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CASE REPORT

# Ruptured Sinus of Valsalva Aneurysm in Apert Syndrome: Case report

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**Abstract**

*Background*: **Sinus of Valsalva aneurysm (SOVA) is a rare anomaly of the aorta that can be congenital or acquired. It can be associated with syndromes such as Marfan syndrome and Ehlers-Danlos syndrome. However, to our knowledge, it has never been described in a patient with Apert syndrome. Although it often presents as an incidental finding on imaging, SOVA is associated with the risk of serious complications, including rupture. A possible connection between the conditions might be the FGFR2 gene mutation in Apert syndrome and the influence of a mutation in fibroblast growth factor 2 (FGF2) on heart development. Here we report a case of acute heart failure secondary to rupture of SOVA into the right atrium in a patient with Apert syndrome.**

*Case presentation*: **A 47-year-old Caucasian woman with a history of Apert syndrome and rheumatoid arthritis presented with shortness of breath, orthopnea, paroxysmal nocturnal dyspnea, and progressive bilateral lower extremity edema for 2 weeks. She was diagnosed with acute right heart failure due to ruptured SOVA. The patient underwent surgical repair of the ruptured SOVA. Unfortunately, her postoperative course was complicated by a stroke leading to brain death.**

*Conclusion*: **Ruptured SOVA is a quite rare but serious condition that can cause life-threatening complications. In this case, SOVA occurred in a patient with Apert syndrome. The case may suggest that these two conditions may be related through the FGFR2 gene mutation associated with Apert syndrome and the related growth factor FGF2 involved in heart development.**

*Keywords:* Right heart failure, Sinus of Valsalva aneurysm, Rupture of sinus of Valsalva aneurysm, Apert syndrome, Case report

## 1. Introduction

Apert syndrome is a rare autosomal dominant disorder that results from mutations in the fibroblast growth factor receptor 2 (FGFR2) gene at locus 10q26 (10q25-26). The prevalence of Apert syndrome is approximately 15.5 in 1,000,000 live births,[1] and FGFR2 mutation incidence is reported to be higher with advanced paternal age.[2,3] Apert syndrome is characterized by craniosynostosis, craniofacial anomalies, and severe symmetrical syndactyly of the hands and feet. Cardiovascular abnormalities are present in 10% of patients, including ventricular septal defect, atrial septal defect, coarctation of the aorta, and patent ductus arteriosus.[4]

To our knowledge, sinus of Valsalva aneurysm (SOVA), has never been described in a patient with Apert syndrome. Here we report a case of acute heart failure secondary to rupture of SOVA into the right atrium in a patient with Apert syndrome.

## 2. Case presentation

A 47-year-old Caucasian woman with history of Apert syndrome and rheumatoid arthritis presented with shortness of breath, orthopnea, paroxysmal nocturnal dyspnea, and progressive bilateral lower extremity edema for 2 weeks. The patient also

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reported a weight gain of 4.5 kg over the last 2 months prior to presentation. She was diagnosed with Apert syndrome in childhood, but her earlier medical records were not available. She did not have any current or previous history of smoking or alcohol use, and her family history was significant for heart failure in her maternal grandfather. Vital signs were significant for tachycardia up to 110 beats per minute, temperature 36.4 °C, blood pressure 141/77 mmHg, respiratory rate 18 breaths per minute, oxygen saturation 96% on room air. Her physical examination showed a 3/6 holosystolic murmur in the right upper sternal border and elevated jugular venous pressure. She did not have other signs of hyperdynamic circulation on examination. Laboratory studies were remarkable for elevated brain natriuretic peptide 1205 pg/mL (normal value [NV] <100 pg/mL), negative troponins, aspartate transaminase 102 U/L (NV 3-34 U/L), alanine transaminase 178 U/L (NV 15-41 U/L), and thyroid-stimulating hormone 4.6 μIU/mL (NV 0.4-4 μIU/mL).

Electrocardiogram (ECG) demonstrated sinus tachycardia and left anterior fascicular block. Chest x-ray revealed a small right-sided pleural effusion. Computed tomography angiography scan of the chest showed small bilateral pleural effusions and cardiomegaly with reflux into the intrahepatic veins, indicating right heart failure. Afterward, the patient underwent a transthoracic echocardiogram (TTE), which demonstrated normal ejection fraction, moderately enlarged right atrium and ventricle, and abnormal increase in color flow jet at the atrial septum. Transesophageal echocardiogram (TEE) was then done, which showed mildly dilated aortic root, noncoronary SOVA with possible communication to the right atrium, suggestive of ruptured SOVA (Fig. 1, Video). To confirm the diagnosis, the patient underwent cine cardiac magnetic resonance imaging (MRI), which was suggestive of communication between aortic sinuses and the right atrium.

