Mitral valve replacement for antiphospholipid syndrome complicated by cerebral infarction and mitral valve thrombosis: A case report

Shun Hiraga (s.hiraga.0730@gmail.com)
Nara Medical University School of Medicine
Yoshihiro Hayata
Nara Medical University School of Medicine
Tomoaki Hirose
Nara Medical University School of Medicine
Ryohei Fukuba
Nara Medical University School of Medicine
Junichi Takemura
Nara Medical University School of Medicine
Rei Tonomura
Nara Medical University School of Medicine
Sayaka Tamada
Nara Medical University School of Medicine
Kazuhiro Mitani
Nara Medical University School of Medicine
Masaya Hanakawa
Nara Medical University School of Medicine
Shinya Yokoyama
Nara Medical University School of Medicine

Case Report

Keywords: Antiphospholipid syndrome, cerebral infarction, mitral valve replacement

Posted Date: July 19th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1856025/v1

Abstract

Background: Antiphospholipid syndrome (APS) is an autoimmune disease that causes arteriovenous thrombosis and death. Valvular heart disease is one of its symptoms. Recurrent cerebral infarction caused by valvular heart disease is an indication for surgery; however, standard treatment, including perioperative anticoagulation, has not yet been established, and surgical mortality is high.

Case presentation: A 41-year-old man had a cerebral infarction six years ago and was positive for antiphospholipid antibodies and lupus anticoagulants. He was diagnosed with primary APS and treated with anticoagulation therapy with warfarin. He had another episode of cerebral infarction four months ago. Transesophageal echocardiography revealed a mass attached to the mitral valve. He underwent steroid therapy and was continued on anticoagulant therapy; however, the mass did not shrink, and surgery was performed. Intraoperative rapid histopathology showed that the mass was an old thrombus, and because of the high degree of mitral valve degeneration, we considered that regurgitation control by the valve platy was difficult. Mitral valve replacement was performed using an On-X mechanical valve. Intraoperatively, the activated clotting time was measured every 30 minutes, and no tendency for thrombus formation was observed. He was continued on warfarin therapy after the surgery and did not experience any recurrence of thromboembolism after two years of surgery.

Conclusions: We encountered a patient with APS, recurrent cerebral infarction, and mitral valve thrombus who underwent mitral valve replacement and continued postoperative anticoagulation therapy without recurrence of thromboembolism.

Background

Antiphospholipid syndrome (APS) is a disease characterized by the presence of autoantibodies called antiphospholipid antibodies in the blood, resulting in pregnancy complications, such as arteriovenous thrombosis at various sites and fetal mortality. Although infrequent, it is sometimes complicated by valvular disease, which is called as antiphospholipid antibody-associated symptom. Surgery for APS complicated with valvular disease is challenging because there are no clear guidelines for perioperative anticoagulation or whether valve replacement or valve plasty should be performed. We report a successful case of mitral valve replacement in a patient with primary APS complicated by cerebral infarction and a mitral thrombus.

Case Presentation

A 41-year-old man with a history of cerebral infarction was referred to our neurology department six years ago. A magnetic resonance imaging (MRI) of the head revealed multiple cerebral infarctions and microbleeds. Carotid ultrasonography and transesophageal echocardiography (TEE) revealed no embolic sources. Blood test results were positive for anticardiolipin antibodies and lupus anticoagulant, and cerebral infarction due to antiphospholipid antibody syndrome was suspected. Since the blood tests that

