CASE REPORT

Subaortic Membrane and Patent Ductus Arteriosus in Rare Association-Case Series

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Abstract

Background: **The combination of subaortic membrane (SAM) and patent ductus arteriosus is very rare. Subaortic stenosis is the second most common form of left ventricular outflow tract (LVOT) obstruction after valvular aortic stenosis. We are reporting the largest case series of SAM and PDA.**

Methods: **We included all patients that were diagnosed with the combination of SAM and PDA at our cardiac center. We have reviewed patients echocardiographic studies, cardiac catheterizations, surgical notes and all the outpatients notes.**

Results: **We have a total of 7 patients. The age at presentation was in the early childhood with 3 patients diagnosed in infancy. Four patients had severe and moderate LVOT obstruction with SAM being very close to the aortic valve and all required surgical intervention. The last three patients had mild LVOT obstruction 2 of them with the SAM being > 4mm away from the aortic valve. Six out of the seven patients had intervention while the last one is under clinical follow up currently. PDA closure did not change the outcome. There were no other postoperative complication like developing new AI or developing complete heart block. There was no relation between gender, height, weight or age at diagnosis to the SAM clinical course.**

Conclusion: **SAM and PDA association is very rare. The underlying pathophysiology is not well understood. When the SAM is closer to aortic valve (≤ 4mm), it carries higher risk of progressive LVOT obstruction. The interventions for SAM and PDA were safe procedures.**

Keywords: Subaortic membrane, Patent ductus arteriosus, Left ventricular outflow tract obstruction

1. Introduction

Patent ductus arteriosus is a common congenital heart disease but its coexistence with SAM is rare. Obstruction of the left ventricular outflow tract is a major congenital heart defect that occurs in 6/10,000 live births [1]. Subaortic stenosis is the second most common form after valvular aortic stenosis [1], however it usually coexists with other pathologies such as ventricular septal defects and other left side lesions. It is rarely seen in infants and newborns [3]. In the literature there are only three articles that reported the presence of SAM and PDA. One of these articles was in 1989 while the other two were before the era of echocardiography and the diagnosis was made by cardiac catheterization [2,4,5]. The largest number in those series were 6 patients. We are reporting the association of SAM and PDA in 7 patients three of which are infants. We are also discussing the need for intervention.

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2. Methods

This is a case series where we report the association of SAM and PDA. We included all the patients that were diagnosed with this combination at King Abdulaziz Cardiac Center, National Guards Health Affairs in Riyadh, Saudi Arabia. The data is collected retrospectively from the electronic cardiac database and Xcelera Echocardiographic database, (Philips, Andover, USA).

PDA is defined as a pathologic persistence of ductus arteriosus after birth [6]. As there are neonates who have PDA closure delay after the birth so, we defined PDA as persistent PDA beyond the neonatal period which did not close spontaneously. Subvalvular aortic stenosis is defined as obstruction of the LVOT below the level of the aortic valve [7]. We defined SAM as a tissue below the aortic valve causing left ventricular outflow tract (LVOT) obstruction. We included all the patients with isolated SAM and PDA. Patients with other congenital heart lesions such as mitral valve abnormality, bicuspid aortic valve, coarctation of aorta or perimembranous ventricular septal defect (VSD) were excluded. We reviewed the patients' electrocardiograms (ECG), chest x-rays, echocardiography, cardiac catheterizations, surgical notes and all the outpatients notes. The following variables were collected; demographic data including age at diagnosis, gender, height and weight. Echo data including SAM size in millimeter, SAM distance from aortic valve in millimeter, Doppler gradient at LVOT was calculated from the spectral Doppler velocity using the modified Bernoulli equation [8] then obstruction is graded as mild (peak gradient/mean gradient < 36/25 mmHg), moderate (peak gradient/mean gradient of 36–64/25–40 mmHg) or severe obstruction (peak gradient/mean gradient of >64/40 mmHg) [9]. Aortic insufficiency (AI) was assessed using color Doppler and graded as none, trivial, mild, moderate or severe according to the assessment of the reviewer of the Echo study. PDA size was categorized as small, moderate or large. All echocardiography studies were reviewed looking for AI progression and SAM recurrence.

