Left Ventricular Thrombus: An Interesting Presentation of Primary Antiphospholipid Antibody Syndrome with a Mini-review of the Literature

G. Ravi Kiran, J. Shashivardhan, P. Chandrasekhar
Department of Cardiology, Government General Hospital, Kurnool, Andhra Pradesh, India

Abstract

Antiphospholipid syndrome (APLS) is characterized by recurrent thrombosis. We report the case of a 36-year-old male who had acute right-sided ischemic stroke and right leg ischemia secondary to left ventricular (LV) thrombus caused by primary APLS. The literature review suggested that the LV thrombus presented most commonly with systemic embolism and was associated with a mortality rate of 22.2% with treatment. Thrombophilic workup in young patients with a systemic thromboembolic episode (s) is advised.

Keywords: Antiphospholipid antibody syndrome, left ventricular thrombosis, lupus anticoagulant, mini-review, stroke in the young

INTRODUCTION

Antiphospholipid syndrome (APLS) is a multisystem autoimmune disease that encompasses primary APLS (P-APLS), secondary APLS (S-APLS), seronegative, and catastrophic APLS. It is characterized by the presence of autoantibodies, hypercoagulability, and vascular thrombosis.\(^1\)

The heart is involved mainly in the form of valvular lesions (immune-mediated) and usually does not cause hemodynamic significance. However, occur of ventricular thrombus is very rare, whose epidemiology is unknown.

CASE REPORT

A 36-year-old male presented with a complaint of 8-day history of weakness of the right upper limb and lower limb. He was an alcoholic (2 units/day) and smoker (5 pack-years) but was nondiabetic and nonhypertensive. There were no other chronic illnesses for which the patient is on medication.

On examination, he was fully conscious with a pulse rate and blood pressure of 84 bpm (regular) and 130/80 mmHg (supine), respectively. He had an upper motor neuron type of weakness (power: 4/5) on his right side, and other systemic examinations were within normal limits.

His electrocardiogram and chest X-ray were normal, and routine blood investigations revealed a white cell count of 7.6 × 10^9/L, hemoglobin of 14.4 g/dL, platelets of 255 × 10^9/L, creatinine of 1.1 mg/dl, and all within reference limits (WRL). Tests for HIV, hepatitis B virus surface antigen, and anti-hepatitis C virus core immunoglobulin M were negative.

His emergency CT brain (plain) showed middle cerebral artery territory acute infarct [later confirmed by MRI brain, Figure 1]. A transthoracic echocardiogram done on the day of his admission revealed normal left ventricular (LV) function (ejection fraction: 63.5%) and cardiac chamber size (indexed LV volume: 41.7 ml/m²) with no regional wall motion abnormality. Notably, a large (5 cm X 4.3 cm) mobile mass (probably thrombus) protruding into the LV outflow tract is identified in the LV cavity (later confirmed by cardiac MRI as thrombus) [Figure 2].

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On day 3, the patient developed weakness of the right leg and pain in the right foot. Color duplex Doppler showed occlusion of the right femoral artery with thrombus, and no flow was detected in the popliteal artery. A provisional diagnosis of primary intracardiac thrombus with multi-site embolism was made. Interestingly, his activated partial thromboplastin time (aPTT) was found to be elevated before the initiation of heparin (54s), so blood samples were sent for a detailed autoimmune antibody panel and the thrombophilic screen. He was treated with unfractionated heparin (UFH), whose dose was adjusted to the lower end of individualized heparin therapeutic aPTT range.[5]

In view of acute limb ischemia, CT peripheral angiogram was done and it showed a total occlusion of the distal superficial femoral artery [Figure 3]. Hence, the patient was offered catheter-directed thrombolysis followed by surgical removal of thrombus, but he refused. After shared decision making with the family, he was continued with UFH infusion.

