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Case Report

Left ventricular thrombus complicated by acute limb ischemia in a patient with HIV ☆

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ABSTRACT

Left ventricular thrombus typically occurs in patients with impaired left ventricular function such as aneurysm, dilated cardiomyopathy, or post-myocardial infarction. Untreated HIV infection is known to increase the risk of venous thromboembolism and cardiovascular disease. However, the pathophysiology remains uncertain; some studies have proposed chronic inflammation as the underlying etiology. Nonetheless, left ventricular thrombus is extremely rare among persons living with HIV with no known underlying cardiac disease. Herein, we report an unusual case of a 55-year-old homeless and heterosexual male with past medical history of HIV, who has mildly reduced left ventricular function and a nonmobile, medium size left ventricular thrombus. Patient was initially treated with therapeutic dose of enoxaparin, and subsequently developed acute embolic occlusion of right femoral artery that lead to an above knee amputation. To our knowledge, left ventricular thromboembolism complicated with acute embolic ischemia in persons living with HIV is extremely rare. The presenting case will definitely add to the current body of knowledge and will raise awareness among physicians, in recognizing the rare association between HIV and arterial thromboembolism.

Background

The introduction of potent, convenient, and well tolerated antiretroviral therapy (ART) has changed the landscape in the long-term prognosis of person living with HIV (PLWH). Human immunodeficiency (HIV) disease has become a relatively benign chronic infection when patients take their ART and have an undetectable virus load; but a subset of patients continues to have a chronic inflammatory state, that may put them at an increased risk of cardiovascular disease and thrombotic events. HIV infection has been reported to be independently

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associated with diastolic dysfunction, increased left atrial volumes and left ventricular (LV) mass index [1]. However, the pathophysiology of HIV and thromboembolism remains unclear. The chronic inflammation in patients with HIV may damage endothelial cells, disrupts the von Willebrand factor [2], causing the release of tumor necrosis factor-alpha (TNF-alpha) and reduce the levels of antithrombin III, anticoagulant protein C and anticoagulant protein S [3,4]. A low CD4 count, the presence of antiphospholipid antibodies, dyslipidemia and antiviral therapy may also affect the risk of thrombosis [5].

There is limited data on the incidence of LV thrombus in PLWH. Lijfering et al., reported that the incidence of arterial thrombus in PLWH was 3% (13/519). Out of this cohort, 5 patients had peripheral artery occlusive disease, 4 patients had ischemic stroke, 3 patients had myocardial infarction and 1 patient had a transient ischemic attack and none of the patients had LV thrombus [6]. Our paper reports a rare case of newly diagnosed patient with AIDS with no known cardiac risk factors and normal LV function, who presented with non-mobile, medium size LV thrombus. He subsequently developed acute limb ischemia.

Case presentation

A 55-year-old homeless and heterosexual male with past medical history of hypertension presented with shortness of breath and productive cough for 2 consecutive weeks. He was hypotensive, tachycardic, and tachypneic on admission (temperature 96.2°F, blood pressure 89/64 mm Hg, heart rate 112/min, respiratory rate 24/min, saturating 92% on room air). Physical examination was notable for cachexia, decreased air entry to the lungs bilaterally with diffuse crackles and rhonchi. Arterial Blood Gas (ABG) on room air showed a pH of 7.42 (7.34-7.44), pCO2 of 23.4 mm Hg (35-48 mm Hg), pO2 of 35.2 mmHg (75-100 mm Hg), and oxygen saturation of 67.4%. Chest X-ray showed right lower lobe pneumonia with mild pulmonary vascular congestion. His lactic acid was 8.6 mmol/L (0-2 mmol/L), procalcitonin was 17.7 ng/mL (0-0.05 ng/mL), and lactate dehydrogenase was 504 U/L (122-222 U/L). Computed tomography (CT) chest showed bilateral centrilobular emphysematous changes with scarring of the bilateral lung apices and right middle lobe as well as diffuse ground-glass opacities over both lungs. He was admitted for sepsis and hypoxic respiratory failure possibly secondary to pneumocystis jiroveci pneumonia with bacterial superinfection.

