Journal of the American Association for Laboratory Animal Science
Copyright 2011
by the American Association for Laboratory Animal Science

Vol 50, No 1
January 2011
Pages 94–97

Sinus of Valsalva Aneurysm in a Göttingen Minipig

Pamela P Ko,[1] Stacy L Pritt,[1,*] Karen E Mundwiler,[1] Valerie K Ackley,[1] Ray V Matthews,[2] and Martin Unverdorben[3]

A 26.6-kg, intact, 9-mo-old female Göttingen minipig was presented for a coronary stent study. Angiography revealed a sinus of Valsalva aneurysm (SVA) in the aortic root that involved both the left and noncoronary sinuses of the heart. Gross histologic examination of the heart revealed 2 regions of aneurysmal formation: one at the ostium to the left main coronary artery, with aortic sinus involvement, and the other at the dorsal aspect of the aortic root involving the noncoronary aortic sinus. With no history of any infectious diseases, and the microscopic findings showing no evidence of necrosis, degeneration, or infection, confirmed that the aneurysmal-like dilation of the sinuses was most likely a congenital anomaly. This case illustrates the diagnosis and comparative findings of a rare cardiac anomaly found in only a few species to date. To our knowledge, antemortem diagnosis of unruptured SVA involving both the left and noncoronary aortic sinuses of the minipig heart has not been reported previously.

Abbreviation: SVA, sinus of Valsalva aneurysm.

The aortic root has 3 aortic sinuses (sinus of Valsalva, sinus of Morgagni, and Petit sinus), including the left, right, and noncoronary sinus, which collectively are known as the sinuses of Valsalva. The left and right coronary arteries arise from the left and right aortic sinuses, respectively. In pigs, as in other quadruped mammals, the noncoronary aortic sinus has a dorsal (posterior) position in the aortic valve. On rare occasions, the sinus of Valsalva may have an outpouching (or dilation), termed 'sinus of Valsalva aneurysm' (SVA).[2] This rare condition has been reported in humans and two other species, including dogs and horses.[1,11,13,14] SVA can be congenital, as in connective tissue diseases (for example, Marfan syndrome in humans), or result from acquired degeneration of connective tissue from atherosclerosis, infection, or trauma. In human and veterinary medicine, aneurysms are found most commonly (76.8%) in the sinus associated with the right coronary vessel, occasionally (20.2%) in that related to the noncoronary vessel, and rarely (3.0%) in the left sinus.[2,7] These aneurysms can enlarge over time, thus becoming clinically relevant in humans; however, reported SVA in animals are incidental findings.

The following case report describes a Göttingen minipig with an SVA that is believed to be congenital in light of the absence of any clinical and histologic signs of inflammatory or connective tissue disease. Although the minipig was acceptable for use for a stent study, the anomaly might have precluded the animal's use in other cardiovascular studies. On the basis of an extensive literature review, we believe that this report is the first description of SVA in Göttingen minipigs.

Case Report

A 26.6-kg, intact female, 9-mo-old Göttingen minipig was presented for a coronary artery stent study that was approved by the facility's IACUC. The pig was purchased from an approved vendor of SPF Göttingen minipigs. Colony health records indicated that the animal was free from relevant infectious, contagious, and communicable diseases.

The research facility conducting the study is registered with the US Department of Agriculture and is AAALAC-accredited. On arrival at the facility, the minipig was housed in a room with another minipig from the same shipment. The pigs were housed in a large pen with raised floors. Relative humidity and room temperature were monitored electronically and maintained at 45% to 87% and 18.3 to 21.1 °C (65 to 70 °F), respectively. The minipig was fed a certified laboratory porcine diet (Teklad Certified Miniswine Diet, Harlan Laboratories, Madison, WI). Animal husbandry and sanitation procedures were in accordance with the Animal Welfare Regulations[3] and the *Guide for the Care and Use of Laboratory Animals*.[10]

The minipig was fasted (food only) for approximately 22 h before surgery on day 1. For the coronary stent study, angiography procedures were performed on days 1 and 36 of the study. All presurgical treatments were identical for both days. On the day prior to the first angiography, 2 doses of 75 mg clopidogrel and a single dose of 50 mg aspirin were administered orally. On the day of angiography, the minipig received an intramuscular injection of 0.26 mg glycopyrrolate (0.01 to 0.02 mg/kg) and then was sedated with an intramuscular injection of 106.4 mg Telazol (4.0 to 6.0 mg/kg; Fort Dodge Animal Health, Fort Dodge, IA) and 58.52 mg xylazine (2.2 mg/kg). To maintain stable anesthesia during surgery, 1.15% isoflurane and 4.0 L/min oxygen were administered by inhalation through a 5.5-French sterile endotracheal tube.