The patient was managed with IV diuresis until she became euvolemic, then underwent repair of the ruptured SOVA, reconstruction of the sinus of Valsalva with a pericardial patch, and resuspension of the aortic valve. The surgery was complicated by bleeding and difficulty in liberating the patient from the cardiopulmonary bypass machine, which resulted in a prolonged aortic cross-clamp time. She required circulatory support with an intra-aortic balloon pump and vasopressors. The surgical pathology report of the aortic root showed benign aortic tissue with medial myxoid change and adventitial hemorrhage with no granulomas or malignancy. The aortic fistula pathology showed benign dense fibroconnective tissue with reactive changes, myxoid degeneration, and mild chronic inflammation with no malignancy or granulomas. After the surgery, the patient was moved to the cardiovascular intensive care unit and was kept on mechanical ventilation, intra-aortic balloon pump, and vasopressors. On day 2 postoperatively, the intra-aortic balloon pump was discontinued. However, she remained on vasopressor support and developed ileus. Unfortunately, after weaning her

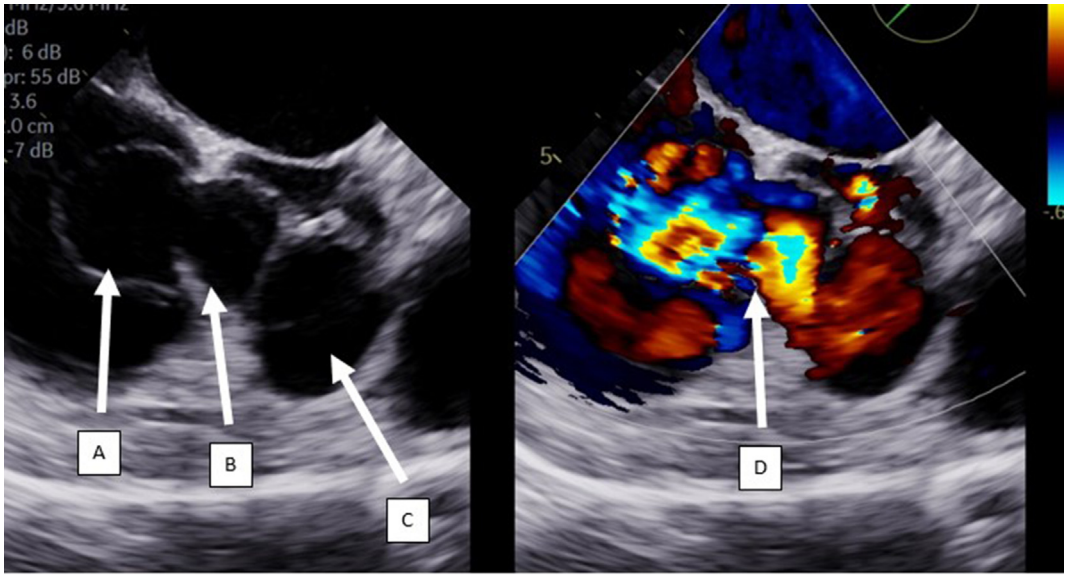


*Fig. 1. Left: Transesophageal echocardiogram short axis. Arrow A, sinus of Valsalva aneurysm, arrow B, left noncoronary cusp, arrow C, coronary cusp. Right: Transesophageal echocardiogram short axis with Doppler. Arrow D, sinus of Valsalva aneurysm. This view does not show rupture.*

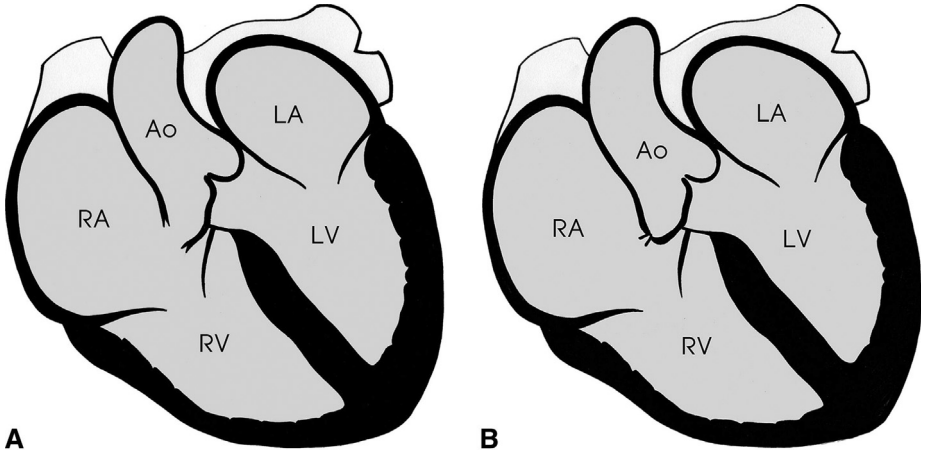


*Fig. 2. Surgical technique used for the repair of ruptured sinus of Valsalva aneurysm (RSVA) to the right atrium (RA). A, RSVA to the RA. B, Primary closure of fistulous communication. From Jung SH, Yun TJ, Im YM et al. Ruptured sinus of Valsalva aneurysm: transaortic repair may cause sinus of Valsalva distortion and aortic regurgitation. J Thorac Cardiovasc Surg. 2008; 135 (5):1153–1158. Reprinted with permission.*

off sedation in preparation for extubation, she was unresponsive, with a flaccid tone, fixed dilated pupils, and absent corneal, pupillary, ocular cephalic, vestibular cephalic reflex, and gag reflexes, which prompted a head computed tomography (CT) scan that showed a massive left cerebral hemisphere stroke with midline shift and herniation. Subsequently, considering her neurological examination and head CT scan findings, she was declared brain dead.

