ESC European Society of Cardiology
European Heart Journal - Case Reports
doi:10.1093/ehjcr/ytab066

CASE SERIES
Cardiac imaging

Submitral aneurysm of varied aetiologies: a case series

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Received 15 July 2020; first decision 7 September 2020; accepted 27 January 2021

Background Submitral aneurysm is a rare disease initially described in the African population. It is usually considered congenital in origin, due to a defect in the posterior portion of the mitral annulus. However, it can be seen in other diseases like ischaemic heart disease, rheumatic heart disease, infective endocarditis, tuberculosis, and syphilis.

Case presentation Case 1 was a 29-year-old female, hypertensive undergoing maintenance haemodialysis for chronic kidney disease and on anti-tubercular therapy. She was found to have a large submitral aneurysm with severe mitral regurgitation, moderate left ventricular dysfunction, and pericardial effusion on echocardiogram. Case 2 was a 58-year-old gentleman presented with inferior wall ST-elevation myocardial infarction and was thrombolyzed with streptokinase for the same. Echocardiogram done 6 months later for evaluation of dyspnoea showed a large inferobasal aneurysm. Case 3 was a 56-year-old hypertensive presented with dyspnoea on exertion and echocardiogram showed a large posterolateral region with transmural late gadolinium enhancement. Case 4 was a 13-year-old boy presented with fever and cerebrovascular accident. Echocardiogram revealed vegetation in the mitral valve and a small submitral aneurysm with vegetation inside it.

Discussion Submitral aneurysm is usually considered congenital in origin. However, it can be due to ischaemic heart disease, rheumatic heart disease, Takayasu arteritis, and tuberculosis. Top dimensional echocardiogram is the investigation of choice. Cardiac magentic resonance imaging helps in identifying the underlying aetiology and delineating the surrounding structures.

Keywords Submitral aneurysms • Tuberculosis • Coronary artery disease • Infective endocarditis • Case series

Learning points

- Submitral aneurysm, though often congenital in origin, can also present due to various other aetiologies, such as coronary artery disease, tuberculosis, and infective endocarditis.
- The most common clinical presentation of submitral aneurysm is with heart failure, which is usually due to mitral regurgitation, though can be due to left ventricular dysfunction in cases caused by coronary artery disease.
- Multimodality imaging including cardiac magnetic resonance, computed tomography, and echocardiogram helps in identifying the aetiology of submitral aneurysm.

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Handling Editor: Andre Dias
Peer-reviewers: Alberto Bouzas-Mosquera; Richard Alexander Brown; Luca Arcari
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Introduction

Submitral aneurysm is a rare cardiac disease of yet unclear aetiology.[1] After initial description in indigenous African populations it is now being frequently reported in other regions including India. It is usually congenital in origin. It can also be seen due to other diseases like ischaemic heart disease, rheumatic heart disease, infective endocarditis, tuberculosis, etc.[2,3] Patients usually present with symptoms of heart failure due to mitral regurgitation (MR), thrombo-embolic phenomena, ventricular tachycardia, or ventricular rupture.[4,5] We describe four cases of submitral aneurysm of different aetiologies and present a brief review of the literature of this rare condition.

Case presentation

Case 1

A 29-year-old female with a medical history of hypertension, end-stage kidney disease undergoing maintenance haemodialysis was referred to us for complaints of dyspnoea on exertion for the past 3 months and pleuritic chest pain for 10 days. Clinical examination showed a pulse rate (PR) of 84/min, blood pressure (BP) of 114/78 mm of Hg, and a pericardial rub on auscultation. Hypertension was first detected during her 2nd pregnancy which was complicated by pre-eclampsia. She also developed end-stage kidney disease following 2nd pregnancy and was receiving renal replacement therapy since then. She was also on empirical anti-tubercular therapy (ATT),