After a surgical plane of anesthesia was achieved, the minipig was placed in dorsal recumbency. The surgical incision site, on the right medial aspect of the right hindlimb, was shaved and prepped by using aseptic surgical techniques with povidone iodine and 70% isopropyl alcohol. Surface electrodes were positioned on the minipig to continuously monitor heart rate. Heart rate and pulmonary function were monitored during the procedure by applying a pulse oximeter (Dash 300, General Electric, Fairfield, CT) to the tongue of the animal. The minipig

Received: 01 Apr 2010. Revision requested: 26 Apr 2010. Accepted: 15 Jul 2010.
[1]B Braun Medical, Biological Test Center, Irvine, California, [2]University of Southern California, Department of Interventional Cardiology, US Cardiovascular Medicine, Los Angeles, California, and [3]B Braun Medical, Scientific Affairs Department, Bethlehem, Pennsylvania.
[*]Corresponding author. Email: stacy.pritt@bbraun.com

http://prime-pdf-watermark.prime-prod.pubfactory.com/ | 2025-02-25

was heparinized immediately prior to surgery to prevent blood coagulation during the procedure. The femoral artery was cannulated with an introducer sheath (B Braun Medical, Bethlehem, PA) and a 6-French guiding catheter (Runway Guide Catheter, Boston Scientific, Plymouth, MN) was advanced into the ostia of the right and left coronary arteries. A fluoroscope, also known as a C-arm, with imaging abilities specific to the cardiovascular system (model OEC 9800, General Electric) was used for the angiographic procedures. Coronary arteries were visualized by using contrast media (OptiRay, 320 Ioversol Injection 68%; Tyco Healthcare, St Louis, MO).

Enlargement of the aortic root was noted during angiography while the guiding catheter was navigated into the coronary ostia. Angiography of the aortic root revealed a SVA involving both the left and noncoronary aortic sinuses of the aortic valve (Figure 1). At the time of SVA identification, we surmised that the presence of the anomaly would not adversely affect the outcome of the stent study; therefore, the minipig was not excluded from the study.

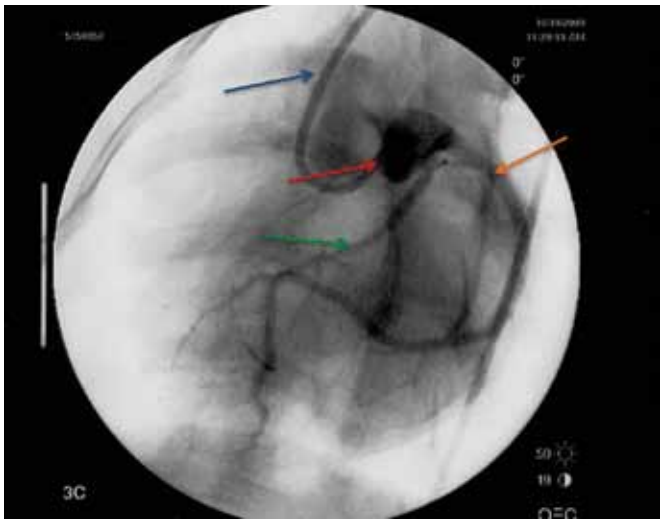

Figure 1. Angiogram taken during injection of the left coronary shows contrast medium refluxing into the sinus of Valsalva involving the ostium of the left main coronary artery. The red arrow indicates the location of the SVA, the blue arrow indicates the placement of the catheter, the green arrow indicates the left anterior descending coronary, and the orange arrow indicates the circumflex coronary

The minipig recovered uneventfully from the stent deployment procedure and was supported by receiving 0.3 mg/mL buprenorphine (Hospira, Lake Forest, IL) intramuscularly immediately after the procedure. Until follow-up angiography on day 36, 75 mg clopidogrel and approximately 40 mg aspirin (half of an 81-mg tablet) were administered orally once daily. No specific treatments were instituted for the SVA condition. During the study (days 1 through 36), the pig experienced no adverse events: all parameters, observed at least once daily, were within normal limits.

