Zel's Broken Heart

Persistent truncus arteriosus in a foal

Kelsie Campbell
Mississippi State University
College of Veterinary Medicine
Class of 2020

Clinicopathologic Conference
March 6th, 2020

Advisor:
Dr. Amy Lack, DVM

Introduction

Horses experience a wide variety of congenital abnormalities; however cardiac malformations are rare. The overall reported prevalence of congenital cardiac defects within the equine species is 0.1-0.5%. The most common defects reported are ventricular septal defects (VSD), tricuspid valve atresia (TVA), and patent ductus arteriosus (PDA).[1] In a study consisting of 15,224 foal necropsies, they reported a 0.14% incidence of equine congenital cardiac malformations. Within this percentage, the incidence of persistent truncus arteriosus (PTA) was 0.0028% or 1:35,714 foals born.[2] PTA is defined as a single, anomalous great vessel arising from the base of the heart. This anomalous vessel is the source of the systemic, pulmonary, and coronary arteries.[3] This defect has been described in a variety of species including horses, dogs, cats, calves, lambs, monkeys, mice, rhinoceros, and humans. PTA is typically recognized within the first days to week of life due to the associated clinical signs.[3] Depending on the cardiac structure, PTAs are classified into different categories, which are the following: pulmonary trunk and aorta originate from the PTA (Type 1), the right and left pulmonary arteries originate in close proximity to the dorsal wall of the PTA (type 2), the pulmonary arteries exit independently from either side of the PTA (type 3), and no pulmonary arteries originate from the truncus (type 4).[3] The severity of clinical signs is dependent on which classification of PTA is present. The most common clinical signs include: exercise intolerance, stunted growth, dyspnea or syncope, and moderate to severe holosystolic heart murmur appreciated bilaterally.[4] Echocardiography is the gold standard to diagnose PTA to confirm diagnosis and locate site of pulmonary venous connection.[5] With few exceptions, congenital cardiac defects in horses are not curable. The most feasible treatment option is euthanasia as prognosis is grave.[6]

History/Presentation/ Diagnostic Approach

The patient that will be discussed in this case report is Zel, a 6-day-old Holsteiner filly who presented to MSU-CVM equine department on April 17th, 2019 for lethargy and colic of one day duration. Zel's birth was attended by her owner who reported that it occurred without complications. Initially, Zel appeared normal to the owner, however over the next 24-48 hours she seemed increasingly lethargic and uncomfortable with a hunched appearance. The owner administered soapy enemas providing short-term improvement. Meconium was passed successfully. The owner reported no issues regarding the mare.

Upon presentation, Zel had a dull mentation but was ambulatory. She weighed approximately 52.1 kg (114 pounds) with a body condition score of 4/9. Her vitals were elevated and were the following: temperature of 102.7 degrees Fahrenheit, pulse of 200 beats per minute, and a respiration rate of 100 breaths per minute. She had a mild eyelid skin tent and appeared to be ~5% dehydrated. Upon examination of her eyes, she had scleral injection with muddy, brown scleral vessels bilaterally. Her mucous membranes were muddy, with a toxic line present. Her capillary refill time (CRT) was approximately four seconds. She was tachypneic with an increased respiratory effort, but no crackles or wheezes were auscultated. Upon cardiopulmonary auscultation, she was tachycardic, but no murmurs or arrythmias were auscultated. Her umbilicus appeared and palpated normally. Zel's hind fetlock joints were effusive bilaterally and warm on palpation, however the rest of her joints were within normal limits.

Initial diagnostic tests included: a complete blood count (CBC), serum chemistry, IgG SNAP test, abdominal ultrasound, and arterial blood gas analysis. The CBC showed a leukocytosis (15.10), increased PCV (46%), and neutrophilia (12684). Her serum chemistry showed electrolyte abnormalities (hyponatremia, 124.8, hyperkalemia, 5.08, hypochloremia

(89.5). Other abnormalities on the serum chemistry were the following: increased anion gap (18) and a decreased total protein (5.6). Whole blood was also submitted to determine her foal IgG levels, which was adequate at >800 mg/dL. Additionally, an arterial blood sample was collected and a blood gas analysis was performed showing hyponatremia (127 mmol/L) and severe hypoxia (PaO2=20 mmHg). Abdominal ultrasound was unremarkable. Based on these results and her clinical state, Zel was hospitalized overnight and maintained on nasal oxygen, 1 L boluses of LRS intravenously every 8 hours, amikacin (25 mg/kg) intravenously every 24 hours, ceftiofur (Naxcel) (6.2 mg/kg) intravenously every 12 hours, sucralfate (1 gram) orally every 8 hours, and ranitidine (300 mg) orally every 8 hours.

