2D echocardiography, anticoagulants.

INTRODUCTION

LV thrombi can occur in several cardiac conditions, including acute anterior myocardial infarction (MI), LV aneurysm, CHF due to DCMP, myocarditis, or both[1,2]. The incidence of LV thrombi in patients with DCMP varies from 11-44%[1]. Mobile thrombi have a high rate of systemic embolisation. Definitive treatment of these thrombi is yet to be established. Anticoagulation, antiplatelet therapy, surgical thrombectomy and thrombolytic therapy are the treatment options. Anticoagulant therapy has had variable success, with thrombus resolution rates ranging from 13 to 59 percent[3]. Thrombolysis with urokinase, streptokinase, and tissue plasminogen activator has been reported, but the risks of hemorrhagic or embolic complications may be unacceptably high[4]. Surgical thrombectomy is also advocated, but generally patients with dilated cardiomyopathies are at an increased risk for perioperative morbidity and mortality. Most studies suggest that when LV thrombus is diagnosed in patients with DCMP or after MI, anticoagulation may be started and surgical treatment may be delayed.

CASE REPORT

A 30 years old female, non-hypertensive and non-diabetic, nonsmoker, presented to Emergency Department, complaining of progressive shortness of breath for the previous 1 month and orthopnea of one week duration. Physical examination revealed a moderately built woman, dyspneic and tachypneic. She had a regular rapid pulse rate of 140 beats/min, blood pressure of 116/72 mm Hg, temperature of 37°C and respiratory rate of 28 breaths/min. Pitting pedal edema was present. Cardiovascular system examination showed a jugular venous pulse of 5 cm above the sternal angle. The apex beat was displaced downwards

and was outside the mid-clavicular line with a normal character. On auscultation, an S3 gallop was present, with pansystolic murmur of mitral regurgitation of grade 3/6. Chest examination revealed bilateral basal rales. Examination of the abdomen revealed tender hepatomegaly. Nervous system examination was unremarkable. Laboratory investigations included complete blood picture with a white blood cell count of 12,600/cc, hemoglobin of 12.6 g/dl, and platelet count of 2.02 lakh/cc. Random blood glucose was 133 mg/dl and renal profile showed creatinine 0.9 mg/dl, urea 40 mg/dl, sodium 136 mmol/l, potassium 5.0 mmol/l. Liver function tests showed bilirubin 1.2 mg/dl, AST 90 U/L, ALT 48 U/L, alkaline phosphatase 85 U/L, albumin 3.7 g/dl, and total protein 5.9 g/dl. Cardiac enzymes (CPK-MB and Troponin-I) were within normal range. The electrocardiogram revealed sinus tachycardia, with LV hypertrophy by voltage criteria and LV strain pattern. The chest radiograph showed moderate cardiomegaly, with evidence of pulmonary edema. Transthoracic 2-D echocardiography revealed dilatation of the LV (LV end-diastolic diameter of 66mm) and left atrium. Global hypokinesia was present with an ejection fraction (EF) of 20-25%, and moderate mitral and mild tricuspid regurgitation. There was a large, mobile "oscillating" LV thrombus of 2.5 x 1.5 cm with attachment to the lateral wall of LV, and protruding into the LV cavity (Figure 1). We concluded that this patient had DCMP with CHF with LV thrombus. She was put on torsemide, ramipril, carvedilol, aspirin, enoxaparin and, later overlapped with warfarin to achieve an international normalized ratio (INR) of 2.5-3. No evidence of embolism was seen during her treatment. These observations highlight that LV thrombi can even occur in patients in sinus rhythm who have reduced LV function and are undergoing

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treatment for heart failure. Our patient's health gradually improved and she was shifted out of the coronary care unit to the general ward. She later refused in-patient treatment and left against medical advice.
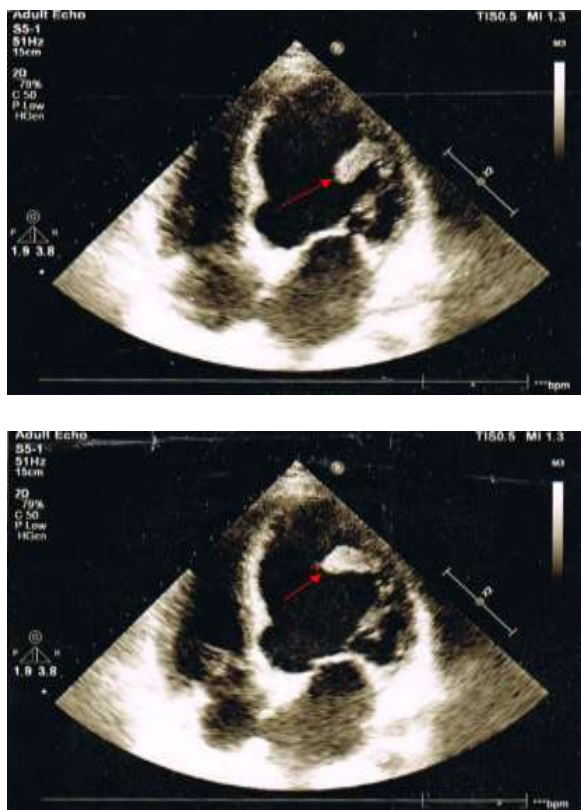