were conducted 12 weeks later were also positive for antiphospholipid antibodies and systemic lupus erythematosus (SLE) was negative, the patient was diagnosed with primary APS. He was administered warfarin to prevent thrombus formation. He had persistent faintness four months ago and was brought to the Department of Neurology in our hospital. An MRI scan of the head showed a point-like diffusion-weighted imaging high-signal and apparent diffusion coefficient low-signal lesion in the left parietal lobe (Fig. 1). He was diagnosed with acute cerebral infarction and hospitalized. TEE, performed to search for an embolic source, revealed a mass attached to the mitral valve, and heparin was administered. He was then administered warfarin with the goal of achieving a prothrombin time-international normalized ratio (PT-INR) of 3.0 to eliminate thrombus. However, TEE did not reveal any reduction in the mass. Cardiac MRI revealed a torn tendon cord, myxoma, and papillary fibroelastoma rather than a thrombus; therefore, immunosuppressive therapy (prednisolone 35 mg/day) was added in accordance with catastrophic APS or SLE complicated by APS. After anticoagulation therapy and one month of oral steroid therapy, the mass did not shrink, and the patient was referred to our department for surgical treatment of the mitral valve mass after completing steroid administration. Physical examination revealed no obvious sequelae of cerebral infarction. His vital signs were temperature of 36.2°C, blood pressure 114/74 mmHg, pulse 67/min and regular, and respiratory rate 12/min. Blood tests revealed a white blood cell count of 12400/μL, C-reactive protein 0.23 mg/dL, PT-INR 2.48, and activated partial thromboplastin time 38.0 s. D-dimer was 0.6 mg/dL which was not elevated. The brain natriuretic peptide level was 44.4 pg/mL which was mildly elevated. The elevated lupus anticoagulant and anticardiolipin antibody levels were 2.19 and > 120 U/mL, respectively. TEE revealed a 7.5 × 7.5-mm mass-like echo pattern on the P3 side of the posterior leaflet of the mitral valve, which moved in conjunction with the valve (Fig. 2). The mitral valve mass was considered to be a mitral valve thrombus formation due to APS, myxoma, or papillary fibroelastoma. We measured the activated clotting time (ACT) every 30 minutes intraoperatively. We decided to perform mitral valve replacement and mitral valve plasty based on the intraoperative findings. Steroid therapy was tapered off and discontinued three weeks prior to the surgery. Surgery was initiated under general anesthesia. The approach was performed through a median sternotomy. The pericardium was incised on the patient’s right side. A small amount of serous pericardial fluid was observed. An 18-French cannula was inserted into the ascending aorta and a 36-French cannula into the superior and inferior vena cava, and the pump was started. After the superior and inferior vena cava were secured with a tape and tourniquet and shifted to complete extracorporeal circulation, the right atrium was incised, and a retrograde myocardial protective catheter was inserted into the coronary sinus under direct vision. The right atrium was closed using 4 – 0 polypropylene. A cannula was inserted into the ascending aorta for antegrade myocardial protection. The ascending aorta was clamped, and cardiac arrest was induced. Left atrial approach was used to reach the left atrium. The posterior commissure of the mitral valve was clumped together owing to inflammation. A partial ulceration of the mitral valve was also observed. The mitral valve was partially resected and subjected to rapid pathological diagnosis, which indicated an old thrombus. The thickened area of the posterior commissure was excised. The excised valve was sutured with 5 – 0 polypropylene, but the mitral stenosis was such that a 20-mm diameter bougie could barely fit. The apex of the valve was also thickened, and considering the patient's age, we decided to perform a mitral valve replacement. The anterior leaflet was resected, and the posterior leaflet was preserved. A total

of 11 sutures with 2 – 0 Ethibond pledget was placed on the valve ring with an everted mattress suture and a 27-mm On-X (Artivion, Florida, United States) was sutured in an intra-annular position. After suturing the left atrium, the aortic clamp was removed. The pump was turned off, and TEE revealed no problems with the mobility of the prosthetic valve. The patient was extubated on the day of the surgery and weaned from ventilatory management. The drain was removed on the second postoperative day (POD), and the patient was treated with continuous heparin and oral warfarin therapy. Heparin administration was terminated on the 12th POD, and the patient was discharged on the 20th POD. After discharge from the hospital, he continued to take warfarin and had no recurrence of thromboembolism after two years of surgery.

