Large In-transient Left Ventricular Thrombus due to Anabolic Steroid-induced Cardiomyopathy

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Abstract

The presence of small or moderate size thrombosis is not uncommon in left ventricle (LV) as results of basic co-moribund disease, but huge LV thrombosis that protrudes to aortic valve in the LV outflow tract (LVOT) tract is an exceptionally rare phenomenon. We report a 34-year-old bodybuilder athlete with cardiomyopathy and massive LV thrombosis. The thrombosis extended to LVOT and protruded through the aortic valve in systole and posed a high risk of systemic emboli. The patient underwent open heart surgery, and the clot was removed. The operation was complicated by low cardiac output syndrome that managed by intra-aortic balloon pump and high dose of inotropic drugs and hemodialysis. The patient died on the 15th day after surgery with multiorgan failures.

Key words: Cardiomyopathies, left ventricular, thrombosis

Introduction

The natural and synthetic derivatives of anabolic androgenic steroids (AAS) have been used illegally to increase sports performance, gain muscle volume, and decrease body fat sources in bodybuilders. Prolonged illicit use of AAS in supraphysiologic doses could be associated with adverse cardiovascular effects such as cardiomyopathy.[1] Evidence of mild LV systolic impairment has commonly been found in AAS users. In opposed to previous studies, a recent study revealed that the prolonged AAS use is associated with significant LV systolic dysfunction.[2] AAS, particularly when used over long durations, may be another cause of toxin-mediated myocardial impairment and could be considered not only among persons with mild LV dysfunction but also in patients with severe LV dysfunction.[3] Our case suggests that AAS-associated cardiomyopathy may be unpredictably related to prolonged use in a way similar to the cardiac toxicity of alcohol. In a few available case reports, the management of LV thrombi is often limited to anticoagulant and thrombolytic therapy with high mortality, but there is no data available to reference optimal management of massive LV clot. However, surgery is indicated in cases with a high risk for embolism or for large in-transient thrombi, where the clot protrudes to ascending aorta and increases risk of sudden large emboli into systemic circulation. On the other hand, thrombolytic therapy, too could potentially increase the risk of embolism.[4] Our case report fits surgical criteria, i.e., a recent emboli and large, in-transient mobile thrombus, that warrants surgical removal. However, the life expectancy in these patients continues to be poor with or without surgery.

Access this article online

Quick Response Code:

Website: www.ijccm.org

DOI: 10.4103/0972-5229.198328

Case Report

A 34-year-old bodybuilder male with a history of prolonged AAS (anabolic androgenic steroids) use presented with a dyspnea and left-hand purple digits. Past medical history revealed a recent cardiac care unit admission for congestive heart failure that was managed medically with digoxin, captopril, carvedilol, diuretics, low-dose Aspirin, and warfarin. The previous TTE showed severe reduced ejection fraction (EF) (30%) with reduced wall thickness and absence of thrombus. The whole septum and apex and anterolateral wall of septum were thin and akinetic with mild mitral regurgitation

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How to cite this article: Sabzi F, Faraji R. Large in-transient left ventricular thrombus due to anabolic steroid-induced cardiomyopathy. Indian J Crit Care Med 2017;21:51-4.

and preserved right ventricle function. Coronary angiography revealed normal arteries. The patient was discharged in good condition. after 3 months, the patient was admitted with dyspnea and cyanosis of the left hand. On physical examination, he was alert and conscious. The heart rate was 80/min, and blood pressure was 160/100 mmHg. Chest, heart, and abdomen were normal. Jugular venous pressure was normal, and peripheral edema was absent. Radial pulse was present on the right side, but was absent on the left side. Both fundi were normal and visual field defects or nystagmus were not observed. Motor movement and neurologic reflexes were normal in the limbs. Complete blood examination was normal, but erythrocyte sedimentation rate and C-reactive protein were in the upper normal range. Fasting blood sugar was normal and liver function test was abnormal, troponin; and other cardiac-specific enzymes and coagulation tests were normal; and his creatine kinase was 450 U/L. Serum triglycerides, total serum cholesterol, and apolipoprotein B were normal. The complete thrombophilia screen including the antiphospholipid antibody screen were negative. Chest X-ray showed cardiomegaly. The electrocardiogram showed sinus rhythm. Q waves were present in leads V1–V6. Echocardiography showed dilated left ventricle (LV) with global hypokinesia and a huge thrombus. Carotid Doppler ultrasound showed no significant stenosis. He discontinued anticoagulants but the cause was uncertain. In transesophageal echocardiography, left ventricular cavity size was enlarged, end diastolic diameter was 7.2 cm, and end systolic diameter was 5.6 cm. The left atrium diameter was 4 cm. Left ventricular EF was 30% and there was a large thrombus [Figure 1], measuring 9.49 cm × 5.47 cm. Thrombus was not smooth and extended to LV outflow tract and protruded into the aortic valve in systole. With the presence of microemboli to left hand, this in-transient clot predisposed the patient to further emboli [Figure 2]. Workup was negative for any malignancy. At surgery cardiopulmonary bypass was instituted by aortic and bicaval cannulation. The aorta was cross-clamped and cardioplegia injected into the aortic root. After cardiac arrest, aortotomy showed bulging of the thrombosis tail to the aortic valve. The thrombus was removed from the LV through ventriculotomy and aortotomy [Figure 3]. Histopathology of the excised mass revealed fine fibrin, clot, granulation tissue, and hemosiderin deposition. Myocardial biopsy showed cardiac muscle fibrosis. The patient experienced postoperative low cardiac output syndrome and acute renal failure that was managed by inotropic drugs, intra-aortic balloon pump, and dialysis, however his condition deteriorated to multiple organ failure and death.

