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Case Report

Total anomalous pulmonary venous connection in a mature dog☆,☆☆

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Abstract A 2-year 10-month, male neutered, crossbreed dog presented for evaluation of cyanosis and exercise intolerance. Doppler echocardiography revealed severe dilation of the right atrium and right ventricle with moderate pulmonary hypertension. Right-to-left shunting across a large ostium secundum atrial septal defect was confirmed by contrast echocardiography. Thoracic radiography revealed a vascular pattern together with cardiomegaly. Computed tomography angiography identified an anomalous pulmonary venous connection in which all pulmonary veins, apart from the right middle vein, coalesced into a single, large aneurysmal vein that then drained into the right atrium via the cranial vena cava. The distal opening of the right middle pulmonary vein could not be determined. A presumptive

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diagnosis of partial anomalous pulmonary venous connection was made. The dog was medically managed with sildenafil (1.5 mg/kg by mouth [PO] every 8 h) and remained clinically stable for 2 months before euthanasia due to worsening exercise intolerance. On postmortem examination, all pulmonary veins, including the right middle vein, were shown to communicate with a single, large central vein. This large vein then connected with the right atrium via the cranial vena cava, consistent with a total anomalous pulmonary venous connection. This case report describes a rare congenital abnormality which has not been previously reported in a mature dog.

Abbreviations

ASD	atrial septal defect
CT	computed tomography
TAPVC	total anomalous pulmonary venous connection

Case description

A 2-year 10-month, male neutered crossbreed dog weighing 16 kg presented to the Royal (Dick) School of Veterinary Studies, University of Edinburgh, for evaluation of cyanosis and exercise intolerance of approximately 4-weeks duration. The dog had been adopted from a shelter 1 year previously. Exercise intolerance was associated with exertional dyspnoea and lingual cyanosis. Occasional coughing was also reported, often associated with regurgitation. The owner did not report a change or abnormality in resting or sleeping respiratory rates. On clinical examination, there was a grade II/VI systolic murmur over the left heart base and cyanosis of the lingual mucosa. The dog was panting, making evaluation of the respiratory rate and effort difficult. The rest of the examination was unremarkable.

Initial diagnostics included a complete blood count and serum biochemistry. Abnormalities included elevated albumin (38 g/l, reference range 26—35 g/l), creatine kinase (446 U/l, reference range 50—200 U/l), and creatinine (141 μmol/l, reference range 40—132 μmol/l). A mild hypophosphataemia was also noted (0.70 mmol/l, reference range 0.90—2.0 mmol/l). Arterial blood gas analysis revealed a respiratory alkalosis (pH 7.47, reference range 7.36—7.44), with hypocapnia (PCO_2 24 mmHg, reference range 36—44 mmHg) and reduced bicarbonate (15.9 mmol/l, reference range 24.0—26.0 mmol/l). Severe hypoxaemia (PO_2 47 mmHg, reference range 90—100 mmHg) was also present, corresponding to a SpO_2 of 86%.

Systolic blood pressure (Doppler) was 147 mmHg. A six-lead electrocardiograph[b] demonstrated sinus rhythm with right axis deviation of the mean electrical axis. The right lateral and dorsoventral thoracic radiographs (Fig. 1a and b) revealed moderate cardiomegaly (vertebral heart score 12) and prominent pulmonary veins and arteries. These findings were accompanied by a large, tubular soft tissue opacity dorsal to the carina, extending from the fourth to the eighth intercostal space visible on the right lateral view (Fig. 1a).

Cardiomegaly and the soft tissue opacity were investigated further by Doppler echocardiography.[c] The right atrium and ventricle were severely dilated. The interventricular septum was flattened, and the left ventricle was small (left ventricular internal dimension in diastole normalised to bodyweight of 1.0, reference range 1.27—1.85 [1]). A large ostium secundum atrial septal defect (ASD), measuring approximately 13 mm, was identified. Interrogation with colour Doppler revealed right-to-left shunting across the defect (Video 1), which was subsequently confirmed by contrast echocardiography. The pulmonary artery was markedly dilated, with elevated flow velocity across the pulmonic valve of 2.1 m/s (reference range 1.2 ± 0.2 [2]) and unremarkable valve leaflets. There was no discernible step-up of flow velocity across the valve, suggesting a relative pulmonic stenosis, i.e. secondary to volume overload, rather than a true pulmonic stenosis. There were moderate tricuspid (3.36 m/s; normal resting value <2.8 m/s [3]) and pulmonic (3.01 m/s; normal resting value <2.2 m/s [3]) insufficiencies present, suggesting a systolic pressure gradient of ~45 mmHg and diastolic pressure gradient of ~36 mmHg, respectively. These values were consistent with pulmonary hypertension [3], but were

[b] AT-102 Plus, Schiller, Switzerland.
[c] Vivid-7, GE-Healthcare, USA.

