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Case Report Rapport de cas

Closure of a patent ductus arteriosus in a 2-week-old llama cria using an Amplatz canine duct occluder

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Abstract – A two-week-old female llama cria was brought to the UC Davis Large Animal Hospital for evaluation of a cardiac murmur and suspected syncopal episodes. A grade IV/VI left basilar continuous murmur was present on cardiac auscultation. Echocardiography revealed a left-to-right shunting patent ductus arteriosus (PDA), mild left ventricular enlargement, scant pericardial effusion, and a suspected persistent left cranial vena cava. The PDA was successfully closed with an Amplatz canine duct occluder. Mild mitral regurgitation was present on echocardiography performed 7 d following PDA occlusion. No syncopal episodes were observed in hospital prior to or following PDA occlusion. At approximately 1 mo following PDA closure, a grade I/VI left apical systolic murmur was present and the cria's body condition was improved.

Key clinical message:

Patent ductus arteriosus closure is achievable in New World camelids using interventional cardiology which provides a minimally invasive treatment option for valuable or companion animals. Since interventional cardiac catheterization is commonly performed in small animal species, veterinary cardiologists are well-equipped to apply these skills to camelids.

Résumé – Fermeture d'un canal artériel persistant chez un lama cria âgé de 2 semaines à l'aide d'un obturateur de conduit canin Amplatz. Une femelle lama cria âgée de deux semaines a été amenée à l'UC Davis Large Animal Hospital pour l'évaluation d'un souffle cardiaque et d'épisodes syncopaux suspectés. Un souffle continu basilaire gauche de grade IV/VI était présent à l'auscultation cardiaque. L'échocardiographie a révélé une persistance du canal artériel avec perméabilité de gauche à droite (PDA), une légère hypertrophie ventriculaire gauche, un léger épanchement péricardique et une suspicion de veine cave crâniale gauche persistante. Le PDA a été fermé avec succès avec un obturateur de conduit canin Amplatz. Une régurgitation mitrale légère était présente sur l'échocardiographie réalisée 7 jours après l'occlusion du PDA. Aucun épisode de syncope n'a été observé à l'hôpital avant ou après l'occlusion du PDA. Environ 1 mois après la fermeture du PDA, un souffle systolique apical gauche de grade I/VI était présent et l'état corporel du cria s'était amélioré.

Message clinique clé :

La fermeture brevetée du canal artériel est réalisable chez les camélidés du Nouveau Monde en utilisant la cardiologie interventionnelle qui offre une option de traitement peu invasive pour les animaux de valeur ou de compagnie. Étant donné que le cathétérisme cardiaque interventionnel est couramment pratiqué chez les petites espèces animales, les cardiologues vétérinaires sont bien équipés pour appliquer ces compétences aux camélidés.

(Traduit par D^r Serge Messier)

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Case description

A 2-week-old female llama cria was presented to the Large Animal Internal Medicine and Cardiology Services for evaluation of a cardiac murmur and possible collapse episodes. The caretakers were unaware that her dam was pregnant, and parturition was not witnessed. The cria was rejected by the dam shortly after birth and was removed from the herd to be supplemented with milk replacer. A cardiac murmur was noted when the referring veterinarian examined the cria at approximately 10 d of age. The cria was treated with an antimicrobial (Excede, ceftiofur crystalline free acid; Zoetis, Kalamazoo, Michigan, USA) and IM selenium. The owner reported 2 episodes of possible collapse; one that appeared to be induced by barking dogs and another that occurred when the cria was pushed.

On clinical examination, the cria was bright, alert, responsive, and ambulatory. The cria was of small stature, body condition was thin, and body weight (7 kg) was low for the cria's age. The cria's heart rate was 90 beats/min and femoral pulses were hyperkinetic and synchronous. A grade IV/VI left basilar continuous murmur was present on cardiac auscultation. Respiratory rate (40 breaths/min) and effort were normal with mildly increased bronchovesicular sounds present ventrally on thoracic auscultation. There was no nasal discharge, tracheal rattle or edema present. Body temperature was normal at 37.8°C. The remainder of the physical examination was clinically unremarkable. Serum cardiac troponin I concentration was normal at 0.04 µg/L [reference range (RR): 0.01 to 0.07 µg/L] (1). Thoracic radiographs were performed due to slight abnormalities detected on thoracic auscultation. A cardiac silhouette that appeared normal in size and a wispy soft tissue opacity in the caudoventral lung suggestive of bronchopneumonia were seen.

