CASE REPORT #5

CASE PRESENTATION

On September 27, 2013, a healthy female giraffe (*Giraffa camelopardalis*) calf was born. The animal was bright, alert, nursing and healthy for the first several weeks. At five weeks of age, keeper staff observed a 2 minute episode of frothy discharge from the calf's mouth and that it was agitated and swinging its head violently. The animal returned to normal within 5 minutes of the episode. One week later, keeper staff reported the calf regurgitated milk and was again exhibiting agitated behavior. A significant amount of milk was found on the head, as well as splattered on nearby walls. Over the next three months, regurgitation episodes became more frequent and keepers reported hearing a "gurgling" sound while the calf was eating or nursing. On February 15, 2014 the animal had a violent regurgitation episode while eating romaine lettuce, expelling both milk and lettuce, followed by an episode with alfalfa one week later. The condition was worsening with the consumption of solid foods, suggesting the presence of an esophageal abnormality.

DIFFERENTIAL DIAGNOSES

The giraffe calf was showing signs of esophageal dysfunction, including regurgitation, difficulty swallowing, and ptyalism. There are a number of different causes of esophageal dysfunction, including esophageal stricture, trauma from a foreign body, esophagitis, neoplasia, megaesophagus, esophageal hypomotility, and a vascular ring anomaly (VRA). Given the age of the giraffe, megaesophagus and esophageal hypomotility were considered unlikely as these most commonly occur in adults. Foreign body ingestion, esophagitis, and neoplasia were also considered unlikely. Esophageal strictures cause regurgitation, ptyalism, dysphagia, and pain. The agitated behavior could potentially be attributed to pain, however

the calf was showing no other signs of pain (Jergens AE).

Another potential condition causing regurgitation is VRA, which is a congenital malformation of major arteries of the heart, leading to entrapment of the esophagus, resulting in obstruction. A number of different VRAs have been reported in dogs and cats, and less frequently in horses and cattle. Affected puppies and kittens will typically present for regurgitation of solid foods when weaning. Previously reported VRAs include persistent right aortic arch (PRAA), persistent left or right subclavian artery, double aortic arch, right ductus arteriosus with left aortic arch, persistent right dorsal aorta, and aberrant intercostal arteries, with the most commonly reported anomaly being PRAA (Jergens AE). During fetal development, pairs of aortic arches present in the heart develop into cardiac vessels or regress during normal development. PRAA anomalies develop when the right 4^{th} aortic arch forms the aorta instead of the left 4^{th} aortic arch. Since the right arch descends on the right side of midline, the left ductus arteriosus, which becomes the ligamentum arteriosum, forms a strap between the right aorta and the left pulmonary artery, which surrounds the esophagus and trachea resulting in entrapment (Butt TD, et al). The presence of a PRAA results in esophageal entrapment at the heart base by the right aorta, the left pulmonary artery, and the ligamentum arteriosum (Jergens AE). This condition obstructs passage of food through the esophagus, resulting in regurgitation and/or food retention and subsequent esophageal dilation anterior to the anomaly (Butt TD, et al). In order to definitively diagnose esophageal stricture or the presence of a VRA, the most common diagnostics performed are radiographic contrast series and/or esophagoscopy. Transesophageal ultrasound and angiography have been used to better identify the anatomy of the aortic arches in order to determine which VRA is present (McKenzie EC, et al).

DIAGNOSTIC EXAMINATION

Due to the inherent risks associated with giraffe anesthesia, less invasive diagnostics such as gastrointestinal contrast radiographs were considered. At 4 months of age, the calf had become too large to safely restrain manually, therefore administration of barium sulfate via gastric tube was not an option. Keepers attempted to train the calf to accept a bottle in order to aid in administration of barium, but the calf was not receptive. The calf was not trained to enter a chute, but could easily be guided into one in order to obtain radiographs. However, the chute was not appropriate for taking radiographs of such a young giraffe as none of the side panels could be removed without posing serious safety concerns to both the calf and the veterinary staff. Since there were no feasible non-invasive diagnostic options, an anesthetic procedure was planned.

On March 13, 2014 the calf was anesthetized for a full diagnostic examination. It received ketamine (1.68 mg/kg, 400 mg) and medetomidine (84.0 mcg/kg, 20 mg) intramuscularly (IM) via a non-metal dart. Initial drug effects were seen in three minutes, and the animal was laterally recumbent within eight minutes. A back board was used to keep the head elevated and the neck supported and straight. The calf was maintained on oxygen via nasal insufflation and was tachypneic throughout the procedure, with respiratory rates as high as 150 breaths per minute. All other vital signs were within normal limits. A full physical examination was performed. Intravenous (IV) catheters were placed in the left auricular vein and the right metatarsal vein and Normosol-R (12 mL/kg/hour, 3 L) was administered IV. Blood was collected from the right jugular vein for serum chemistries, a complete blood count (CBC), and serum banking, and also from the right auricular artery for blood gas analysis. Survey left lateral radiographs were taken of the thorax, thoracic inlet, and the neck. Esophagoscopy was performed by a consulting equine specialist using a 3 meter flexible endoscope. A cardiac ultrasound was also performed by the consulting equine specialist. Due to the increased susceptibility of this animal to aspiration, ceftiofur crystalline