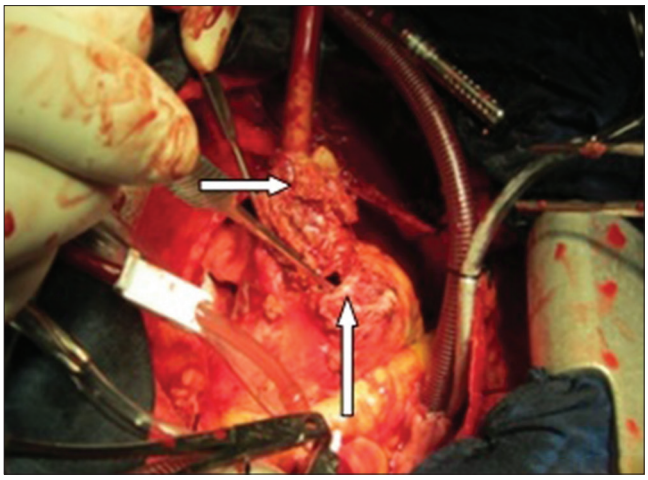

Figure 1: Removal of huge clot (black arrow) from left ventricle, curve lines depict edges of ventriculotomy.

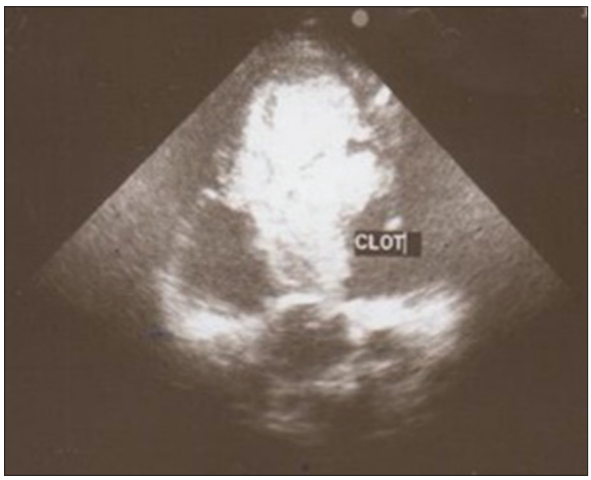

Figure 2: Echocardiography shows huge clot in left ventricle (surrounded by curve lines).

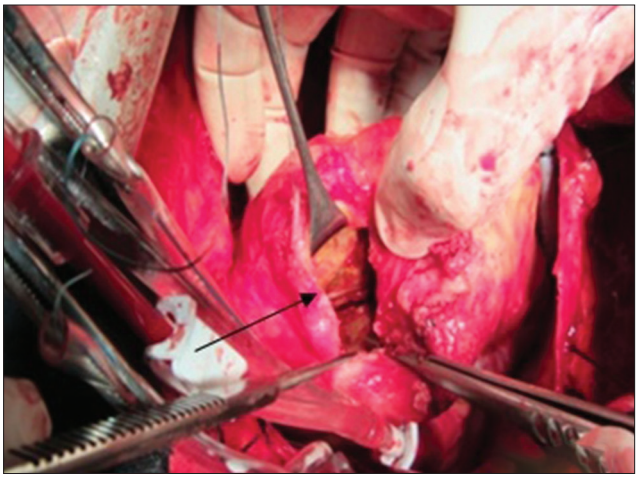

Figure 3: Left ventricular apex and internal wall of left ventricle after removal of clot.