The second angiographic procedure was performed on day 36, the scheduled end of the study. This procedure followed the same anesthesia protocol as previously described. While under anesthesia and after angiography, the minipig was euthanized with a commercially available euthanasia solution (Euthasol, Virbac Animal Health, Fort Worth, TX). The heart was perfused with 0.9% normal saline, rapidly excised en bloc, and then perfused with 10% neutral buffered formalin for approximately 24 hours. Immediately after perfusion, the heart was submitted for histopathologic analysis to a pathology laboratory specializing in cardiovascular studies (CVPath Institute, Gaithersburg, MD). A board-certified veterinary pathologist performed the histologic evaluations.

Gross histologic examination revealed 2 regions of aneurysmal formation: one at the ostium to the left main coronary artery, and the other at the dorsal aspect of the aortic root (Figure 2). The aortic root, with surrounding myocardium and the attached coronary arteries then were dissected from the heart (Figure 3).The dilation, located in the noncoronary (dorsal) sinus of Valsalva, measured 0.9 cm in diameter. Sectioning revealed a mildly thin aortic wall. The left coronary sinus and ostium to the left main coronary were dilated (diameter, 1.0 cm), although the aortic wall and main coronary in the region did not grossly appear to be attenuated (Figure 4).

The microscopic findings showed no evidence of necrosis, degeneration, or infection and confirmed the hypothesis

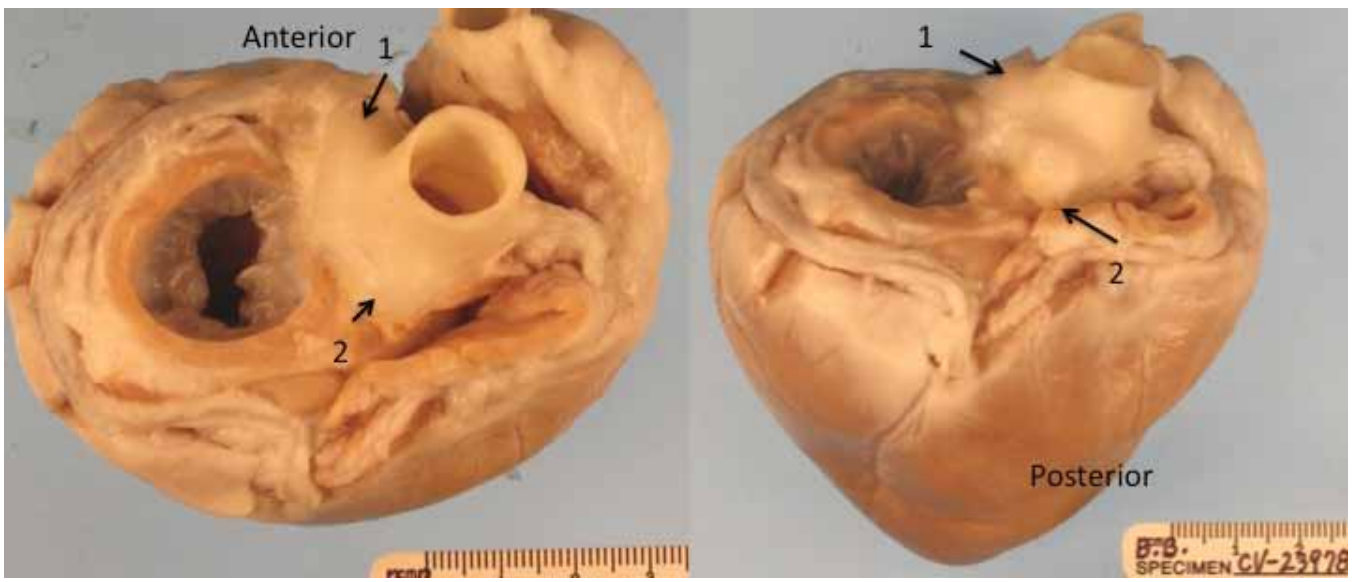

Figure 2. Postmortem specimen showing craniocaudal and dorsoventral views of the swine heart. Gross histologic examination indicated 2 regions of aneurismal formation. Arrow 1 indicates position of the SVA in the region of the left main coronary artery. Arrow 2 indicates the position of the SVA in the dorsal region of the aortic root.

