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SUBAORTIC MEMBRANE PRESENTING AS ATYPICAL CHEST PAIN IN AN ADULT: CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT
Discrete subaortic stenosis or subvalvular aortic stenosis (SAS) or obstructive subaortic membrane (SAM) tends to be a progressive, severe defect that occurs most often in children. The symptoms and electrocardiographic findings of discrete subaortic stenosis are similar to those of aortic valve stenosis. The usual criteria for diagnosis, localization of the gradient below the aortic valve at cardiac catheterization or angiographic demonstration of discrete subaortic stenosis, are not always evident. Echocardiography may aid in determining the diagnosis by demonstrating the membrane in the left ventricular outflow tract (LVOT) and moreover, recognising the early systolic closure of the aortic valve leaflets. An acceptable low surgical mortality rate can be achieved; however, some patients require aortic valve replacement or multiple operations for adequate repair of their defect. Patients with a thin membrane generally have a more favorable result than those with fibro-muscular collar or secondary muscular hypertrophy. Aortic regurgitation is not always predictable and may recur or progress postoperatively. We are presenting a case report of a 52 year old obese female afflicted with discrete SAM with associated bicuspid aortic valve (BAV) and LVOT obstruction alongwith atypical chest pain.

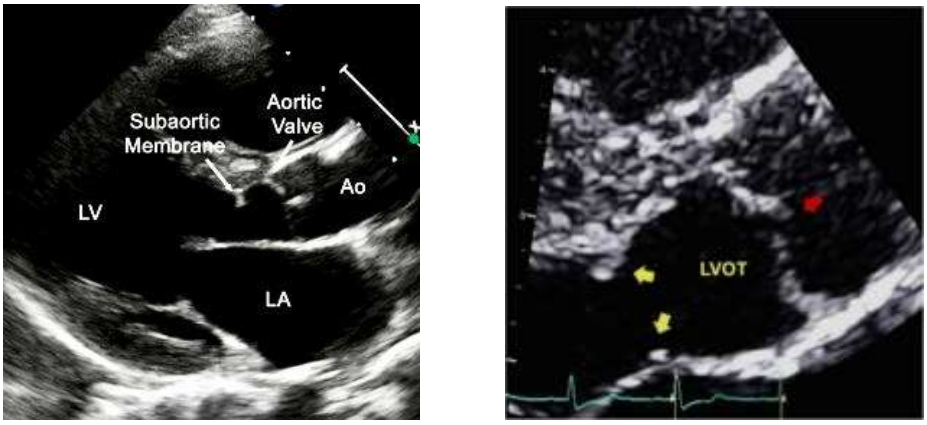
KEYWORDS: Subaortic membrane, Subaortic stenosis, Bicuspid aortic valve, Bicuspid aortic valve stenosis, LVOT obstruction.

INTRODUCTION

SAM is the second most common type of aortic stenosis (AS), accounting for 14% of LVOT obstruction, with valvular aortic stenosis being the most common cause (70%).[1] The prevalence of SAM is 6.5% of all the adult congenital heart diseases.[2] It predominantly involves males, with a male-to-female ratio of 2:1. SAM is associated with defects such as ventricular septal defect (VSD), atrioventricular septal defect (AVSD), or conotruncal anomalies in 60% of cases and may develop after patch closure of a perimembranous or malaligned VSD or AVSD.[3,4]

SAM is considered an acquired disease. It is rarely diagnosed during infancy, but it often manifests in the first decade of life with features of progressive LVOT obstruction, left ventricular hypertrophy (LVH), and aortic regurgitation (AR).[5] A familiar form of this disease, Shone syndrome, has also been described.[6]

SAM occurs in the LVOT just below the aortic valve and is characterized by an abnormal fibrous tissue, causing obstruction of blood flow from the left ventricle to the aorta (Figure 1).[7]