Discussion And Conclusions

APS is an acquired autoimmune disease with a predilection to thrombogenesis. It causes arteriovenous thrombosis, pregnancy complications (fetal mortality and placental dysplasia), and thrombocytopenia, and some patients have symptoms related to SLE [1]. Patients with APS have antiphospholipid antibodies and are positive for lupus anticoagulant, anticardiolipin, and anti-β-glycoprotein antibodies. Antiphospholipid antibodies are pathogenic autoantibodies that induce inflammation [2]. In the revised Sapporo APS classification, APS is diagnosed when at least one clinical symptom of vascular thrombosis and pregnancy morbidity, and at least one positive laboratory test result of lupus anticoagulant, anticardiolipin antibody, and/or anti-β_2 glycoprotein-I antibody are present [3]. The annual risk of thrombus formation is < 4% in patients with SLE and < 1% in patients without SLE [4]; this patient had primary APS without SLE but had a history of cerebral infarction and thrombus on the mitral valve. Anticoagulation therapy is important in the treatment of thromboembolic events, which cause serious complications such as stroke, myocardial infarction, deep vein thrombosis, and pregnancy morbidity and death during the treatment of APS [1, 5]. In 2003, the consensus recommended low-dose aspirin administration in patients with no history of thrombosis and no vegetation or valve dysfunction on echocardiography and anticoagulation with a PT-INR of 2.0–3.0 for patients with valve vegetation or systemic embolic symptoms secondary to valvular disease [6]. In our case, steroids were administered preoperatively; however, regarding the efficacy of steroids, a report on rivaroxaban plus hydroxychloroquine, corticosteroids, and low-molecular-weight heparin, states a reduction in size by half at one week and complete disappearance at six months [7]. Autopsy studies have reported decreased non-bacterial thrombotic endocarditis in steroid-treated patients [8]. Steroids may promote the healing of valve-attached vegetation and prevent scarring and valve dysfunction [9]. In our case, we administered steroids preoperatively, tapered them off subsequently, and then performed the surgery.

APS occurs in 5% of the general population and 30% of SLE patients with valvular disease as one of the several clinical manifestations [1]. Valvular disease is present in 14.3% of patients with APS and is characterized by unusual nodules and vegetation and moderate-to-severe valve dysfunction in the absence of rheumatic fever or infective endocarditis [5]. Valvular disease of the left heart system, especially mitral valve failure, is common in APS as is the presence of a mass in the mitral valve in our

case. Valvular disease in APS is characterized by localized thickening of the valve (> 3 mm), including the proximal or middle portion of the leaflet and irregular nodules in the atrial portion of the mitral valve [10]. APS-associated valve degeneration is non-specific and characterized by fibrosis, calcification, vascularization, and thrombus formation in the endocardium on the valve surface and in capillaries [11]. The immune complexes are considered to damage the endocardium and cause valve fibrosis [1, 5]. The risk of stroke is ten times higher in patients with valvular disease due to APS, and valvular damage is usually moderate, with an 8% chance of progression to valvular disease. In a retrograde study of 284 patients with APS, 159 diagnosed with primary APS showed an association between valvular heart disease and central nervous system symptoms, such as epilepsy, migraine, cerebrovascular accidents, and transient ischemic attack [12]. In our case, recurrent cerebral infarction and a mitral valve mass formation probably caused by APS were also observed. In addition to mitral thrombus formation due to APS, intraoperative findings suggested that the mitral valve was degenerating, and mitral valve replacement was performed.

