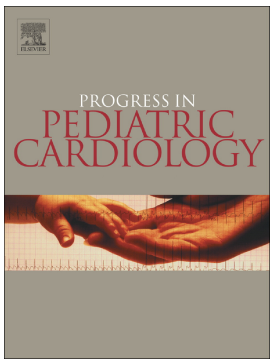

Anomalous origin of left coronary artery from pulmonary artery (ALCAPA) presenting as a murmur

Emily DiLillo, Eva Nunlist

PII: S1058-9813(20)30130-2

DOI: https://doi.org/10.1016/j.ppedcard.2020.101261

Reference: PPC 101261

To appear in: *Progress in Pediatric Cardiology*

Received date: 14 May 2020

Revised date: 15 June 2020

Accepted date: 17 June 2020

Please cite this article as: E. DiLillo and E. Nunlist, Anomalous origin of left coronary artery from pulmonary artery (ALCAPA) presenting as a murmur, *Progress in Pediatric Cardiology* (2020), https://doi.org/10.1016/j.ppedcard.2020.101261

Progress in Pediatric Cardiology

(Nemours ECHO Supplement)

Title: Anomalous Origin of Left Coronary Artery from Pulmonary Artery (ALCAPA) Presenting as a Murmur

Emily DiLillo[1], Eva Nunlist [1,2]

[1]Nemours Cardiac Center, Nemours Children's Hospital, Orlando, FL

[2] Department of Pediatrics, University of Central Florida College of Medicine, Orlando, FL

Corresponding Author:

Eva Nunlist DO FAAP FACC

Nemours Cardiac Center

6535 Nemours Parkway

Orlando FL 32827

Office: 407-650-7470

Email: Eva.Nunlist@nemours.org

Abstract:

As clinicians and sonographers, we frequently encounter referrals for heart murmurs. Fortunately, for most patients, their murmurs are innocent or benign in nature. Anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) is an incredibly rare but serious congenital heart disease that may lead to progressive myocardial ischemia, mitral regurgitation due to papillary muscle necrosis, left ventricular dysfunction, dilated cardiomyopathy, ventricular arrhythmias, and even sudden cardiac arrest. The anomalous coronary artery may be diagnosed by echocardiography but may require additional imaging to confirm the diagnosis prior to surgical repair. Computed tomography angiography and cardiac magnetic resonance imaging (MRI) may both aid in making a definitive diagnosis of ALCAPA. However, the gold standard of diagnosis has traditionally been through invasive angiography. ALCAPA is a surgical emergency and if left untreated may result in significant morbidity and mortality. In this report, we review a case of ALCAPA, presenting as a heart murmur to a sub-specialty clinic appointment and discuss the role echocardiography played in making the initial diagnosis.

Keywords:

anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA); echocardiography; computed tomography angiography; magnetic resonance angiography; murmur; mitral regurgitation

Case:

A seven-week-old male infant born at 38 weeks gestation with an unremarkable prenatal course was noted to have polydactyly in the newborn period. During his pediatrician's exam, he was also heard to have a heart murmur. He was subsequently referred to plastic surgery for evaluation of the polydactyly and to cardiology for the heart murmur. His weight was at the 5th percentile and height at the 50th percentile for age. He was scheduled to see plastic surgery prior to cardiology. At the time of his plastic surgery visit, his mother reported a five-day history of nasal congestion and two-day history of progressively worsening respiratory distress. At his initial exam his vitals were: weight 4.49 kilograms, pulse 195 beats/minute, blood pressure 68/52 mmHg, respiratory rate 43 breaths/minute, temperature 35.8 degrees Celsius and pulse oximetry 95% on room air. He was noted to be in respiratory distress with nasal flaring and intercostal retractions with a harsh grade 3/6 holosystolic murmur at the apex. He was immediately brought to the emergency room for further evaluation. Workup included a chest x-ray that demonstrated cardiomegaly and atelectasis at the lung bases. An electrocardiogram showed sinus tachycardia at a rate of 196 bpm, rightward axis, Q waves in leads I, aVL, V5, and V6, and ST depression with concern for subendocardial injury. Laboratory markers showed no signs of infection with negative respiratory viral panel and procalcitonin. However, evidence of myocardial involvement was demonstrated with an elevated Troponin I of 1.5 ng/mL and elevated NT-proBNP of 256,000 pg/mL. He also had a metabolic acidosis, with a pH of 7.2. He was started on high flow nasal cannula and subsequently required intubation. An echocardiogram demonstrated a severely dilated left ventricle with severely diminished systolic function and low ejection fraction of 17-19% (Fig. 1). The left coronary artery arose