Figure 1: 2-D Echocardiography showing a large, mobile "oscillating" LV thrombus attached to the lateral wall of LV

DISCUSSION

LV thrombus is a frequent complication in patients with idiopathic DCMP, acute anterior wall MI and its sequelae, LV aneurysm[1,2]. Dilated LV (LV end-diastolic diameter >60 mm), low EF, atrial fibrillation, regional wall motion abnormalities and apical aneurysm appear to be major risk factors in thrombus formation and subsequent embolisation[5]. DCMP is associated with dilatation of both left and right ventricles with reduced systolic function. The resultant biventricular stasis promotes the formation of thrombus, most frequently in the LV, followed by the right ventricle. The characteristics of thrombus associated with heightened propensity for embolisation include large size, increased friability, mobility, protrusion into the LV cavity, diffuse LV dilatation, and impaired systolic function[5,6].

The incidence of LV thrombus in patients with DCMP is 11-44%[1]. Embolic events are estimated to occur in 4% of DCMP patients who have a LVEF ≤35%[7]. Foster *et al.,* [8] in a retrospective study of 104 patients with non-ischemic DCMP, reported an 18% frequency of thromboembolic events and an incidence of 3.5 clinically apparent events/100 patient-years. Katz *et al.,*[9] prospectively followed 264 DCMP patients and reported that the incidence of stroke was 1.7/100 patient-years. In the Vasodilators in Heart Failure trials (V-HeFT)[10,11], the overall rate of thromboembolism was between 2.2 and 2.5/100 patient-years. Patients with a lower LVEF had a higher risk of stroke. Based on data from V-HeFT, there was no statistically significant difference in the rate of thromboembolism between patients with ischemic and non-ischemic DCMP. In the Survival and Ventricular Enlargement (SAVE) trial[12,13], the incidence of stroke was 1.5/100 patient-years. Risk was increased in patients who were old and those who had lower LVEF. Patients with an LVEF ≤28% had a nearly twofold increase in relative risk of stroke compared with patients with an LVEF >28%. For every 5% decrease in LVEF, there was an 18% increase in stroke rate. The retrospective review of Studies of Left Ventricular Dysfunction (SOLVD)[14] analysed the incidence of thromboembolic events in patients with cardiomyopathy. Although the overall incidence of thromboembolic events was similar to that for other large clinical trials, an unexpected finding was that women were at increased risk for thromboembolic events compared with men (2.4 events/100 patient-years vs. 1.8 events/100 patient-years). This finding may be due to gender differences in the clotting or fibrinolytic system, the effects of hormonal variations or simply chance.

2-D Echocardiography has a sensitivity of 92–95% and a specificity of 86–88% for the detection of a LV thrombus[15]. It provides a noninvasive means of imaging the LV and its apex with precise spatial orientation and theoretically is the best tool for the detection and follow-up of a LV thrombus.

Anticoagulant therapy decreases the incidence of embolisation in idiopathic DCMP, and should be instituted if atrial or ventricular thrombus is detected by 2-D echocardiography[16]. Limited information, however, is available concerning the effect of anticoagulants on the morphologic features of LV thrombus[6]. Several reports in the literature confirm that anticoagulation suffices to resolve even large thrombi within days. Mallory *et al.,* reported complete resolution of a mobile LV thrombus attached to the anterior septum and extending into the LV outflow tract, in a patient of ischemic cardiomyopathy who was treated with low molecular weight heparin (enoxaparin) for 14 days[17]. High-dose intravenous heparin effectively treats thrombi that are mobile or that protrude into the LV cavity[3]. Complete resolution of 83 percent of thrombi has been documented after a mean of 14 days of treatment, but hospitalization and

monitoring of the partial-thromboplastin time are required[4,17]. Zaidi *et al.,* [18] also reported a case of 32 year old male with DCMP and a large mobile LV apical thrombus showing complete resolution within 2 weeks of anticoagulation therapy. Butman[19] reported rapid resolution of a massive LV thrombus by systemic anticoagulation. Quintana *et al.,*[20] demonstrated 2 patients with severe LV dysfunction and mobile mural thrombi, which disappeared with anticoagulant therapy. Bozkurt *et al.,* [21] and Sivasankaran *et al.,*[22] also reported complete resolution of LV thrombus with anticoagulation alone. It is advisable; however, to closely follow thrombus morphology by repeated echocardiographic studies when anticoagulants are being administered in order to be able to timely refer patients for thrombectomy should the thrombus undergoes "malignant" change in morphology[6]. LV thrombectomy might be an effective treatment for patients with mobile, pedunculated, LV thrombi. However, additional experience is required to compare surgical and medical treatment.