Timeline

Case	Age	Presenting complaints and medical history	Investigations	Management	Outcome and follow-up
1	29	Medical history Pre-eclampsia, chronic kidney disease on maintenance haemodialysis Evaluated for pyrexia of unknown origin Presenting complaints Dyspnoea for 3 months Pleuritic chest pain for 10 days	Echocardiogram—Initially submitral aneurysm (SA), Ejection fraction (EF) 35 %, moderate mitral regurgitation (MR). Later pericardial tamponade. Computed tomography (CT) coronary angiogram—No obstructive coronary artery disease. Cardiac magnetic resonance (CMR) imaging—SA	Anti-tubercular therapy for pyrexia of unknown origin. Pericardiocentesis for pericardial tamponade. Antibiotics for purulent pericardial fluid. Beta-blockers for heart failure.	Mortality at home due to sudden cardiac death
2	56	Medical history ST elevation (STE) inferior wall myocardial infarction. Presenting complaints Dyspnoea on exertion.	Echocardiogram—SA.	Thrombolysis and angioplasty to right coronary artery Dual antiplatelets and heart failure therapy	Stable at 12 months follow-up.
3	58	Medical history Diabetes, hypertension, smoker. Presenting complaints Dyspnoea on exertion.	Echocardiogram— EF 30 %, SA with thrombus, moderate MR. CMR—Transmural late gadolinium enhancement in inferoseptal and apical regions, SA.	Aspirin, warfarin and heart failure therapy	Stable at 6 months follow-up.
4	13	Medical history Nothing significant Presenting complaints Fever, hemiparesis, sudden loss of vision.	Echocardiogram—vegetation on mitral valve, severe MR CMR—Submitral aneurysm with vegetation Brain magnetic resonance imaging—Infarct in posterior and middle cerebral artery territory. Blood culture—*Staphylococcus aureus* (methicillin sensitive)	Intravenous antibiotics.	Vision 6/6 Power 4+/5 Awaiting mitral valve replacement.

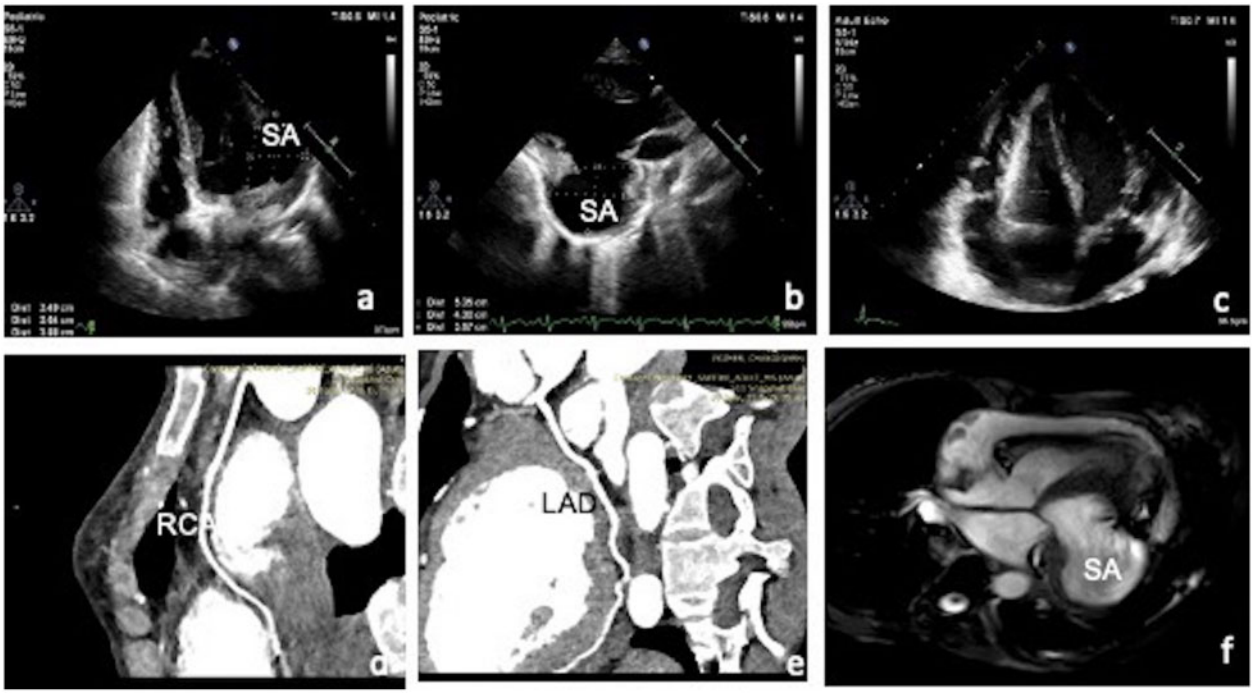
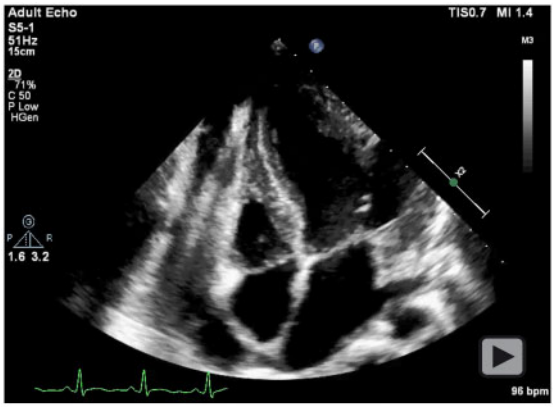