Hematology performed just before referral revealed a mild, mature neutrophilia of 17 656 cells/µL (RR: 2502 to 13 411 cells/µL) and mild hyperfibrinogenemia of 6.81 g/L (RR: 1 to 4 g/L), consistent with inflammation. Clinically important alterations in serum biochemistry included panhypoproteinemia of 41 g/L (RR: 47 to 70 g/L) characterized by hypoalbuminemia of 27 g/dL (RR: 29 to 50 g/L) and hypoglobulinemia of 14 g/L (RR: 15 to 26 g/L), and mildly increased blood urea nitrogen of 13.93 mmol/L (RR: 3.21 to 12.86 mmol/L) (2). Evaluation of adequate transfer of passive immunity was not performed on the farm at 24 to 48 h of age. It is not possible to determine if the alterations observed in serum protein levels were due to partial failure of transfer of passive immunity, waning maternal antibodies, consumption, or a combination of these processes as the cria was 2 wk old. Due to evidence of mild inflammation on the complete blood (cell) count, mild hypoglobulinemia, and slight bronchopneumonia, the cria received a plasma transfusion and intravenous antimicrobials during hospitalization.

Routine transthoracic echocardiography (TTE, Philips iE 33 Ultrasound; Philips Healthcare Solutions, Andover, Massachusetts, USA) was performed to further investigate the cause of the cardiac murmur. The examination was completed using an 8-3 MHz phased array transducer to optimize 2D imaging and a 5-1 MHz phased array transducer to optimize

quality of color and Spectral Doppler. The cria was not sedated and was restrained in right and then left lateral recumbency. The left atrium, right atrium, right ventricle, atrioventricular valves, and semilunar valves were unremarkable (Figure 1 A, B). The left ventricular internal dimensions in diastole measured at the upper limits of normal to mildly enlarged using reference ranges for healthy, neonatal llamas and alpacas in the first 2 wk of life (3). Specifically, the absolute left ventricle dimensions (LVD) in diastole were 33 mm, 29 mm, and 30 mm when measured in 2D right parasternal long axis, and 2D and M-mode right parasternal short axis (Figure 1 C) views, respectively. The reported upper limit for LVD in diastole in healthy crias was 28.6 mm (3). A left to right shunting patent ductus arteriosus (PDA) with a pulmonic ostium of 2.6 mm and a peak velocity of 4.67 m/s was identified (Figure 1 D, E). Additional findings included scant pericardial effusion and a dilated coronary sinus which raised suspicion for a possible persistent left cranial vena cava (PLCVC). Normal sinus rhythm was present on the electrocardiogram performed during the TTE, with periods of sinus bradycardia that coincided with sleep. The equivocal LV enlargement supported possible hemodynamic significance of the PDA, although it was considered unlikely to be the cause of the reported collapse episodes. It was decided to occlude the PDA to prevent potential development of left-sided congestive heart failure.