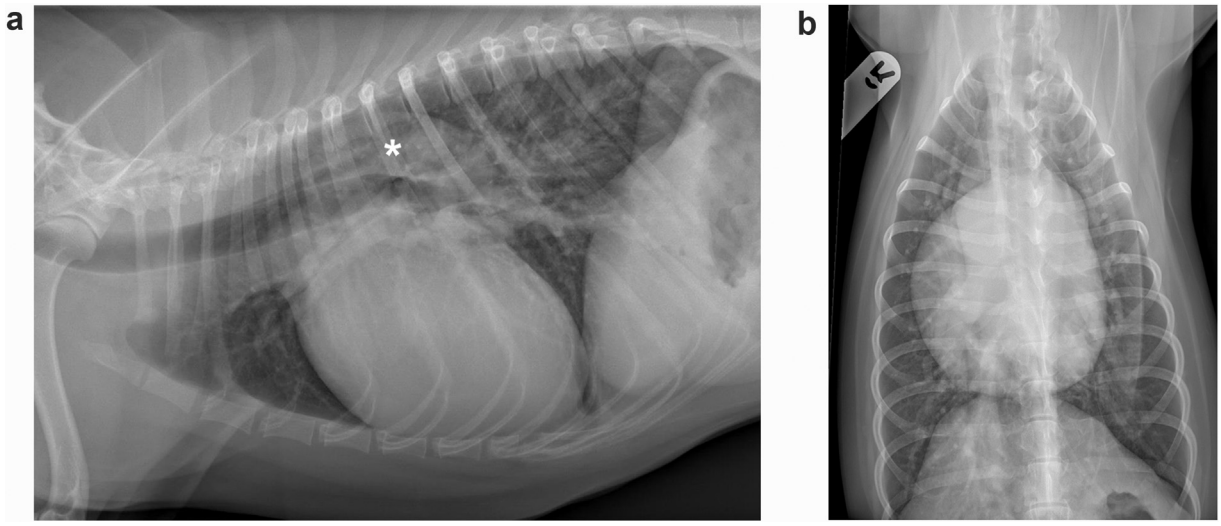

Fig. 1 Right lateral (a) and dorsoventral (b) thoracic radiographs showing moderate cardiomegaly together with a vascular pattern. *A soft tissue opacity is present dorsal to the carina on the lateral projection.

presumed to underestimate pulmonary artery pressure, given the dilated right atrium and hepatic venous congestion identified later using multidetector computed tomography (CT).[d] Pulmonary-systemic flow ratio (Qp:Qs) was estimated using two-dimensional echocardiography and pulsed wave spectral Doppler. The estimated shunt ratio was 5.6, indicating a greater pulmonic vs. systemic flow [4]. Systolic function of the right ventricle was adequate based on a tricuspid annular planar systolic excursion of 15 mm (reference range according to [5]), fractional area change of the right ventricle of 35% (reference range 35.6—59.2% [6]) and S′ 10.1 cm/s (reference range 8.0—21.0 cm/s [6]). Neither pulmonary veins nor entrance of the pulmonary venous flow could be visualised on standard and non-standard views of the left atrium.

A bedside enzyme-linked immunosorbent assay (ELISA) test for *Angiostrongylus vasorum*,[e] performed because of pulmonary hypertension, was negative.

To investigate further causes of pulmonary hypertension, CT angiography was performed. Contrast medium[f] was injected into the right cephalic vein (2 ml/kg, 4 ml/s) via a power injector system.[g] Dextro and levo phases of the heart followed by a late phase of the thorax were performed. Moderate dilation of the right atrium and right ventricle was observed together with a generalised increased vascular pattern especially in the right hemithorax. The course taken by venous drainage from the right middle lung lobe was not clearly identifiable. The venous drainage from the other lobes merged into two distinct pulmonary veins, one from the left cranial and caudal lung lobes and one from the right cranial, caudal, and accessory lung lobes. These two vessels subsequently fused into a common large, aneurysmal, tortuous vessel that was dorsal to the mainstem bronchi (Fig. 2) and entered the right atrium via the cranial vena cava (Fig. 3). In an early dextro cardiac phase, contrast medium entering the right atrium 4 s after injection crossed the interatrial septum through the ostium secundum ASD and entered the left atrium. In the venous phase, moderate distension of the hepatic vasculature was highlighted. This was consistent with hepatic congestion upstream of elevated right atrial pressure. No other congenital abnormalities, e.g. asplenia, were identified based on this CT examination which was extended to include the cranial abdomen.