Figure 1 Echocardiogram showing large submitral aneurysm (SA) measuring approximately (*A*) in A4C view 3.8 cm × 3.6 cm with a neck diameter of 3.5 cm. (*B*) in PLAX view 5 cm × 4 cm with a wide neck of size 3.67 cm. (*C*) Echocardiogram showing pericardial effusion with multiple thick strands and organized fluid at some places. (*D* and *E*) Computed tomography coronary angiogram showing no obstructive lesions in right coronary artery (*D*) and left anterior descending artery (*E*). (*F*) Cardiac magnetic resonance (CMR) bright blood image [frame from cine steady state free precession (SSFP) sequence] in 4Ch-view showing the large submitral aneurysm.



Video 1 Echocardiogram in apical four-chamber view showing left ventricular submitral aneurysm with severe left ventricular dysfunction. Note also made of pericardial effusion.

after evaluation for pyrexia of unknown origin and mediastinal lymphadenopathy with necrotic core on contrast-enhanced computed tomography (CT). As, tuberculosis is an endemic disease in India, in this patient with pyrexia of unknown origin (i.e. after unsuccessful reasonable evaluation for aetiology of pyrexia) we have started her on anti-tubercular therapy. In this case, for aetiology of tuberculosis, induced sputum for acid-fast bacilli (AFB) was done thrice, sputum for GeneXpert, fine needle aspiration cytology of lymph nodes with Ziehl-Neelsen (ZN) staining for AFB were done. All turned out to be negative for tuberculosis. Mantoux test (intradermal purified protein derivative injection) was also performed, which revealed 14 mm induration at 48 h but its diagnostic accuracy is considered modest in endemic areas.

Her fever responded to the ATT. Transthoracic echocardiogram revealed a large submitral aneurysm, moderate MR, moderate left ventricular dysfunction due to global hypokinesia (*Figure 1A–C*) (*Video 1*). Cardiac magnetic resonance (CMR) imaging confirmed that the aneurysm is a true aneurysm (*Figure 1F*). Her CT coronary angiography showed no obstructive lesions (*Figure 1D and E*). She was started on guideline-directed therapy for her heart failure. During follow-up, her dyspnoea worsened along with fever and pleuritic type of chest pain. Repeat echocardiogram showed large pericardial effusion with tamponade physiology. Pericardiocentesis revealed foul-smelling purulent fluid. Fluid analysis revealed lymphocyte rich cellular infiltrate, high protein (4.5 g/dL, normal levels < 3 g/dL), low sugar (38 mg/dL, normal levels 60–80 mg/dL), and high adenosine deaminase (ADA) of 80 IU/L (ADA levels > 40 u/L suggestive of

