Case Series

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Clinical features and surgical outcomes of membranous subaortic stenosis in three siblings: a case series and literature review

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Introduction: Subvalvular aortic stenosis (SAS) is a rare heart condition that can cause LVOT obstruction and lead to serious complications. While surgery is the main treatment, recurrence is a concern. This case series highlights the challenges in managing SAS in young patients.

Case Series: Three young brothers presented with symptoms of shortness of breath and chest tightness. All were diagnosed with membranous SAS through echocardiography and Doppler ultrasound. Surgical intervention was performed to remove the obstruction, but all three patients experienced recurrence within 2 years.

Discussion: This case series of three brothers suggests a genetic predisposition. Symptoms included exertional dyspnea and chest tightness, diagnosed via echocardiography. Surgical intervention is the primary treatment, but its timing is debated due to recurrence risks and complications.

Conclusions: This case series suggests a possible genetic predisposition to SAS. Despite successful initial surgery, the high recurrence rate highlights the need for improved management strategies and long-term follow-up. Further research is crucial to understand the causes of recurrence and optimize treatment for children with SAS.

Keywords: aortic stenosis, cardiology, genetics, heart defect, pediatrics

HIGHLIGHTS

- Subvalvular aortic stenosis (SAS) is a rare heart condition causing LVOT obstruction.
- Three brothers with shortness of breath and chest tightness were diagnosed with membranous SAS via echocardiography.
- All three underwent surgery to remove the subaortic membrane, but SAS recurred within 2 years, requiring more surgeries.
- The presence of SAS in three siblings suggests a potential genetic predisposition.
- The high recurrence rate postsurgery highlights the need for better management and long-term follow-up.
- Further research is needed to understand SAS recurrence and optimize treatment strategies.

Introduction

Subvalvular aortic stenosis is a rare condition seen in infants and newborns. It is the second most prevalent form of aortic stenosis and represents about 1% of all congenital heart defects, occurring in ~8 out of every 10 000 births[1]. It is associated with left ventricular outflow tract (LVOT) obstruction and accounts for 8–20% of all cases[2]. SAS is often incidentally found during evaluations for other heart defects. Exertional dyspnea is the most common symptom, occurring in 40% of symptomatic patients[1]. Moreover, patients may progress to develop severe stenosis or aortic regurgitation[3]. Echocardiography is the primary diagnostic tool for SAS, and an ECG may show a Q wave in the left precordial leads, indicating septal hypertrophy[1,4]. Distinguishing SAS from hypertrophic cardiomyopathy with obstruction remains challenging due to similar clinical manifestations, such as asymmetric septal hypertrophy[4]. Surgical intervention is recommended when the LVOT gradient exceeds 40 mmHg. There are three types of subaortic stenosis, two of which are associated with congenital heart disease. The subaortic membrane, the most common type, is further divided into discrete membranous SAS and diffuse fibromuscular SAS.

This case series has been reported in line with the preferred reporting of case series in surgery (PROCESS) criteria[5].

Case series

Case 1

A 3.5-year-old child was admitted to our hospital due to complaints of intermittent chest tightness, shortness of breath, and