Cardiac catheterization for PDA device occlusion was reviewed including echocardiographic evaluation for residual PDA shunt, aortic arch obstruction and pulmonary artery branches obstruction. We reviewed patient clinical data postoperatively looking for possible complications including residual PDA shunt, residual LVOT obstruction or new AI. We have also reviewed the postoperative ECG to assess the possibility of heart block.

3. Results

In this case series we have a total of 7 patients. Two patients were diagnosed after birth to have moderate PDA and at the age of 6 months both were diagnosed also to have SAM. Another patient was diagnosed with moderate PDA after birth and SAM at the age of 14 months (Table 1). The other four patients were referred to our center soon after diagnosis of isolated SAM and PDA at different ages. They were referred at ages 18 months, 20 months, 5 years and 8 years (Table 1).

Out of seven patient, two patients had severe LVOT obstruction with SAM being very close to the aortic valve but not tethered to the valve (Fig. 1). The tissue size measured 4 mm and 5 mm. Other two Patients had SAM with moderate LVOT obstruction. One of them was very close to the aortic valve with 5 mm SAM tissue. The other patient had a SAM tethered to the aortic valve and the tissue measured 4 mm. The last three patients had mild LVOT obstruction. One of them had SAM close to aortic valve (1 mm) and the tissue measured 2 mm. The other 2 patients had the SAM away from the aortic valve (4 and 5 mm) and SAM size measured 2 mm (Fig. 2). All the seven patients had AI with different severity. Three patients had trivial AI which was not progressive during follow up. Four patients had mild AI (Table 1), two of them had AI continued to progress to moderate.

Six out of the seven patients had intervention while the last one is under clinical follow up currently. Three patients underwent PDA device closure while surgical PDA ligation was performed in the other three patients. None of them had residual shunt or obstruction to the aortic arch or pulmonary artery branches. SAM resection was done for four patients. Two of them had no residual SAM or LVOT obstruction. Two patients had

Table 1. LVOTO severity and SAM-AV distance and AI at time of intervention.

LVOTO[a]		Age at Dx[b]	Gender	SAM-AV Distance	AI[c]
Severe	2	6	M	1 mm	Mild
		60	M	1 mm	Mild
Moderate	2	6	F	0 mm	Trivial
		18	F	1 mm	Trivial
Mild	3	14	F	1 mm	Mild
		20	M	4 mm	Trivial
		96	M	5 mm	Mild

AI: aortic insufficiency, AV: Aortic valve, Dx: diagnosis, LVOTO: left ventricular outflow tract obstruction. SAM: subaortic membrane.

[a] LVOTO at intervention.

[b] Age at diagnosis in months.

[c] AI at time of intervention.

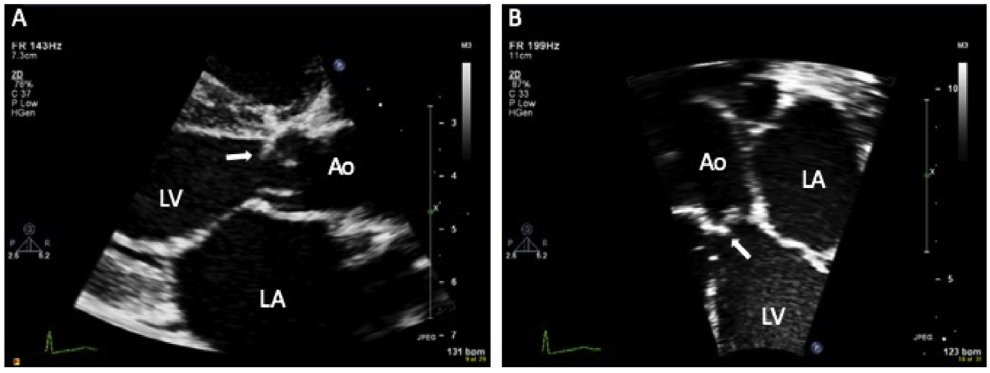

Fig. 1. A: LVOT parasternal long axis showing SAM close to aortic valve. B; Apical 5 chambers view showing SAM close to aortic valve for the same patient. Ao: Aorta, LA: Left atrium, LV: Left ventricle. Arrow: SAM.

recurrence of SAM, one of them had residual SAM and LVOT obstruction which was progressive and required another surgical intervention. The last patient had residual small SAM with mild LVOT obstruction and moderate AI. He is still under follow up and he may require another intervention. There were no other postoperative complications such as developing new AI or developing complete heart block.