The cria was premedicated with ceftiofur sodium (Naxcel; Zoetis, Kalamazoo, Michigan, USA), 5 mg/kg, IV, flunixin meglumine (Banamine; Merck, Madison, New Jersey, USA) 0.5 mg/kg, IV, midazolam (Midazolam Injection; Hospira, Lake Forest, Illinois, USA), 0.2 mg/kg, IV, and atropine (Atropine Sulfate Injection; Accord Healthcare, Durham, North Carolina, USA) 0.02 mg/kg, IM. Anesthesia was induced with ketamine (Zetamine; Ketamine Hydrochloride Injection, VetOne, Boise, Idaho, USA), 4 mg/kg, IV and maintained with inhalant isoflurane (Fluriso, Isoflurane, USP; MWI, Boise, Idaho, USA) and sufentanil (Sufentanil Citrate Injection, USP; Akorn, Lake Forest, Illinois, USA) constant rate infusion. The cria was placed in right lateral recumbency to facilitate access to the right femoral artery which was isolated *via* sharp and blunt dissection. A 21-gauge × 4 cm percutaneous entry needle was used to facilitate placement of a 0.35" × 150 cm long hydrophilic guide wire (HiWire; Cook, Bloomington, Indiana) through the femoral artery. A 5 Fr introducer with dilator (Flexor Check-Flo Introducer Ansel 1 Modification and Dilator; Cook) was placed over the hydrophilic guide wire and advanced to the level of the ductus in the descending aorta. The position of the introducer was monitored *via* fluoroscopy. The dilator and guide wire were removed while the introducer was held in place. An angiogram was performed through the introducer using 1 mL/kg of non-ionic contrast media (Omnipaque; GE Healthcare, Marlborough, Massachusetts, USA). Angiography allowed visualization of the ductal morphology and size (Figure 2 A). Transesophageal echocardiography (TEE, Philips iE 33 Ultrasound; Philips Healthcare Solutions, Andover, Massachusetts, USA) to measure minimal ductal diameter (MDD) during the procedure was unsuccessful. Measurements of the MDD were therefore based on a combination of TTE