Owing to financial constraints, surgical management could not be considered. Medical management consisted of sildenafil PO (1.5 mg/kg q 8 h) to address the pulmonary hypertension. After 2 months, exercise intolerance and cyanosis had become so marked that the owner requested euthanasia.

On postmortem examination, there was right-sided cardiomegaly with marked right atrial dilation and severe engorgement of all the lobar branches of the pulmonary veins. The lobar branches, including the right middle vein (Fig. 4),

[d] Somatom Volume Zoom, Siemens, Germany.
[e] Angio Detect™, IDEXX, Wetherby, UK.
[f] Iomeron® 400 mg/ml Iomeprol, Bracco, Italy.
[g] Mark V Plus®, Medrad®, UK.

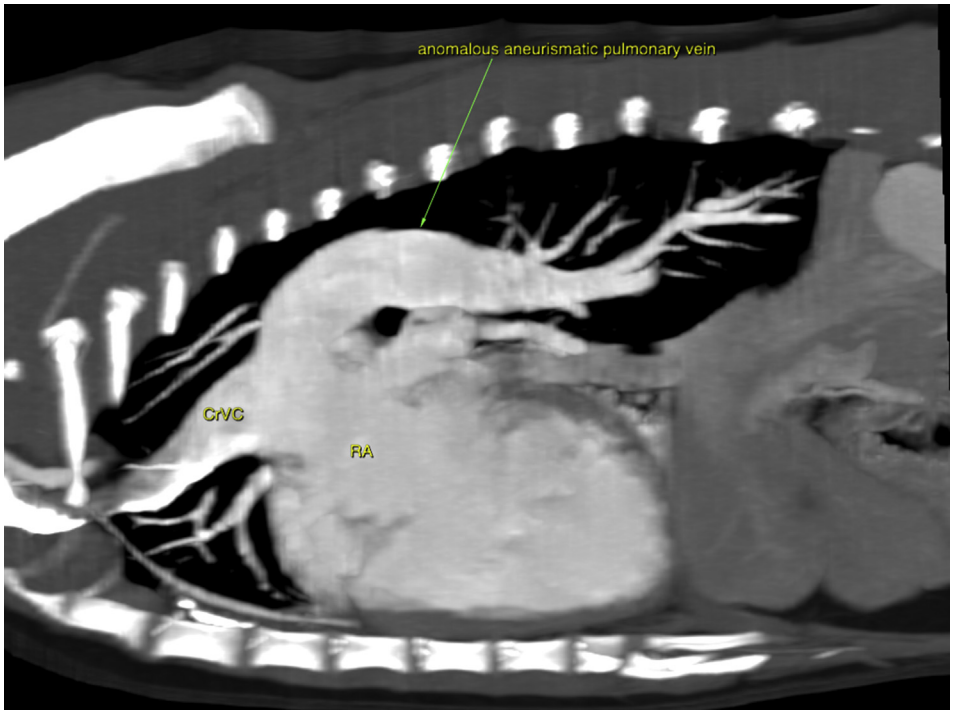

Fig. 2 Computed tomography image showing the large dilated anomalous vessel in the dorsal thorax. RA, right atrium; CrVC, cranial vena cava.

entered two distinct left and right pulmonary veins that then merged to join a single, severely dilated pulmonary vein that communicated with the cranial vena cava before entering the right atrium. Entry of the cranial and caudal venae cavae into the right atrium was unremarkable. No pulmonary veins (left or right lobar) entered the left atrium. A 20-mm wide ostium secundum ASD was present distal to the opening of the cranial vena cava within the right atrium. The pulmonary artery was markedly distended (22-mm wide) relative to the aorta (11-mm wide), consistent with pulmonary hypertension and volume overload of the right side of the heart with relative underloading of the left side. This corresponds to the clinical picture and the results of imaging modalities which suggested a large pulmonic flow (Qp:Qs) and dilation of pulmonary veins in the absence of left-sided congestive heart failure. Overall, the findings were consistent with a total anomalous pulmonary venous connection (TAPVC) [7].