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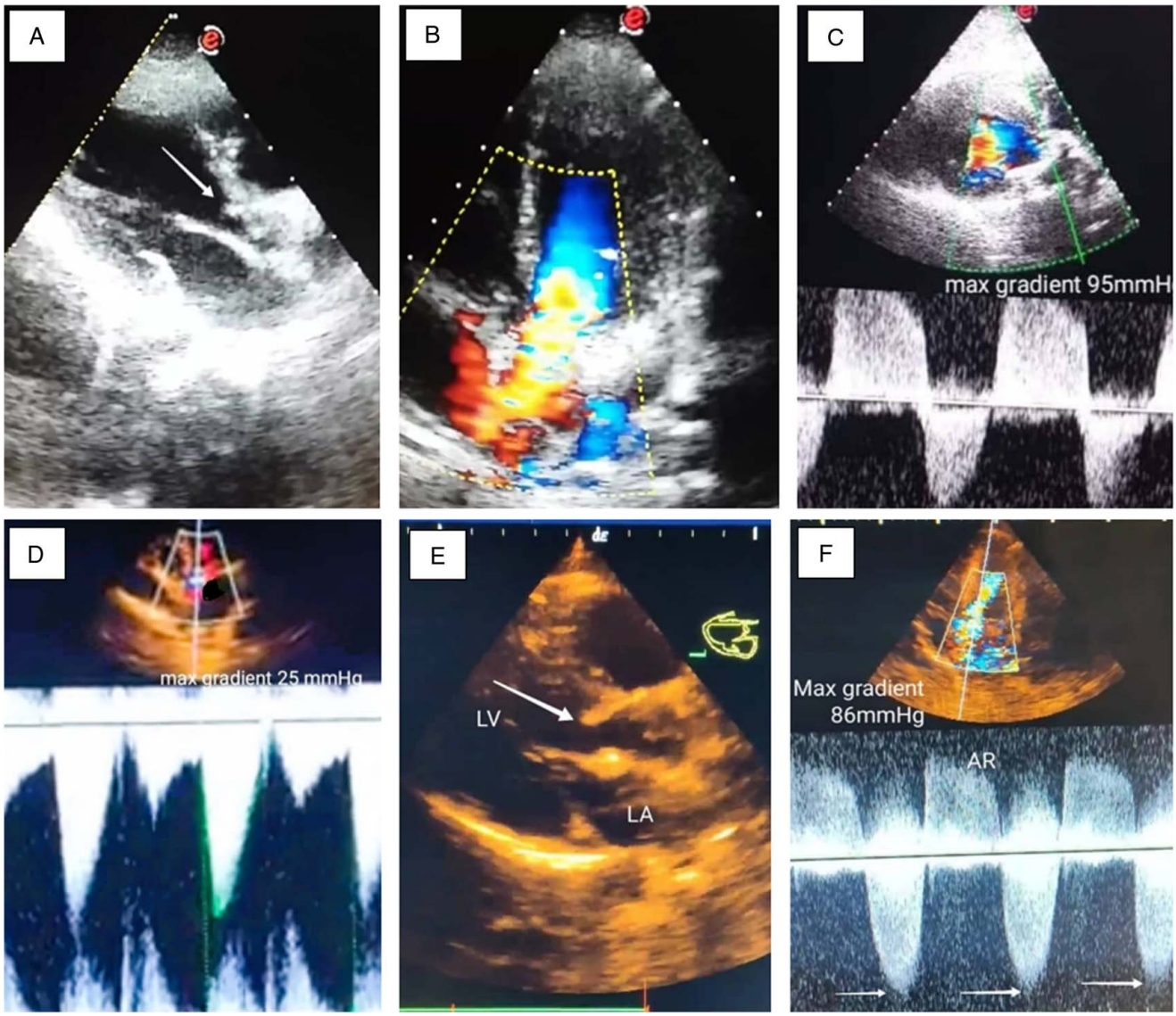

Figure 1. A: Apical five-chamber view, the arrow points at the subaortic membrane; B: Apical five-chamber view revealed a significantly increased systolic blood flow at the SAS; C: Doppler ultrasound revealed a maximum gradient of 95 mmHg; D: maximum gradient after first surgery of 25 mmHg; E: recurrent subaortic membrane 2 years after the first surgery; F: recurrent subaortic stenosis with 86 mmHg maximum gradient.