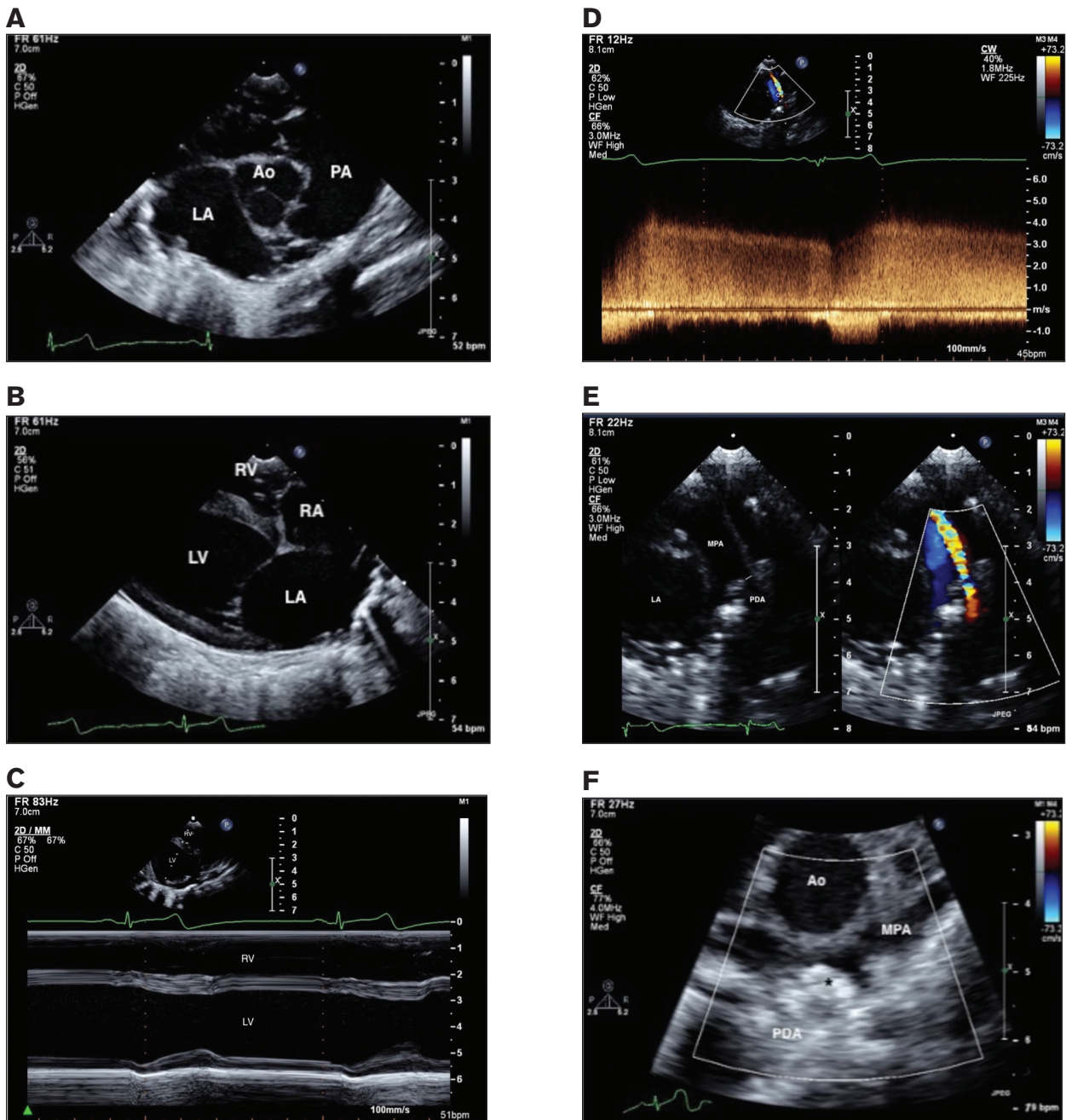


Figure 1. Transthoracic echocardiographic images of the patent ductus arteriosus. A – A 2-dimensional (2D) right parasternal short axis view at the level of the heart base showing normal left atrial size (LA – Left atrium, Ao – Aorta, PA – Pulmonary artery). B – A 2D right parasternal long axis view (LV – Left ventricle, LA – Left atrium, RA – Right atrium, RV – Right ventricle). C – An M-mode image of the right parasternal short axis at the level of the left ventricular chordae tendineae showing left ventricular size in diastole and systole. D – Continuous wave Doppler across the patent ductus arteriosus revealing continuous flow throughout systole and diastole with a maximum velocity of 4.7 m/s. E – A 2D image with an adjacent color Doppler comparison revealing continuous flow across the patent ductus arteriosus (PDA) to the main pulmonary artery (MPA). The white line on the 2D image represents the pulmonic ostium. F – A zoomed in imaged of the right parasternal short axis view at the level of the heart base and branching of the main pulmonary artery. The ACDO (*) can be seen as a hyperechoic structure with hard shadow occluding the ductus (PDA) as it enters the main pulmonary artery (MPA).

performed before the procedure (2.6 mm) and contrast angiography (2.0 mm) performed during the procedure. A 4-mm Amplatzer canine ductal occluder (ACDO, Amplatzer Canine Duct Occluder; Infiniti Medical, Plymouth, Minnesota, USA) was chosen based on the recommended device waist diameter to MDD ratio of 1.5 to 2. The tip of the introducer was

positioned across the ductus and into the pulmonary artery. The ACDO attached to a delivery wire was advanced through the introducer across the ductus (Figure 2 B) and deployed as previously described (4). Color Doppler and 2D imaging using TEE confirmed successful ACDO placement and occlusion of the ductus (Figure 1 F). Following placement, all catheters and