There was no relation between gender, height, weight or age at diagnosis to the SAM clinical course. One of our patients had a small mid-muscular VSD, two patients had patent foramen ovale (PFO) and one patient had a small secundum atrial septal defect (ASD). All of them closed spontaneously.

4. Discussion

The combination of SAM and PDA is very rare and it has been reported only in three previous papers. We are reporting the largest case series of isolated SAM and PDA and we are the first to report this pathology combination in infancy. All of our patients were diagnosed in early childhood. Three patients were born in our hospital and they were diagnosed in infancy, while the other 4 patients were referred at 1–8 years of age. Steinherz L et al. reported female predominance with a ratio of 5:1 while there was no significant relation to the gender in our series with a ratio of 3:4.

The left ventricle outflow tract obstruction is one of the important variables to observe during follow up. The severity of LVOT obstruction was related to the distance between SAM and the aortic valve. Four of our patients had significant LVOT obstruction that required intervention and all of them had the SAM close to the aortic valve (Fig. 1). Patients with more than 4 mm distance between SAM and aortic valve did not require LVOT intervention (Fig. 2). Our study is consistent with the finding of Bezold et al., they indicated that LVOT obstruction was affected by the distance between the discrete subaortic stenosis and aortic valve. They found that patients who had SAM to aortic valve distance of 5.5 ± 3.3 mm tend to have non progressive LVOT obstruction, while patients who had distance of 3.0 ± 2.1 mm had progressive LVOT obstruction ($p < 0.05$) [10].

Aortic valve insufficiency is another major complication and a reason for surgical intervention in patients with SAM. Subaortic obstruction can result in a progressive aortic valve destruction which will lead to AI [4,5,10–14]. Lopes et al. found that aortic insufficiency develops in half of patients with subaortic stenosis, and if left untreated it may affect more than 80% [15]. All of our patients had AI with variable severity. The AI developed early in our patients as three of them were diagnosed in infancy and they had AI before reaching the age of 2 years. Worsening of AI is directly related to the progression of LVOT obstruction. Two of our patients had worsening of AI to moderate when their LVOT obstruction progressed from mild to moderate. AI develops secondary to a turbulent flow in LVOT which is generated by subaortic obstruction. Brauner et al. indicated that intervention should be done before LVOT obstruction reaches a maximum peak gradient of 40 mmHg to prevent aortic valve damage, recurrence and the need for reoperation [16]. Two of our patients underwent PDA device occlusion and the SAM was left untouched. The two patients had small SAM size with mild LVOT obstruction. Both patients had SAM away from AV (≥4 mm) (Table 1). The decision for PDA occlusion without SAM resection was based SAM size, distance from AV and severity of LVOT obstruction and non-significant AI.

Subaortic membrane is a progressive lesion and it carries high risk of recurrence [2,16–20]. The risk of