## 3. Discussion

SOVA is an abnormal dilation of the area between the aortic root annulus and the sinotubular ridge (Fig. 2).[5] Normally, the sinuses of Valsalva permit the opening of the aortic valve during systole without obstructing the coronary artery ostia. SOVA is a rare anomaly that affects the right coronary sinus in almost all cases, followed by the non-coronary sinus and left sinus.[6]

SOVA can be either acquired or congenital. Congenital aneurysms result from localized weakness of the elastic lamina at the junction of aortic media and annulus fibrosus. This is usually seen in hereditary collagen diseases such as Marfan syndrome and Ehlers-Danlos syndrome.[6–9] Acquired aneurysms result from elastic connective tissue degeneration leading to weakness of the sinus wall, which can be caused by infectious diseases such as bacterial-endocarditis and syphilis and from noninfectious diseases such as deceleration trauma.[10–12] Acquired SOVA can also be iatrogenic as a complication of aortic valve replacement[13–16] or ascending aortic dissection repair.[17]

Ruptured SOVA has been reported in about 35% of cases with only 25% presenting with acute symptoms.[17,18] The most common location of rupture is the right ventricle, followed by the right atrium.[6] Complications of ruptured SOVA vary depending on its anatomical location and communication with heart chambers (Fig. 2). In our case, rupture of the non-coronary sinus led to communication between the aorta and the right atrium, creating a left to right shunt and eventually right-sided heart failure.[18,19]

TTE and TEE are considered appropriate initial imaging modalities in diagnosing ruptured SOVA, which show continuous flow in systole and diastole on color Doppler.[20,21] Cardiac CT scan also has been used as a supplemental or confirmatory test.[22] Cine cardiac MRI is considered the gold standard test. However, it is not required if other imaging modalities sufficiently provide the diagnosis along with pertinent anatomic and physiologic details.[19]

SOVA is classified as a lesion with moderate complexity in the 2018 American Heart Association/American College of Cardiology (AHA/ACC) guidelines for the management of adults with congenital heart disease.[23] The mainstay of treatment is surgical, but there are no specific guidelines for SOVA surgical repair. Transcatheter closure has been reported in small number of cases in the literature with promising results.[23]

Untreated ruptured SOVA carries a poor prognosis with estimated mean survival of 1–2 years.[24] However, surgical intervention has an excellent prognosis in SOVA with estimated long-term survival of 90% at 15 years,[25] and surgical in-hospital mortality is quite low at 3.6%.[26] We believe that our patient's poor prognosis resulted from having a ruptured SOVA and having a prolonged intraoperative aortic cross-clamp time due to bleeding intraoperatively. To our

knowledge an association between Apert syndrome and SOVA has not been previously described. It is possible that this patient has two separate rare and unrelated disorders. The alternative explanation is that there is an association between Apert syndrome and SOVA. Apert syndrome is caused by FGFR2 gene mutation, and fibroblast growth factor 2 (FGF2) is involved in cell proliferation, angiogenesis, and heart development.[27] Heart defects are reported in 10% of Apert patients.[4] A mutation in FGF2 or its receptor might theoretically lead to higher risk of developing aneurysm.

## 4. Conclusion

Ruptured SOVA is a quite rare but serious condition that can cause life-threatening complications. In this case, SOVA occurred in a patient with Apert syndrome. The case may suggest that these two conditions are related through the FGFR2 gene mutation associated with Apert syndrome and the related growth factor FGF2 involved in heart development.

## Consent for publication

Our institution does not require IRB approval for case reports because, as reports on an individual patient intended to be shared for medical or educational purposes, case reports do not meet the definition for human subject research under the purview of an IRB. HIPAA requires written authorization, but if it is not possible to obtain authorization then the patient's PHI must be de-identified before submission to a journal or any other disclosure. We were not able to obtain written consent from the patient because brain death occurred and the patient died and consent from a family member was not possible because we were unable to reach the family member noted in the chart after multiple attempts. We ensured that we met all conditions to properly de-identify the patient's PHI in accordance with our institution's HIPAA guidance.

## Availability of data and materials

Not applicable.

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The authors declare that they received no funding for this study.

## Author contributions

M.H. and L.A. wrote the manuscript, reviewed the literature, and revised the manuscript for intellectual content. S.B. wrote the manuscript. L.C. and D. W. reviewed the literature and revised the manuscript for intellectual content. All authors read and approved the final manuscript.

## Conflict of interest

The authors declare that they have no competing interests.

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