http://prime-pdf-watermark.prime-prod.pubfactory.com/ | 2025-02-25

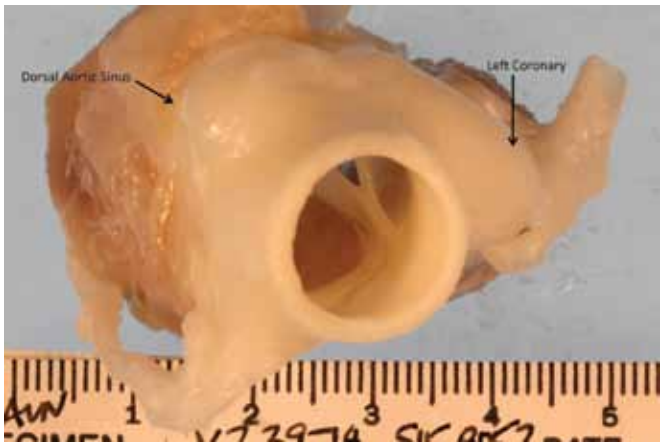

Figure 3. Cranial view of the aortic root. The arrows indicate 2 bulging regions (dorsal aortic sinus and left main coronary artery), which mark the presence of the SVA.

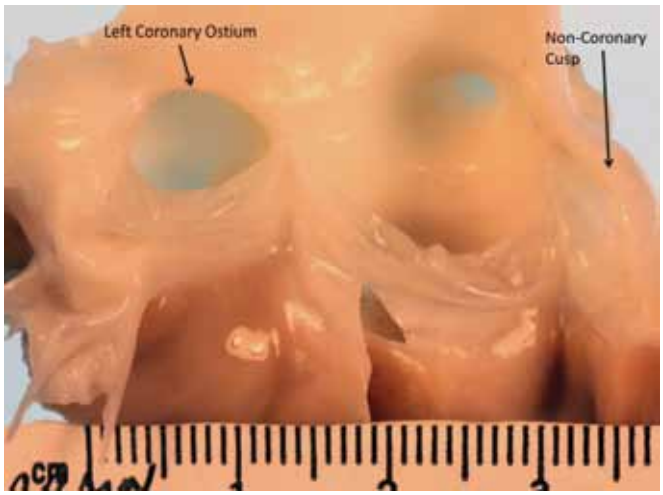

Figure 4. Aorta opened through the noncoronary (dorsal) sinus. The left arrow indicates the dilated left coronary ostium; the right arrow indicates the SVA in the region of the noncoronary sinus.

that the aneurismal-like dilation of the sinuses most likely represents a preexisting anomaly, with no relation to the stent study test device.

Discussion

An SVA is defined as a localized weakness of the wall of the sinus of Valsalva, leading to focal bulging of the aortic sinus, which may rupture into an adjacent cardiac chamber and create an aortocardiac fistula.[6] This presentation is distinct from the diffuse dilation of all sinuses seen in patients with connective tissue disorders.[4] SVA can present in unruptured or ruptured forms. Unruptured SVA are usually incidental findings of routine echocardiography or when connective tissue diseases trigger the search for an anomaly of the aorta. When associated with aortic valve disease, SVA may become symptomatic, with heart murmurs, chronic chest pain, shortness of breath, or dyspnea as the chief complaints, or may be noticed after surgical procedures.[2] Ruptured SVA may result in sudden cardiac death as a consequence of the acute onset of congestive heart failure, arrhythmia, cardiac tamponade, or ischemia.[12] Transthoracic echocardiography is the most common diagnostic approach for SVA, because this technique visualizes the aortic root. Color-coded Doppler color echocardiography is the primary technique used to capture ruptured aneurysms with their associated aberrant blood flow.[13,14] Transesophageal echocardiography is more appropriate when a clear image of a fistulized aneurysm is desired. In asymptomatic SVA, regular follow-up using noninvasive imaging techniques determines the indication for elective surgery with typically excellent results. Acute symptomatic and complicated SVA require emergency surgery, with excellent results.

SVA are rare anomalies in humans and are found infrequently in both human and veterinary medicine.[9] In humans, the male-to-female incidence ratio is 3.5:1. A 5-y retrospective study reported an apparently increased rate of SVA in patients of Asian origin.[8] As congenital SVA progresses, symptoms usually develop in adulthood.[6] There are limited case reports of ruptured and unruptured SVA in humans. For example, a pregnant Korean woman, who had a congenital heart defect since childhood, developed a heart murmur during her third pregnancy. Transthoracic echocardiography revealed a thinned wall, slightly aneurysmal dilation of the right coronary sinus of Valsalva of the aortic sinus.[12] The physiologic hemodynamic changes during pregnancy—including decreased systemic vascular resistance, increased cardiac stroke volume in the first and second trimesters but slightly decreased in the third trimester, increased (40% to 50%) blood volume, and increased (30% to 50% above baseline) cardiac output— may contribute to the worsening of cardiac status in patients with anatomic cardiac defects. Pregnancy places hemodynamic strain on the cardiovascular system and can be risky in women with underlying cardiac disease. In the case of the pregnant woman with asymptomatic SVA,[10] medical management focused on treating the heart failure, arrhythmia, and endocarditis that occurred during the pregnancy period. In addition, cardiac surgery during pregnancy has been found to reduce the likelihood of fetal loss.[5]