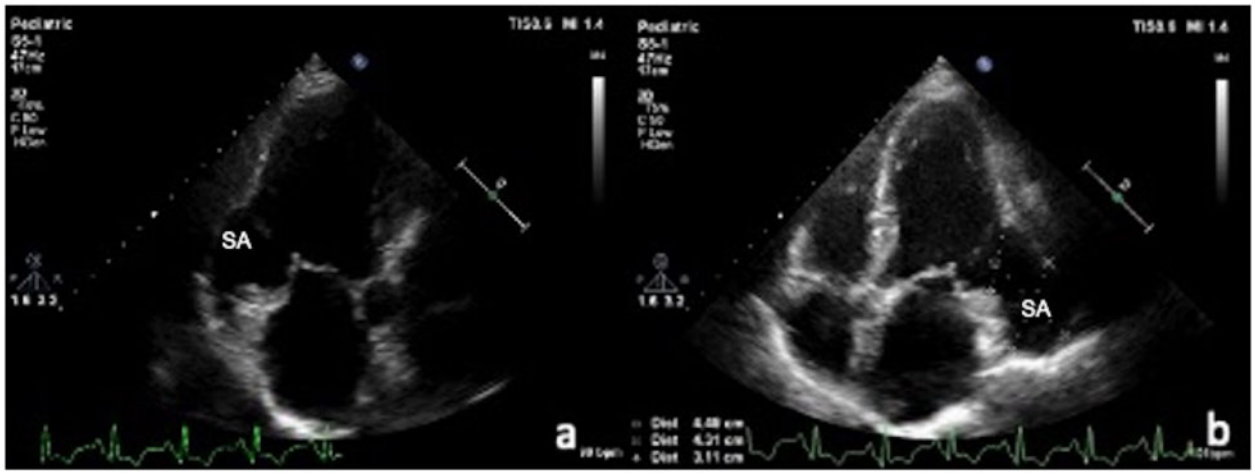
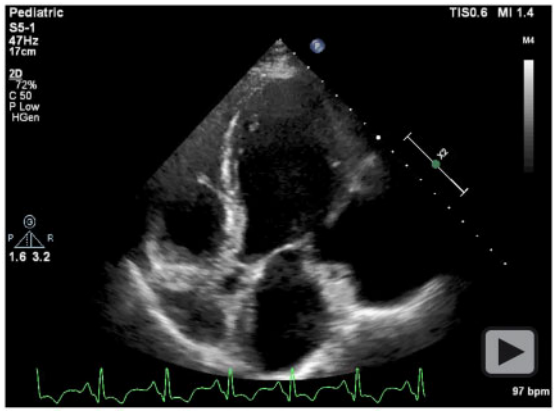


Figure 2 (*A* and *B*) Echocardiogram showing large submitral aneurysm (SA) (4.5 cm × 4.3 cm) with a wide neck (3.1 cm) underneath the posterior mitral leaflet with thrombus.



Video 2 Echocardiogram in apical four-chamber view showing left ventricular submitral aneurysm with moderate left ventricular systolic dysfunction.

tuberculosis pericarditis). Cartridge-based nucleic acid amplification test (CB-NAAT) for Mycobacterium tuberculosis was negative. She was managed with IV antibiotics with the continuation of anti-tubercular therapy. Subsequently, she defervesced with no further accumulation of fluid. She was discharged after 2 weeks of IV antibiotics, on anti-tubercular therapy, beta-blockers, and was advised aneurysmal repair surgery and a pericardial window. She succumbed at home, 18 days after discharge due to sudden cardiac arrest.

Case 2

A 58-year-old male smoker, with no significant medical history presented to the emergency department with 12 h of chest pain. His electrocardiogram (ECG) showed ST-elevation in inferior leads. His echocardiogram revealed hypokinesia in the inferobasal region and no MR. He was thrombolyzed at a local hospital with streptokinase. He underwent angioplasty of the right coronary artery. He was discharged on dual antiplatelets, statins, angiotensin-converting enzyme inhibitors (ACEI), and beta-blockers. Five months later he presented with dyspnoea on exertion. Clinical examination showed PR of 76/min, BP of 124/60 mmHg, and no crepts or S_3 on auscultation. Electrocardiogram showed q waves in the inferior leads and normal R wave progression. Echocardiogram revealed a large submitral aneurysm with a wide neck, moderate left ventricular dysfunction, and no thrombus or MR (*Figure 2A,B*) (*Video 2*). He was managed with dual antiplatelets, diuretics, beta-blockers, ACE inhibitors, and mineralocorticoid receptor antagonists (MRA). With the above therapy, his dyspnoea resolved and currently is stable after 12 months follow-up.