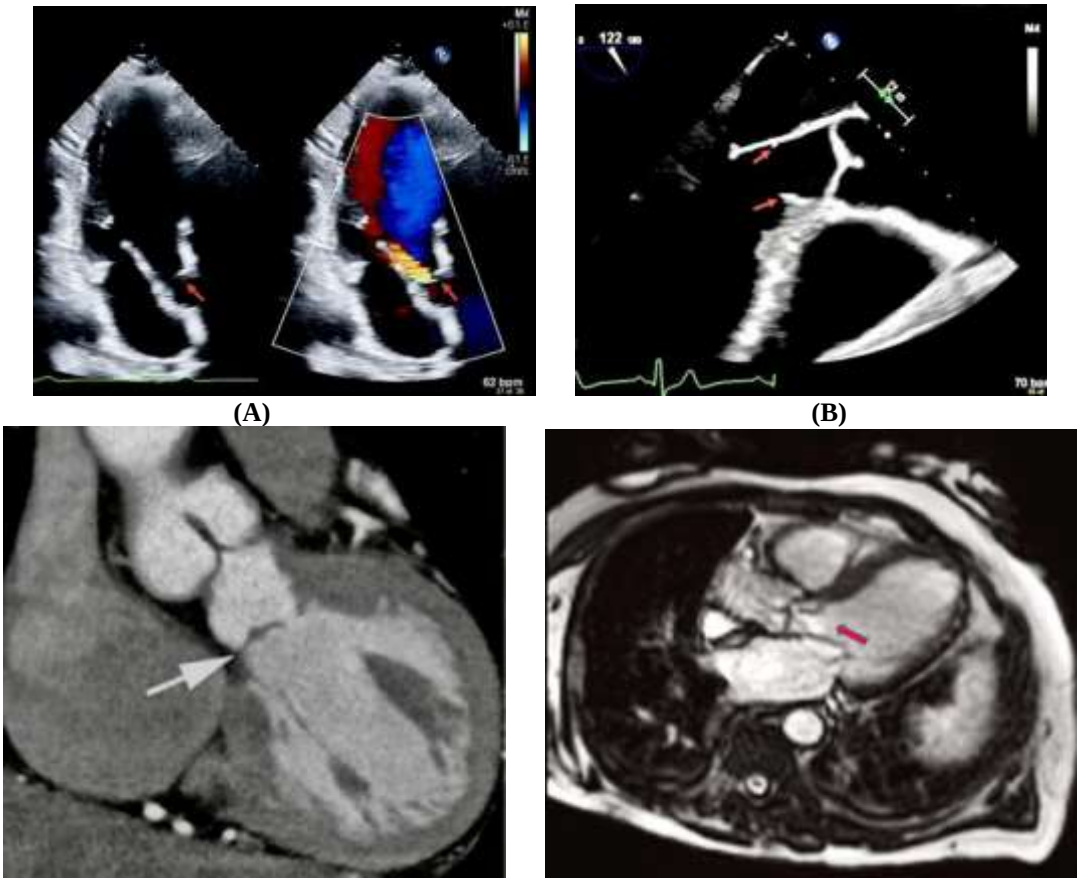


(A) **(B)**

Figure 1: A) Transthoracic echocardiogram in parasternal long axis view (LX) identifying the SAM, B) Focused view of LVOT with SAM and aortic valve on Transthoracic echocardiogram in LX view.

SAM can cause a range of symptoms, including dyspnea, chest pain, palpitations, and heart failure.[7] Guidelines are clear on the management of SAM if the patient has myocardial ischemia, heart failure, or has a resting peak gradient of >50 mmHg when asymptomatic.[8] However, the guidelines are less clear on the management of adults who present incidentally, have minimal or no symptoms, and have mild AS or AR that does not meet the threshold of intervention. In addition, there is insufficient guidance on how to pursue surveillance in these patients and the risk of progression of AS and AR is not well known.[9]

Currently, SAM can be effectively illustrated (Figure 2) by multiple imaging modalities:
(i) Transhthoracic echocardiography (TTE)
(ii) Transesopheal echocardiography (TEE)
(iii) Cardiac CT
(iv) Cardiac MR



(A) **(B)**

(C) **(D)**

Figure 2: A) TTE with and without color doppler demonstration of a SAM causing regurgitation through the aortic valve, B) TEE demonstrating the presence of a SAM, C) Cardiac computed tomography showing a discrete LVOT obstruction by SAM, D) Cardiac MR - the red arrows points towards the SAM.

The newer imaging techniques for diagnosing various causes of LVOT include CMR and CT.[10] CMR may be used to measure flow velocity and elucidate anatomy. One drawback of CMR is that the region of interest is frequently hidden by the spin dephasing artifact.[10] This issue makes visualization challenging, especially when taking into consideration the subaortic membrane's thinness. Conversely, cardiac CT complements the role of TTE in diagnosing a subaortic membrane.[11]

Surgery remains the gold standard for treating severe and symptomatic subaortic stenosis secondary to a subaortic membrane.[13] Recurrence is not unusual and occurs in up to 30% of patients, especially those with the tunnel variant and those with multiple levels of obstruction.[12,13] Progression of aortic regurgitation from none to mild or mild to moderate is also not uncommon, especially in patients with a preoperative peak LVOT gradient $\geq$ 80 mmHg.[14]

Case report

A fifty-four year old obese female recently detected to be having a heart murmur, was referred to us for a detailed transthoracic echocardiography (TTE). On clinical evaluation, she was found to be suffering from multiple comorbidities besides obesity: (i) Diabetes mellitus, (ii) Hypertension, (iii) Dyslipidemia, (iv) Hypothyroidism and (v) Obstructive sleep apnea. Her chief complaints were atypical chest pain not related to effort for many years, shortness of breath on moderate effort and occasional palpitation. There was no history of presyncopal or syncopal episodes.

On clinical examination, her height was 162 cm, weight was 85 kg, pulse rate was 80/min, BP was 150/80 mmHg, in the right upper limb in sitting posture, SPO2 was 98% at room air and respiratory rate was 16/min. On cardiovascular examination there was presence of Grade 2/6 ejection murmur at the base of heart alongwith normal Ist and IInd heart sound. No ejection click or LV gallop sounds were heard. All the peripheral pulses were normal and there was no radio-femoral delay. Rest of the systemic examination was unremarkable.

Resting ECG (Figure 3) identified left ventricular hypertrophy with strain, normal sinus rhythm and a left axis deviation with QRS axis of -45 degree.

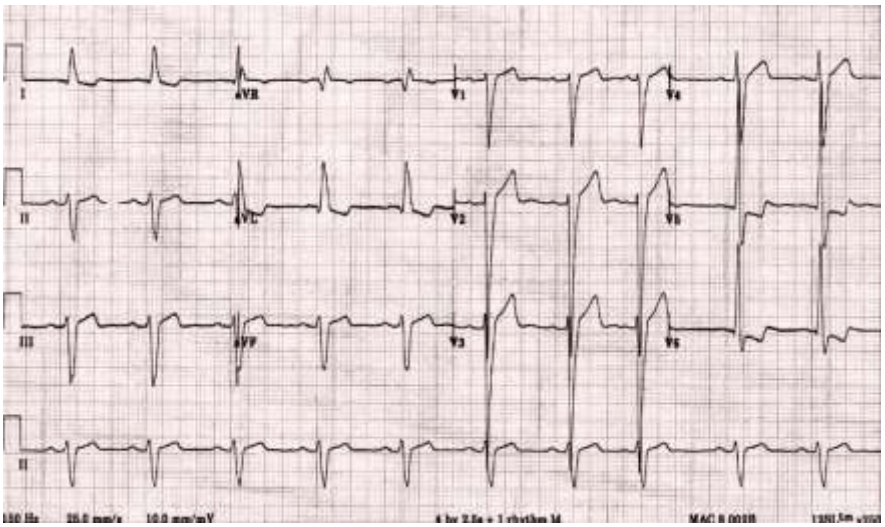


Figure 3: Resting ECG is consistent with left ventricular hypertrophy with strain, normal sinus rhythm and a left axis deviation (QRS axis -45 degree).