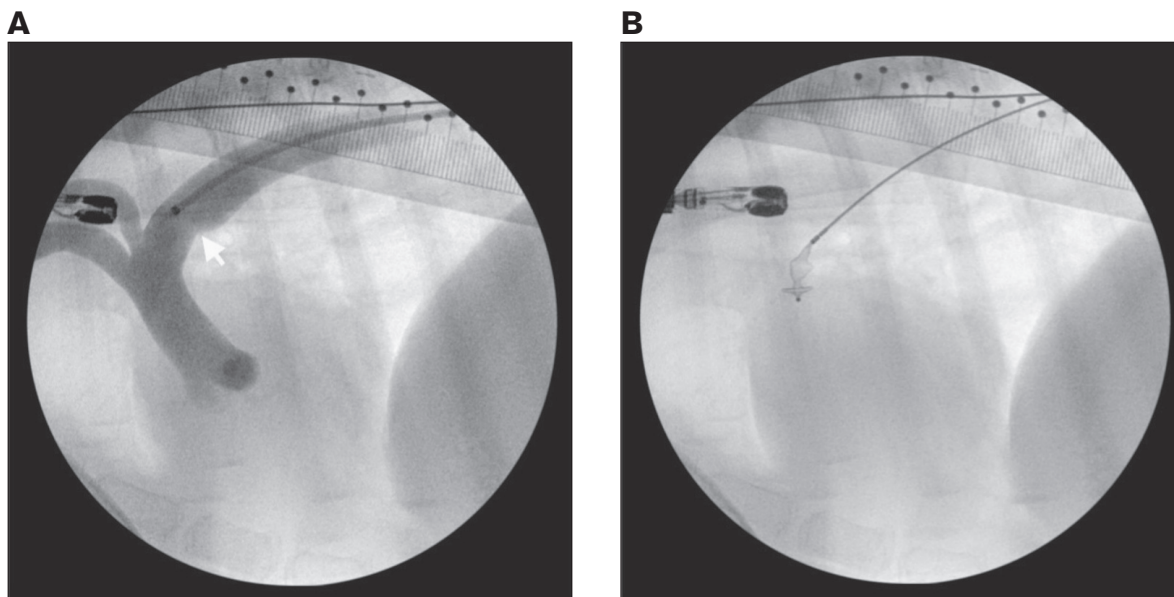


Figure 2. A – Ductal angiogram. Angiogram is performed through the introducer in the aorta slightly cranial to the ductus arteriosus. The ampulla of the ductus is shown (arrow). B – The distal and proximal discs of the ACDO have been exteriorized across the pulmonary and aortic side of the ductal ampulla and have not yet been released from the delivery cable.

guidewires were removed. The right femoral artery was ligated with 0 silk suture and routine closure was performed. Recovery from anesthesia was prolonged and required opioid reversal with naloxone (Naloxone Hydrochloride Injection; Mylan Institutional LLC, Morgantown, West Virginia, USA).

Following general anesthesia for closure of the PDA, the cria developed gastrointestinal ileus and aspiration pneumonia, and remained in hospital for treatment of these conditions with intravenous fluids, parenteral and enteral nutrition, and antimicrobials in addition to nebulization with saline, acetylcysteine (American Reagent, Shirley, New York, USA) and ceftiofur sodium (Naxcel; Zoetis, Kalamazoo, Michigan, USA). The left basilar continuous murmur resolved immediately with PDA occlusion; however, a grade II/VI left apical systolic murmur was noted during daily physical examinations. Femoral pulse quality was normal. No syncopal or collapse episodes were observed throughout the duration of hospitalization. Repeat TTE was performed 7 d following PDA occlusion. Trace mitral regurgitation (MR) with a centrally directed jet was present and there was no residual flow through the PDA. The previously noted scant pericardial effusion had resolved. There was no change in LV size, and LV systolic function was reduced, as indicated by a fractional shortening of 21.4% in M-mode derived from the right parasternal short axis at the level of the chordae tendineae. Reduced indices of LV systolic function are a typical finding following PDA occlusion (5). The murmur was attributed to the mild MR and was projected to improve or resolve over time with the heart chambers returning to normal following occlusion.

The cria was discharged after approximately 12 d of hospitalization and returned 2 wk later, at approximately 1.5 mo of age, for a recheck examination. The cria was reported to be doing well with no collapse episodes witnessed on the farm. Her body condition was improved, as was body weight at 12.5 kg. A grade I/VI left apical systolic murmur was present and pulmonary

auscultation was normal. Repeat TTE was not performed, which is a major limitation of this case report. Since that time and over the following 6 mo, no cardiac murmurs were detected by the primary care veterinarian during routine health visits.

Discussion

This is the first report of interventional closure of a PDA using an ACDO in a neonatal llama cria and the second report to document the use of an ACDO in a New World camelid. Use of an ACDO for successful closure of a PDA has been previously reported in a 6-month-old alpaca (4). In addition, this is the first report to discuss the presence of a persistent left cranial vena cava in a llama.

Congenital heart defects are the most often reported abnormalities of the cardiovascular system in camelids. In one retrospective study, congenital heart defects were identified in 3.6% of llama crias evaluated at Colorado State University over a 7-year period. In this population, ventricular septal defect was the most common congenital abnormality followed by PDA (6). The incidence of PDA is less common in other reports and is often associated with complex congenital heart defects; however, large epidemiological studies are lacking (7). Although the exact time frame for ductus arteriosus closure in camelids is not known, it is rare to auscultate the characteristic continuous left basilar murmur or identify ductal flow *via* echocardiography beyond 3 to 4 d of age (3). The distinctive murmur, persistent ductal flow documented using TTE, and lack of other complex congenital cardiac abnormalities in this 2-week-old llama cria were consistent with an isolated PDA.

