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Sinus of Valsalva Aneurysms in Non-marfan Patients: An Underestimated Entity? A Case Series

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Authors' contributions

This work was carried out in collaboration between all authors. Author MC was responsible for data collection, performed the literature search and wrote the first draft of the manuscript. Author MNS provided all histopathological data and reviewed the manuscript. Author WL provided the echocardiographic data and reviewed the manuscript. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Aims: Sinus of Valsalva aneurysms are rare anomalies. Aneurysmal dilatation of the sinuses of Valsalva in Marfan syndrome has been extensively studied. The aim of this study was to investigate clinical manifestation, diagnosis, histopathological findings and management of sinus of Valsalva aneurysms in non-Marfan patients.
Study Design: Retrospective analysis, case-series.
Methodology: A search of digital echocardiographic recordings, histopathology and electronic patient databases in our institution for the period 2004 – 2012 was performed. All patients with asymmetrical dilatation of at least one coronary sinus of Valsalva at postmortem and ruptured (or dissected) aneurysms on echocardiogram were included. Patients with Marfan syndrome and those with non-ruptured sinus of Valsalva aneurysms on echocardiogram were excluded.
Results: A total of 12 patients (7 males; mean age 36.1 years) were studied. The right coronary sinus was the most commonly affected (9/12). Involvement of more than 1 sinus was seen in 3/12 cases. Four patients died suddenly and another 6 had acute or

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rapidly worsening symptoms. Three sudden deaths were due to dissection or rupture with haemopericardium and tamponade. Five cases had concomitant congenital heart defects.

Conclusion: Sinus of Valsalva aneurysms are an uncommon cause of morbidity and mortality in non-Marfan patients. They are associated with certain congenital heart defects. There is often associated aortopathy. Sudden death can be the first manifestation and is most commonly due to aneurysm rupture or aortic dissection into the pericardial space. Echocardiography is the investigation of choice for diagnosis and follow-up. Prompt surgical or percutaneous intervention has an excellent long-term outcome.

Keywords: Sinus of valsalva aneurysm; congenital cardiac defect; echocardiography; Marfan syndrome.

1. INTRODUCTION

The three cusps of the aortic valve are attached in a semilunar manner to the aortic root. The aortic sinuses of Valsalva are the spaces between the luminal surface of the aortic leaflets and the bulges in the aortic root wall. Two of the sinuses, almost invariably those adjacent to the pulmonary valve and also known as the facing sinuses, usually give rise to the right and left coronary arteries. They are intrapericardial and in close proximity to all the cardiac chambers, the atrial and ventricular septum and the atrioventricular node [1]. Sinus of Valsalva aneurysms result from weakness in the wall of the sinuses, which in turn can be congenital or acquired [2,3]. Congenital aneurysms can be associated with abnormalities of elastic tissue, as those found in connective tissue disorders like Marfan syndrome [4] and congenital cardiac anomalies including ventricular septal defects and bicuspid aortic valve [5]. With acquired aneurysms, the walls of the sinuses are weakened by infection, as in cases of infective endocarditis mainly on the aortic valve, inflammatory processes as in conditions like syphilis and Behçet's disease, or trauma [4,5].

Aneurysmal dilatation of the aortic root at sinus level in Marfan syndrome has been extensively studied [6,7]. Sinus of Valsalva aneurysms outside the context of Marfan syndrome are rare anomalies, yet they often lead to important symptoms if left untreated [2]. The aim of our study was to investigate sinus of Valsalva aneurysms in non-Marfan patients concentrating on clinical manifestation, diagnosis, histopathological findings and management.

2. METHODOLOGY

The cases were selected from the adult congenital heart disease digital echocardiogram database and patients registry within our institution (about 8000 patients) and all the heart specimens (about 1200 specimens) that reached our histopathology department during the 8-year period between 2004 and 2012.

We included all cases of documented asymmetrical aneurysmal dilatation of at least one coronary sinus of Valsalva, with or without rupture or dissection, from the postmortem specimens and ruptured aneurysms from the echocardiography database. All sizes of aneurysm were included. On echocardiogram, the criteria for diagnosing a sinus of Valsalva aneurysm included an origin above the aortic annulus, a saccular shape, and normal

dimensions of the adjacent aortic root and ascending aorta. A ruptured sinus of Valsalva aneurysm was diagnosed when a communication was present between the aneurysm and the adjacent cardiac chamber on colour flow mapping and a high-velocity continuous flow was detected on continuous wave Doppler.