Transthoracic Echocardiography (Figures 4-8)

All echocardiographic evaluations were performed by the author, using-My Lab X7 4D XStrain echocardiography machine, Esaote, Italy. The images were acquired using a harmonic variable frequency (1-5 Mhz) electronic single crystal array transducer while the subject was lying in left lateral decubitus position.

Conventional M-mode, two-dimensional and pulse wave doppler (PWD) echocardiography was performed from parasternal long-axis, short axis and apical four chamber views and following parameters were derived: interventricular septum and LV posterior wall thickness in end-systole (IVS d and LVPW d, respectively), LV internal dimension at end-diastole and end-systole (LVID d and LVID s, respectively), LV end-diastolic and end-systolic volumes (LVEDV and LVESV respectively), ejection fraction (EF%), LV Mass in distole (LV Mass d).

M-Mode Echocardiography

The echocardiographic features of M-mode echocardiography are outlined.

LV	
IVS d	11.0 mm
LVID d	45.1 mm
LVPW d	11.7 mm
IVS s	16.5 mm
LVID s	27.5 mm
LVPW s	18.2 mm
EF	69 %
%LVFS	39 %
LVEDV	93.0 ml
LVESV	28.4 ml
ESV	64.6 ml
CO	4.13 l/min
LV Mass	184 g

2-Dimensional Echocardiography

- A discrete and thin subaortic membrane was delineated, just below the aortic valve, arising from the ventricular septum.
- Presence of associated calcific, non-stenotic, bicuspid aortic valve was identified.
- Concentric hypertrophy of LV.

Continuous Wave Doppler Echocardiography

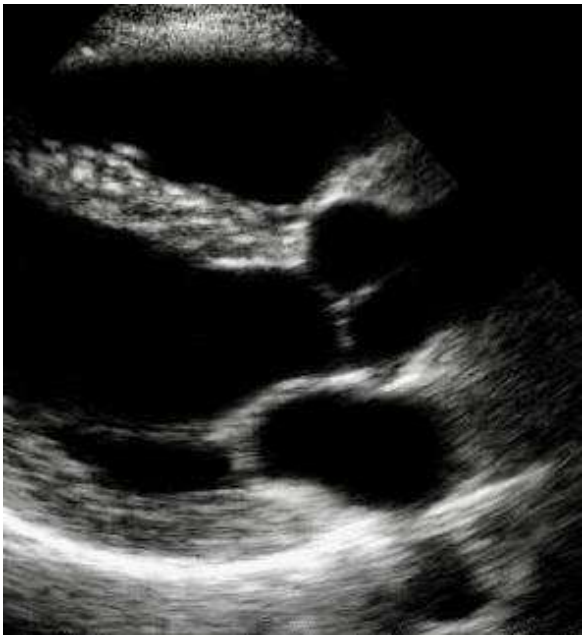
On placing the continuous wave doppler (CWD) sample volume across the LVOT a CWD signal of mild subaortic stenosis was displayed with a peak and mean gradient of 28.5/15 mmHg.

Color Doppler Echocardiography

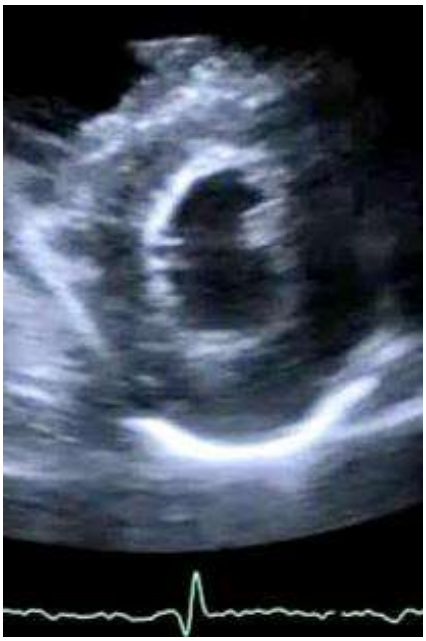
- On color doppler examination of the LVOT in the 5CH view a highly turbulent mosaic pattern flow was demonstrated.
- Additionally, a mild aortic regurgitation (AR) jet with a jet width of 3.5 mm, and occupying 20% of LVOT, was depicted.
- Mild tricuspid regurgitation was present with an estimated right ventricular systolic pressure/pulmonary artery pressure of 37 mmHg, suggestive of mild pulmonary arterial hypertension.

On summarizing, the following characteristics were present:

- A discrete, thin SAM, peak/mean gradient across SAM 28.5/15 mmHg.
- Bicuspid aortic valve, calcific and non-stenotic.
- Mild AR.
- Concentric hypertrophy of LV.
- Normal biventricular systolic function and dimensions.
- Normal LVEF 69%.
- No regional wall motion abnormality of LV was observed.
- Mild pulmonary arterial hypertension (PAH).