Throughout the day, Zel appeared to improve. Her afternoon physical examination showed that her vitals had normalized. Her mentation remained abnormal; however, was improved from presentation. Zel was seen standing and nursing normally several times. She did not pass any fecal material but continued to urinate normally. At approximately 4:00am on April 18th, 2019 Zel was noted to be open mouth breathing, tachypneic, with an increased respiratory effort, and cyanotic mucous membranes. Flow-by oxygen, which had been discontinued the previous evening was restarted. Her respiratory rate and effort returned to normal and supplemental oxygen was discontinued after several hours.

During Zel's morning physical examination on April 18th, 2019, she had a dull mentation and elevated vital parameters: temperature of 102.0 degrees Fahrenheit, pulse of 200 beats per minute, and a respiration rate of 100 breaths per minute. Her mucous membranes appeared to be less cyanotic with a CRT of <3 seconds. As she was receiving her 1 L LRS fluid bolus, she collapsed and was unresponsive. Supplemental flow-by oxygen was provided again for

approximately 20 minutes where she eventually became more alert and her respiration rate decreased to normal.

Due to Zel's deteriorating status and episodic tachypnea, additional diagnostics were performed. Thoracic radiographs showed mild rounding of the left ventricular region on the ventrodorsal projection, which was likely caused by a phase of the cardiac cycle, but mitral valve dysplasia and septal defects could not be ruled out. There was a mild, focal, unstructured interstitial pulmonary pattern within the right caudal lung lobe that was thought to be superimposition of structures and atelectasis; however, pneumonia could not be ruled out. Next, an echocardiogram was performed stall-side. Zel was lightly restrained and no sedation was administered due to her systemic compromise. The only abnormality found during this procedure was a blunted and incomplete interventricular septum with the following differential diagnosis: ventricular septal defect, endocardial cushion defect, or tetralogy of Fallot. During this procedure, Zel became extremely cyanotic, so it was terminated early. Several arterial blood gases were performed, which showed her hypoxemic state to be stagnant (PaO_2= 21, 21, 21 mmHg). An additional echocardiogram under general anesthesia or computed tomography (CT) was advised to fully evaluate Zel's heart.

Later that day, Zel was placed under general anesthesia to undergo a computed tomography (CT) with contrast. CT imaging showed a single, large, anomalous vessel at the heart base that received contrast from both the left and right ventricles. The pulmonary lobar arteries converged and originated from this single anomalous vessel. An incomplete intraventricular septum was confirmed. Lastly, the right ventricular free wall and interventricular septum was subjectively thickened. An echocardiogram was then performed while Zel was anesthetized to confirm the CT findings. This revealed a ventricular septal defect that allowed

communication between the left and right ventricles. The communicating ventricles had a single outflow tract with turbulent blood flow. Pulmonary pressures were not evaluated. With these changes to the aorta and pulmonary lobar arteries, subjective right ventricular hypertrophy, and the ventricular septal defect, Zel was diagnosed with a persistent truncus arteriosus.

Pathophysiology

Persistent truncus arteriosus (PTA) is a conotruncal defect that occurs when there is failed separation between the aorta and pulmonary artery creating a single, common truncus (vessel).[6] The separation can be complete or incomplete, however both lead to aorta and pulmonary flow through a common trunk.[4] During normal embryologic development, the aorta and pulmonary artery originate from equivalent structures, the bulbus and the truncus. During early heart development, the bulbar ridges arise from the endocardial lining of the heart and fuse together creating a septum that divides the truncus and the unabsorbed section of the bulbus into an aorta and pulmonary trunk. From here, the ventricular septum develops and increases in height from the base of the common ventricle ultimately creating two separate ventricles. The proximal septum is incomplete for a short time until the interventricular foramen fuses with the proximal bulbar septum. However, the lack of initial division of the truncus and bulbus ultimately causes a PTA.[8] Due to the underdevelopment of the pulmonary infundibulum, as the bulbus does not properly divide, a high ventricular septal defect is always present below the truncus.[6,9] The truncus most commonly has one, large, abnormal valve that can consist of two to five cusps.[3] Most commonly in humans, PTA originates from the right ventricle (42%), however some can originate from both ventricles (41%) and from the left ventricle (16%).[9] With these anatomical defects, the common truncus gives origin to systemic, pulmonary, and coronary

blood supply with an admixture of oxygenated and deoxygenated blood between both ventricles and the common truncus.[4,7]