The exclusion criteria were symmetrical aortic root dilatation involving all 3 sinuses and aneurysmal aortic dilatation of any type in patients with a confirmed diagnosis of Marfan syndrome. Cases from the echocardiographic database with only aneurysmal dilatation of the sinuses of Valsalva but no rupture were also excluded.

Further details of clinical manifestation and procedures undergone were obtained from the case notes.

3. RESULTS

There were a total of 12 patients identified (7 males; mean age 36.1 years). The clinical details are summarised in Table 1, where each case has been assigned a number for ease of reference in the text.

The right coronary sinus of Valsalva was the most commonly affected sinus (9/12; 75%), followed by the non-coronary sinus in 6/12 (50%). In 2/12 patients (16.67%), 2 sinuses were involved and 1 patient (8.33%) had aneurysms involving all 3 sinuses. In 5/12 (41.67%) patients, there were concomitant congenital cardiac defects – bicuspid aortic valve in 2, ventricular septal defect in 2 and subaortic stenosis needing trans aortic subvalvular myectomy in 1.

An associated aortic dissection was present in 3/12 (25%) patients and a ruptured aneurysm of the sinus of Valsalva was found in another 8/12 (66.67%) patients. Only 1 patient, marked as case 4 in Table 1, with a history of Klippel-feil syndrome, was known to suffer from hypertension and was on antihypertensive medication.

3.1 Clinical Presentation

Four patients died suddenly. One of these patients (case 1) was under investigation for a connective tissue disorder other than Marfan syndrome and was awaiting aortic root surgery. Another patient (case 4) was known to have Klippel-Feil syndrome with associated hypertension and hearing impairment and gave a history of increasingly frequent palpitations over the weeks preceding her death. The other 2 cases of sudden death had previously been well with no relevant past medical history.

Six other patients experienced acute or rapid symptomatic deterioration. One (case 10 in Table 1) was diagnosed after an out-of-hospital cardiac arrest while running at his local gym and was successfully resuscitated. The other 5 patients showed features of decompensated heart failure and were all found to have ruptured sinus of Valsalva aneurysms with important left-to-right shunts. In 4 of these, the main complaint was worsening breathlessness, while one patient with rupture into the right ventricular outflow tract had predominantly ‘right-sided’ failure with marked hepatic congestion and severe hepatic enzyme derangement.

Table 1. Summary of the clinical details, sinuses of Valsalva involved, associated defects and management for the 12 patients included in our study

Case no.	Sex	Age (yrs)	SoV involved	Findings on investigation	Other defects/ conditions	Management
Sudden deaths						
1	M	29	RC	2 dissection tears above aortic valve + haemopericardium	'Connective tissue disorder' – Marfan excluded	---
2	M	34	RC + NC	Dissection with tear in NC SoV + haemopericardium	---	---
3	M	38	RC + LC + NC	RCA stretched over aneurysm with no occlusion; no histological ventricular changes	---	---
4	F	33	NC	Ruptured NC SVA with haemopericardium	Klippel-Feil syndrome & HT	---
5	F	32	RC	SVA rupture into RVOT	BAV + AR	Surgery
6	M	39	NC	SVA rupture into RA	BAV + AR	Surgery
7	M	36	RC	SVA rupture into RVOT	Resected SAS	Surgery
8	M	46	RC	SVA rupture into RV body + RA	---	Surgery
9	F	25	RC	SVA rupture into RV body	VSD (subaorticperimembranous)	Surgery
10	M	46	LC + RC	Dissection + thrombus in LC SVA	---	Surgery
Asymptomatic						
11	F	48	NC	Small SVA rupture into RA	---	Percutaneous device closure
12	F	27	RC	Small SVA rupture into RV body	VSD (small muscular VSD)	Surgery

Abbreviations: SoV = sinus of Valsalva; LC = left coronary; NC = non-coronary; RC = right coronary; Ao = aorta; Asc = ascending; SVA = sinus of Valsalva aneurysm; RCA = right coronary artery; RA = right atrium; RV = right ventricle; RVOT = right ventricular outflow tract; LVH = left ventricular hypertrophy; BAV = bicuspid aortic valve; VSD = ventricular septal defect; AR = aortic regurgitation; f/h = family history; SAS = subaortic stenosis; HT = hypertension

Only 2/12 patients were asymptomatic. Both had chronic ruptured aneurysms with small left-to-right shunts, which were diagnosed incidentally on imaging.