(A)



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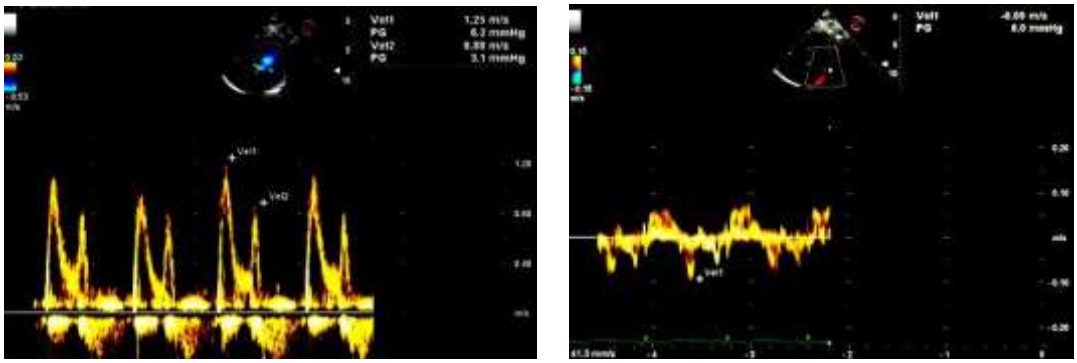
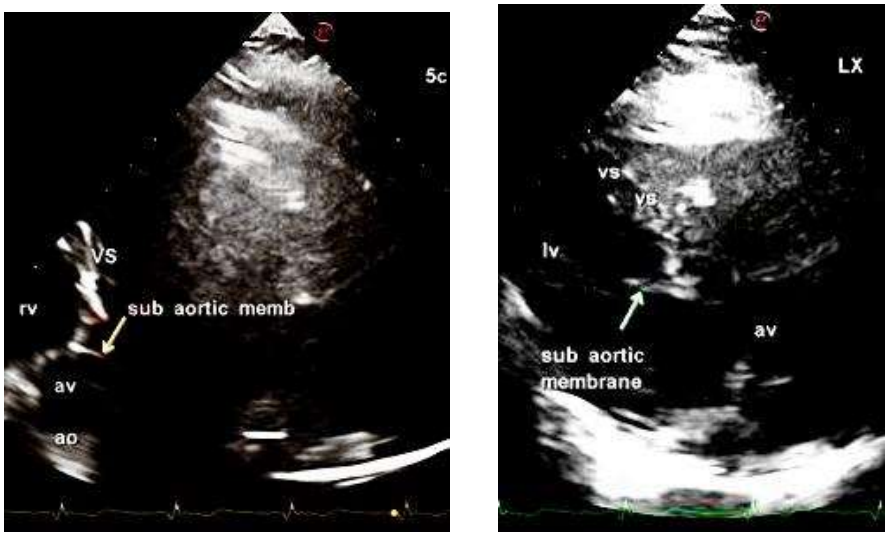


(C) (D)

Figure 4: A) LX View. Demonstrates concentric hypertrophy of LV, B) SX View. Shows concentric hypertrophy of LV, C) Pulse Wave Doppler analysis of mitral flow. Normal mitral flow pattern, D) Tissue Doppler Imaging (TDI) of lateral wall of LV. The TDI was normal.



(A) (B)

Figure 5: A) 5CH View. A discrete subaortic membrane is identified. B) LX View. A distinctive discrete subaortic membrane is seen.

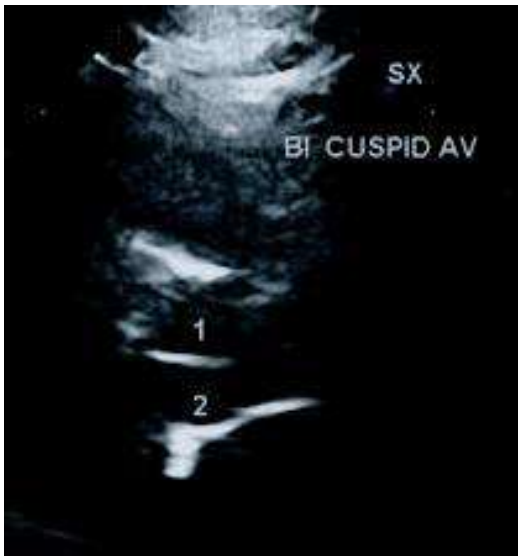
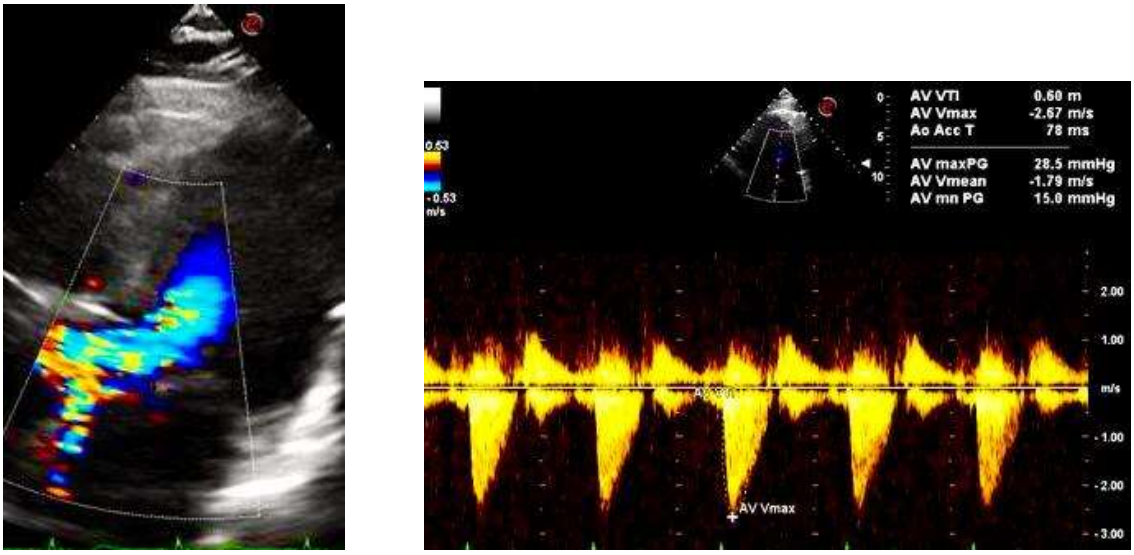


Figure 6: SX View. Bicuspid aortic valve is recognised.