anomalously from the main pulmonary artery, making the diagnosis of ALCAPA (Fig. 2). Additionally, there was moderate to severe mitral regurgitation (Fig. 3). The left atrium was severely dilated, and there was a patent foramen ovale shunting left to right with mean gradient of 13 mmHg, suggestive of left atrial hypertension. Within the left ventricle, the papillary muscles were echogenic, suggestive of ischemic injury with suspected flail chordae (Fig. 1). With moderate to severe mitral regurgitation and endocardial fibroelastosis of the left ventricle, further advanced imaging with chest computed tomography angiography was performed to fully delineate the coronaries, and the diagnosis of ALCAPA was confirmed (Fig. 4). It was consistent with ischemic injury to the myocardium. Due to these findings, he was supported with inotropic agents and scheduled for urgent surgical correction. A pre-operative transesophageal echo confirmed the flail chordae of the mitral valve (Fig. 5). He underwent re-implantation of the anomalous left coronary artery into the aorta with a single coronary transfer technique and subsequently required mitral valve replacement.

Discussion:

First described in 1886, anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) is a rare but serious congenital heart disease that causes significant morbidity and mortality.[1] In a normal heart, the coronary arteries branch off the aorta immediately after the aortic valve. However, in cases of ALCAPA, the left coronary artery arises from the pulmonary artery. This defect occurs in about 0.25-0.5% of congenital heart disease patients and is often singular.[1] In about 5% of cases it is associated with other defects such as a ventricular septal defect, patent ductus arteriosus, tetralogy of Fallot, or coarctation of the aorta.[1,2] Although some patients survive into adulthood undetected, without correction, about 90% of children with this defect die within the first year of life.[1-3] Most who do survive without correction have a high

risk of sudden cardiac death, especially with exercise. Given the seriousness of this condition, it is of utmost importance to detect ALCAPA early and accurately. Patients typically present with nonspecific symptoms such as irritability and fussiness, and quickly progress to heart failure.[1,2] The gold standard for diagnosis is an invasive coronary angiogram, but due to the invasive nature of the procedure other modalities have emerged.[3] In particular, echocardiography has shown promise as an ideal noninvasive imaging modality.[3,4] Sonographers and clinicians, who read echocardiograms, play a crucial role in the detection of coronary anomalies. Many children may be uncooperative during exam. However, attention to institutional protocol for segmental analysis of the heart in pediatric patients, especially the coronary artery origins, is very important. Coronary artery imaging should be performed in all new patients receiving an echocardiogram, as the detection of a coronary anomaly may be life-saving.

Coronary artery vascular development requires complex cellular interactions and signaling pathways. Anomalous origin of the left coronary artery from the pulmonary artery may develop due to abnormal septation of the conotruncus or due to persistence of aortic buds, which normally become the coronary arteries.[1] This defect often remains undetected in fetal life, as the pressure in the lungs equals systemic pressure in utero, allowing for myocardial perfusion from the pulmonary artery through the anomalous coronary artery.[1] After birth, most infants are asymptomatic until the pulmonary vascular resistance starts to drop. This typically occurs over the first 8 weeks as the patent ductus arteriosus closes and the pressure in the lungs slowly decreases. The coronary flow goes from the aorta, down the right coronary artery via collaterals to the left coronary artery and then flows into the pulmonary artery.[1,2] This creates a relative "steal" from the coronary circulation known as the coronary steal phenomenon, which leads to decreased myocardial perfusion of the left ventricle and water shed infarction of the