Upon praecordial auscultation, all patients with a ruptured sinus of Valsalva aneurysm had a continuous murmur, though in some cases this was clinically misinterpreted as representing separate systolic and diastolic murmurs.

3.2 Histopathological Findings

Postmortem data was available for all 4 cases of sudden death. 2/4 cases of sudden death had aortic dissection with associated haemopericardium. Case 1 had a 21mm aneurysm of the right coronary sinus of Valsalva as well as an aneurysm of the aorta measuring 80mm in diameter for a length of 90mm from the aortic valve to the brachiocephalic trunk. There were 2 dissection tears located 30mm and 42mm above the aortic valve. Case 2 had aneurysms of the right coronary and non-coronary cusps with a total circumference of 110mm. In this case, the dissection tear was located in the non-coronary sinus aneurysm 50mm from the aortic valve (Fig. 1). Case 4 had an aneurysm of the non-coronary sinus of Valsalva measuring 60mm x 50mm x 30mm with rupture into the pericardial space resulting in haemopericardium (Fig. 2). Case 3 had a 50mm aneurysm of the right coronary sinus, a 40mm aneurysm of the non-coronary sinus and a 30mm aneurysm of the left coronary sinus. There was no evidence of dissection or rupture. The right coronary sinus aneurysm was bulging into the triangle of Koch involving the atrioventricular nodal conduction system and the right coronary artery was stretched over the aneurysm. There was no evidence of thrombosis or occlusion of the coronary artery and no histological features of ventricular infarction. Tissue histology in cases 1 and 2 showed widespread cystic medial degeneration of the aortic wall. In case 3, the cystic medial degeneration was limited to the sinuses with the rest of the aorta being normal. In case 4, histology of sections from the aneurysm showed thinning of the wall with diffuse replacement of elastin by fibromyxoid connective tissue, while sections from the uninvolved aorta were normal.

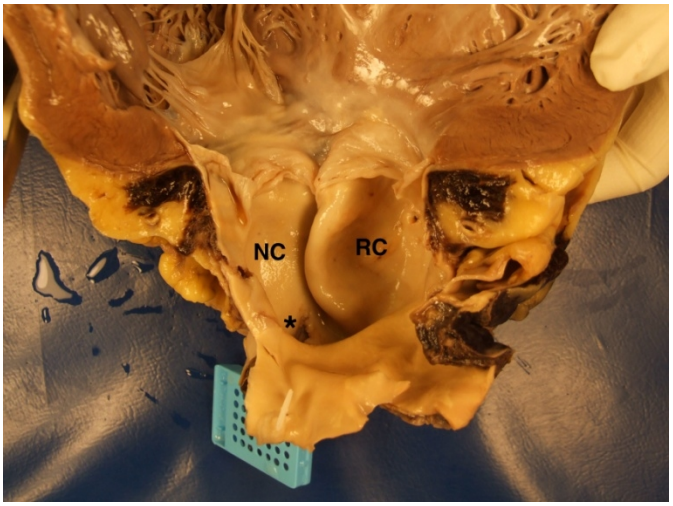

Fig. 1. Postmortem image for case 2 showing aneurysms of right coronary (RC) and non-coronary (NC) sinuses (labelled) with a dissection tear in the non-coronary sinus leading to haemopericardium (asterisk)