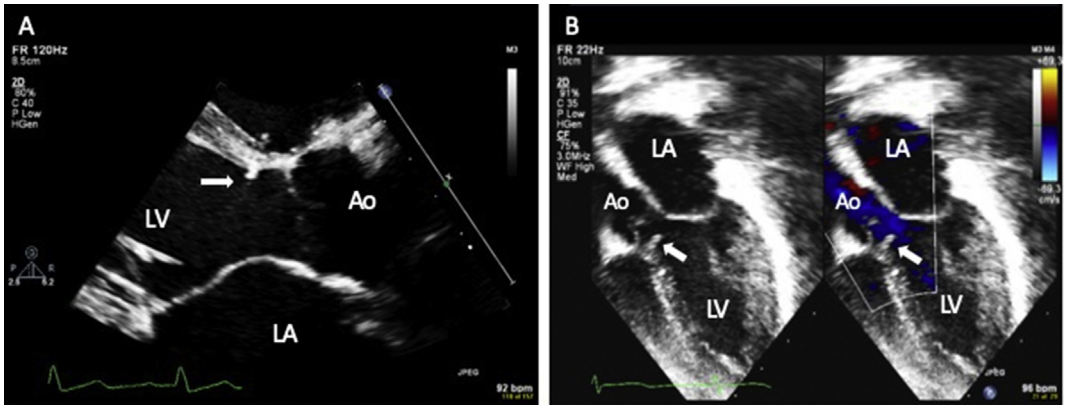

Fig. 2. A: LVOT parasternal long axis showing SAM away from aortic valve. B: Apical 5 chambers view with color compare showing SAM away from aortic valve. Ao: Aorta, LA: Left atrium, LV: Left ventricle. Arrow: SAM.

recurrence is reported to be between 6% and 30% [18]. Similar to what has been reported, two of our patients had recurrence of SAM and required re-intervention. After the PDA device occlusion, one of the patients had improved AI from mild to trivial. Although they were followed for 1–2 years, both patients had static mild LVOT obstruction. Multiple studies had been done aiming to evaluate risk of recurrence predictors. As indicated in multiple studies, we were observing for predictors of recurrence which include higher gradient at LVOT at the time of surgery, younger age at repair and shorter distance between the membrane and the aortic valve [10,21,22]. All of our patients who underwent SAM resection did well postoperatively with no complications such as worsening AI, heart block or residual LVOT obstruction. One patient had mild residual LVOT obstruction due to tethered SAM to the aortic valve. This confirms that surgical resection of SAM is a safe procedure with low risk of morbidity and mortality [5,21,23]. PDA intervention is also safe in this group of patients. Six of our patients underwent PDA closure (3 devices and 3 surgical ligation) with smooth postoperative course and no obstruction to the pulmonary artery branches or the aortic arch.

SAM is a common pathology in association with other congenital heart disease like ventricular septal defect. Jose maria et al., concluded that discrete subaortic stenosis in adults is increasing and it is related to the greater number of repaired CHD in childhood [24]. As of now, the SAM pathophysiology is not fully understood. Sir Arthur Keith has postulated that the reason of SAM development is secondary to incomplete atrophy of the bulbus cordis [25]. While Troyer believed that an embryonic membrane failed to undergo normal atrophy which leads to development of the SAM [5]. Van Mierop suggested that SAM happens secondary to malformation of the truncal septum at the proximal part where it joins the conus septum [26], while Van Praagh et al. objected that because the conal septum is muscular while the membrane is a fibrous structure. They suggested that the membrane origin is coming from the abnormal endocardial cushions [27]. Ezon believes that the interventricular septum at the LVOT is exposed to chronic shear stress that well lead to an abnormal endothelial and muscle proliferation resulting in LVOT obstruction. He has indicated that there are several factors which may increase the shear stress such as a narrow LVOT, exaggerated aortic override, increased mitral-aortic septation, and steep atrioventricular septal angle which may result in a chronic flow disturbance [28]. We think that isolated SAM and PDA have different underlying pathophysiology than SAM in other congenital heart diseases. We can postulate that, in the absence of congenital heart diseases, the genetic factors may play a role in development of isolated SAM and PDA.

5. Conclusions

The combination of subaortic membrane and PDA is a rare and interesting pathology. The need for intervention depends on the proximity of SAM to the aortic valve, worsening LVOT obstruction and AI. Intervention for both lesion is safe.

Author contribution

Conception and design of Study: Hussain Moafa, Alhabshan F. Supervision of the research; Funding for the researchand materials: Alhabshan F. Data collection: Hussain Moafa, Mohammed Alnasef, Obayda M. Diraneyya. Literature review and critical review: Hussain Moafa, Mohammed Alnasef, Obayda M. Diraneyya, Alhabshan F. **Drafting of**

manuscript: Hussain Moafa, Mohammed Alnasef; Alhabshan F

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Conflicts of interest

The authors declare no potential conflicts of interest.

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