Surgery is considered in cases of severe valve dysfunction or recurrent thromboembolism, despite continued anticoagulation therapy. Severe valve regurgitation requiring surgery is seen in 4–6% of APS cases complicated by valvular heart disease [10]. A retrospective study of 32 patients with APS who underwent valve replacement reported a mortality rate of 12.5%; however, in the same study, any event was reported in the half of patients [13]. A previous study reported mortality rates of > 20% [5]. Regarding the choice of valves, biological valves are generally superior to mechanical valves in terms of antithrombotic properties [14]. However, some reports recommend the use of mechanical valves since many patients are young and require anticoagulant therapy to prevent thromboembolism [15]. Additionally, there is a possible risk of an immune response to the bioprosthetic valve. One study found no difference between valve types [13]. Since the patient was relatively young and had already been anticoagulated with warfarin, a mechanical valve was selected as the prosthetic valve. Two years have passed since surgery and there is no evidence of valve dysfunction. Currently, the long-term results of different prosthetic valves after valve replacement for APS are unclear, and further findings are awaited. There is a report on the use of On-X, which has excellent antithrombotic properties, in revision surgery for patients with trapped prosthetic valves owing to thrombus formation caused by APS [16]. The five-year thromboembolic-free rate for mitral valve replacement with On-X has been reported to be 97.7 ± 0.9% under INR control of 2.0–3.0 [17]. In our study, no valve dysfunction or thromboembolic events were observed after two years of surgery using On-X. There is no clear protocol for anticoagulation during intraoperative cardiopulmonary bypass, with only six case reports describing perioperative anticoagulation [18–21]. None of the reports showed intraoperative complications due to inadequate anticoagulant therapy; the anticoagulant used was heparin and ACT was used for monitoring. ACT was measured every 30 s in our case, and no intraoperative thromboembolic events were observed. There are few reports on anticoagulation therapy during open heart surgery with cardiopulmonary bypass in patients with APS, and more knowledge needs to be accumulated. We report a patient with APS complicated with valvular disease who underwent surgery under cardiopulmonary bypass with heparin and continued postoperative anticoagulation with oral warfarin without thromboembolic events. Further

case studies are needed to determine the appropriateness of intraoperative and postoperative anticoagulation for patients with APS complicated with valvular disease.

Abbreviations

APS
antiphospholipid syndrome
ACT
activated clotting time
POD
postoperative day
PT-INR
prothrombin time-international normalized ratio
MRI
magnetic resonance imaging
SLE
systemic lupus erythematosus
TEE
transesophageal echocardiography

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: Written informed consent was obtained from the patients' parents and participants for the publication of this case report and any accompanying images.

Availability of data and materials: Not applicable

Competing interests: The authors declare that they have no competing interests.

Funding: Not applicable

Authors' contributions

SH is responsible for the design of this study; TH, YH, and SY collected the detailed information; RF and JT cooperated in the revision of the manuscript; all authors read and approved the final manuscript.

Acknowledgments

The patient signed an informed consent form for this case report. We thank the patient and doctors who participated in this study for their cooperation.