exertional dyspnea for several months. The patient has no family history of hypertension, sudden cardiac death (SCD), or cardiac or metabolic disorders. The patient was aware and responsive and examination at admission revealed that all his vital signs were stable. However, the cardiac auscultation revealed an aortic systolic ejective murmur at the right upper sternal border. Laboratory test results were all within normal ranges. ECG showed sinus rhythm and signs of left ventricular (LV) hypertrophy. Echocardiography demonstrated a slightly hypertrophic LV, mild left-atrium ectasia, mild mitral and tricuspid valve insufficiency, mild aortic regurgitation, and normal systolic function. The apical five-chamber view revealed a 2.5 mm membrane that is 3 mm below the level of the aortic valve (Fig. 1A arrow) with moderate-to-severe subaortic stenosis (SAS). Doppler ultrasound revealed a significantly increased systolic blood flow at the SAS (Fig. 1B) with a maximum pressure difference of 95 mmHg (Fig. 1C). As a result, a diagnosis of membranous subaortic stenosis was established. The child underwent surgical intervention to resect the subaortic membrane. One month following the surgery, the maximum pressure difference became 25 mmHg (Fig. 1D), but over the next 2 years, symptoms returned with recurrent subaortic membranes (Fig. 1E). A subsequent Doppler ultrasound revealed a maximum gradient of 86 mmHg (Fig. 1F) with severe SAS and mild aortic insufficiency. Four months later, a second surgery was performed, and the patient recovered and was stable.

Case 2

A 2.5-year-old child was admitted with shortness of breath and exertional dyspnea lasting for a few months. As his sibling, the patient came with no family history of any cardiac or metabolic disorders. Physical examination at admission revealed normal

vital signs with a wind-like systolic murmur over the aortic valve area. ECG showed normal rhythm and signs of LV hypertrophy. The apical five-chamber view of the echocardiogram showed a subaortic membrane and 2/4 subaortic stenosis (Fig. 2A). Doppler ultrasound confirmed a significant increase in blood flow at the SAS area (Fig. 2B) with a maximum gradient of 100 mmHg (Fig. 2C). After surgical intervention, the maximum gradient decreased to 22 mmHg (Fig. 2D). On a routine examination two years later, a Doppler ultrasound indicated a recurrent membrane and a recurrent flow blood pressure difference of 92 mmHg (Fig. 2E). The patient underwent a second surgery to remove the recurrent membrane and recovered well following the surgery.