His was tested positive for lupus anticoagulant (LA: by clot-based assay). IgG anticardiolipin antibody (aCL: 42.71 GPL/ml) and IgG anti-β-2 glycoprotein antibody (β2 GPI: 50.6 GPL/ml) were elevated in high titers (by enzyme-linked immunosorbent assay method), and antinuclear antibody was negative. His homocysteine, protein C, protein S, and antithrombin III levels were WRL. Thus, a diagnosis of primary antiphospholipid antibody syndrome was made.[4]

Due to financial constraints, hemolytic workup, Coombs test, and anti-dsDNA workup were not done. On day 4, the patient experienced sudden death presumably due to coronary embolism.

**DISCUSSION AND MINI-REVIEW OF THE LITERATURE**

APLS is characterized by arterial and more commonly venous thromboembolic events.[10] Although intracardiac thrombus is rare, it is reported to be most common in the right atrium and is more frequently associated with P-APLS as compared to S-APLS.[6] Although there are no data specific to LV thrombus, available literature suggests that the presence of high levels of LA and aCL was significantly associated with arterial[7] and intracardiac thrombosis.[8] A 5-year prospective study also showed that the median time to a recurrent thrombotic event is shorter in patients with high titer of aCL antibody and intracardiac thrombus.[9]

Due to the rarity of this association, we did a systematic search in the MEDLINE database for cases of LV thrombi in APLS. We used MeSH terms such as “intracardiac” or “cardiac thrombus” AND “antiphospholipid” or “APLS” or “antiphospholipid antibodies.” Only retrievable English language citations were included in the study. A total of 138 citations were found. Thirty-nine cases met our criteria [Figure 4 and Supplementary Material].

A total of 40 cases of APLA syndrome associated with LV thrombus were reported (including our patient), with a mean age of 35.7 years (one patient age is unknown) and male: female ratio of 1.05:1. 27.5% of the patients have documented S-APLS (SLE being most common). There is a paucity of complete data on the autoantibody pattern; only 4% (1/25) and 7.1% (2/28) of the documented case(s) were negative for LA and aCL antibodies, respectively. In 3 patients, data on clinical presentation were not published, and in the remaining (37), the most common (62.1%) presentation was systemic embolism. 27.5% of the patients have documented underlying myocardial dysfunction. Different strategies employed for treating LV thrombus were anticoagulation, corticosteroids, and surgery. Embolic manifestations were treated with catheter-directed thrombolysis or embolectomy or percutaneous interventions or surgical bypass. Based on the retrievable data, the mortality rate among patients treated...
with medical therapy (antithrombotics +/- corticosteroids) alone for LV thrombus was 16.7% (4/24), and 80% (8/10) of the patients who underwent surgical removal were alive. The overall reported mortality rate was 22.2% (8/36).

Although the available literature suggests a more than 80% recovery rate with medical management, our patient died. This is probably because, our patient presented with a large, protruding, mobile thrombus, which is considered as risk factor for embolization and thus complications\[11\] including death. Due to higher risk for systemic thromboembolism when treated with anticoagulation alone, these high-risk thrombi should be treated with thrombectomy.\[10\] Accordingly, our patient was planned for surgical removal of thrombus, which the patient refused and ultimately succumbed to death.

**CONCLUSION**

LV thrombus is a rare manifestation of antiphospholipid antibody syndrome (APLS), which can occur even in the absence of valvular involvement and cardiac dysfunction. This case highlights the importance of evaluation for thrombophilic disorder in young (<40 years) patients with a systemic thromboembolic episode(s), in particular, if it involves an atypical site or multiple sites.

The literature review suggests that LV thrombus in APLS presents most commonly with the systemic embolic phenomenon. This association has a mortality rate of 22.2% with treatment.