Discussion

Total anomalous pulmonary venous connection is a rare congenital cardiopulmonary condition. Reports in the veterinary and medical literature tend to use the words 'connection,' 'drainage,' and 'return' interchangeably; however, there are subtle differences between 'connection' and 'drainage'. Total anomalous pulmonary venous connection refers to pulmonary veins that have no connection to the left atrium, instead the pulmonary veins connect to a systemic vein; total anomalous pulmonary venous drainage occurs if the veins drain into the right atrium, i.e., 'connection' is an anatomical relationship, but 'drainage' is a physiological one [7,8]. To the author's knowledge, there are only three published reports of total anomalous pulmonary venous abnormalities in the veterinary literature, involving two dogs [9,10] and one foal [11]. In all cases, juvenile animals were affected. This case report describes the use of multiple imaging modalities to diagnose TAPVC antemortem in an adult dog. A definitive diagnosis was made postmortem.

Preliminary complete blood count did not reveal evidence of secondary appropriate erythrocytosis which might be expected with severe generalised hypoxaemia as shown by lingual cyanosis and the results of the arterial blood gas [12]. The absence of polycythaemia may be related to the age of the dog as in the early stages of the disease, right-to-left shunting of deoxygenated blood may be minimal until pulmonary hypertension develops causing greater mixing of oxygenated and deoxygenated blood [7]. In dogs,

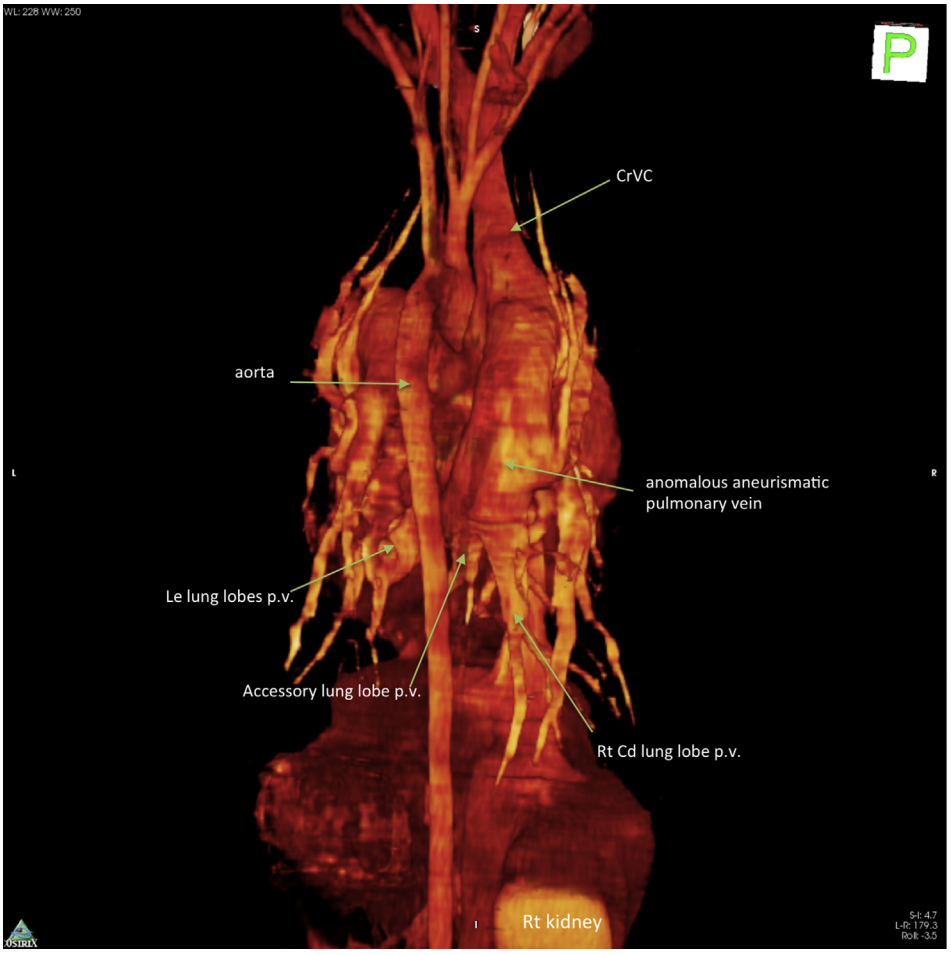

Fig. 3 Reconstructed CT image showing the veins from the right caudal, left, and accessory lung lobes merging before connecting to the large venous structure, which subsequently joined the right atrium via a single opening. CrVC, cranial vena cava; p.v., pulmonary vein; Le, left; Rt, right; CD, caudal; CT, computed tomography.

with right-to-left shunting, patent ductus arteriosus erythrocytosis may not be seen until after 24 months of age [13]. The remainder of the biochemical abnormalities was not specific for a right-to-left shunting cardiac anomaly.