The reported case fatality rate for untreated PDA in dogs is approximately 65% within the first year of diagnosis (8). Ductal closure is important for long-term survival and may also result in reverse cardiac remodeling. Prognosis for long-term survival following closure of an uncomplicated PDA is excellent, with a

median survival time of > 11.5 y in 1 study in dogs (5). Ductal closure can be achieved through various methods including surgical ligation, coil embolization, Amplatzer vascular plugs, and ACDO. In small companion animals, femoral artery size is a limiting factor for ACDO use and animals weighing < 3 kg generally require alternative methods of closure (9). Femoral artery size is not a limiting factor for ACDO use in this species since most normal llama crias weigh 9 to 18 kg at birth (10). Although the llama cria in this case was underweight at admission with mild comorbidities, this did not preclude the placement of an ACDO in the first few weeks of life. Failure to thrive and stunted growth are commonly reported in crias with congenital heart defects, although syncope is usually only observed in animals with complex congenital defects (3,6). Arguably, the procedure could have been delayed a few weeks to months for monitoring, although it was considered unlikely that the PDA would close at that point without intervention. Given the concern for LV enlargement, prompt ductal closure was elected and was successful.

The development of mild MR following PDA occlusion in this case was interesting. Mitral regurgitation was not present in the cria during preoperative or intraoperative imaging. Recheck TTE post-operatively confirmed trace MR with normal valve appearance. In addition, left atrial size remained normal and LV size was static. Following ductal occlusion, a reduction in preload leads to a decrease in left atrial and ventricular size which should result in improvement or resolution of any pre-existing functional MR. An increase in afterload is another immediate effect of PDA closure and the increase in systemic vascular resistance may have altered LV pressure enough to induce the trace MR while the cardiac chambers were continuing to return to normal. In a study evaluating the outcome of PDA closure in 520 dogs, the development of severe MR within 24 h of PDA occlusion negatively affected survival times (5). Given the mild nature of the MR and lack of additional structural cardiac changes, the development of MR was not considered to be clinically important or negatively affect outcome in this case. In fact, the murmur was no longer detected at the time of follow-up on the farm and the cria continued to grow and thrive.

In humans, persistent left superior vena cava is an uncommon vascular anomaly, although it is the most common congenital anomaly of the thoracic venous return system. This anatomical variation of the great vessels arises due to failed regression of the embryologic left anterior cardinal vein (11). Early in the advent of cardiac catheterization and angiography, the reported prevalence of persistent left superior vena cava in the general population was 0.3%, with most humans being asymptomatic. In humans with congenital heart disease, the prevalence increased to 4.3% and was associated with various other cardiac abnormalities (12). Similarly, the reported prevalence of PLCVC in dogs with congenital cardiovascular defects is < 5% (13). There are no reports in the literature of PLCVC in camelids, although there are reports in other domestic animal species including dogs, cats, ruminants, equids, and pigs (14–16). Right-to-left shunting can occur if the PLCVC drains to the left atrium, which is reported in 10% of humans with persistent left supe-

rior vena cava (17). However, this appears to be a rare finding in domestic animals with only one clear case presented in the literature (16). Diagnosis of PLCVC can be made with echocardiography, angiography, computed tomography, magnetic resonance imaging, or during necropsy evaluation and is usually incidental. The PLCVC in the case of this cria was suspected on TTE due to characteristic coronary sinus dilation and although a noteworthy additional vascular anomaly, it was considered an incidental finding. Further characterization with angiography was not pursued to limit time under general anesthesia.

Interventional PDA closure is achievable in New World camelids using the ACDO and provides a minimally invasive treatment option for valuable or companion animals. Since interventional cardiac catheterization is commonly performed in small animal companion species, veterinary cardiologists are well-equipped to transfer these skills to camelids and other suitable species.

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