Our extensive search of the veterinary literature revealed only 2 case studies of SVA. The single antemortem case report referred to an 18-mo-old, 25-kg, male Dalmatian with rupture of the left aortic sinus into the pulmonary artery.[1] The postmortem case report described a 15-y-old, Standardbred broodmare with an aortic sinus aneurysm, which ruptured and subsequently led to rupture of chorda tendinea of the tricuspid valve, tricuspid regurgitation, and acute right-sided congestive heart failure.[13]

In this minipig case study, the possible genetic and congenital anomaly was first identified by angiography. This case illustrates the diagnosis and comparative findings of a rare cardiac anomaly reported in only a few species to date. A symptomatic SVA are likely under-reported in the literature because routine examinations would not detect the anomaly. To our knowledge, antemortem diagnosis of unruptured SVA, involving both the left and noncoronary aortic sinuses of the minipig heart, has not been reported previously. The current report represents a unique case in veterinary and laboratory animal medicine.

References

1. **Abbott JA, Prozio P.** 1998. Rupture of the left aortic sinus into the pulmonary artery in a Dalmation dog. Vet Radiol Ultrasound. **39:**544–550.
2. **Alexi MM, Melissa MC.** 2009. Sinus of Valsalva aneurysm. Proc (Bayl Univ Med Cent). **22:**338.
3. **Animal Welfare Regulations.** 2008. 9 CFR 3.125–3.142.
4. **Banerjee S, Jagasia DH.** 2002. Unruptured sinus of Valsalva aneurysm in an asymptomatic patient. J Am Soc Echocardiogr **15:**668–670.

http://prime-pdf-watermark.prime-prod.pubfactory.com/ | 2025-02-25

5. **Becker RM.** 1983. Intracardiac surgery in pregnant women. Ann Thorac Surg **36:**453–458.
6. **Choudhary SK, Bhan A, Sharma R, Airan B, Kumar AS, Venugopal P.** 1997. Sinus of Valsalva aneurysm: 20 years'experience. J Card Surg **12:**300–308.
7. **Chu SH, Hung CR, How SS, Chang H, Wang SS, Tsai CH, Liau CS, Tseng CD, Tseng YZ, Lee YT.** 1990. Ruptured aneurysms of the sinus of Valsalva in Oriental patients. J Thorac Cardiovasc Surg **99:**288–298.
8. **Dong C, Wu QY, Tang Y.** 2002. Ruptured sinus of Valsalva aneurysm: a Beijing experience. Ann Thorac Surg **74:**1621–1624.
9. **Edwards JE, Burchell HB.** 1957. The pathological anatomy of deficiencies between the aortic root and the heart, including aortic sinus aneurysms. Thorax **12:**125–139.
10. **Institute for Laboratory Animal Research.** 1996. Guide for the care and use of laboratory animals. Washington (DC): National Academies Press.
11. **Jandrey KE, Smarick SD, Burkitt JM, Labelle P, Mohr FC, Kittleson MD.** 2005. Giant unruptured aneurysm of the left sinus of Valsalva in the left ventricular outflow tract of a young dog. J Vet Intern Med **19:**602–605.
12. **Latzman J, Makaryus AN, Rosman D.** 2006. Ruptured sinus of Valsalva aneurysm in a pregnant woman. Tex Heart Inst J **33:**66–69.
13. **Roby KAW, Reef VB, Shaw DP, Sweeney CR.** 1986. Rupture of an aortic sinus aneurysm in a 15-year-old broodmare. J Am Vet Med Assoc **189:**305–308.
14. **Sleeper MM, Durando MM, Miller M, Habecker PL, Reef VB.** 2001. Aortic root disease in four horses. J Am Vet Med Assoc **219:**491–496.

http://prime-pdf-watermark.prime-prod.pubfactory.com/ | 2025-02-25