References

1. Cervera R. Antiphospholipid syndrome. Thromb Res. 2017;151;Suppl 1:S43-7.
2. Shoenfeld Y, Blank M, Cervera R, Font J, Raschi E, Meroni PL. Infectious origin of the antiphospholipid syndrome. Ann Rheum Dis. 2006;65:2–6.
3. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost. 2006;4:295–306.
4. Barbhaiya M, Erkan D. Primary thrombosis prophylaxis in antiphospholipid antibody-positive patients: where do we stand? Curr Rheumatol Rep. 2011;13:59–69.
5. Colli A, Mestres CA, Espinosa G, Plasín MA, Pomar JL, Font J, et al. Heart valve surgery in patients with the antiphospholipid syndrome: analysis of a series of nine cases. Eur J Cardiothorac Surg. 2010;37:154–8.
6. Lockshin M, Tenedios F, Petri M, McCarty G, Forastiero R, Krilis S, et al. Cardiac disease in the antiphospholipid syndrome: recommendations for treatment. Committee consensus report. Committee consensus report. Lupus. 2003;12:518–23.
7. Ruiz-Irastorza G, Khamashta MA. The treatment of antiphospholipid syndrome: A harmonic contrast. Best Pract Res Clin Rheumatol. 2007;21:1079–92.
8. Zuily S, Huttin O, Mohamed S, Marie PY, Selton-Suty C, Wahl D. Valvular heart disease in antiphospholipid syndrome. Curr Rheumatol Rep. 2013;15:320.
9. Brenner B, Blumenfeld Z, Markiewicz W, Reisner SA. Cardiac involvement in patients with primary antiphospholipid syndrome. J Am Coll Cardiol. 1991;18:931–6.
10. Cervera R, Tektonidou MG, Espinosa G, Cabral AR, González EB, Erkan D, et al. Task force on catastrophic antiphospholipid syndrome (APS) and Non-criteria APS Manifestations (I): catastrophic APS, APS nephropathy and heart valve lesions. Lupus. 2011;20:165–73.
11. Roldan CA, Gelgand EA, Qualls CR, Sibbitt WL. Valvular heart disease as a cause of cerebrovascular disease in patients with systemic lupus erythematosus. Am J Cardiol. 2005;95:1441–47.
12. Erdogan D, Goren MT, Diz-Kucukkaya R, Inanc M. Assessment of cardiac structure and left atrial appendage functions in primary antiphospholipid syndrome: a transesophageal echocardiographic study. Stroke. 2005;36:592–96.
13. Gorki H, Malinovski V, Stanbridge RDL. The antiphospholipid syndrome and heart valve surgery. Eur J Cardiothorac Surg. 2008;33:168–81.
14. Erdozain JG, Ruiz-Irastorza G, Segura MI, Amigo MC, Espinosa G, Pomar JL, et al. Cardiac valve replacement in patients with antiphospholipid syndrome. Arthritis Care Res. 2012;64:1256–60.
15. Berkun Y, Elami A, Meir K, Mevorach D, Naparstek Y. Increased morbidity and mortality in patients with antiphospholipid syndrome undergoing valve replacement surgery. J Thorac Cardiovasc Surg. 2004;127:414–20.

16. Koga A, Okamoto K, Tazume H, Fukui T. Use of an on-x prosthetic valve in a 42-year old female with antiphospholipid syndrome. Heart Surg Forum. 2018;31;21:E026-7.
17. Karkar AM, Castresana MR, Odo N, Agarwal S. Anticoagulation dilemma in a high-risk patient with On-X valves. Ann Card Anaesth. 2015;18:257–60.
18. Sheikh F, Lechowicz A, Setlur R, Rauch A, Dunn H. Recognition and management of patients with antiphospholipid antibody syndrome undergoing cardiac surgery. J Cardiothorac Vasc Anesth. 1997;11:764–6.
19. Ducart AR, Collard EL, Osselaer JC, Broka SM, Eucher PM, Joucken KL. Management of anticoagulation during cardiopulmonary bypass in a patient with a circulating lupus anticoagulant. J Cardiothorac Vasc Anesth. 1997;11:878–9.
20. Hogan WJ, McBane RD, Santrach PJ, Plumhoff EA, Oliver WC Jr, Schaff HV, et al. Antiphospholipid syndrome and perioperative hemostatic management of cardiac valvular surgery. Mayo Clin Proc. 2000;75:971-6.
21. East CJ, Clements F, Mathew J, Slaughter TF. Antiphospholipid syndrome and cardiac surgery: Management of anticoagulation in two patients. Anesth Analg.2000;90:1098–101.