free acid (CFA) (6 mg/kg, 1600 mg) was administered subcutaneously (SQ). Additionally the calf was opportunistically vaccinated with rabies (IMRAB 3, 2 mL) and tetanus toxoid (2 mL), both SQ. Regardless of measures taken to keep the neck straight, a slight kink was observed mid-procedure in the mid-cervical region, with knotted, taught neck muscles. Keeper staff massaged the area throughout the remainder of the procedure, and upon recovery the neck was normal. Medetomidine was reversed with atipamezole (0.2 mg/kg, 50 mg) IM and recovery was quick and smooth. The calf appeared sedate later in the day and was observed stumbling and holding its head down, but was still standing. It was left with the dam overnight and was normal the next morning.

EXAM FINDINGS

Physical exam findings were within normal limits. Respiratory sounds were loud but clear on both sides. The calf was in good body condition and weighed 238 kg. The survey radiographs were unremarkable and blood work showed a relative neutropenia with serum chemistries all within normal limits (Appendix 1). The cardiac ultrasound was normal, with the exception of poor ventricular contractility, which was attributed to the use of medetomidine. During the esophagoscopy, the oral cavity was visualized to be normal. The endoscope was passed easily for approximately 50 cm, at which point it would pass no further. There was a tight stricture in the esophagus at the level of the heart base. The area was insufflated with air, and the distal esophagus was found to be markedly dilated with a small amount of a brown-colored fluid present. The dilated area had developed into a diverticulum, which was likely the source of the "gurgling" sound that the keepers had been reporting. Based on the esophagoscopy findings, the calf was diagnosed with a VRA, most likely PRAA, causing stricture of the distal esophagus.

While plans were being made for surgical correction of this condition, keeper staff modified

the calf's feedings. Keeper staff offered small meals several times throughout the day, and avoided romaine lettuce and alfalfa hay. The calf continued to remain bright and alert, and the modified feedings decreased the regurgitation episodes.

SURGICAL INTERVENTION

One day prior to surgery, the calf received haloperidol acetate (0.08 mg/kg, 20 mg) IM via a non-metal dart to decrease anxiety during transport to the surgery center. On April 8, 2014 the calf was coaxed into a trailer without incident and transported to a local veterinary teaching hospital. The calf was monitored via a live video camera during the transport, which went smoothly. Upon arrival at the hospital, the calf was darted in the trailer with ketamine (1.68 mg/kg, 400 mg) and medetomidine (84 mcg/kg, 20 mg) IM with a non-metal dart. Within 7 minutes, the giraffe was laterally recumbent, however it required additional ketamine (0.84 mg/kg, 200 mg) IV via the right auricular vein for safe transport into the hospital. The calf was intubated with a 16 mm endotracheal tube and maintained on isoflurane throughout the surgery via a ventilator. A back board was placed under the head and neck with additional padding to prevent kinking. Two IV catheters were placed, one in the left jugular vein and the other in the left lateral metatarsal vein. Additionally, arterial catheters were place in the right auricular and ventral tail arteries. Anesthesia was monitored cooperatively by the anesthesia staff at the veterinary teaching hospital and the zoo's veterinary team. Given the large and unique body size of the calf, thoracic echocardiography would not be diagnostic. Attempts were made to perform a thoracic computed tomography (CT) scan in order to definitively diagnose the VRA, however due to the animal's size it would not fit into the CT gantry. Since a VRA was still suspected, the calf was prepared for surgery.

The animal was transported into surgery where it was shaved and prepped with

chlorhexidine, saline, and povidone iodine prior to surgery. During surgery, the calf received ceftiofur sodium (10 mg/kg, 2400 mg) IV, ceftiofur CFA (6.72 mg/kg, 1600 mg) SQ, diazepam (0.05 mg/kg, 12mg) IV, ketamine (1.0 mg/kg, 240 mg) IV, lidocaine (1.68 mg/kg, 400 mg), fentanyl (238 mg/kg, 1mg) IV, hetastarch (1L) IV, and hypertonic saline (1L) IV. It also received constant rate infusions of ketamine (2.88 mL/hour), calcium gluconate (52 mL/hour), lidocaine (36 mL/hour), midazolam (12mg/hr), fentanyl (720 mcg/hour), and dobutamine (14 mg/hour initially, then 7 mg/hour) to help maintain anesthesia, provide analgesia, and maintain physiologic parameters. Immediately prior to surgery, a cervical subluxation was observed. The neck was massaged continuously throughout the surgery but the subluxation never fully resolved. Surgery was performed by a team of small animal and equine surgeons. Upon entering the thoracic cavity, the surgeons found that visualization of the cranial aspect of the heart, the great vessels, and the ductus arteriosus were hampered by the inability to adequately retract the thoracic limb cranially. The limb was manually retracted cranially as far as possible by the zoo's veterinary team throughout the surgery. Esophagoscopy was again performed by an equine specialist to aid in finding the vascular anomaly, and the ductus arteriosus was identified and dissected. The ductus arteriosis proved to be friable and as it was ligated it tore resulting in substantial hemorrhage. The hemorrhage was controlled with the application of vascular clamps, but the vessels were too friable to hold sutures. Other closure options were discussed, such as hemoclips, but were considered not applicable in this case. Due to the fact that the hemorrhage could not be controlled without the vascular clamps and no suitable options existed for closure of the vessel, the calf was humanely euthanized with pentobarbital (98.3 mg/kg, 23,400mg) IV.