**Patient consent**
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**
There are no conflicts of interest.

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### Supplementary Material: Literature review on left ventricular thrombus in APLA syndrome

| Publication | Form | Age | Sex | CC-T | Presentation | Treatment | Outcome | LA | aCL | Ab2GPI |
|-------------|------|-----|-----|------|--------------|-----------|---------|----|-----|--------|
| Gorelick et al. (Arch Neurol. 1985) | SLE | 25 | F | LV | Left CVA | Surgery + AC | Dead | U | U | U |
| Gur et al. (J Rheumatol. 1988) | SLE | 16 | F | LV | CCF + right CVA | AC + IS | Dead | +ve | U | U |
| Eber et al. (Dtsch Med Wochenschr. 1991) | P | 34 | F | LV | Incidental | U | U | +ve | U | U |
| Kaplan et al. (Am Heart J. 1992) | SLE | 38 | F | LV | Left CVA | AC alone | Alive | +ve | +ve | U |
| Barjatya et al. (J Assoc Physicians India, 1992) | SLE | 32 | F | LV | incidental | AC + CS | Alive | +ve | U | U |
| Rojas et al. (Ann Cardiol Angeiol, Paris, 1993) | P | 42 | M | LV | RVT | CS | Alive | U | +ve | U |
| Baum et al. (South Med J. 1994) | P | 58 | F | LV | ALI | Surgical removal + AC + toe ampt. | Alive | +ve | +ve | U |
| Santos et al. (Rev Port Cardiol. 1994) | P | 14 | F | LV | Systemic embolism (site: U) | AC alone | Alive | U | +ve | U |
| Bruce et al. (Br Heart J. 1995) | SLE | 41 | F | LV | Left CVA | AC alone | Alive | +ve | +ve | U |
| Atallah et al. (Arch Mal Coeur Vaiss. 1995) | SLE | 14 | F | LV | Incidental | Surgical removal + AC | Alive | U | U | U |
| Plein et al. (J Am Soc Echocardiogr. 1996) | P | 13 | F | LV | Incidental | Surgical removal + AC + CS + CQ | Alive | U | +ve | U |
| Aguilar et al. (J Am Soc Echocardiogr. 2000) | P | 19 | F | LV | Right CVA | Surgical removal + AC | Alive | U | +ve | U |
| Voyer et al. (Arch Mal Coeur Vaiss. 2000) | U | 48 | F | LV | CAD + ALI | AC alone | Alive | U | +ve | U |
| Emre et al. (Dig Surg. 2001) | U | 33 | F | LV | U | AC alone | Alive | U | U | U |
| Sivasankaran et al. (Indian Heart J. 2002) | ARF | 14 | M | LV | Fever + arthralgia | AC + CS | Alive | U | +ve | U |
| Best et al. (Heart Lung. 2002) | P | 32 | F | LV | TIA | AC alone | Alive | +ve | +ve | U |
| Cattaneo et al. (Ital Heart J Suppl. 2003) | P | 39 | M | LV | Incidental | Surgical removal + AC | Alive | +ve | +ve | U |
| Willens et al. (Echocardiography. 2003) | SLE | 43 | M | LV | CVA | AC alone | Alive | U | +ve | U |
| De Silva AN et al. (Rev Port Cardiol. 2003) | SLE | 34 | U | LV | CCF | AC + CS + CQ | Death | +ve | U | U |
| Erdogan et al. (Stroke. 2005) | U | U | U | LV | U | U | U | +ve | U | U |
| Morel et al. (Thromb J. 2005) | P | 42 | M | LV + RV + RA | STEMI | AC + PTCA + abciximab | Alive | +ve | +ve | −ve |
| Massoudy et al. (Eur J Cardiothorac Surg. 2005) | U | 59 | F | LV + RV | H/O CVA | Surgical removal + AC + CS + PP | Alive | U | +ve | U |
| Bahlmann et al. (J Am Soc Echocardiogr. 2006) | P | 68 | M | LV | Subacute myocardial infarction (CCF) with IMH | AC + CABG | Alive | +ve | +ve | U |
| Guedes-Barbosa LS et al. (Arthritis Rheum. 2007) | P | 36 | M | LV | CCF + ALI | U | Died | +ve | +ve | U |
| Amigo et al. (Clin Rev Allergy Immunol. 2007) | P | 26 | M | LV + LA + RA + PA | Sepsis | U | dead | +ve | +ve | U |
| Cianciulli et al. (Cardiol J. 2009) | P | 39 | M | LV | Left CVA + peripheral embolism (site: U) | Surgical removal + AC | Alive | +ve | −ve | U |
| Koch et al. (Clin Nephrol. 2009) | P | 38 | F | LV | TIA | Urokinase + danaparoid | Alive | +ve | U | U |
| Tomas FC et al. (Cardiology J. 2009) | SLE | 36 | M | LV | TIA | AC alone | Alive | +ve | −ve | U |
| David S Kotlyer et al. (Blood J. 2010) | P | 39 | M | LV | U | AC alone | Alive | +ve | +ve | U |
| Acikel S (Echocardiography. 2010) | SLE | 36 | F | LV + PA | DVT + PTE | AC + AP + CS | Alive | U | U | U |