Based on anatomical differences, Collett and Edwards created a classification system in 1949 that is still followed today classifying the various types of PTA. A type 1 has a single, pulmonary trunk and a single ascending aorta originating from the PTA. In a type 2, the right and left pulmonary arteries arise close in proximity from the dorsal wall of the PTA. The difference of a type 3 is that one (or both) pulmonary arteries exit independently from either side of the PTA, rather than both from the dorsal wall. Lastly, in a type 4 no pulmonary arteries originate from the truncus and pulmonary circulation is solely provided by the bronchial arteries.[3] The most common type diagnosed in humans is type 1, however with it being so incredibly rare in horses the most common type is unknown. [9]

The definitive etiology of this cardiac abnormality in horses is unknown, but hypotheses regarding genetics and toxin exposure has been made in humans. In humans, there is an increased incidence of PTA within families suggesting it is an autosomal inheritance. Studies have focused on mutations causing deletion of chromosome 22, leading to abnormalities in development of neural crest cells to the third and fourth pharyngeal pouches causing cardiovascular underdevelopment. Due to this, the patient undergoes a failure of separation of the cardiac outflow tract resulting in a single outflow tract, which is a PTA. Another speculation is toxic exposure to the following: bis(dichloroacetyl)diamine, fetal alcohol syndrome, Tedral (asthmatic medication) containing theophylline, ephedrine, and phenobarbital, and thalidomide, which have all experimentally induced PTA.[2] Although no further studies of this hypothesis has been made in veterinary medicine. The only study regarding veterinary medicine regarding the etiology of PTA was conducted on mice with chromosomal mutations. Experimentally, mice

with a mutation of the Pax3 gene and Trisomy 16 gene have been shown to have a higher incidence of PTA development. Both genes disrupt neural crest development which then lead to underdevelopment and disorganization of the mouse' aorticopulmonary system since neural crest cells are involved in the separation of the truncus arteriosus.[10] Based on current literature of PTA in horses, neither of these, genetic or toxins, have been shown, so the etiology remains unknown.

In diagnosing PTA in horses, the gold standard is echocardiography. However, tentative diagnosis of a cyanotic congenital cardiac disease can be based on clinical signs, cyanosis, and arterial blood gas analysis, severe hypoxemia. Echocardiogram diagnosis is contingent on visualization of a large. single arterial trunk overriding the VSD with the inability to visual an independent pulmonary trunk.[2,7] Common echocardiography findings are the following: right ventricular and atrial enlargement, left atrium atrophy, and right-to-left bulging of the atrial septum. Post-mortem diagnosis of PTA can be made upon necropsy examination, which would feature all the abnormalities seen on echocardiography.[2]

Clinical signs vary depending on the anatomical features and magnitude of pulmonary blood flow.[5] In the literature, signs of venous admixture predominate in foals causing weakness, exercise intolerance, tachypnea, tachycardia, cyanosis, and a moderate to severe holosystolic murmur auscultated bilaterally.[2] The holosystolic heart murmur present with PTA are a result of the VSD being present causing turbulent blood flow between both ventricles.[6] When pulmonary vascular resistance is lower than systemic vascular resistance, blood will flow into the pulmonary circulation causing an increase in pulmonary blood flow resulting in pulmonary hypertension.[3] This results in left heart volume overload and can cause left heart failure. If the foal survives and the PTA continues to circulate, desaturated venous blood from the right ventricle will be ejected

into systemic circulation, due to the pressure differences, resulting in right-to-left shunting. This shunting is the cause of the common clinical signs, hypoxemia and cyanosis.[3,7]