myocardium.[1,2] The papillary muscles are particularly prone to myocardial ischemia as they sit at the end of the coronary distribution tree. Some patients develop adequate intercoronary collaterals that allow them to survive beyond infancy.[1] When collateral vessels form between the right and left coronary arteries, sufficient perfusion and oxygenation may be provided to the tissues.[1] While this may allow the patient to survive longer, these vessels ultimately fail due to worsening coronary steal, leading to arrhythmias, mitral regurgitation, and ischemic cardiomyopathy.[2,3] There have been case reports of patients surviving beyond 35 years of age without surgical treatment, but these are rare.[3]

Myocardial ischemia in infancy commonly presents with symptoms of feeding intolerance, pallor, and irritability, which may progress to signs and symptoms of heart failure such as tachypnea, tachycardia, diaphoresis, and failure to thrive.[1,2] Other physical exam findings may include a gallop rhythm or a new murmur of mitral regurgitation. Our patient had relative failure to thrive (weight 5%) and developed a murmur with progressive respiratory symptoms between birth and 7 weeks of age. Given the nonspecific exam findings that most infants present with for this abnormality, the differential diagnoses are broad, including colic, gastro-esophageal reflux, milk protein allergy, bronchiolitis, Kawasaki syndrome, vasculitis, Ehlers Danlos syndrome, and trauma.[2,5] A thorough work-up is needed to obtain an accurate diagnosis. Chest x-rays and electrocardiograms are often obtained and may show cardiomegaly with pulmonary edema and ischemia, respectively.[1] However, these findings are nonspecific and non-diagnostic. Echocardiograms play a vital role in the diagnosis and long-term management of patients with ALCAPA. Imaging the coronary arteries in uncooperative infants and children may be challenging. However, echocardiograms have the ability to directly visualize the anomalous left coronary artery originating from the pulmonary artery with retrograde flow by

two-dimensional and color Doppler assessment.[1,4] They are also able to identify indirect signs of ALCAPA including an enlarged right coronary artery, abundant collaterals, mitral regurgitation, and may provide important information about anatomy, function, and hemodynamics.[3-5] Multiple studies have shown that echocardiograms have 90% accuracy in identifying the abnormality.[3,4] The most common misdiagnoses occurred in adults, and were identified as primary endocardial fibroelastosis, a coronary-pulmonary artery fistula, or rheumatic heart disease.[3,4]

If echocardiography is non-diagnostic, then advanced cardiac imaging with computed tomography angiography and cardiac MRI may enhance direct visualization of the anomalous origin of the left coronary artery and additionally identify retrograde flow, dilated vessels, left ventricular hypertrophy, poor left ventricular function, ischemic areas, hypokinesis, and delayed subendocardial enhancement.[2] However, both come with their own positives and negatives.[2] Computed tomography angiography provides good spatial resolution with fast examination time, and may not require anesthesia, which is ideal for infants, but complex, expensive, and has high radiation exposure.[2,3] Cardiac MRI has no radiation, but is a long exam and has poor spatial resolution.[2] However, due to its ability to provide information about myocardial function and viability, cardiac MRI is an excellent tool for guiding therapeutic decision making in older patients with moderate chronic ischemia and limited necrosis.[2] If there is extensive subendocardial delayed gadolinium enhancement on cardiac MR imaging due to infarction then surgery should be performed.[2] The gold standard for definitive diagnosis is invasive coronary angiography.[2,3] However, angiography has the risks of any invasive vascular procedure (vessel injury, thromboembolic event, injury to the heart, arrhythmia or even death) as well as a risk for radiation exposure.[2,3]