Discussion

Many studies have demonstrated a significant increase in muscle mass and fiber size with increase muscle protein synthesis, and ultimately muscle mass with ASS. This increase in skeletal muscle mass is essentially the result of muscle fiber hypertrophy and involves myocyte cell activation and hypertrophy of the muscle fiber. Many bodybuilders abuse AAS to improve their performance or even their appearance with increasing muscle mass. Bodybuilders

with prolonged AAS abuse have a high potential for thrombophilia, arterial hypertension, stroke, dyslipidemia and cardiomyopathy. The latter is the most serious cardiac sequel of AAS.[5] AAS abuse induced apoptosis in ventricular myocytes in mice *in vitro* and increased the expression of specific proapoptotic oncogene Bax-alpha, as assessed by reverse transcription-polymerase chain reaction, increases intracellular Ca^{2+} influx and mobilization, leading to the release of apoptogenic factors. These results clearly indicate that AASs induce apoptotic cell death in a dose-dependent manner. This finding may have important implications in understanding of the pathogenesis of ventricular remodeling, cardiomyopathy, and sudden cardiac death associated with AAS abuse.[6] Several authors have shown that serum of lipoprotein(a) (Lp[a]) concentrations reduced with treatment with testosterone enanthate in men, and in hemodialysis patients. However, high dose of AAS caused increased level of LP(a). As opposed to the aforementioned study, serum Lp(a) concentrations were lower in AAS user in bodybuilder than in their non users and altered the serum concentrations of apolipoproteins, high-density lipoprotein cholesterol, it's sub fractions; unfavorably, Changes in intracellular calcium concentration and could alter endothelial hemostasis, predisposing to the early endothelial cell activation, macrophage and monocyte entrapment in media that is responsible for vascular atherosclerosis frequently.[8] Several authors have suggested that LV clot or thrombus with the following features have higher rate of emboli and may have an indication of surgical intervention: (1) Clot protruding into the left ventricular chamber, (2) in-transient thrombus, (3) high mobility, and (4) recurrent emboli in the presence of LV thrombus. A thrombus is defined as protruding mass when it protrudes mainly into the LV chamber and considered as mural thrombus when in TTE appears flat in parallel with the endocardial surface.[9-17] Domenicucci *et al*. revealed that these echocardiographic features have a significant variability in the first 60 days of acute infarction and therefore showed that the evaluation of these features was not helpful. The author showed that 40% of LV thrombi had a significant morphological change in their shape and 30% had an important change in the mobility.[18] On the other hand, up to 30% of thromboembolism cases appear in patients whose clot is neither mobile nor protruding into ventricular cavity. Other thrombus features, such as clot size,[16] hypolucency of central part of clot[17] or hyperkinesia or paradoxical motion of the myocardium below to the thrombus,[4] are accompanied with an increased risk of thromboembolism. Other factors that associated increasing risk of emboli and may be an indication of surgery are: (1) Congestive heart failure, (2) severe systolic LV dysfunction and dilatation, (3) recurrent embolization, (4) atrial fibrillation, and (5) patient age more than 70 years. In patients who are not candidates for surgical intervention, the following options may be used for therapy.

Thrombolysis

Vaitkus and Barnathan *et al*.[19] showed that the incidence of LV clot formation or mortality in patients receiving thrombolytic therapy was not different from those without. In another study, the incidence of recurrence in patients treated with either thrombolytic therapy or heparin was not different.[5]

In a retrospective study, thrombolytic therapy was used for the treatment of documented LV clot. In a study of twenty participants with a LV clot on trans thoracic echocardiography (TTE), streptokinase was used intravenously at a dose of 60,000 U/h for a mean of 5 days along with intravenous heparin (100 units/h). LV clot dissolution was successful in two-thirds of the patients. No case of systemic emboli was reported in these patients. Thrombolytic therapy was discontinued in one patient due to bleeding.[33]. In another study, four patients with hypermobile LV clot received thrombolytic therapy by streptokinase. In half of the patients, thrombolysis was documented without any clinical complication. In the remaining two patients, systemic thromboembolism occurred and one case had diplopia and the other had fatal stroke.[1] The authors concluded that thrombolytic drugs are effective in rapid lysing of cardiac thrombi, but may be associated with catastrophic complications such as stroke and massive bleeding.

Heparin

Published data on Heparin for LV clot are conflicting. In a prospective study, patients with recent acute myocardial infarction, who received anticoagulant doses of intravenous heparin (12,000 units every 12 h) had a lower rate of LV clot formation compared to those patient receiving low dose of heparin (5000 units every 12 h) during the first 2 weeks of the event.[9] In another study, however, high-dose intravenous heparin therapy did not prevent clot formation.[10] In a study, 24 patients with mobile LV clot, high-dose intravenous heparin was infused intravenously during a time frame of 2–3 weeks. In all these patients, size of LV clot decreased, and the high-risk characteristics resolved at follow up TTE. Complication of anticoagulation was found in only one patient.

Vitamin K antagonist

Based on current studies, Vitamin K antagonist therapy reduced the risk of emboli in patients with LV clot after acute myocardial infarction.[20] However, this drug does not seem to affect the probability of the thrombus resolution.

Due to the risk of fatal bleeding, the potential benefit of oral anticoagulant treatment combined with dual antiplatelet therapy could not outweigh the increased risk of bleeding.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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