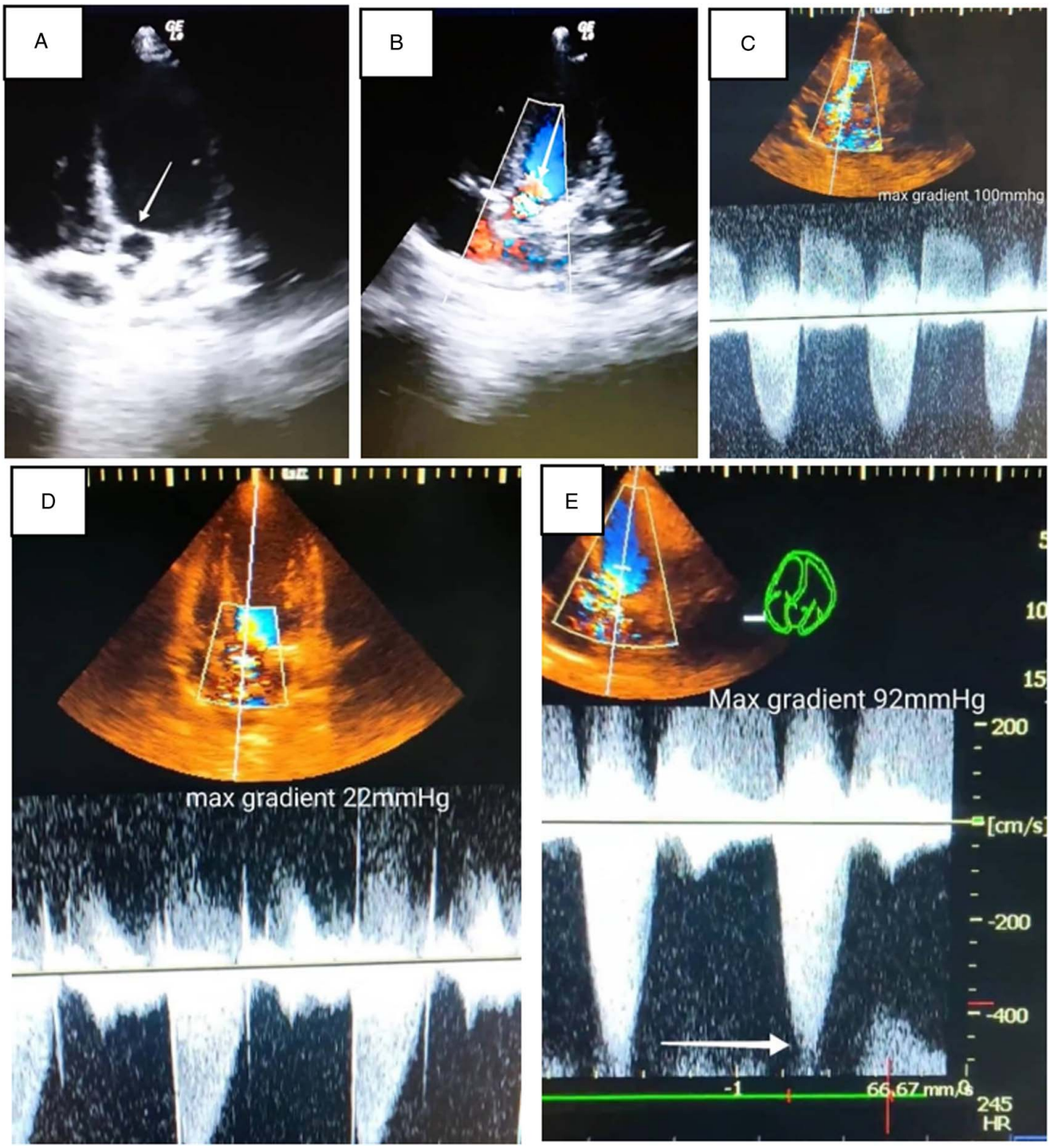

Figure 2. A: Apical five-chamber view revealed the subaortic membrane; B: Doppler ultrasound showed a significant increase in blood flow; C: Doppler ultrasound showed a maximum gradient of 100 mmHg; D: Maximum gradient for the second child is 22 mmHg after the first surgery; E: The recurrent high maximum gradient.

Case 3

A 1-year-old male with no significant prenatal or postnatal history was brought by his parents to the cardiology clinic complaining that the child has been experiencing episodes of unexplained dyspnea, especially during feeding, increased physical activity, and in warm environments.

His family history revealed a membranous subaortic stenosis in two of his brothers with significant gradient and mild aortic regurgitation. Physical examination revealed a systolic heart murmur and reduced oxygen saturation during episodes of dyspnea.

Laboratory test results were all within normal ranges. ECG revealed a left axis deviation with signs of LV hypertrophy. Echocardiogram demonstrated moderate concentric left ventricular wall hypertrophy, mild left atrial enlargement, mild tricuspid regurgitation, mild mitral regurgitation, a 2.5 mm membranous protrusion at the left ventricular outflow tract 3 mm away from the aortic valve leaflets, an ejection fraction (EF) of 55–60%, and pulmonary pressure of 25–30 mmHg (Fig. 3A).

Doppler ultrasound demonstrated a significant increase in blood flow at the SAS area with a maximum gradient of 80 mmHg.