Case 3

A 56-year-old gentleman with a medical history of diabetes, hypertension, and smoking presented to cardiology out-patient services with dyspnoea on exertion for the past 3 months. Clinical examination showed PR of 80/min, BP of 120/84 mm, and no crepts or S_3 on auscultation. His ECG revealed left ventricular hypertrophy with a strain pattern. Echocardiogram revealed a large aneurysm of size 7 mm × 8 mm with a wide neck and partially filled with thrombus in the posterolateral region of the left ventricle with moderate MR and an ejection fraction of 30% (*Figure 3A,B*) (*Video 3*). CMR confirmed a large pseudoaneurysm of size 11 cm × 6 cm with thrombosis and a wide neck (3.7 cm) at the basal region near the mitral valve (*Figure 3C,D*). Myocardial infarction was the likely cause of submitral aneurysm in this case considering the transmural LGE (late gadolinium enhancement) at the inferoseptal region in CMR. He was started on aspirin, warfarin, atorvastatin, diuretics, beta-blockers, ACEI, and

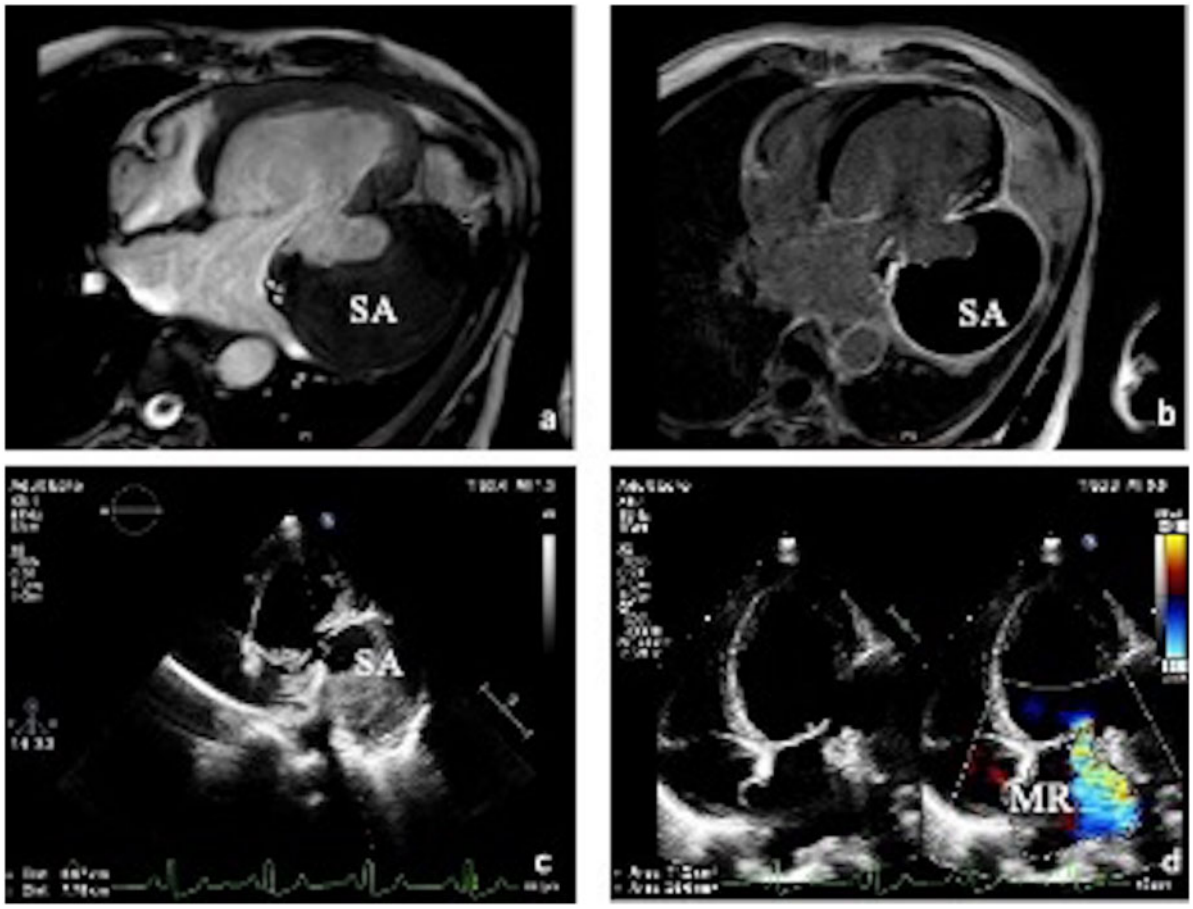
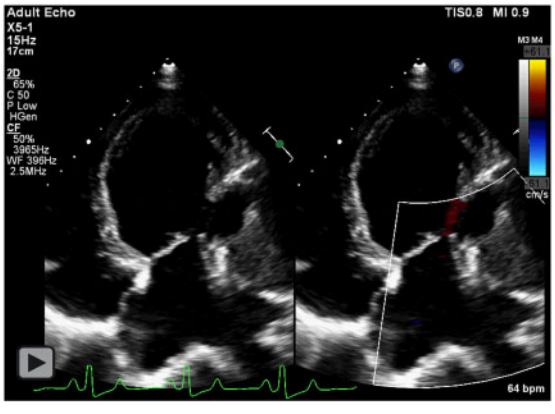