Initial management of ALCAPA includes treatment for heart failure: diuretics, afterload reduction, and inotropes.[1] Ultimately, however, this defect requires surgical correction. There are two approaches: develop a one coronary system or two coronary system. Historically, a one coronary system involves ligating the left coronary artery to prevent coronary steal with reliance upon the sole right coronary artery to maintain cardiac function. However, this approach was associated with significant complications.[1] Most of the recent surgical approaches have adopted a two-coronary system, and involve direct anomalous left coronary artery to aorta re-implantation or the Takeuchi procedure, which involves tunneling in the pulmonary artery to connect the ostium of the anomalous left coronary artery to the aorta.[1,3] Another option for adults includes ligating the left coronary artery at its origin of the pulmonary artery to stop competitive flow in combination with coronary artery bypass grafting using the internal mammary artery or saphenous vein.[2] Following surgical repair, mechanical ventricular support with extracorporeal membrane oxygenation may be required as the ventricle recovers. Overall, surgical outcomes tend to be good, with minimal residual defects.[5,6] One study reported long-term survival up to 98%, and up to 81% of patients required no further surgical intervention at the end of the study.[6] The most common reason necessitating further surgeries was significant residual mitral regurgitation,[6] as seen in our patient.

Conclusion:

Heart murmurs are common in infants and children, and are usually benign. Pediatric cardiologists and sonographers who perform pediatric echocardiograms must always perform complete segmental assessment of the heart to avoid missing rare forms of congenital heart disease that may lead to sudden cardiac arrest, such as the detection of a coronary anomaly. Anomalous left coronary artery from the pulmonary artery is an incredibly rare disease and one

of the most uncommon forms of congenital heart disease. Early diagnosis and prompt surgical correction is necessary for long-term survival. This case highlights the role of echocardiography in the management of a patient with anomalous left coronary artery from the pulmonary artery.

References:

1. Lardhi AA. Anomalous origin of the left coronary artery from pulmonary artery: A rare cause of myocardial infarction in children. J Family Community Med. 2010;17(3):113-116.

2. Pena E, Nguyen ET, Merchant N, Dennie C. ALCAPA Syndrome: not just a pediatric disease. Radiographics. 2009;29(2):553-565.

3. Yuan XC, Hu J, Zeng X, Zhou AY, Chen L. Echocardiographic diagnosis of anomalous origin of the left coronary artery from the pulmonary artery. Medicine (Baltimore). 2019;98(47):e18046.

4. Li RJ, Sun Z, Yang J, et al. Diagnostic Value of Transthoracic Echocardiography in Patients With Anomalous Origin of the Left Coronary Artery From the Pulmonary Artery. Medicine (Baltimore). 2016;95(15):e3401.

5. Moshref L, Moshref R, Faden M, Al-Radi O. The outcome of surgical repair of anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) in infants. Cardiothorac Surg. 2019;27(2).

6. Naimo PS, Fricke TA, d'Udekem Y, et al. Surgical Intervention for Anomalous Origin of Left Coronary Artery From the Pulmonary Artery in Children: A Long-Term Follow-Up. Ann Thorac Surg. 2016;101(5):1842-1848.

Highlights:

- **ALCAPA causes significant morbidity if not surgically corrected.**
- **Early and accurate detection is important for good clinical outcomes.**
- **Invasive angiography has been the traditional diagnostic tool for ALCAPA, but is costly and invasive.**
- **Echocardiography is an accurate, cost effective, and noninvasive imaging modality to diagnose ALCAPA.**

Funding:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Special thanks to Dr. Peace Chike Madueme for providing chest CT angiogram and transesophageal echocardiogram images.