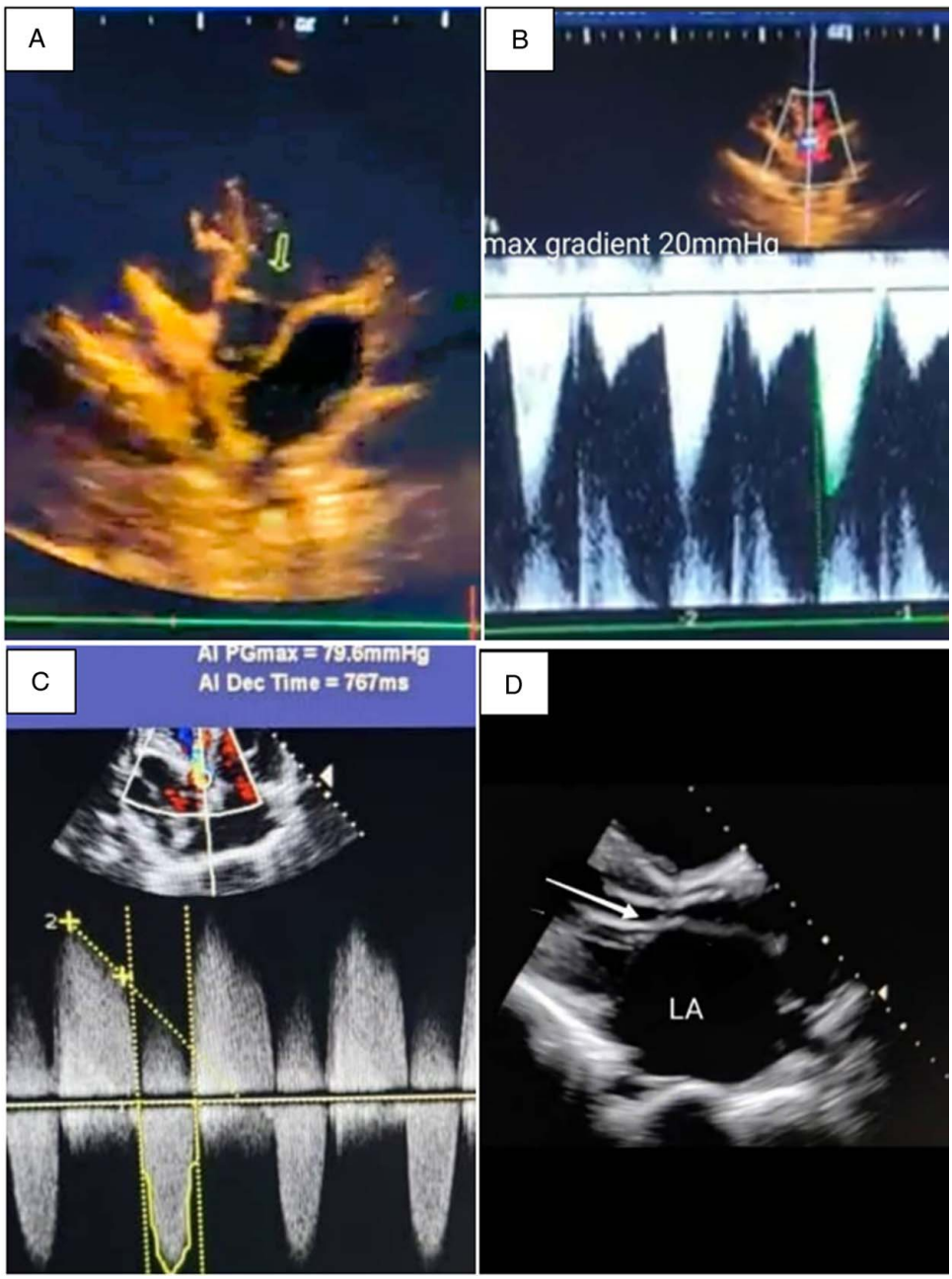

Figure 3. A: Apical five-chamber view revealed the subaortic membrane (arrow); B: Doppler ultrasound revealed a maximum gradient decreased to 20 mmHg after the first surgery; C: Doppler ultrasound demonstrated the recurrence of the subaortic membrane with an increase of maximum gradient to 79.6 mmHg; D: Parasternal long-axis echocardiogram demonstrated the membrane recurrence in a tunnel-like narrowing form (arrow).