In people, TAPVC is thought to account for four to six per 100,000 live births [14]. The incidence in dogs is unknown. One epidemiological study identified a single case of anomalous venous return of 290 dogs with congenital heart disease [15]. Another reported one case from 976 dogs with congenital defects [16]. It is unclear from these reports whether the cases identified were partial or TAPVC.

In children, TAPVC is repaired surgically, and the outcome is ultimately dependent on whether univentricular or biventricular physiology exists. Children who undergo surgical repair of TAPVC with biventricular physiology have a better long-term prognosis, with the majority living symptom and medication free to adulthood [17,18]. Untreated cases in adults are rare due to advances in foetal echocardiography. However, reports of surgical correction of TAPVC in adults exist [19]. Affected individuals experience clinical signs related to right-sided volume overload and right-to-left shunting, including cyanosis and heart failure. Cyanosis is normally mild and may go unnoticed in childhood. It becomes more noticeable when pulmonary hypertension develops secondary to the increased blood flow through the pulmonary vasculature, as was observed in this dog, because pulmonary hypertension promotes right-to-left shunting.

Total anomalous pulmonary venous connection is classified according to the location of the anomalous connection with respect to the heart and whether obstruction at the level of the pulmonary veins is present. There are four types of anomalous connections: supracardiac, in which the common pulmonary venous confluence drains into the superior vena cava or innominate vein, cardiac where

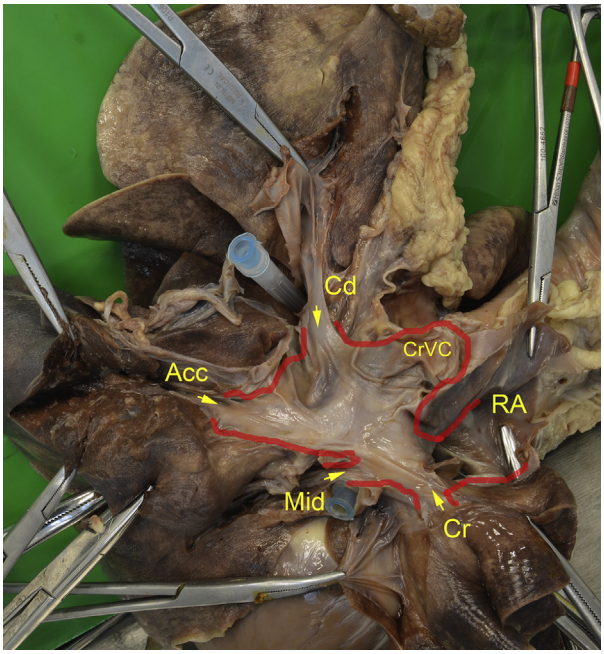

Fig. 4 Fixed tissue. Ventral view of the right lung illustrating the anomalous drainage of all right pulmonary veins into the large central vein (highlighted in red). Lobes: Cd, caudal; Acc, accessory; Mid, middle; Cr, cranial; CrVC, caudal vena cava.

drainage of the common pulmonary vein is into the coronary sinus, infracardiac where the common pulmonary venous confluence empties into the portal or hepatic veins, and mixed where there is drainage at two or more levels [7]. The most commonly reported types in people are supracardiac and cardiac [17,18]. The type identified in this case report was supracardiac. In all types of TAPVC, survival beyond the neonatal period requires a communication between the right and left sides of the heart to allow oxygenated blood to flow through the aorta. In most cases, an ASD or patent foramen ovale is present, although patent ductus arteriosus and ventricular septal defects may also be found [7]. The result is a composite bidirectional shunt, where oxygenated blood from the pulmonary veins mixes with deoxygenated blood within the right atrium, and then the right atrial blood shunts into the left atrium. Whether cyanosis develops is dependent on the degree of mixing of deoxygenated and oxygenated blood within the right atrium and the volume of the right atrial blood that crosses the ASD, the latter dependent on the relative compliance of the right and left ventricles. Regardless of classification, affected hearts have right atrial and right ventricular dilation and hypertrophy, with a relatively normal-to-undersized left side. The pulmonary artery is also usually dilated owing to pulmonary hypertension [7]. If pulmonary venous obstruction is present, the heart appears very similar to non-obstruction, but the person presents with pulmonary oedema early in life [7]. Obstruction was not present in the dog reported here.