Figures

Fig. 1

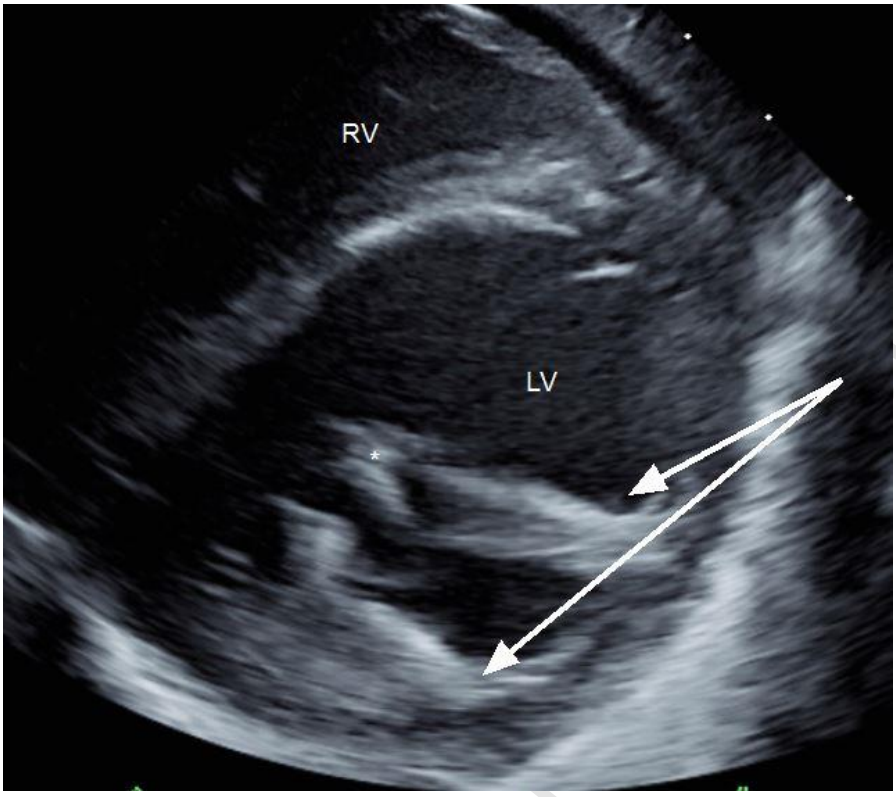

Fig. 2 (needs to be in color)

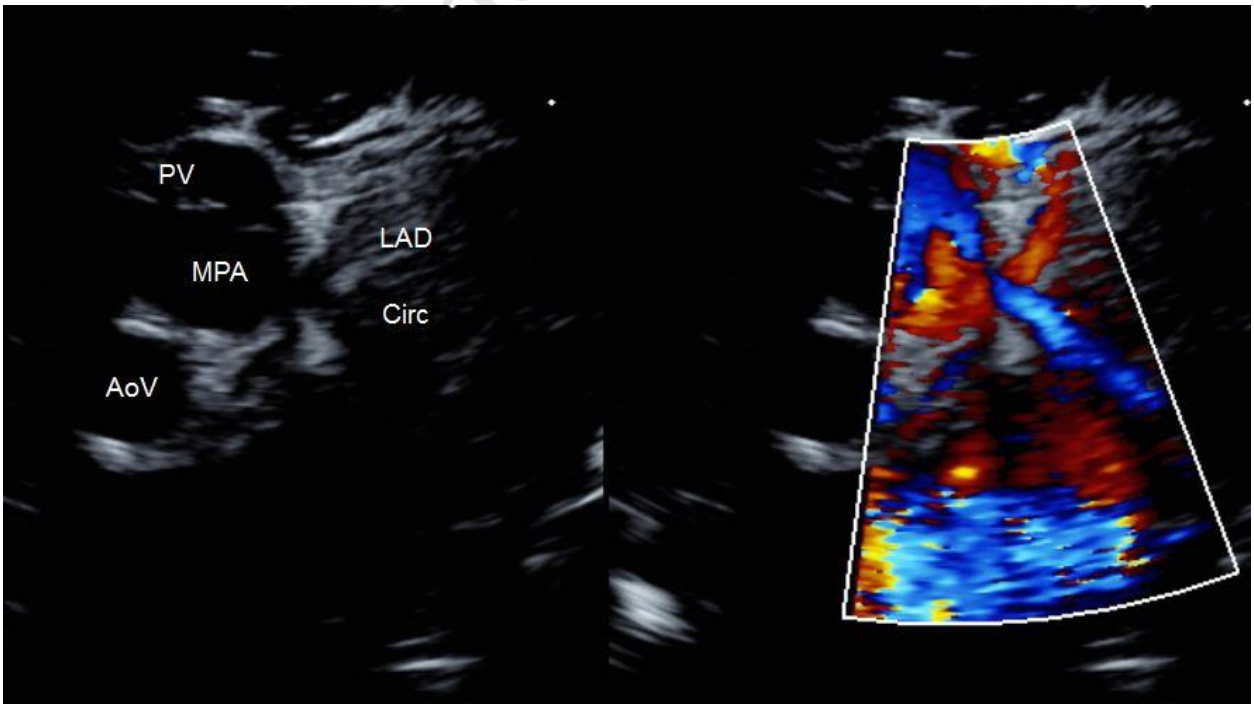

Fig. 3 (needs to be in color)