The European Heart Journal guidelines of 2012 state that patients with mural thrombi require oral anticoagulation with vitamin K antagonist therapy for up to 6 months. According to the 2013 American College of Cardiology/American Heart Association (ACC/ AHA) guidelines, vitamin K antagonist therapy can be limited to three months in these patients[23]. The combination of oral anticoagulation with dual antiplatelet therapy increases the risk of bleeding. Accordingly, most clinicians suggest oral anticoagulation with one antiplatelet agent. Given the existing controversy surrounding the duration of oral anticoagulation therapy and case reports of the recurrence of ventricular thrombi[23], some authorities advise lifelong therapy or therapy until improvement in the LV function[24].

Although certain groups of patients with DCMP have well defined indications for chronic anticoagulation (previous thromboembolic event, atrial fibrillation and the presence of a newly formed LV thrombus[25,26]), evidence from published reports does not demonstrate convincingly that the benefits of anticoagulation exceed the risks in other subgroups (i.e. reduced LV function in sinus rhythm). Moreover, the fluctuating metabolic state of patients with DCMP may predispose to bleeding complications of chronic anticoagulation. DCMP patients often have a chronically low cardiac output that may impair hepatic and renal functions. Furthermore, they often require multiple medications that may interact with oral anticoagulants (e.g. warfarin). Thus, the benefits of anticoagulants for patients with depressed LV function in sinus rhythm have yet to be established[27]. Indeed,

the reduced risk of ischemic stroke in response to warfarin is offset by a risk of hemorrhage[27].

Analyses of the SAVE[13] and SOLVD[14] databases have shown that low dose aspirin may be quite useful in preventing thromboembolism and may be much less risky than warfarin. In V-HeFT I[28], the incidence of thromboembolism in patients receiving aspirin monotherapy was 0.5 events/100 patient-years compared with 2.7 events/100 patient-years in patients receiving no antiplatelet or anticoagulant agents. Thus, to summarise, the only clear-cut indications for anticoagulation in most patients with DCMP are atrial fibrillation, a previous thromboembolic event or LV thrombus. For DCMP patients without these complications, aspirin monotherapy is a favorable option.

LV thrombectomy should be considered in selected patients in whom a very high-risk thrombus morphology is detected[6,29,30]. These thrombi are usually of a pedunculated, globular nature connected to the endocardium by a very narrow stalk, moving freely in a "wavy" motion within the LV lumen, and constitute a risk for embolization approaching 60-80%[6,29,30]. Thrombectomy is usually carried out by left ventriculotomy and is associated with subsequent LV dysfunction, arrhythmias and aneurysm formation[30].

Whether the presence of a large mobile LV thrombus should be an indication for surgical removal remains a troublesome clinical dilemma. There are no specific scientifically validated guidelines as to the best therapeutic approach. The case reports mentioned above[4,17,29,20,21], confirm the efficacy of anticoagulant therapy in large, mobile LV thrombus, and give clinicians an opportunity of deferring surgical removal of intra-ventricular thrombi, in favor of anticoagulant therapy, where considered appropriate, on an individual basis. Also, the risk of surgery is high in patient with severe LV dysfunction and heart failure. However, surgical removal should be considered especially with prior or repeated embolisation in the face of adequate anticoagulation.

Thrombolysis is indicated when patients have evidence of systemic embolisation and are poor candidates for thrombectomy[31]. Streptokinase, urokinase and recombinant tissue plasminogen activator (rt-PA) were used in several case reports with the latter favored due to its better safety profile, since rt-PA is a highly fibrin-specific serine protease[31]. In general, fibrinolysis is not a preferred modality as it carries the risk of embolisation at the time of lysis of the thrombus[32]. Additionally, it carries higher risk of hemorrhagic complications.

More randomized clinical trials or observational retrospective data will delineate the future course of patients presenting with LV thrombi formation secondary to DCMP.

This case of a large, mobile LV thrombus with attachment to the lateral wall of LV is extremely unusual in DCMP. The most common and important consideration for clinicians is to take an immediate decision regarding the line of treatment in such cases. Anticoagulant therapy is still a valid option to treat a large size intra-cardiac thrombi and heparin has been demonstrated to aid in the resolution of the clot. 2-D echocardiography should be routinely performed to follow the thrombus morphology during heparin-assisted resolution. It can be concluded that LV thrombus formation is a potentially dangerous complication of DCMP especially in patients with very low LVEF. Resolution of LV thrombus with anticoagulation demonstrates the effectiveness of such therapy in preventing the dreaded complications of clot embolism.

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Source of support: Nil
Conflict of interest: None Declared