Table 1

Other causes of left ventricular outflow tract (LVOT) obstruction.

Cause	Description	Diagnosis	Management
Hypertrophic obstructive cardiomyopathy (HOCM)	A genetic disorder characterized by asymmetrical septal hypertrophy causing obstruction of the left ventricular outflow tract	Echocardiography, MRI, genetic testing	Medications (beta-blockers, calcium channel blockers), surgery if severe
Bicuspid aortic valve	Congenital malformation where the aortic valve has only two cusps instead of three	Echocardiography, MRI	Surgical repair, balloon valvuloplasty
Supravalvular aortic stenosis	The least common cause; can occur in conditions such as Williams syndrome	Echocardiography, MRI	Surgical intervention with excision or patch enlargement
Coarctation of the aorta	Congenital Narrowing of the aorta, usually near the ductus arteriosus	Echocardiography, MRI	Surgical repair, balloon angioplasty
Mitral valve prolapse with systolic anterior motion (SAM)	Anterior motion of the mitral valve, leading to dynamic outflow obstruction of the left ventricle	Echocardiography, MRI	Beta-blockers, monitoring; surgical intervention if symptomatic

Surgical removal of the subaortic membrane was performed, and the patient was discharged in good condition (Fig. 3B). Upon 2-year follow-up, an echocardiogram showed a recurrence of the subaortic membrane that was previously excised, with severe stenosis at the ventricular outlet, along with signs of 2/4 aortic insufficiency (Fig. 3C, D). Therefore, the patient underwent another surgery to remove the recurrent membrane.

Discussion

Subvalvular aortic stenosis (SAS) is a cardiac condition that poses diagnostic and therapeutic challenges, especially in pediatric patients. With a male-to-female ratio of 2:1 to 3:1, SAS accounts for 10–20% of LVOT cases. It presents as a progressive and potentially fatal disease characterized by left ventricular outflow tract (LVOT) obstruction due to a subvalvular fibrous, fibromembranous, or fibromuscular ring[6]. The precise etiology remains unclear, with factors such as anatomical modifications to the interventricular septum and mitral valve apparatus proposed as potential causes[6,7]. Some patients may experience a quick progression of discrete subaortic stenosis, while others may have a slower course[6]. In our case series, this disease occurred in three brothers, even though it is not usually considered a hereditary disorder. While the exact genetic basis for familial membranous subaortic stenosis remains unclear, a review by Fatimi *et al*.[2] highlighted the complexity of inheritance patterns in discrete subaortic stenosis (DSS), suggesting possible genetic and envir onmental interactions without establishing a clear inheritance mode. This emphasizes the need for further research to explore the genetic underpinnings of DSS in larger cohorts. All three cases involved young children presenting with symptoms of exertional dyspnea, chest tightness, and aortic systolic murmurs, leading to the diagnosis of membranous subaortic stenosis confirmed by echocardiography and Doppler ultrasound.

SAS may manifest in conjunction with other cardiac abnormalities, such as mitral valve abnormalities or an interrupted aortic arch with a ventricular septal defect. Patients often have a normal tricuspid valve with aortic valve thickening that may be widespread. Most of the time, the left ventricle is hypertrophied concentrically. If SAS is not treated, it can eventually lead to aortic insufficiency (AI), arrhythmia, and even death[8]. Although it is infrequently identified in the first 10 years of life, it frequently presents with increasing LVOT blockage, left ventricular hypertrophy (LVH), and aortic regurgitation (AR). Shone syndrome, a hereditary variation of this disease, has also been reported[9]. In our case series, a systolic cardiac murmur was discovered during the physical examination. A left axis deviation and indications of left ventricular hyper trophy were seen on the ECG, and echocardiography revealed aortic regurgitation, mitral valve insufficiency, left atrium ectasia, and a hypertrophic left ventricle.