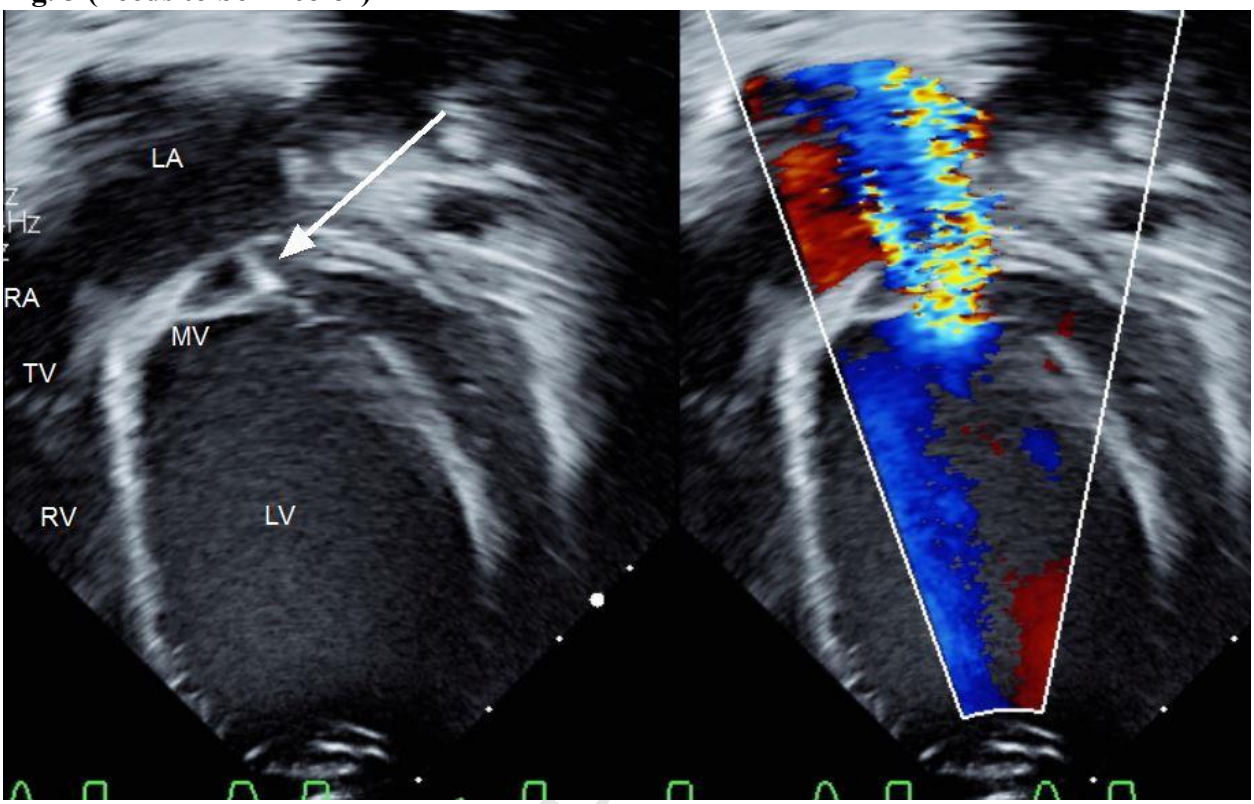

Fig. 4

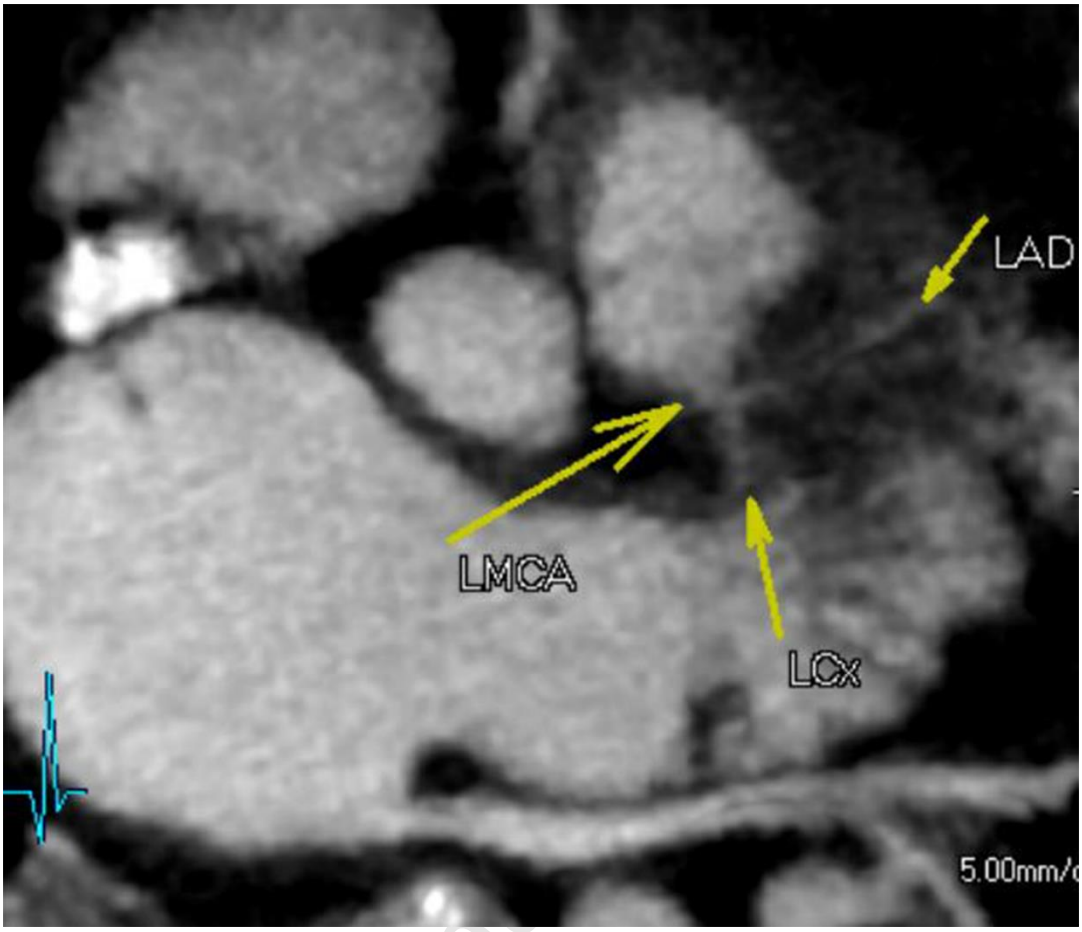

Fig. 5

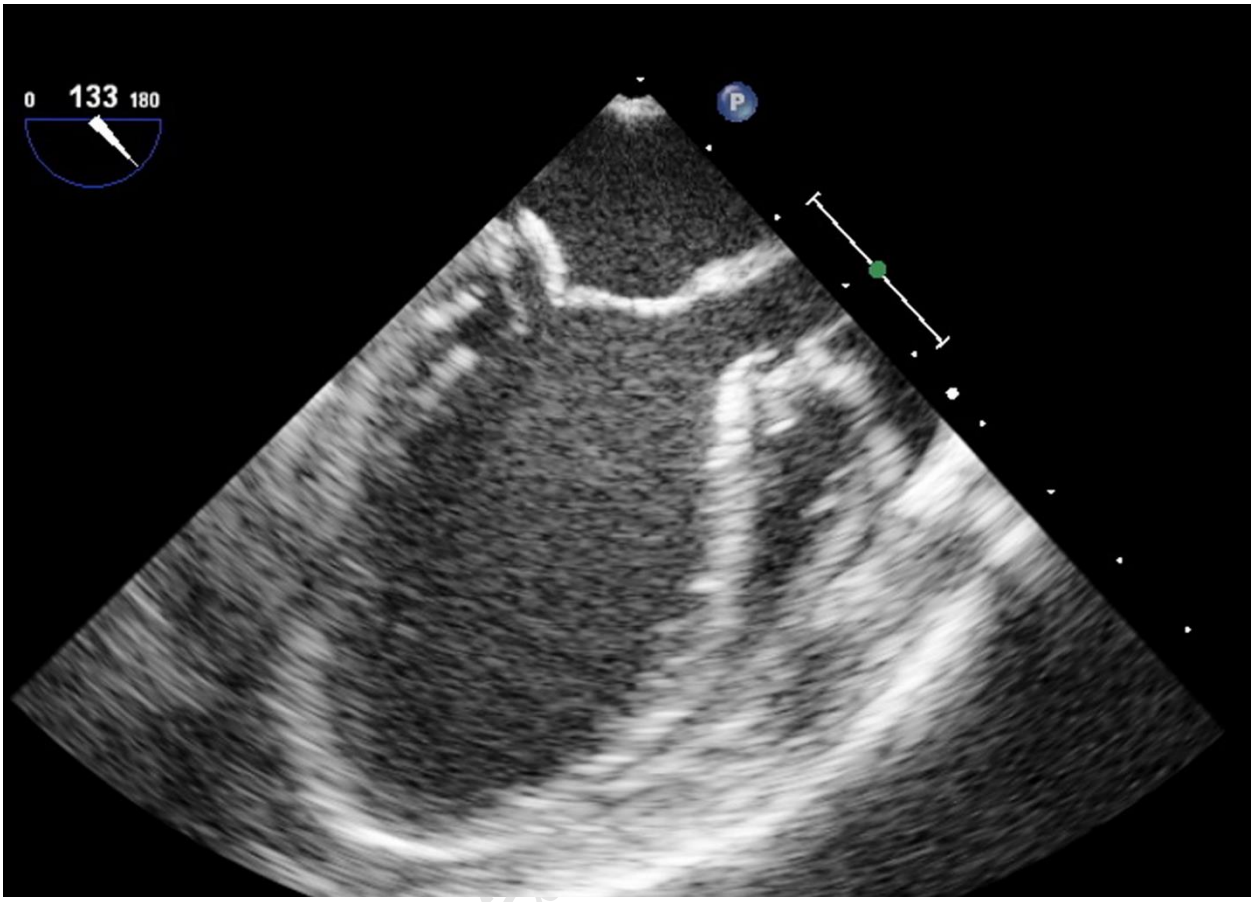

Figure Captions:

Fig. 1 Severely dilated left ventricle with echogenic papillary muscles and myocardium suggestive of ischemic injury and flail chordae of mitral valve. *RV* right ventricle, *LV* left ventricle, arrows pointing to papillary muscles, ***** denotes suspected flail mitral valve chordae.

Fig. 2 The proximal left coronary artery arises anomalously from the main pulmonary artery and bifurcates into the left anterior descending and circumflex coronary arteries. *AoV* aortic valve, *PV* pulmonary valve, *MPA* main pulmonary artery, *LAD* left anterior descending coronary artery, *Circ* circumflex.

Fig. 3 Mildly dilated mitral valve annulus with flail chordae and moderate to severe mitral valve regurgitation. Echogenic appearance of myocardium. *RA* right atrium, *RV* right ventricle, *LA*, left atrium, *MV* mitral valve, *LV* left ventricle.

Fig. 4 Axial CT image showing the left main coronary artery (LMCA) arising from the pulmonary artery and bifurcating into the left anterior descending (LAD) and left circumflex (LCx) arteries.

Fig. 5 Transesophageal image showing the echobright flail chordae of the mitral valve that has prolapsed into the left atrium.