Figure 3 (*A*) Cardiac magnetic resonance bright blood image (frame from Cine SSFP sequence) in four-chamber view showing large aneurysm arising from the basal inferolateral wall of LV with large eccentric hypointense thrombus. (*B*) Corresponding late gadolinium-enhanced image showing enhancement of the thinned out aneurysmal wall with large internal non-enhancing thrombus. (*C*) Echocardiogram showing large submitral aneurysm (SA) (7.7 cm × 6.6 cm) with wide neck and organized thrombus. (*D*) Colour Doppler across mitral valve (MV) showing moderate MR.

MRA. With the above management, his dyspnoea resolved and he is doing well at 6-month follow-up visit.

Case 4

A 13-year-old boy presented with a high-grade fever for 1-month, loss of vision, and weakness of the right upper and lower limb for 1 week. On examination, he had a high-frequency pansystolic murmur at the apex and weakness of the right upper and lower limbs (4/5) with brisk deep tendon reflexes. Brain magnetic resonance imaging revealed a large infarct in the posterior and middle cerebral artery territory. Echocardiogram revealed two vegetations on the mitral valve (MV) with severe MR (*Figure 1A*) (Supplementary material online, *Video S1*). Transoesophageal echocardiogram confirmed the same (*Figure 1B*). CMR revealed a small submitral aneurysm with vegetation attached to aneurysmal wall (*Figure 1C,D*). His blood culture revealed the growth of *Staphylococcus aureus* (methicillin-sensitive). He was managed with intravenous antibiotics for 6 weeks. Blood samples from the central venous catheter showed candidial growth. Antifungal was added for the same. With the above



Video 3 Echocardiogram in apical four-chamber view showing left ventricular submitral aneurysm with severe left ventricular systolic dysfunction. Colour Doppler showing moderate to severe mitral regurgitation.