Two previous cases of total anomalous pulmonary venous abnormalities have been reported in dogs. The first was a 5-month-old Great Dane with right-sided congestive heart failure and total anomalous pulmonary venous return [10]. Diagnosis was made via angiocardiography and confirmed postmortem. The second case was an 8-week-old Brittany spaniel with total anomalous pulmonary venous drainage suspected after echocardiography and, again, confirmed postmortem [9]. Neither of these reports included CT in the diagnostic evaluation, which would have characterised the underlying pathology further and can facilitate surgical planning. Partial anomalous pulmonary venous connection has been described in several dogs [20—23] and one cat [24]. Three of these reports detailed the use of multidetector CT in the diagnostic evaluation [20,22,24], but this case describes the first application of this modality to canine TAPVC.

In people, CT and MRI are routinely used to diagnose complex congenital cardiac defects. They provide detailed information about cardiac and thoracic structure and function when compared with other standard diagnostic methods such as thoracic radiographs and echocardiography. Indeed, an elegant study used CT and silicone endocasts to provide detailed information regarding pulmonary vein anatomy in the normal canine heart [25]. Although postmortem examination was required for a definitive diagnosis in the case reported here, CT provided more anatomical information than any other imaging modality. It identified the soft tissue opacity dorsal to the carina on thoracic radiography as a large aneurysmal vessel that appeared to communicate with most of the pulmonary vessels. It also provided further characterisation of the pulmonary hypertension, making an underlying respiratory cause less likely. The only disparity between CT and postmortem findings was the path taken by the right middle pulmonary vein. On CT, there was close contiguity between the vein and the dorsal aneurysmal vein at the level of the cardiac silhouette, but direct communication could not be demonstrated. Instead, it was suspected that the right middle vein emptied into the left atrium because it did not have any of the dilatory (compared with the corresponding pulmonary artery) or tortuous features of the other pulmonary veins. However, connection with the left atrium could not be demonstrated directly on CT. Postmortem

examination was required to fully evaluate the path of the right middle lobar vein which merged with all the other pulmonary veins to form a large, single vein that then opened in to the right atrium.

Conclusion

Evaluation of dogs with evidence of right-sided volume overload and unexplained pulmonary hypertension should include advanced imaging techniques when possible. This case report describes a rare congenital condition in an adult dog in which multidetector CT provided an antemortem diagnosis. To our knowledge, this is the first veterinary case report of TAPVC diagnosed by multiple imaging modalities, including multidetector CT, and the first report of such a defect in an adult dog.

Conflicts of interest statement

The authors do not have any conflicts of interest to disclose.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jvc.2018.11.003.

Video table

Video 1	Ostium secundum defect	Right parasternal short axis at the level of the left atrium showing an ostium secundum defect with right-to-left shunt.

References

[1] Cornell CC, Kittleson MD, Della Torre P, Haggstrom J, Lombard CW, Pedersen HD, Vollmar A, Wey A. Allometric scaling of M-mode cardiac measurements in normal adult dogs. J Vet Intern Med 2004;18:311—21.

[2] Kirberger RM, Blandvandenberg P, Grimbeek RJ. Doppler echocardiography in the normal dog .2. Factors influencing blood-flow velocities and a comparison between left and right heart blood-flow. Vet Radiol Ultrasound 1992;33:380—6.

[3] Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, Solomon SD, Louie EK, Schiller NB. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 2010;23:685—713.

[4] Grossman W, Moscucci M. Shunt detection and quantification. In: Moscucci M, editor. Grossman and Baim's Cardiac Catheterization, Angiography, and Intervention. 8th ed. Philadelphia, USA: Lippincott Williams and Wilkins; 2014. p. 261—71.

[5] Pariaut R, Saelinger C, Strickland KN, Beaufrere H, Reynolds CA, Vila J. Tricuspid annular plane systolic excursion (TAPSE) in dogs: reference values and impact of pulmonary hypertension. J Vet Intern Med 2012;26:1148—54.