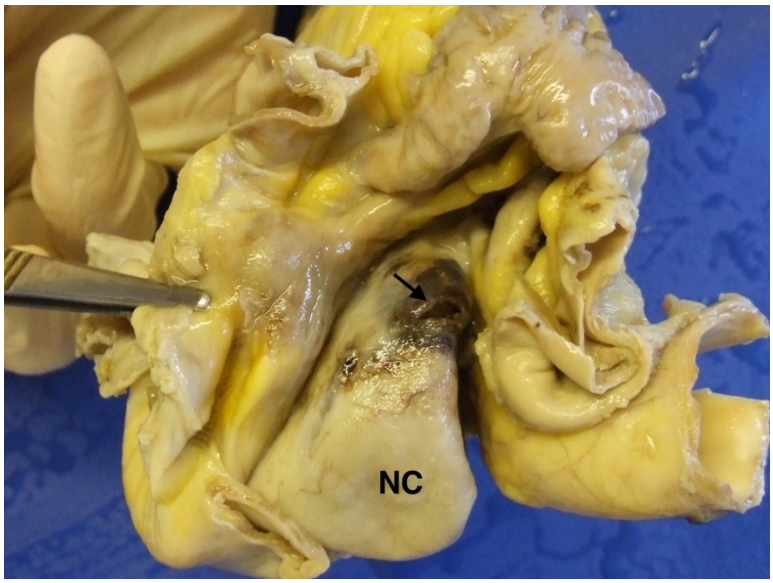

Fig. 2. Postmortem image for case 4 showing site of rupture (arrow) of the free wall of non-coronary sinus of Valsalva (NC) (labelled) resulting in a large haemopericardium

Histological information was available for 2/7 patients (case 5 and 6) who underwent surgical repair. In case 5, sections of the right coronary sinus of Valsalva aneurysm showed it to be lined by dense collagen with focal calcification and Lambl excrescence formation. Sections of the aortic wall away from the aneurysm showed focal disorganization of the elastic layers with an increase in smooth muscle cells. In case 6, the fistulous connection resulting from the ruptured non-coronary sinus of Valsalva into the right atrium consisted of fibrous tissue at one end of which was a cystic nodule lined with histiocytes. Sections of aortic wall showed focal nodular medial and subintimal fibrosis but no cystic medial degeneration.

3.3 Findings on Cardiac Imaging

Echocardiography was the main diagnostic imaging modality in the 8 live patients in our series. 7/8 patients had evidence of rupture, showing as a turbulent left-to-right jet on colour Doppler and a continuous high-velocity shunt on spectral Doppler interrogation (Figs. 3, 4). Rupture into the right ventricle occurred in 5 cases (3 into the right ventricular body and 2 into the right ventricular outflow tract) and the right atrium in 2 cases. A transoesophageal echocardiogram in the remaining case (case 10) showed aneurysmal dilatation predominantly of the left coronary sinus with evidence of dissection and thrombus inside the sinus (Fig. 5). Cardiac computed tomography was also used in this case to give more detailed three-dimensional information (Fig. 6).

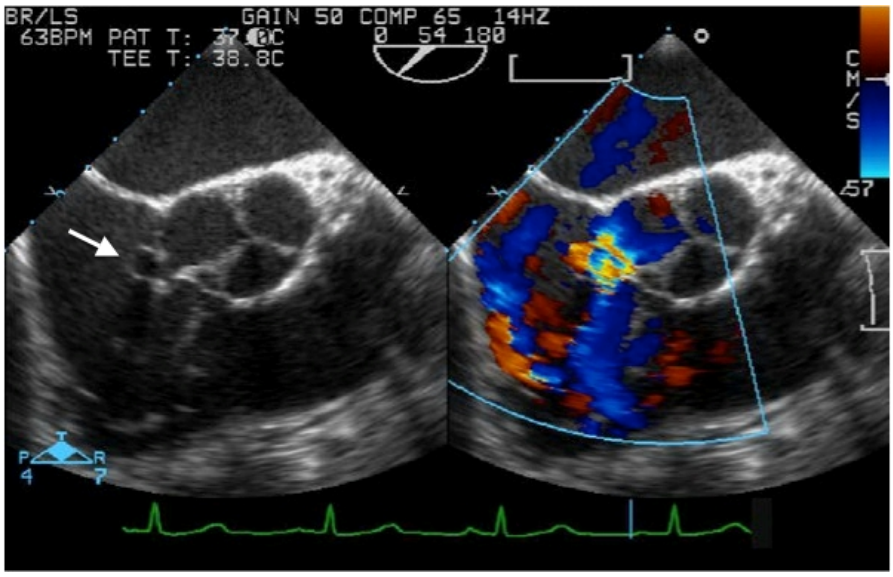

Fig. 3. Transoesophageal echocardiogram from case 11 showing a non-coronary sinus of Valsalva aneurysm (arrow) with a turbulent jet across the site of rupture into the right atrium