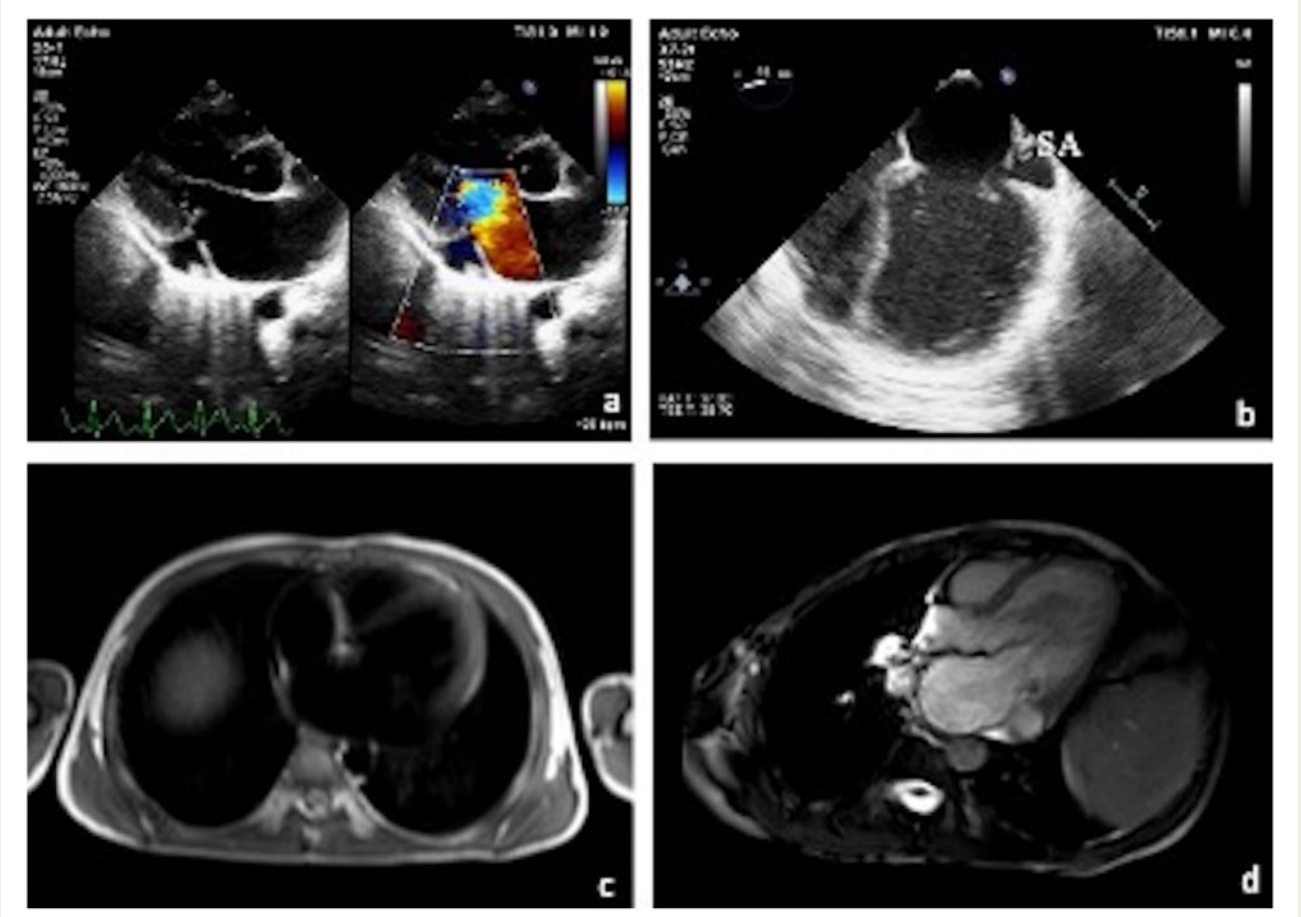


Figure 4 (*A*) Echocardiogram showing submitral aneurysm (SA) under the posterior mitral leaflet communicating with the left ventricle with vegetation inside the aneurysm. Colour Doppler showing blood in and out of the aneurysm. (*B*) Transoesophageal echocardiogram (TOE) showing vegetation over the posterior mitral leaflet and also in the aneurysm. (*C*) Cardiac magnetic resonance black blood image [frame from half-Fourier single-shot turbo spin-echo (HASTE) axial sequence]. (*D*) Bright blood image (frame from SSFP sequence) showing small submitral aneurysm.

treatment, he became afebrile. His vision improved to 6/6 and power to 4+/5. Currently, he is awaiting MV replacement.

Discussion

Submitral aneurysm or posterobasal aneurysm is a rare condition first described by Abrahams *et al.*[1] and is usually seen in indigenous African populations. Most of the available literature is from Africa and India. They are considered to be congenital in origin; however, multiple associations with various inflammatory and infective diseases like tuberculosis, rheumatic heart disease, endocarditis, ischaemic heart disease, syphilis, and Takayasu arteritis were proposed.[2,3] A possibility of genetic aetiology was also considered due to racial predilection, with frequent occurrence in Africans. They were also described in a foetal echocardiogram supporting congenital origin.[6]