POST MORTEM FINDINGS

After euthanasia the calf was transported to a nearby diagnostic laboratory for a full necropsy.

On gross examination, pale tan, friable material was found extending from the aorta at the base of the subclavian artery and also from the main pulmonary trunk at the former location of the ligamentum arteriosum. A 1.5 cm linear full thickness laceration was found at the base of the subclavian artery. There was marked attenuation observed in the distal esophageal musculature directly subjacent to the surgery site. The esophageal musculature in this area was found to be approximately one-third the thickness of the normal muscle. Two tracheal rings in the affected area were slightly compressed. Histologic examination revealed that the pulmonary artery, subclavian artery, and aorta had moderately decreased density of collagen and elastin fibers in the outer third to half of the tunica media of each vessel.

According to the pathologist's report, these findings confirmed the presence of a PRAA with ductus originating from the left subclavian artery, restricting the esophagus and trachea. The etiology of the arterial degeneration was not apparent in the examined sections of tissue. Two suggested possible causes of the degeneration could be a result of a congenital defect of the extracellular matrix proteins in the vessel wall or a result of local hypoxia due to compression of small vessels supplying the outer portions of the vascular wall. There are no documented disorders in giraffes that are characterized by defects in the formation of certain extracellular matrix proteins, though a few disorders have been documented in humans. Local hypoxia could have been due to the presumed pressure placed on these vessels by the trachea and the esophagus as the animal grew.

CONCLUSION

This case of a persistent right aortic arch is the first documented in this species. The close working relationship between this animal and its keeper staff allowed for diagnosis of the condition early in life, giving a much greater chance of successful repair and survival. Though this condition is routinely diagnosed and surgically corrected in dogs, cats, and

humans, the size and anatomy of this species presented a number of challenges during diagnosis and surgery. Even with these challenges, a successful surgical outcome might have been obtained if not for the significant degeneration of the vessels.

REFERENCES

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Appendix 1: Blood work results for 0.1 giraffe (*Giraffa camelopardalis*), 13 March 2014

TEST	RESULT	ISIS NORMAL REFERENCE RANGES
WBC (* 10^3 cells/UL)	6.11	3.38-21.91
RBC (* 10^3 cells/UL)	13.58	5.17-15.51
Hemoglobin (g/dL)	11.5	6.9-15.6
Hematocrit (%)	31.64	19.6-46.9
MCV (fL)	23.3	22.4-43.4
MCH (uug)	8.47	8.2-14.5
MCHC (gm/dL)	36.3	29-40
Neutrophils (* 10^3 cells/UL)	0.165	1.58-17.40
Lymphocytes (* 10^3 cells/UL)	5.627	0.45-5.33
Monocytes (cells/UL)	202	61-1110
Eosinophils (cells/UL)	98	48-1077
Basophils (cells/UL)	18	47-670
Platelet count (* 10^3 cells/UL)	216	94-1041
Glucose (mg/dL)	269	57-273
Blood urea nitrogen (BUN) (mg/dL)	10	12601
Creatinine (mg/dL)	1.8	0.7-2.8
BUN:creatinine ratio	5.56	4.2-27.6
Calcium (mg/dL)	10	7.1-12.9
Phosphorus (mg/dL)	9.8	3.2-13.9
Calcium:Phosphorus ratio	1.02	0.6-2.5
Sodium (mEq/L)	136	136-155
Potassium (mEq/L)	5.1	3.1-6.2
Sodium:Potassium ratio	26.7	22.9-44.2
Total Protein (gm/dL)	5.7	4.5-10
Albumin (gm/dL)	2.5	1.7-4.1
Globulin (gm/dL)	3.1	1.7-6.8
Albumin:Globulin ratio	0.806	n/a
Alanine Aminotransferase (IU/L)	14	2-40
Total Bilirubin (mg/dL)	0.3	0.1-2.9
Amylase (IU/L)	0	1-136
Alkaline Phosphatase (IU/L)	910	67-1512
Aspartate Aminotransferase (IU/L)	68	31-163
Creatine phosphokinase (IU/L)	1054	90-3144
Gamma Glutamyltransferase (IU/L)	8	9-84