As described in our diagnostic workup, we conducted comprehensive evaluations to exclude other possible causes of LVOT obstruction (Table 1). This included detailed echocardiographic assessments, which consistently identified membranous subaortic stenosis as the primary etiology in all cases. Additionally, the patients were evaluated for other potential anatomical or functional contributors to LVOT obstruction, such as hypertrophic, cardiomyopathy, and congenital heart defects, but none were identified.

Since most pediatric patients are asymptomatic, medical therapy has no role in the treatment of SAS. As the condition progresses, intervention may be needed to relieve the obstruction in the LVOT. Surgical correction is the best option for treating subvalvular aortic stenosis. Treatment may involve removing the membrane or more extensive procedures, such as ring resection with or without myectomy, or a Konno procedure[10,11].

In our described three cases, the surgical approach involved a median sternotomy with cardiopulmonary bypass, followed by a transverse aortotomy to access and resect the subaortic membrane and any associated fibromuscular tissue. The aortic valve was inspected during the procedure, but no further intervention was required beyond the membrane resection. Despite complete resection, all patients experienced a recurrence of the membrane within 1–2 years, necessitating a second surgery, which involved a more extensive removal of the tissue.

The appropriate timing and criteria for intervention in these patients remain a matter of controversy. The potential benefits of early intervention are weighed against the elevated risks of postoperative recurrence, delayed reoperation, and the onset of aortic regurgitation following the relief of the obstruction[12,13]. The long-term results of surgery for discrete subaortic membranes, as investigated in the study by Talwar *et al*., demonstrate positive outcomes. The surgical resection, particularly when combined with septal myectomy, showed good results in reducing left ventricular outflow tract gradients and improving aortic regurgitation[14]. Another study by Valeske *et al*.[13] investigated surgical outcomes for subaortic stenosis in 81 children. While surgery successfully reduced gradients without mortality, 31% experienced recurrence, particularly in complex cases. This recurrence happened in our case series of three patients.

On the other hand, in the study conducted by Tal *et al*.[8], evaluating long-term aortic valve function in patients with discrete subaortic stenosis, surgical intervention demonstrated

limited immediate postoperative benefits, with subsequent deterioration observed in nearly half of the patients. These findings raise questions about the efficacy of current surgical approaches in preventing long-term aortic valve insufficiency, highlighting the need for further research to identify optimal intervention timing and understand the underlying causes of progression in subaortic stenosis patients.

This study has several limitations. First, it involves only three siblings, which is a small sample size and limits the ability to generalize the findings. Since it is a small case series rather than a larger observational study, we cannot draw broad conclusions or establish general patterns. Additionally, the follow-up period of 2 years may not capture all long-term outcomes or recurrence patterns.

Conclusions

By presenting this case series, we discuss membranous subaortic stenosis as a differential diagnosis in pediatric patients presenting with exertional dyspnea and chest tightness. Despite successful surgical intervention, the high recurrence rate of SAS necessitates regular follow-up and re-evaluation. Genetic factors may contribute to the condition, and further research is needed to optimize management strategies and improve long-term outcomes for patients with SAS. Physicians should remain vigilant in monitoring these patients to prevent the progression of aortic insufficiency and other complications associated with this condition.

Ethical approval

Patient anonymity is maintained throughout this manuscript. Ethical approval and consent were obtained for publication from the patient's parents.

Consent

Written informed consent was obtained from the patient's parents/legal guardian for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

M.A.: was involved in conceptualization, writing the main manuscript, preparing figures, and revising the final manuscript; A.A.: participated in writing the original manuscript and gathering data; H.H.: participated in writing the original manuscript; H.A. and S.K.: participated in preparing the original manuscript and figures; L.B.: participated in preparing the original manuscript; S.T.: was involved in patients care and management, reviewing, and supervision. All authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

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