Sinus of Valsalva Aneurysm and Infective Endocarditis Involving a Bicuspid Aortic Valve in an Infant With Trisomy 21

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ABSTRACT

A 19-month-old girl with trisomy 21 and a congenitally bicuspid aortic valve died following a short febrile illness. Autopsy disclosed pericarditis, epimyocardial abscess, infective endocarditis, and a sinus of Valsalva aneurysm. Microscopy demonstrated continuity between the aortic wall and valve leaflet, consistent with an acquired aneurysm. Abnormal hemodynamics associated with the valve malformation likely facilitated endocarditis. *Acad Forensic Pathol.* 2018 8(3): 763-768

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STATEMENT OF HUMAN AND ANIMAL RIGHTS

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INFORMATION

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INTRODUCTION

A 19-month-old girl with trisomy 21 became unresponsive while at home and died soon after being brought to the emergency room of a local hospital.

She had been born at 36 weeks and five days gestation via cesarean section to a 40-year-old gravida two para one mother with pre-eclampsia and diabetes. Neonatal echocardiogram disclosed a patent ductus arteriosus and bicuspid aortic valve (BAV), as well as a small, perimembranous ventricular septal defect (VSD) that was deemed hemodynamically insignificant.

One month following her most recent well-child check, the patient became ill with a fever and rhinorrhea for two days. The day of her death she was given acetaminophen and put to bed. One hour later, the mother found her unresponsive. Upon emergent transport to the local hospital, the patient had a temperature of 35°C, a Glasgow coma score of 3, and was found to be acidotic. After a failed trial of resuscitation, she was pronounced dead.

The local medical examiner performed an autopsy and found the patient had cardiomegaly (fresh weight: 80 g; normal: 43 g for height - 76.2 cm and weight - 10.4 kg) (1) and a purulent pericardial effusion. *Escherichia coli* was isolated from blood and pericardial fluid cultures. The cause of death was deemed consequences of sepsis due to pericarditis. The formalin-fixed heart was sent to University of California, San Francisco Pathology for further evaluation by a cardiovascular pathologist.

Examination of the enlarged heart showed an epimyocardial abscess and evidence of pericardial exudate (**Image 1**). A close-up view of the anterosuperior epicardial surface of the dissected specimen showed a protuberant mass with a 1.5 cm diameter between the right atrial appendage and the ascending aorta (**Image 1A**). A histologic section of the mass disclosed hemorrhage and intense inflammation of the abscess with numerous polymorphonuclear cells (**Image 1B and C**).

Dissection disclosed a minute ventricular septal defect sealed by tricuspid valve tissue. The BAV included conjoined right and left aortic coronary leaflets with a raphe (trisinate). While the smaller aortic valve leaflet appeared normal, the conjoined coronary leaflet had a flat vegetation on the ventricular aspect. A close-up view of the left ventricular outflow tract showed the bicuspid aortic valve with its relatively normal noncoronary leaflet as well as the adjacent conjoined leaflet, which had largely been destroyed by a vegetation (**Image 2**). Histology disclosed infective endocarditis with numerous coccobacilli. Just proximal to the aortic valve and beneath the infected leaflet, there was a fibrotic endocardial plaque consistent with traumatic callus.

In addition to the BAV involved by infective endocarditis, there was a broad, nonruptured, smooth-walled sinus of Valsalva aneurysm (2 cm in greatest diameter) involving the right sinus, as evidenced by the presence of the normally situated right coronary ostium (**Image 2**). The aneurysm was visible as a mild bulge externally. A histologic section of the aneurysmal wall and leaflet attachment disclosed continuity between the vessel media and the valve leaflet, similar to the normal anatomy seen in a corresponding section of the non-coronary sinus and leaflet.

Finally, histologic evidence of extensive subendocardial acute necrosis in the left ventricle was consistent with recent low-output state. Taken together, these findings affirmed the patient died from consequences of low-output state heart failure secondary to septic shock in association with infective endocarditis.