He received normal saline bolus, intravenous trimethoprim-sulfamethoxazole, ceftriaxone and steroid. He was put on BiPAP for ventilatory support. HIV test was positive with a CD4 count of 22 (560-2700 × 10^3/uL) and treatment with bictegravir 50 mg, emtricitabine 200 mg and tenofovir alafenamide 25mg (Biktarvy) was initiated. Additionally, his Brain Natriuretic Peptide (BNP) on admission was found to be elevated to 926. Subsequent echocardiogram showed slight reduction in ejection fraction with EF of 45-50%, with a left ventricular round apical thrombus, non-mobile and measuring about 1 × 2 cm, impaired left ventricular relaxation (Fig. 1). He was started on therapeutic enoxaparin (1 mg/kg).

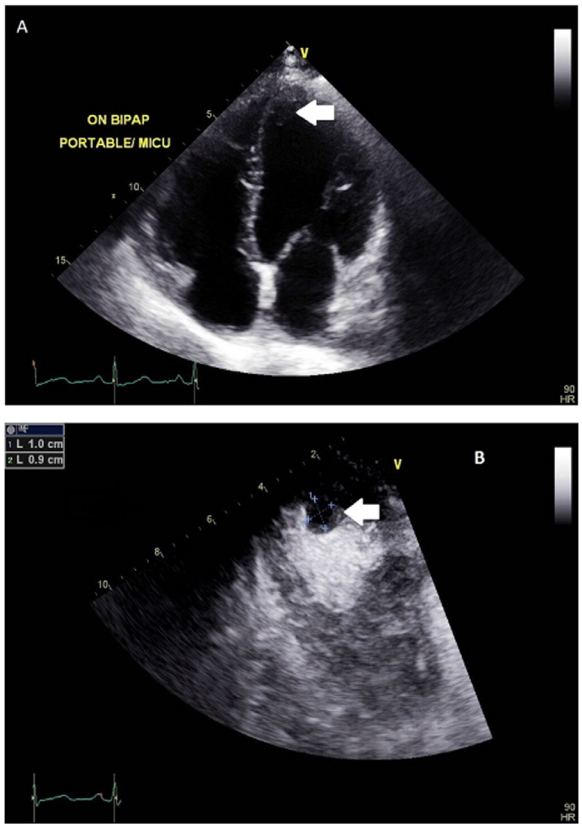

Fig. 1 – On Day 4 of admission, picture A showing Left ventricular round apical thrombus (white arrow) on Echocardiogram without contrast, picture B showing the filling defect (white arrow) on Echocardiogram with contrast.

On Day 8 of admission, he started to complain of right lower extremity numbness and the leg was cold upon palpation. Physical examination revealed absence of posterior tibialis and dorsalis pedis pulses. Bedside duplex of right lower extremity showed arterial thrombus extending from the popliteal artery down to the tibial artery. CT angiogram subsequently showed an acute embolic occlusion within the right popliteal artery (Fig. 2). Therapeutic enoxaparin (1 mg/kg) was discontinued and patient was started on heparin drip. Emergent femoral embolectomy was performed. Unfortunately, there was extensive gangrene of the right foot with severe distal small vessel disease, he subsequently required above knee amputation of his right leg.

Repeated echocardiogram 3 months later showed no evidence of LV thrombus. LVEF 60-65% improved from 45% to 50% on earlier echocardiogram with mild mitral regurgitation (Fig. 3). He was discharged with aspirin and warfarin for the thrombotic event after his lung function improved. Hypercoagulable work up including lupus anticoagulant, anticardiolipin antibody, anti-beta-2 glycoprotein antibody levels were negative. Protein C, protein S, antithrombin III levels were all within normal limits. Patient was also screened negative for Factor V Leiden and prothrombin gene mutation. In light of