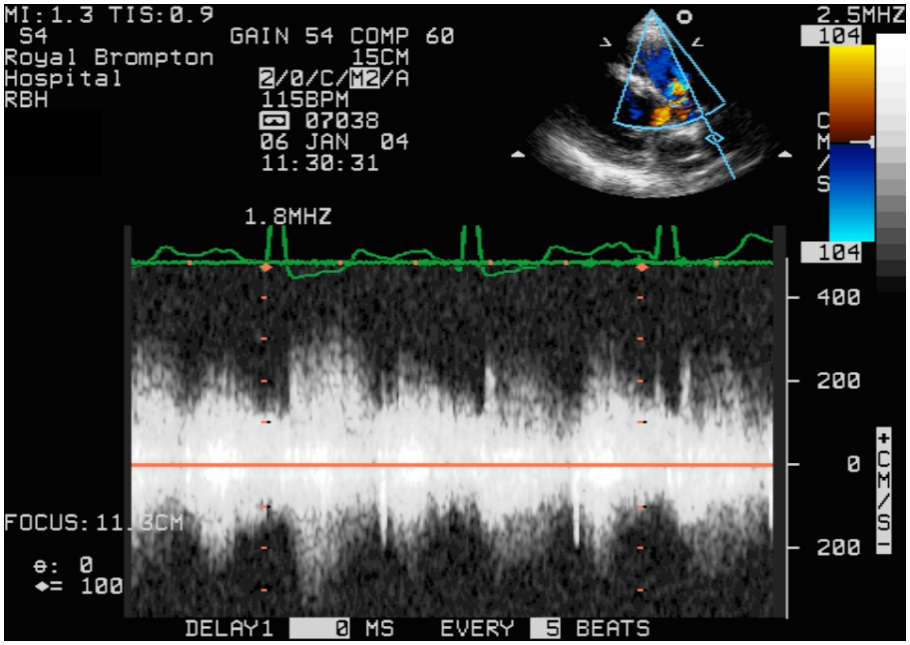

Fig. 4. Continuous-wave Doppler across the site of aneurysm rupture on parasternal long-axis view for case 7 demonstrating a continuous high-velocity shunting throughout the cardiac cycle

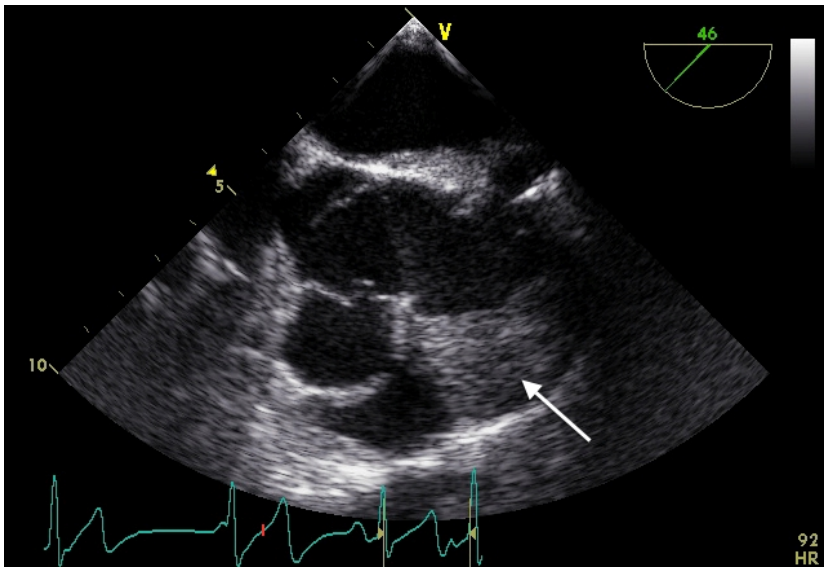

Fig. 5. Two-dimensional transoesophageal echocardiogram from case 10 showing aneurysmal dilatation of left coronary sinus with thrombus (arrow) in situ