DISCUSSION

A sinus of Valsalva aneurysm (SoVA) is defined as an enlargement of the aortic root area between the aortic valve annulus and the sinotubular ridge (2). A sinus of Valsalva aneurysm can be congenital or acquired and is caused by any process that weakens the elastic lamina at the junction of the aortic media and valve leaflet (2, 3). Congenital SoVA is seen in connective tissue disorders such as Marfan syndrome and Ehlers-Dan-

Image 1: Epimyocardial abscess. **A)** Protuberant mass between the right atrial appendage (RAA) and the ascending aorta (Asc Ao). **B)** A histologic section shows hemorrhage and intense inflammation of the abscess (H&E, x12.5). **C)** High magnification demonstrates numerous polymorphonuclear cells (H&E, x400).

Image 2: A close-up view of the left ventricular outflow tract. The right coronary artery ostium (arrowhead) denotes the epicardial position of the abscess. The sinus of Valsalva aneurysm at the conjoined leaflet is dilated as compared with the normal sinus at the noncoronary leaflet.

los syndrome (2, 4). Acquired SoVA has been linked to similar connective tissue disorders, infectious etiologies, atherosclerosis, medial degeneration, chest trauma, aortitis, and iatrogenic injury (2, 4). Sinus of Valsalva aneurysm has also been associated with other cardiac abnormalities, including ventricular septal defects, aortic regurgitation, and aortic stenosis (2, 4).

The structural basis for congenital SoVA has long been controversial. Some studies attribute the dilatation to a malformation that creates a gap between the aortic wall media and the valve annulus (5). Other studies have shown that both congenital and acquired lesions have a normal connection, making a definitive distinction between congenital and acquired SoVA based on the histologic appearance of the connection challenging (5).

In our patient, the lack of a gap between the aortic media and the valve annulus could not help differentiate between a congenital or acquired SoVA. However, review of her neonatal echocardiogram showed no evidence of SoVA; thus, the aneurysm was likely an acquired lesion. The size of the aneurysm and lack of aortitis suggest that it preceded the infection, which implicates a cause other than the endocarditis in its formation.

Bicuspid aortic valve is a common cardiac malformation affecting 0.5% – 2% of the population, while SoVA has an estimated prevalence of only 0.09% (2, 4). There have been case reports of BAV (6, 7) and SoVA (3, 8) in patients with trisomy 21, but the relative risk of either anomaly's association with trisomy 21 has not been reported.

Patients with BAV may be at increased risk of developing SoVA. One study found that 9% of patients with SoVA had a concurrent BAV (2). A SoVA initially forms as a diverticulum due to forces acting on the aortic root. Congenital defects that exacerbate pressure in this area could lead to development of a SoVA (2). In a living patient, cardiac magnetic resonance imaging has documented the impact of abnormal hemodynamics due to bicuspid aortic valve in relation to a SoVA, suggesting an etiologic basis for

the dilated sinus (9). Our patient had congenital BAV and a ventricular septal defect, raising the possibility of a synergistic effect on her risk of developing SoVA.

While it is possible the SoVA was caused by elastic tissue weakening secondary to infection, based on our gross and microscopic findings, we speculate that the SoVA in our patient preceded the endocarditis and instead developed because of abnormal hemodynamics in association with the BAV, with possible contributions from her VSD prior to its closure.

The role of the aneurysm in the eventual development of infective endocarditis is open to debate. Bicuspid aortic valve is common among cases of endocarditis in infants (10). In our patient, there was no definitive evidence of chronic damage to the valve leaflet on microscopy; however, the area of injury that led to bacterial deposition was likely obscured by the vegetation. In children with native valve endocarditis, the most common isolates are viridans streptococci and *Staphylococcus aureus*. Although Gram negative enteric organisms, such as *Escherichia coli*, frequently cause bacteremia in infants, Gram negative organisms rarely cause infective endocarditis (11). Despite this, the results of blood and pericardial fluid culture support *E. coli* as the causative pathogen in our case.

CONCLUSION

This case of bicuspid aortic valve and acquired sinus of Valsalva aneurysm in a 19-month-old girl with trisomy 21 illustrates how the convergence of multiple cardiac anomalies can make the determination of cause and mechanism of death a challenge. For natural deaths occurring in the pediatric population, a thorough understanding of cardiovascular anomalies can prove invaluable in understanding mechanism of death.

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