(A) **(B)**

Figure 7: A) Color flow imaging in the 5 CH view, depicts a turbulent mosaic pattern flow in the LVOT, consistent with subaortic stenosis. B) Continuous wave Doppler analysis across the LVOT. Mild subaortic stenosis is observed with a peak and mean gradient of 28.5/15 mmHg.

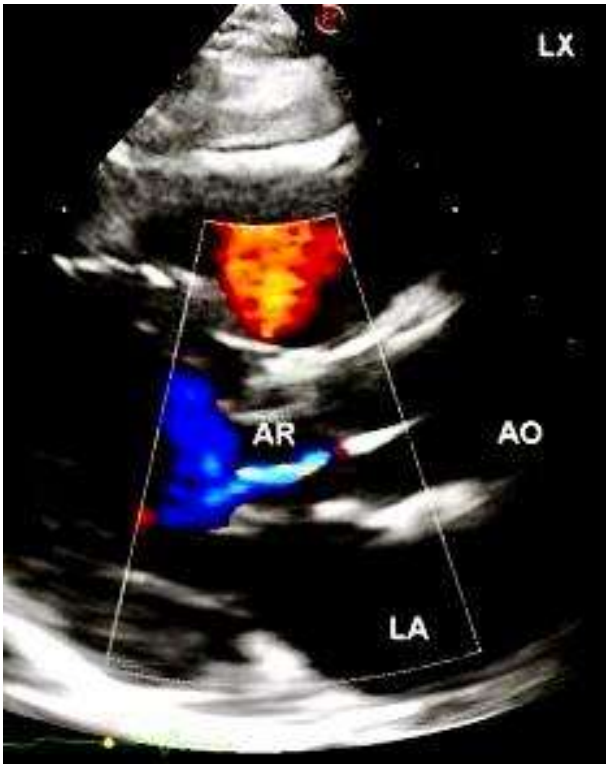


Figure 8: LX View. Mild aortic regurgitation is appreciated.

Treadmill stress test (TST) was performed on a Bruce protocol to rule out the presence of coronary artery disease and it was inconclusive. Because of the ambiguous TST result a 128 slice CT coronary angiography was conducted (Figure 9) which illustrated a calcium score of 0 and normal coronary arteries.

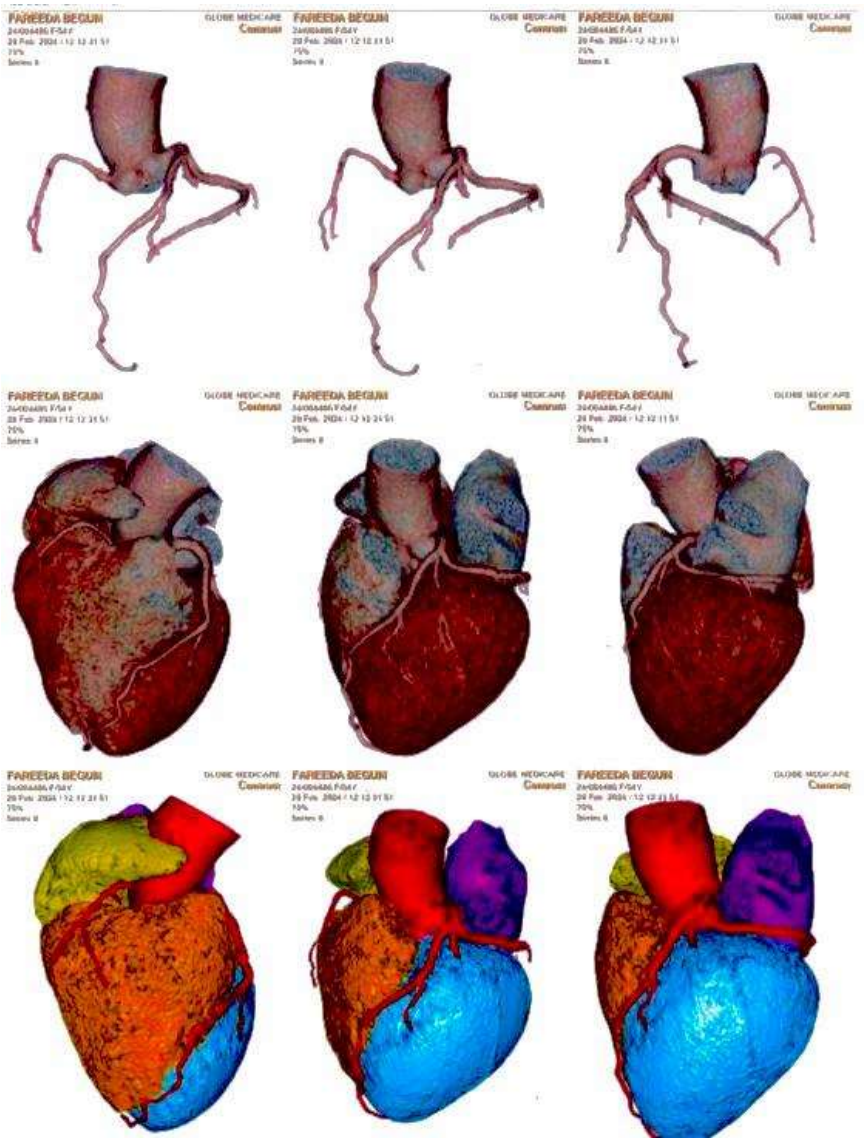


Figure 9: 128 slice CT coronary angiography. The calcium score was 0. Coronary arteries are normal.