[6] Visser LC, Scansen BA, Schober KE, Bonagura JD. Echocardiographic assessment of right ventricular systolic function in conscious healthy dogs: repeatability and reference intervals. J Vet Cardiol 2015;17:83—96.

[7] Brown D, Geva T. Anomalies of the pulmonary veins. In: Allen D, Shaddy RE, Penny DJ, Feltes TF, editors. Moss and Adams' Heart Disease in Infants, Children and Adolescents. 9th ed. Philadelphia, USA: Wolters Kluwer; 2016. p. 888—903.

[8] Mascarenhas E, Javier RP, Samet P. Partial anomalous pulmonary venous connection and drainage. Am J Cardiol 1973;31:512—8.

[9] Hogan DF, Green 3rd HW, Van Alstine WG. Total anomalous pulmonary venous drainage in a dog. J Vet Intern Med 2002;16:303—8.

[10] Hilwig RW, Bishop SP. Anomalous pulmonary venous return in a Great Dane. Am J Vet Res 1975;36:229—33.

[11] Diaz OS, Desrochers A, Hoffmann V, Reef VB. Total anomalous pulmonary venous connection in a foal. Vet Radiol Ultrasound 2005;46:83—5.

[12] Stokol T. Anemia, erythrocytosis. In: Ettinger S, Feldman EC, Etienne C, editors. Textbook of Veterinary Internal Medicine. 8th ed. St. Louis, Missouri: Elsevier; 2017. p. 229—35.

[13] Beijerink NJ, Oyama MA, Bonagura JD. Congenital heart disease. In: Ettinger SJ, Feldman EC, Etienne C, editors. Textbook of Veterinary Internal Medicine. 8th ed. St. Louis, Missouri: Elsevier; 2017. p. 1211—7.

[14] Perloff J, Marelli A. Atrial septal defects. In: Perloff J, Marelli A, editors. Perloff's Clinical Recognition of Congenital Heart Disease. 6th ed. Phildalephia, USA: Elsevier; 2012. p. 243—54.

[15] Patterson DF. Epidemiologic and genetic studies of congenital heart disease in the dog. Circ Res 1968;23:171—202.

[16] Oliveira P, Domenech O, Silva J, Vannini S, Bussadori R, Bussadori C. Retrospective review of congenital heart disease in 976 dogs. J Vet Intern Med 2011;25:477—83.

[17] Karaci AR, Harmandar B, Aydemir NA, Sasmazel A, Balci AY, Saritas T, Yekeler I, Bilal MS. Early and intermediate term results for surgical correction of total anomalous pulmonary venous connection. J Card Surg 2012;27:376—80.

[18] Kelle AM, Backer CL, Gossett JG, Kaushal S, Mavroudis C. Total anomalous pulmonary venous connection: results of surgical repair of 100 patients at a single institution. J Thorac Cardiovasc Surg 2010;139:1387—94.

[19] Jian XH, Huang J, Ding Y, Xiao XJ, Wu M, Chen JM, Zhuang J. Surgical outcome of isolated total anomalous pulmonary venous connection in adults: a 14-year experience. J Card Surg 2012;27:736—9.

[20] Fujii Y, Ishikawa T, Sunahara H, Sugimoto K, Kanai E, Kayanuma H, Mishina M, Aoki T. Partial anomalous pulmonary venous connection in 2 Miniature Schnauzers. J Vet Intern Med 2014;28:678—81.

[21] Shively MJ. Anomalous pulmonary venous connection in a dog. J Am Vet Med Assoc 1975;166:1102—3.

[22] Thorn CL, Ford NR, Sleeper MM. Partial anomalous pulmonary venous connection in a dog. J Vet Cardiol 2017;19:448—54.

[23] Abraham LA, Slocombe RF. Asymptomatic anomalous pulmonary veins in a Siberian Husky. Aust Vet J 2003;81:406—8.
[24] Nicolson G, Daley M, Makara M, Beijerink N. Partial anomalous pulmonary venous connection with suspected pulmonary hypertension in a cat. J Vet Cardiol 2015;17:S354—9.
[25] Brewer FC, Moise NS, Kornreich BG, Bezuidenhout AJ. Use of computed tomography and silicon endocasts to identify pulmonary veins with echocardiography. J Vet Cardiol 2012;14:293—300.