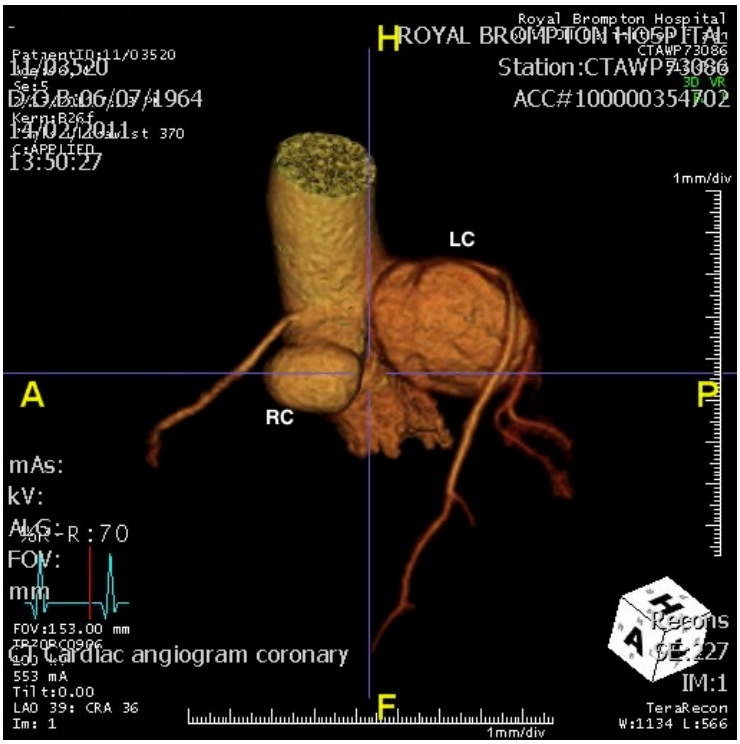

Fig. 6. Computed tomographic angiogram with three-dimensional reconstruction from case 10 showing a large left coronary sinus of Valsalva aneurysm measuring 45mm in its maximum diameter and a smaller right coronary sinus aneurysm measuring 23mm in its maximum diameter (labelled) with stretching of the left coronary artery

3.4 Management

7/8 live patients underwent surgical excision of the aneurysm and repair of any associated abnormalities shortly after the diagnosis was made. One patient (case 11) had a percutaneous device closure of the ruptured sinus. 7 patients remain well to date, while one patient (case 10) is presently awaiting aortic valve surgery for significant aortic regurgitation that has progressed since his initial surgery.

4. DISCUSSION

4.1 Prevalence and Clinical Presentation

Sinus of Valsalva aneurysms are rare. First described in 1839 by Hope et al [8], they have been found in 0.09% of 8138 autopsy subjects and in 0.15%–3.5% of patients who underwent open heart surgery [2]. Their rarity has been confirmed by the numbers found in our study: 7 ruptured and 1 dissected sinus of Valsalva aneurysms out of a population of 8000 adult congenital heart patients and 4 cases out of 1200 cardiac specimens assessed by our histopathology department.

The clinical presentation of sinus of Valsalva aneurysms varies extensively [2,4,5] as is also suggested by our case series. At one end of the spectrum are patients who are asymptomatic and at the other extreme are those who die suddenly; in between these 2 extremes are the majority of patients, who are those with significant ruptures who most commonly present with symptoms of heart failure from large-volume left to right shunting. Three of the 4 sudden deaths in our series were the result of haemopericardium and tamponade secondary to dissection or rupture into the pericardial space. Both cases of aortic dissection had histological evidence of cystic medial degeneration, suggesting that cystic medial degeneration is necessary for dissection to occur [9], even in patients who do not have Marfan syndrome. Also, the finding of abnormal aortic wall histology away from the sinus aneuryms (as seen in cases 1 and 2 as well as 5 and 6) suggests that, at least in certain patients, the presence of sinus of Valsalva aneurysms could be a manifestation of a more widespread aortopathy.

Aneurysm rupture into a cardiac chamber with the development of an acute significant left-to-right shunt most commonly causes symptoms of worsening heart failure, as seen in 5 cases in our series. A new loud continuous murmur along the sternal border in patients with these symptoms should raise the suspicion of rupture. In these cases, prompt surgery or intervention is necessary to prevent symptomatic deterioration [10].