Figures

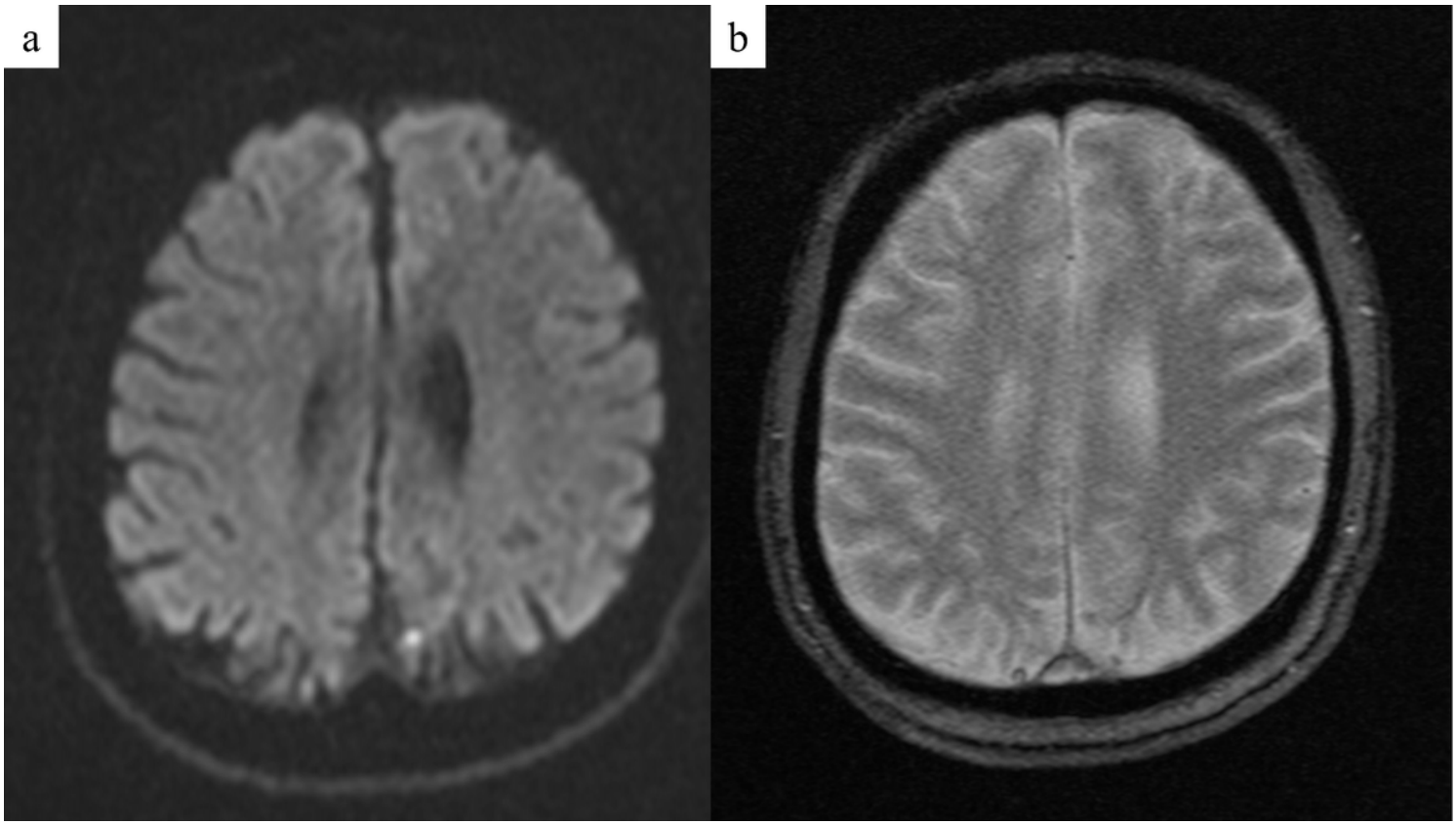

Figure 1

Magnetic resonance imaging revealed a high-signal point lesion in the left occipital lobe on diffusion weighted image (a) and a low-signal lesion on apparent diffusion coefficient (b).