Contd...
## Supplementary Material: Literature review on left ventricular thrombus in APLA syndrome. Contd...

| Publication                       | Form | Age | Sex | CC-T | Presentation                        | Treatment                           | Outcome | LA | aCL | Ab2GPI |
|-----------------------------------|------|-----|-----|------|-------------------------------------|-------------------------------------|---------|----|-----|--------|
| Abid L (Pan Afr Med J. 2011)      | P    | 30  | M   | LV   | B/L ALI                             | AC + AP + embolectomy               | dead     | +ve| +ve | U      |
| Nadine A et al. (Eur Heart J Cardiiovase Imaging. 2012) | P    | 39  | M   | All 4 | CCF + PUO                           | Surgical removal + AC               | Dead     | −ve| +ve | −ve    |
| Sculley et al. (Int Med Case Rep J. 2013) | P    | 59  | M   | LV   | ALI + AKI                           | AC alone                            | Alive    | +ve| +ve | +ve    |
| Le BB et al. (Clin Nucl Med. 2016) | P    | 44  | F   | LV   | Right CVA + systemic embolism (kidney and bones) | AC + CS + PP                      | U        | U  | U  | U      |
| Suzuki K et al. (Ann Thorac Surg. 2016) | P    | 45  | F   | LV   | Incidental                          | VATS + removal                      | Alive    | U  | U  | U      |
| Rayan Jo Rachwan et al. (Front Cardiiovase Med. 2017) | P    | 38  | M   | LV + BiAoV | TIA                                  | AC alone                           | Alive    | +ve| +ve | U      |
| Vergara-Uzcategui CE et al. (Arch Cardiol Mex. 2017) | P    | 45  | U   | LV + RV | CCF (DCMP)                          | AC alone                           | Alive U  | +ve| U    |
| Mohammed ayan et al. (PROC (Bayl Univ Med Cent). 2019) | P    | 23  | M   | LV   | CAD                                  | AC + AP                             | Alive U  | +ve| +ve | U      |
| Ariel González-Cordero et al. (SAGE Open Med Case Rep. 2019) | P    | 26  | M   | LV   | CAD - ACS                           | AC + PTCA + AP + Hydroxy- CQ + ICD  | Alive    | +ve| +ve | −ve    |
| Ravi Kiran et al. (Our report -2019) | P    | 36  | M   | LV   | CVA                                  | AC + CDT                           | Alive    | +ve| +ve | −ve    |

P=P-APLAS, S=Secondary-APLAS, M=Male, CC-T=Cardiac chamber with thrombus, F=Female, RA=Right atrium, LA=Left atrium, RV=Right ventricle, LV=Left ventricle. All 4=LA + RA + LV + RV, AWMI=Anterior wall myocardial infarction, CVA=Cerebrovascular accident, ALI=Acute limb ischemia, CHF=Congestive heart failure, FUO=Fever of unknown origin, SLE=Systemic lupus erythematosus, TIA=Transient ischemic attack, URI/PNA=Upper respiratory infection with pneumonia, Pos=Positive, Neg=Negative, CS=Corticosteroids, CQ=Chloroquine, IgG=Immunoglobulin G, IgM=Immunoglobulin M, S=Surgery to remove thrombus, AC=Anticoagulation, AP=Antiplatelets, U=Unknown, PP=Plasmapheresis, CVA=Cerebrovascular accident/stroke, CABG=Coronary artery bypass surgery, CDT=Catheter-directed thrombolysis, VATS=Video-assisted thoracoscopy