Another recognised potentially fatal complication of sinus of Valsalva aneurysms is coronary artery obstruction [11] which was seen in 2 cases (case 3 and 10) in our series. In both these cases, the main sinus involved was one giving rise to a coronary artery (right coronary in case 3 and left coronary in case 10). The coronary arteries originating from the aneurysmal sinus in both these cases appeared to be stretched over the aneurysm though in neither of the cases did the coronary artery appear to be occluded. One could speculate that, in such cases, the mechanism behind the cardiovascular collapse is the development of malignant arrhythmias triggered by transient ischaemia from stretching of the coronary artery. Only 2 patients in our series were asymptomatic and both had chronic aneurysm ruptures with only a small left to right shunt. Timely surgical repair or percutaneous device occlusion of rupture can be life-saving and both have a very good long-term outcome[12].

4.2 Pathogenesis

The right coronary sinus is most commonly involved, followed by the non-coronary sinus, [2,12] and this trend was confirmed in our series, with 10 patients having aneurysms of the right coronary sinus. The aetiology of aneurysms in our series is likely to be congenital. Three patients had evidence of a non-Marfanaortopathy and one had Klippel-Feil syndrome – a multisystem condition in which sinus of Valsalva aneurysms have been documented in the literature [13,14]. Another 5 patients had an accompanying congenital cardiac anomaly – 2 had a ventricular septal defect, 2 a bicuspid aortic valve and 1 had undergone resection of subaortic stenosis. Both patients with an associated ventricular septal defect had aneurysms of the right coronary sinus. In case 9, the ventricular septal defect was perimembranous while in case 12 it was a small muscular defect. This differs from trends in the literature showing a higher incidence of right coronary sinus aneurysm with doubly-committed ventricularseptal defects and non-coronary sinus aneurysms with perimembranous defects [9].

4.3 Role of Imaging

Echocardiography plays an important role in diagnosing sinus of Valsalva aneurysms and rupture. According to the published case reports from the past, more than 90% cases were diagnosed by colour Doppler echocardiography [2]. In our series, all 8 live patients had a diagnosis of sinus of Valsalva aneurysm and rupture (or dissection) made on echocardiogram, confirming this to be the first-line imaging investigation [15]. Two-dimensional echocardiography demonstrates the site of aneurysm and its relation to adjacent structures. Colour Doppler shows turbulent flow across the site of rupture and spectral Doppler confirms a high-velocity continuous shunt throughout the cardiac cycle (Figs. 3, 4). The high-velocity continuous nature of the jet spanning the entire cardiac cycle helps distinguish aneurysm rupture into the right ventricle from a ventricular septal defect, where the flow is restricted mainly to the systolic phase. Although in some adult patients with ventricular septal defect and increased left ventricular end-diastolic pressure, diastolic left to right shunt can be present, the diastolic flow velocity is usually low (less than 2 m/s) as left ventricular diastolic pressure is much lower than diastolic pressure in the ascending aorta. With large ruptures, Doppler interrogation in the descending aorta can also demonstrate diastolic flow reversal. Echocardiography is also important for the long-term follow-up and monitoring of patients known to have sinus of Valsalva aneurysms to look for changes in size or complications such as aortic regurgitation. Further delineation of the anatomy of aneurysms can be obtained by cardiac magnetic resonance and electrocardiogram-gated contrast-enhanced computed tomography (Fig. 6). They also provide much better spatial resolution of cardiac structures and give detailed anatomic depiction of the Valsalva aneurysms in relation to surrounding structures [2].

4.4 Management

Aneurysmal dilatation of the aortic sinuses has been extensively studied in Marfan syndrome and there are clear guidelines for follow-up and management [6,7]. The behaviour of sinus of Valsalva aneurysms in non-Marfan patients is less known and most documentation in the medical literature consists of isolated case reports or surgical series relating to management of rupture. Our series suggests that, even in the non-Marfan population, sinus of Valsalva aneurysms can result in serious complications which are often life-threatening. On the basis of these findings, we would advise that patients with large non-ruptured aneurysms should

undergo elective surgical repair even if asymptomatic, also as such surgical repair is documented to be of low risk [12]. Prompt intervention, either surgical or transcatheter, of ruptured aneurysms should be undertaken to prevent clinical deterioration. Asymptomatic patients with smaller non-ruptured sinus of Valsalva aneurysms should have close follow-up and regular imaging, mainly by transthoracic echocardiography, to look for any increase in size of aneurysm and detect any rupture or complications like aortic regurgitation. Patients with certain congenital abnormalities, particularly ventricular septal defects and bicuspid aortic valve, should be screened for sinus of Valsalva aneurysms by Doppler echocardiography.