The pathogenesis is not clear and various proposed mechanisms include false aneurysm occurring due to the defect or weakness in the posterior part of the mitral fibrous annulus, or disjunction between the left ventricular (LV) and left atrial (LA) musculature.[7] The presence of potentially weak membranous curtain extending along the various lengths of the posterior portion of the annulus, or congenitally weak but not yet aneurysmal annulus predisposes to aneurysm formation. Submitral curtain when compounded by repeated stress from increased left ventricular pressures as in Takayasu arteritis[2], chronic inflammation as in tuberculosis,[8–10] rheumatic heart disease, and infective endocarditis leads to submitral aneurysm formation. Depending on the extent of involvement of the posterior portion of the annulus and the number of necks, Du Toit *et al.*[11] classified them as type 1 containing a single neck type 2 as containing multiple necks, and type 3 as involving the entire posterior portion of the annulus.

Coronary artery disease-related aneurysm usually occurs following transmural infarction and are predominantly apical. Although rare, the occurrence of submitral aneurysm due to infarction has been reported in the past and is the likely cause in two of our cases.[4]

Similar to our case no 1, Baruah *et al.*[9] defined a case of submitral aneurysm in a patient with tuberculosis, pericardial effusion with tamponade, and hypotension who succumbed after surgery.

Submitral aneurysms can have variable presentations. The usual presentation is dyspnoea caused by MR secondary to imperfect coaptation of the leaflets. It is usually preceded by a long asymptomatic period. They can also present with life-threatening ventricular arrhythmias, thromboembolic phenomena, compression of a coronary artery, heart failure, rupture leading to death.[4,5] Thrombo embolism due to submitral aneurysm is rare owing to the narrow neck of the aneurysm with very few cases described.[12]

In our cases related to coronary artery disease, only one case presented as an acute coronary syndrome (ACS), the other case had no angina suggesting that aneurysm formation can occur even without angina or ACS. The predominant complaint in patients of ischaemic heart disease-related aneurysm is dyspnoea.

Diagnosis is usually made by transthoracic echocardiography. It helps in identifying the size of the aneurysm, location, extent, size of the neck, presence of thrombus, the severity of mitral regurgitation, and ventricular function. CMR and CT further help in delineating the length of the neck and presence of thrombus, relationship with the surrounding structures, and helps in planning surgical management. Coronary CT angiogram or invasive angiogram may be helpful in selected cases when ischaemic aetiology is suspected.

Treatment includes initial stabilization of heart failure with medical therapy followed by surgical repair. Surgical treatment of the aneurysm includes extracardiac or intracardiac (transatrial) repair with pericardial patch placement and mitral valve repair or replacement.[11] Intracardiac approach offers better visualization of MV. Other therapeutic interventions like EPS—RFA for intractable arrhythmias, anticoagulation for thrombo-embolic phenomena are needed. Surgical outcomes are poor.[11]

In this series, we have described four cases of submitral aneurysm with three different aetiologies. Our series is unique in that it presents submitral aneurysm of varied aetiology, although we could not prove tuberculosis and infective endocarditis as the reason for aneurysm formation. The causal relationship has been well established in cases of ischaemic heart disease-related aneurysm in two cases (Cases 2 and 3) and it is not clear in Cases 1 and 4. However, the presence of tubercular effusion and the mediastinal lymphadenopathy favours tuberculosis as the possible aetiology in Case 1. In one of the cases, the aneurysm was not present during the hospital admission for ACS but was detected 5 months later during evaluation for complaint of dyspnoea. This can be explained by the fact that 50% of the aneurysms occurs within 48 h after the ACS and the rest within 2 weeks. Post ACS aneurysms predominantly (80%) occur in the anterior wall and/or apex. If the LV aneurysm is 20% of LV circumference then congestive heart failure may occur.[13]

Submitral aneurysm is an uncommon disorder, with varied aetiologies apart from the congenital origin. Management is usually surgical, with medical management focused on underlying aetiology.

Lead author biography

Krishna Prasad is pursuing DM Cardiology (Fellowship) at PGIMER, India an institute of national importance. He has many national and international publications as a lead author. He has interest in complex coronaries and structural intervention. After the fellowship, he will pursue advanced fellowships in structural heart disease.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from all the patients and father of the case four patient in line with COPE guidance.

Conflict of interest: None declared.

Funding: None declared.

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