Treatment and Management

The prognosis for foals exhibiting complex congenital cardiac defects, such as PTA, is grave as corrective surgery, the mainstay of treatment for this disease, is not feasible to perform.[2] In humans, survivability of the procedure has improved although one-third of patients remain symptomatic post-surgery and approximately half of them require additional surgical intervention.[9,10] Surgical goals are closure of the VSD with connection of the truncus to the left ventricle and connection of the pulmonary arteries to the right ventricle.[9] During the surgery, an aortic homograft is used to create a pulmonary trunk. A hole is made within the right ventricle where the homograft is sutured to and the VSD is repaired. The pulmonary arteries are then detached from the PTA and sutured to the graft, which creates independent blood flow.[10] Since cardiac surgery is not an option for foals, the only medical management option is the treatment for cyanotic heart disease, rather than PTA alone. Treatment options include preventing hyper-viscosity syndrome by phlebotomy, fluid replacement as needed, and by maintaining a high-normal systemic blood pressure; nevertheless, even with these treatments the foal's prognosis remains grave.[6]

Case Outcome

As Zel continued to decline, Zel's grave prognosis was communicated with the owners. Due to Zel's grave prognosis, her owner's elected humane euthanasia. Zel was humanely euthanized on March 18th, 2019 and her body was submitted for necropsy. Necropsy examination

showed a transposed/overriding aorta, high ventricular septal defect, a single anomalous vessel that likely contained the aorta and main pulmonary artery, and a malformed pulmonary artery that branched off the aorta furthering our diagnosis of type 3 PTA. The ventricular hypertrophy noted during the echocardiogram was not appreciated during gross examination. In examining Zel's liver, there was severe, centrilobular and multi-focal hepatocellular necrosis most likely secondary to the systemic hypoxemia.

References

[10] Brandt, D. J., Canfield, D. R., Peterson, P. E., & Hendrickx, A. G. (2002). Persistent truncus arteriosus in a rhesus monkey (Macaca mulatta). *Comparative Medicine, 52*(3), 269-272.

[4] "Chapter 4: Disorders of the Cardiovascular System." *Knottenbelt and Pascoe's Color Atlas of Diseases and Disorders of the Horse*, by Siobhan B. McAuliffe and Derek C. Knottenbelt, Saunders/Elsevier, 2014, pp. 162–163.

[7]Chuzel, Thomas, et al. "Persistent Truncus Arteriosus in a Cat." *Journal of Veterinary Cardiology*, vol. 9, no. 1, 2007, pp. 43–46., doi:10.1016/j.jvc.2005.06.001.

[1] Hall, T.l., et al. "Congenital Cardiac Defects in Neonatal Foals: 18 Cases (1992â 2007)." *Journal of Veterinary Internal Medicine*, vol. 24, no. 1, 4 Jan. 2010, pp. 206–212., doi:10.1111/j.1939-1676.2009.0445.x.

[6] Jesty, Sophy A. "Chapter 120: Congenital Cardiovascular Conditions." *Robinson's Current*

Therapy in Equine Medicine, by Kim A. Sprayberry and N. Edward Robinson, Elsevier, 2015, pp. 503–505.

[2] Jesty, S. A., et al. “Persistent truncus Arteriosus in Two Standardbred Foals.” *Equine Veterinary Education*, vol. 19, no. 6, 2007, pp. 307–311., doi:10.2746/095777307x213946.

[3] Kittleson D. Mark. *Small Animal Cardiovascular Medicine Textbook: Chapter 18: Truncus and Pseudotruncus Arteriosus.* 2005 February.

[5] Seco Diaz, Olga, et al. “Total Anomalous Pulmonary Venous Connection in a Foal.” *Veterinary Radiology & Ultrasound*, vol. 45, no. 1, Jan. 2005, pp. 83–85., doi:https://doi.org/10.1111/j.1740-8261.2005.00017.x.

[9] Serres, François, et al. “Ante-Mortem Diagnosis of Persistent Truncus Arteriosus in an 8-Year-Old Asymptomatic Dog.” *Journal of Veterinary Cardiology*, vol. 11, no. 1, 2009, pp. 59–65., doi:10.1016/j.jvc.2008.11.001

[8] Steyn, P.F., et al. “The Angiocardiographic Diagnosis of a Persistent Truncus Arteriosus in a Foal.” *Journal of the South African Veterinary Association*, vol. 60, no. 2, 1989, pp. 106–108.