5. CONCLUSION

Sinus of Valsalva aneurysms are a rare but important entity that affects younger age groups. They could be a manifestation of a more widespread aortopathy even outside the context of Marfan syndrome and can be complicated by dissection or rupture, which carry a high morbidity and mortality. They are often associated with congenital abnormalities of the aortic wall. Patients diagnosed with such aneurysms should be followed up closely by means of regular echocardiograms. Early intervention is advisable both on large non-ruptured aneurysms to prevent serious and potentially fatal complications and on ruptured aneurysms irrespective of size to avoid clinical deterioration from left-to-right shunting.

CONSENT

Not applicable.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

The authors have no competing interests.

REFERENCES

1. Ho SY. Structure and anatomy of the aortic root. Eur J Echocardiogr. 2009;10(1):3–10.
2. Bricker AO, Avutu B, Mohammed T-LH, Williamson EE, Syed IS, Julsrud PR et al. Valsalva sinus aneurysms: findings at CT and MR imaging. Radiographics. 2010;30(1):99–110.
3. Edwards JE, Burchell HB. The pathological anatomy of deficiencies between the aortic root and the heart, including aortic sinus aneurysms. Thorax. 1957;12(2):125–139.

4. Ott D. Aneurysm of the sinus of Valsalva. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2006;13:165–176.
5. Feldman DN, Roman MJ. Aneurysms of the sinuses of Valsalva. Cardiology. 2006;106(2):73–81.
6. Stuart AG, Williams A. Marfan's syndrome and the heart. Arch Dis Child. 2007;92:351–356.
7. Baumgartner H, Bonhoeffer P, De Groot NMS, de Haan F, Deanfield JE, Galie N et al. ESC Guidelines for the management of grown-up congenital heart disease. Eur Heart J. 2010;3123:2915–2957.
8. Hope J. Case of an aneurysmal pouch of the aorta bursting into the right ventricle. In: Hope J, editor. A Treatise on the Diseases of the Heart and Great Vessels. Lea and Blanchard, Philadelphia. 1839;466-471.
9. Angelini P. Aortic sinus aneurysm and associated defects: can we extrapolate a morphogenetic theory from pathologic findings? Tex Heart Inst J. 2005;32:560–562.
10. Pasteuning WH, Roukema JA, van Straten AHM, van der AA M, Wonnink-de Jonge WF. Rapid hemodynamic deterioration because of acute rupture of an aneurysm of the sinus of Valsalva: the importance of echocardiography in early diagnosis. J Am Soc Echocardiogr. 2002;15:1108–1110.
11. Lijoi A, Parodi E, Passerone GC, Scarano F, Caruso D, Iannetti MV. Unruptured aneurysm of the left sinus of Valsalva causing coronary insufficiency. Tex Heart Inst J. 2002;29:40–44.
12. Moustafa S, Mookadam F, Cooper L, Adam G, Zehr K, Stulak J et al. Sinus of Valsalva aneurysms - 47 years of a single center experience and systematic overview of published reports. Am J Cardiol. 2007;99:1159-1164.
13. Nenci I, Malaguti R. [Congenital aneurysm of Valsalva's sinus in the Klippel-Feil syndrome]. Riv Patol Clin Sper. 1967;8:493–517. Italian.
14. Kawano Y, Tamura A, Kadota J. Klippel-Feil syndrome accompanied by an aneurysm of the non-coronary sinus of Valsalva. Intern Med. 2006;45:1191–1192.
15. Chiang CW, Lin FC, Fang BR Kuo CT, lee YS, Chang CH. Doppler and two-dimensional echocardiographic features of sinus of Valsalva aneurysm. Am Heart J. 1988;116:1283–1288.

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