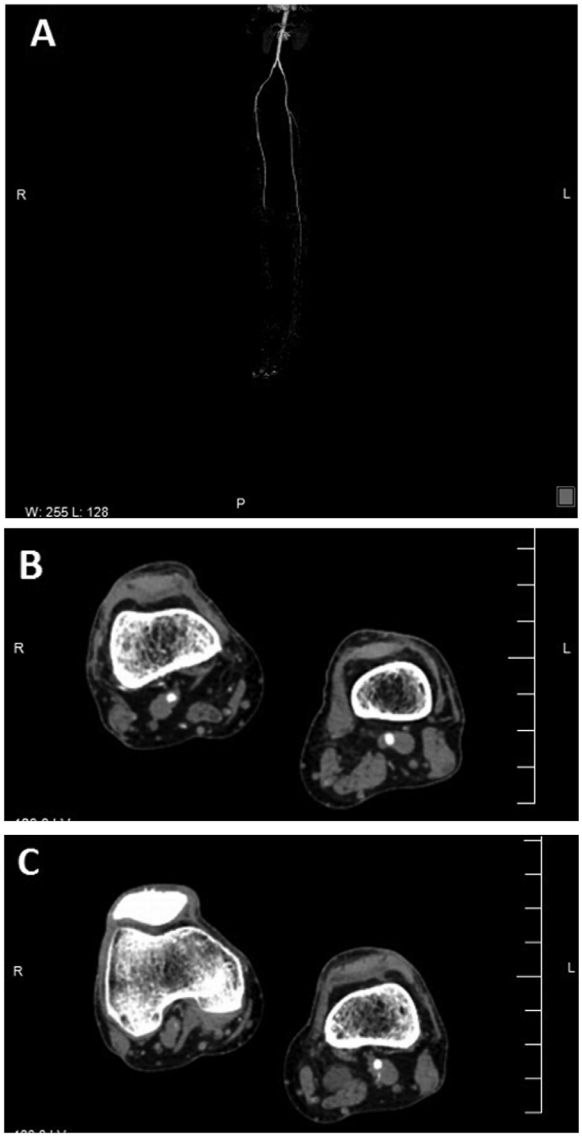

Fig. 2 – On Day 8 of admission, CT angiogram showing embolic occlusion within the right popliteal artery (A); (B) and (C): illustrating the transition the filling defect in the popliteal artery

the potential HIV thrombophilia, patient was started on long term anticoagulation together with antiretroviral therapy.

Discussion

Untreated HIV constitute a chronic inflammatory state with increased risk of hypercoagulability; however, data on the risk of arterial thrombosis and LV thrombus in patients with HIV is limited. In a systematic review by Klein et al, 2005, it was reported that PLWH are at 2- to 10-fold increased risk of venous thrombosis, compared to the general population of the same age [7]. Moreover, in a retrospective study from the National Hospital Discharge Survey, from 1996 to 2004, conducted by

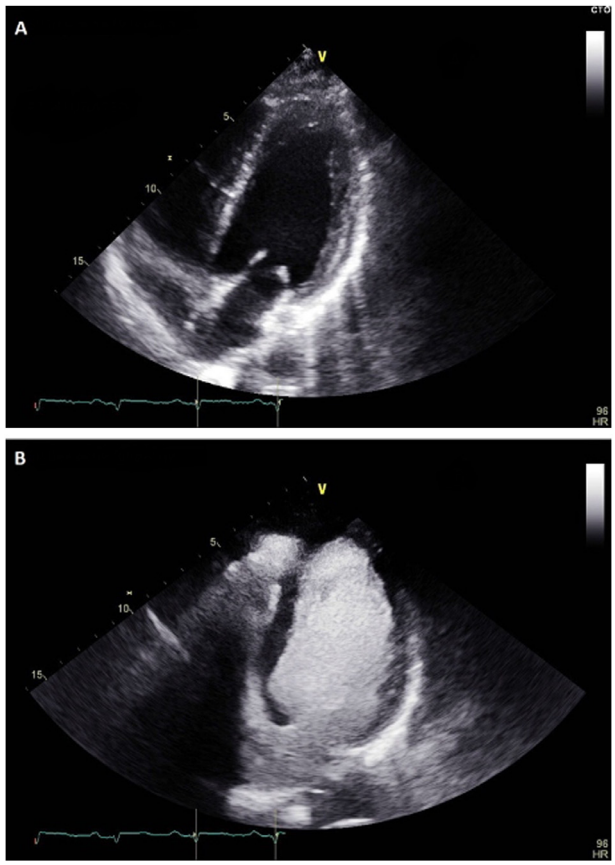

Fig. 3 – Echocardiogram 3 months later showed no evidence of vegetation or LV thrombus on predischarge (picture A). Echocardiogram without contrast, picture B showing no filling defects on echocardiogram with contrast.