In view of mild subaortic stenosis, calcific, non stenotic bicuspid aortic valve, mild AR, normal LVEF and the presence of a NYHA functional class 2; our patient was advised medical management alongwith strict control of obesity diabetes, hypertension and dyslipidemia to the target goals. Moreover, she was suggested a meticulous use of continuous positive airway pressure (CPAP) device for her accompanying obstructive sleep apnea (OSA).

We did not consider any interventional or surgical procedure at this stage of the disease.

DISCUSSION

SAM is characterized by the formation of a fibrous membrane obstructing the left ventricular outflow tract (LVOT). SAM occurs in about 6% of children with congenital heart defects.[15,16] and is responsible for 8–30% of total LVOT obstructions in children and up to 20% of obstructions that require intervention.[17,18] Key features of the disease are its rapid progression and its association with both a high-velocity jet and a high-pressure gradient across the LVOT.[19-21] The membrane that causes SAM can present with a variety of morphologies.

The angiocardiographic classification.[22] defines SAM into four types

Type I. A thin membranous diaphragmatic stenosis.
Type II. A fibrotic ring stenosis.
Type III. A fibromuscular additional tissue stenosis.
Type IV. A tunnel-like stricture of the left ventricular outflow tract.

Morphological classification of SAM (Figure 10), suggested by Torres et al,[23] categorizes SAM into three types

A. Fibromuscular ridge type
B. Crescent-shaped type
C. Filamentous-shaped type

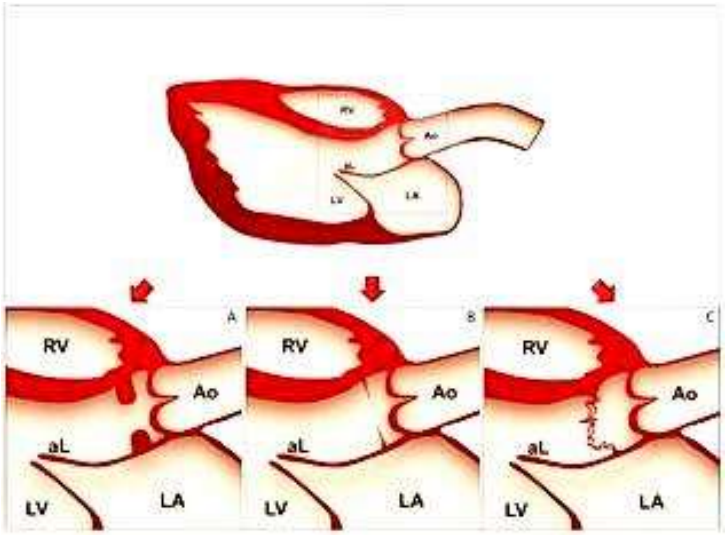


Figure 10: Different morphologies of subaortic membranes. (A) Fibromuscular ridge type; (B) Crescent-shaped type; (C) Filamentous-shaped type. aL: anterior leaflet of mitral valve; Ao: aorta; LA: left atrium; LV: left ventricle; RV: right ventricle.

SAM consists of five tissue layers,[24]: (1) endothelial layer, (2) glycosaminoglycans in the sub-endothelial layer, (3) fibroelastic layer with collagen bundles and elastin fibrils, (4) smooth muscle layer with a thickened basement membrane, and (5) fibrous layer with increased collagen.[25] The location of this membrane can range from just below the aortic valve where it sometimes fuses with the leaflets, to lower within the LVOT where it can become attached to the anterior mitral valve leaflet (Figure 11).

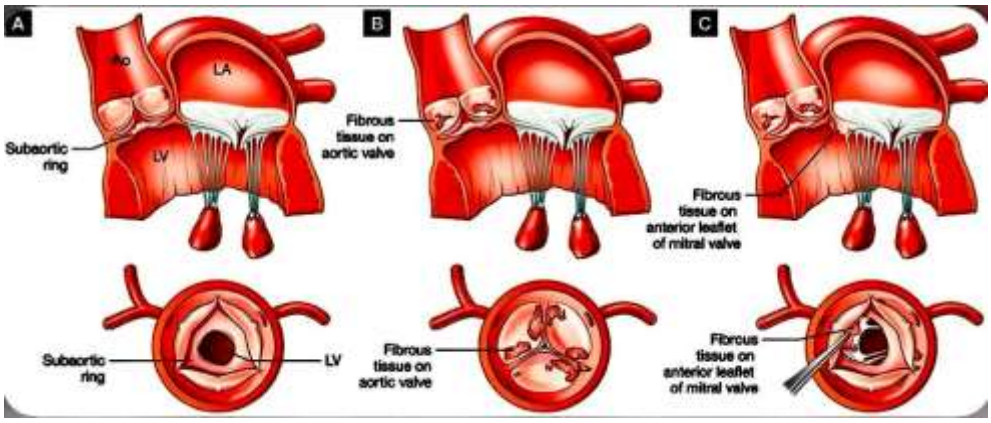


Figure 11: (A) isolated geometry; (B) involvement with the aortic valve; and (C) involvement with the mitral valve (Ao, aorta; LA, left atrium; LV, left ventricle).