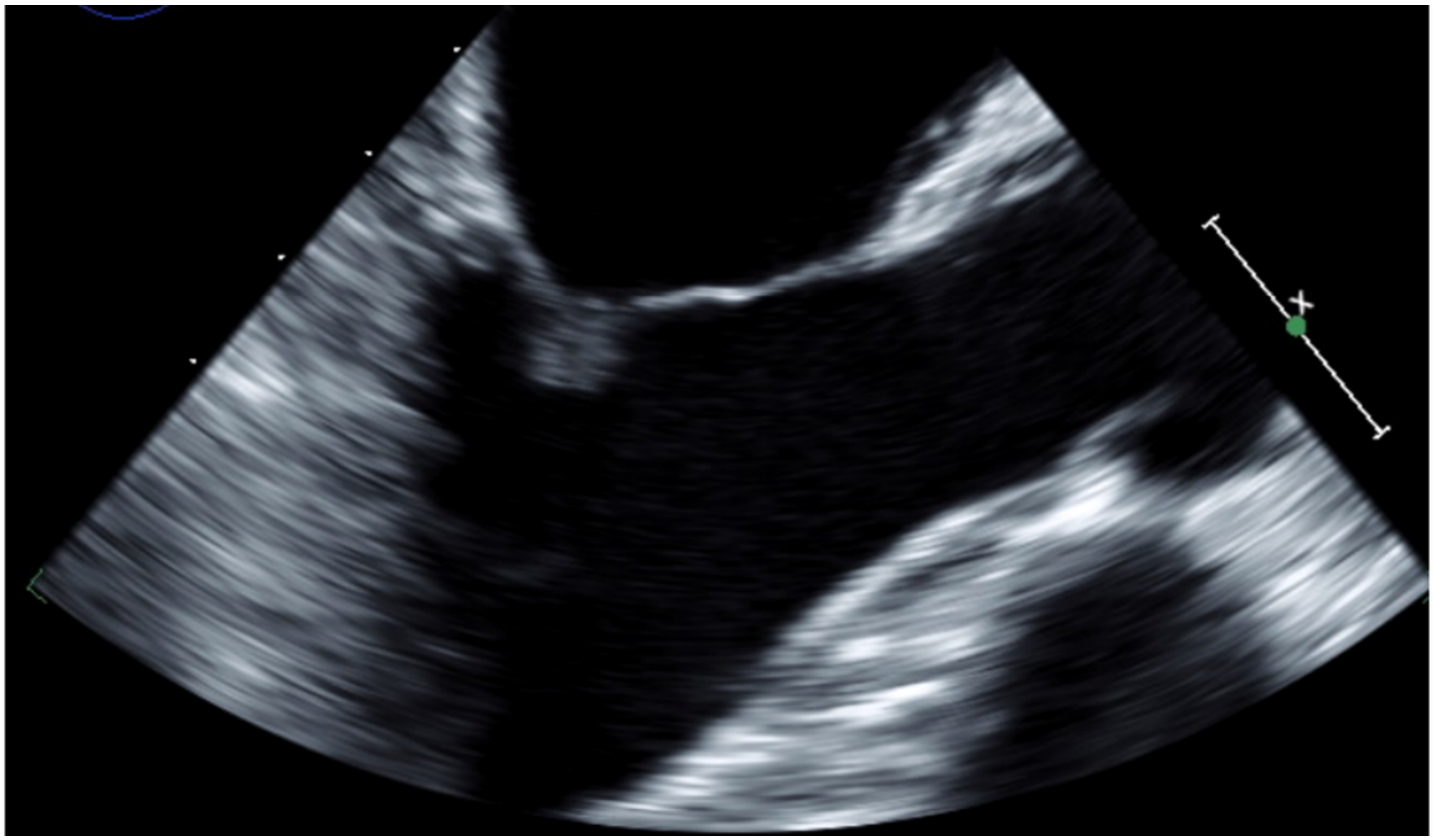

Figure 2

Transesophageal echocardiography revealed a 7.5-mm diameter mass-like echo pattern moving in conjunction with the posterior leaflet of the mitral valve.