Malek et al., 2011, suggested that the odds of developing pulmonary embolism among PLWH were 43% greater, compared to controls, matched for age [8].

The hypercoagulable state observed in patients infected with HIV may be due to an increase in procoagulant factors (microparticles, antiphospholipid, and lupus anticoagulant) and a decrease in anticoagulant factors (Antithrombin III, protein C and protein S) [6]. Numerous reports have proposed that these acquired coagulopathies, may be the underlying mechanism that increase the incidence of venous and arterial thrombosis in patients infected with HIV.

Numerous articles have documented that HIV positive patients had an increased risk of developing thrombosis with the incidence of 2-10 times greater, compared to patients without HIV, especially in those patients with CD4 count less than 200 [9]. Some has linked the mechanism to endothelial activation as during the course of HIV infection with cytokines such as tumor necrosis factor alfa, interleukin-1 and interleukin-6 markedly up-regulated, leading to coagulation cascade activation and the production of fibrinolytic proteins inhibition. Lijfering et al., reported that HIV can cause an imbalance between procoagulant proteins (ie, increases factor VIII and fibrinogen concentrations) and anticoagulant proteins (ie, decreases protein C and protein S) which increase

the risk of VTE [6]. Thus, in theory, using HAART to treat patients with AIDS could eliminate the increased risk of developing thromboembolic disease by achieving immunologic reconstitution [10]. Moreover, studies have shown that patients with HIV treated with HAART had less cardiovascular and cerebrovascular complications, including thrombosis and death [10].

Thrombosis usually occurs when there is alteration of Virchow triad mainly blood flow (stasis), endothelial damage or hypercoagulable state (inherited vs acquired) [11]. LV thrombosis, on the other hand, mostly develops in patients with cardiac risk factors such as LV malfunction that leads to wall hypokinesis (such as myocardial infarction, dilated cardiomyopathy, severe systolic dysfunction), which results in stasis and turbulence inside the left ventricular chamber, eventually leading to thrombus formation [12]. Thus, having LV thrombus in a young patient with no risk factors is extremely uncommon.

The natural history of LV thrombus is complete resolution and endothelialization and the risk of embolization may happen prior to this [13]. Prompt revascularization has decreased the incidence of LV thrombus and anticoagulation is used to reduce embolic complication [14]. Thrombus mobility and thrombus protrusion are two major risk factors for embolization in patients with LV thrombus. Management of LV thrombus in general involves anticoagulation. It can also be managed with thrombolytic therapy, followed by heparin to prevent rebound thrombosis [15]. If the thrombus is large with increased risk of embolization before or after thrombolytic therapy, henceforth surgery can be performed [16]. The roles of new oral anticoagulant agents (NOACs) in the setting of left ventricular thrombosis are poorly understood. There are scatter case reports encourage the use of these agents [17,18]. More studies are still needed to explore the potential role of NOACs on LV thrombus.

In our case, a 55-year old patient with a past medical history of HTN and newly diagnosed AIDS without any thrombophilic risk factors had a left heart echocardiogram revealing a round LV thrombus that was medium in size. The hypercoagulable work up was negative and he was treated with anticoagulant and the thrombus embolized to the right lower extremity, which led eventually to gangrene for which the patient had above knee amputation done. Subsequent echocardiogram showed resolution of the thrombus.

Conclusion

LV thrombus is extremely rare in an otherwise healthy individual with no known cardiac risk factors. In our patient, HIV may be the independent risk factor leading to arterial thrombosis and LV thrombus formation. To our knowledge, the presenting case of LV thromboembolism complicated with acute embolic ischemia in HIV patient is extremely rare. Our case highlights the importance of high suspicion for thrombosis, especially in advanced HIV disease; and the importance of appropriate imaging to make the diagnosis and start aggressive anticoagulation as soon as possible.

Ethics approval and consent to participate

Not available.

Consent for publication

Patient has given both verbal and written informed consent to publish the case including publication of images.

Availability of data and materials

Data has been presented in the text.

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Author Contributions

KHC and AR contributed to the conception and design, acquisition, analysis and interpretation of data, as well as participate in drafting and revision of the manuscript. SLL and EA actively participate in analysis of data, drafting and revision of manuscript. AS, JS and HS contributed to idea design, data analysis and critically revised the manuscript and as well as approved the final submission of manuscript.

Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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