Etiopathogenesis

Many mechanisms contribute to the development of SAM[26]

- Genetic factors.
- Hemodynamic abnormalities seen in other cardiac lesions.
- Underlying left ventricular outflow tract morphology that increases the turbulence at the outflow tract.
- A narrow LVOT.
- Exaggerated aortic override.
- Increased mitral-aortic septation.
- Steep atrioventricular septal angle.

These factors increase the fluid shear stress on the interventricular septum and induce an abnormal endothelial and muscle proliferation resulting in the formation of a fibromuscular ridge. This may account for the development of subvalvular aortic stenosis. The repair of associated congenital heart defects may modify the left-sided outflow increasing the turbulence and fluid shear stress on the interventricular septum contributing to the development of SAM.

Epidemiology

SAM is a rare disorder seen in infants and newborns but is the second most common type of aortic stenosis. It is responsible for approximately 1% of all congenital heart defects (8 in 10,000 births) and 15% to 20% of all fixed left ventricular outflow tract obstructive lesions.[27,28]

10-14% of SAM is observed amongst children with congenital aortic stenosis.[27,28] It is more common in males and is responsible for 65% to 75% of the cases,[27,28] with a male to female ratio of 2:1. The prevalence of SAM is 6.5% of all the adult congenital heart diseases.[2]

SAM is associated with other cardiac malformations in 50% to 65% of cases.[3,29]. In a report of 35 patients,[29] associated lesions encountered were:

- Ventricular septal defect (VSD) (20%)
- Patent ductus arteriosus (34%)
- Pulmonic stenosis (9%)
- Aortic coarctation (23%)
- Miscellaneous other lesions (14%)

Management

Since most pediatric patients are asymptomatic, medical therapy has no role in the treatment of subvalvular aortic stenosis. Nonetheless, because the disease is progressive, in adults intervention is needed at some point to relieve the left ventricular outflow tract obstruction. Surgical correction of the obstruction is the definitive therapy for the subvalvular aortic stenosis. This may range from simple removal of the membrane to extensive ring resection, with or without myectomy. However, if the patient develops heart failure or clinically significant left ventricular dysfunction, the patient is started on medical treatment until the surgery can be performed.

Indications for Intervention

The criteria and timing of intervention for subvalvular aortic stenosis are controversial. Early intervention in these patients is counterbalanced by the high postoperative incidence of recurrence, late reoperation and development of aortic regurgitation after relieving the obstruction.[30,32]

- In children and adolescents with Doppler mean gradient of less than 30 mmHg and no left ventricular hypertrophy, the management of subvalvular aortic stenosis is nonintervention and medical follow up.
- In children and adolescents with Doppler mean gradient of 50 mmHg or more should be surgically treated
- In children and adolescents with Doppler mean gradients of 30 to 50 mmHg, may be considered for surgery if they are symptomatic with angina, syncope, or dyspnea on exertion or if they are asymptomatic and in the older age group, but develop changes on ECG at rest or with exercise.
- Prevention of aortic regurgitation alone is generally not a criterion for surgery. However, the progression and worsening of regurgitation to a significant grade is an indication for surgery.

CONCLUSION

Subaortic membrane is a rare pathologic entity that usually presents in adults and typically consists of a thin fibrous membrane in the LV outflow tract. The membrane is most commonly described as a fibromuscular ring of tissue, an incomplete shelf, or ridge-like structure that causes discrete subaortic stenosis. Discrete subaortic stenosis can result in LV hypertrophy and dysfunction, aortic regurgitation, endocarditis, arrhythmias, and death. Although there are data to guide the threshold for intervention, controversy exists with regard to the optimal timing of surgery because of the high risk of recurrence. Discrete subaortic stenosis is complex disorder that remains largely unexplained, with difficult treatment principles.

Managing SAM in adult patients is challenging due to the limited treatment options and potential complications. While imaging and non-surgical workup allow us to make definitive conclusions on the presence and extent of disease, surgical resection remains the definitive treatment. The recurrence rate with surgical resection is high, so regular echocardiographic follow-up is required. In our patient any interventional procedure was not contemplated because the patient was having mild gradient across SAM and was minimally symptomatic.

REFERENCES

1. Barekatain A, Fanari Z, Hammami S, et al. Subvalvular aortic stenosis. Del Med J., 2015; 87: 346–348.
2. Oliver JM, González A, Gallego P, et al. Discrete subaortic stenosis in adults: increased prevalence and slow rate of progression of the obstruction and aortic regurgitation. J Am Coll Cardiol, 2001; 38: 835–842.
3. Leichter DA, Sullivan I, Gersony WM. "Acquired" discrete subvalvular aortic stenosis: natural history and hemodynamics. J Am Coll Cardiol, 1989; 14: 1539–1544.
4. Sigfússon G, Tacy TA, Vanauker MD, et al. Abnormalities of the left ventricular outflow tract associated with discrete subaortic stenosis in children: an echocardiographic study. J Am Coll Cardiol, 1997; 30: 255–259.
5. Sharma BD, Mittal S, Kasliwal RR, et al. Discrete subvalvular aortic stenosis. J Assoc Physicians India, 2000; 48: 1103–1106.
6. Urbach J, Glaser J, Balkin J, et al. Familial membranous subaortic stenosis. Cardiology, 1985; 72: 214–217.
7. Mulla S, Siddiqui WJ. Subaortic stenosis. StatPearls [Internet]. StatPearls Publishing, Treasure Island (FL); 2023.
8. Stout KK, Daniels CJ, Aboulhosn JA, et al., 2018. AHA/ACC guideline for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. Circulation, 2019; 139: 0–800.
9. Van der Linde D, Takkenberg JJ, Rizopoulos D, et al. Natural history of discrete subaortic stenosis in

adults: a multicentre study. Eur Heart J., 2013; 34: 1548–56.
10. Mun H.S., Wann L.S. Noninvasive evaluation of membranous subaortic stenosis: complimentary [sic] roles of echocardiography and computed tomographic angiography. Echocardiography, 2010; 27: E34–E35.
11. Baumgartner H., Hung J., Bermejo J., et al. Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. J Am Soc Echocardiogr, 2017; 30: 372–392.
12. Barkhordarian R., Uemura H., Rigby M.L., et al. A retrospective review in 50 patients with subaortic stenosis and intact ventricular septum: 5-year surgical experience. Interact Cardiovasc Thorac Surg, 2007; 6: 35-38.
13. Devabhanktuni S.R. Chakfeh E., Malik A.O., Pengson J.A., Rana J., Ahsan C.H. Subvalvular aortic stenosis: a review of current literature. Clin Cardiol, 2018; 41: 131-136.
14. Van der Linde D., Roos-Hesselink J.W., Rizopoulos D., et al. Surgical outcome of discrete subaortic stenosis in adults: a multicenter study. Circulation, 2013; 127: 1184-1191, 1191.e1-4.
15. Hoffman JIE, Christianson R. Congenital heart disease in a cohort of 19,502 births with long-term follow-up. Am J Cardiol, 1978; 42: 641–7.
16. Etnel JRG, Takkenberg JJM, Spaans LG, Bogers AJJC, Helbing WA. Paediatric subvalvular aortic stenosis: a systematic review and meta-analysis of natural history and surgical outcome. Eur J Cardio-thoracic Surg, 2015; 48: 212–20.
17. Sadeghian H, Karimi A, Ahmadi SH, Lotfi-Tokaldany M, Fallah N, Zavar R, et al. Discrete subvalvular aortic stenosis: severity of aortic regurgitation and rate of recurrence at midterm follow-up after surgery. J Tehran Univ Hear Cent, 2008; 3: 219–24.
18. Donald JS, Naimo PS, Richardson M, Bullock A, Weintraub RG, Brizard CP, et al. Outcomes of subaortic obstruction resection in children. Hear Lung Circ, 2017; 26: 179–86.
19. Ozsin KK, Toktas F, Sanri US, Yavuz S, Yavuz S. Discrete subaortic stenosis in an adult patient. Eur Res J., 2016; 2: 66.
20. Krieger EV., Stout KK, Grosse-Wortmann L. How to image congenital left heart obstruction in adults. Circ Cardiovasc Imag, 2017; 10: e004271.
21. Aboulhosn J, Child JS. Left ventricular outflow obstruction: subaortic stenosis, bicuspid aortic valve, supravalvar aortic stenosis, and coarctation of the aorta. Circulation, 2006; 114: 2412–22.
22. Deutsch V, Shem-Tov A, Yahini JH, Neufeld HN. Subaortic Stenosis (Discrete Form). Radiology, 1971; 101: 275-286.
23. Torres, F & Moral, Sergio & Robles, R & Ballesteros, Esther & Morales, Marise & Frigola, J & Albert, Xavier & Muntaner, L & Ramos, Ruan & Rigau, Pau & Brugada, R. P1760 Cardiac prognosis of patients with subaortic membrane according to their morphology. European Heart Journal - Cardiovascular Imaging, 2020; 21.
24. Foker JE. Outcomes and questions about discrete subaortic stenosis. Circulation, 2013; 127: 1447–50.
25. Muna WF, Ferrans VJ, Pierce JE, Roberts WC. Ultrastructure of the fibrous subaortic “ring” in dogs with discrete subaortic stenosis. Lab Investig, 1978; 39: 471–82.
26. Ezon DS. Fixed subaortic stenosis: a clinical dilemma for clinicians and patients. Congenit Heart Dis., 2013; 8: 450-6.
27. Kitchiner D, Jackson M, Malaiya N, Walsh K, Peart I, Arnold R. Incidence and prognosis of obstruction of the left ventricular outflow tract in Liverpool (1960-91): a study of 313 patients. Br Heart J., 1994; 71: 588-95.
28. Liu CW, Hwang B, Lee BC, Lu JH, Meng LC. Aortic stenosis in children: 19-year experience. Zhonghua Yi Xue Za Zhi (Taipei), 1997; 59: 107-13.
29. Choi JY, Sullivan ID. Fixed subaortic stenosis: anatomical spectrum and nature of progression. Br Heart J., 1991; 65: 280-6.
30. Karamlou T, Gurofsky R, Bojcevski A, Williams WG, Caldarone CA, Van Arsdell GS, Paul T, McCrindle BW. Prevalence and associated risk factors for intervention in 313 children with subaortic stenosis. Ann Thorac Surg, 2007; 84: 900-6; discussion 906.
31. Rohlicek CV, del Pino SF, Hosking M, Miro J, Côté JM, Finley J. Natural history and surgical outcomes for isolated discrete subaortic stenosis in children. Heart, 1999; 82: 708-13.
32. Mukadam S, Gordon BM, Olson JT, Newcombe JB, Hasaniya NW, Razzouk AJ, Bailey LL. Subaortic Stenosis Resection in Children: Emphasis on Recurrence and the Fate of the Aortic Valve. World J Pediatr Congenit Heart Surg, 2018; 9: 522-528.