“Kanili’s Conundrum”

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Class of 2021

Clinicopathologic Conference

June 26, 2020

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Introduction:

There are numerous diseases of the trachea that can result in respiratory compromise, but relatively few have been reported in goats. This case report will discuss the clinical signs, physical exam, and diagnostic findings of a young pygmy goat suffering respiratory distress due to tracheal disease. Differential diagnoses that should be considered in a young goat with suspected tracheal disease include tracheitis, tracheal collapse, or tracheal hypoplasia. Any of the aforementioned diseases can result in life threatening tracheal stenosis and respiratory compromise[3, 9, 16].

Tracheitis is most commonly reported in goats secondary to trauma. Traumatic events include being tethered, injury from a herd mate, or inappropriate administration of medications with a rough-ended balling gun[2]. Tracheitis secondary to dust, ammonia, and other airborne irritants should also be considered[18]. Infectious bovine rhinotracheitis can cause tracheitis, cough and nasal discharge experimentally in goats, however it is rare to isolate IBR in a natural setting[16]. Cilia-associated respiratory bacillus is known to cause tracheitis in laboratory rats and cattle. While it has been isolated from goats with chronic tracheitis, the clinical significance of this has not been established[18]. A sequel to severe tracheitis is tracheal stenosis[16]. Tracheal stenosis is narrowing or constriction of the tracheal lumen[19].

Tracheal collapse is a common condition in toy breed dogs that can be due to a congenital predisposition to tracheobronchomalacia, or it can be an acquired condition[11]. Intrathoracic tracheal collapse in an animal will present with respiratory distress most notable on expiration, accompanied by coughing and wheezing. An animal with cervical tracheal collapse will typically make stertorous noises, and respiratory distress will be most notable on inspiration[11]. While

relatively well-known in miniature horses, donkeys, and calves, tracheal collapse has been rarely documented in goats[2]. An adult goat showed no clinical signs of a respiratory condition until suddenly he became severely dyspneic and died. On necropsy, he was diagnosed with a grade II tracheal collapse[3]. In Texel sheep, tracheal collapse was diagnosed secondary to a recessive genetic disorder resulting in chondrodysplasia[20]. The chondrodysplasia resulted in severely thickened tracheal walls and narrowed tracheal lumens, along with other cartilage abnormalities. The lambs were so severely affected that after exercise, the tracheal collapse resulted in apnea and death[20].

Tracheal hypoplasia is a congenital anomaly where the diameter of the tracheal lumen is decreased along the entire length of the trachea[8]. Tracheal hypoplasia is a difficult diagnosis in goats, as the diameter of a goat's trachea is smaller than expected[16]. The best way to diagnose tracheal hypoplasia in goats is to compare them to their healthy counterparts[18]. Tracheal hypoplasia was confirmed in lambs with congenital tracheal stenosis. The lambs developed congenital tracheal stenosis after their dams ate *Veratrum californicum* on days 31-33 of gestation[9]. Lambs were also born with other defects including cyclopia and left lung lobe hypoplasia. Congenital tracheal stenosis occurs in humans as well, however the cause is unknown[9]. There have not been reports of does ingesting *Veratrum californicum* that produce kids with similar defects.

History and Presentation:

Kanili was a 6-month-old, intact female African pygmy goat (doeling) that was presented to the MSU-CVM Food Animal Department on August 28, 2019 for a nearly 2-month history of reported coughing and, recently, respiratory distress. Kanili lived predominantly indoors with

one other adult female African pygmy goat. Two weeks prior to the start of clinical signs, Kanili received an oral Vitamin D drench, and the owners thought she aspirated some of it. Around the same time, Kanili was seen eating a small amount of ant poison and had soft stool for several days following, which quickly resolved. Two weeks after the vitamin drench, Kanili developed a cough which had progressively worsened. Kanili's owners tried multiple medical treatments including florfenicol, penicillin G procaine, and oxytetracycline for presumptive aspiration pneumonia. Kanili was also administered dexamethasone, cannabidiol oil, and dewormers including panacur and ivermectin for possible lungworm infection. Despite treatment, Kanili continued to worsen and began to experience exercise intolerance. At the time of presentation, the only medication Kanili was receiving was albuterol. Originally only administered twice daily, Kanili's owners administered albuterol nearly every 3 hours since it was the only thing keeping Kanili out of respiratory distress. Despite her respiratory condition, Kanili continued to eat and drink.

Upon presentation, Kanili was bright, alert and responsive. She was open mouth breathing and significant stridor was heard. Her heart rate was 140 beats per minute, with a normal heart rate being between 70 to 90 beats per minute[13]. Her respiratory rate was 44 breaths per minute, with 12 to 24 breaths per minute being a normal respiratory rate[13]. Her rectal temperature was mildly elevated at 103.2º F. Kanili weighed 11 kilograms at presentation and was in good body condition with a body condition score of 3 out of 5. Harsh lung sounds were heard throughout the lungs, with loud wheezes auscultated at the thoracic inlet. Auscultation of her trachea revealed harsh breath sounds that were louder than the lungs. Minimal pressure on her trachea induced a cough. The remainder of the physical exam was unremarkable.

Diagnostic Approach/Consideration

Due to the easily inducible cough, a collapsing trachea was considered for the primary differential causing Kanili's condition[11]. However, tracheitis and aspiration pneumonia were not ruled out. A blood sample was obtained for a complete blood count and chemistry panel, both of which had no significant findings. Cervical and thoracic radiographs were obtained to confirm the suspected collapsing trachea. The cervical radiographs showed undulating tracheal margins with diffuse and severe narrowing of the cervical trachea at up to 90%, with the most severe being at the thoracic inlet. The thoracic radiographs revealed both a mild diffuse bronchial pulmonary pattern as well as an unstructured interstitial pulmonary pattern. The intrathoracic trachea was also narrowed. During normal respiration cycles, the trachea can narrow up to 25% of normal[1]. The pulmonary patterns are most likely consistent with infectious/inflammatory etiologies and atelectasis, respectively. The undulating margins of the trachea are consistent with tracheal collapse and/or tracheitis[1]. The top differential for the narrowed trachea was considered chondromalacia leading to tracheal collapse[1]. These radiographic findings were consistent with the working diagnosis of collapsing trachea, however tracheitis and/or tracheal hypoplasia were not excluded.

When medical management fails, treatment for tracheal collapse in small animals is most commonly a tracheal stent[11]. With the owner's permission, Kanili underwent bronchoscopy to confirm tracheal collapse and measure for placement of a tracheal stent. During the bronchoscopy, it was found the trachea was diffusely nodular and erythematous with a narrow tracheal lumen the entire length. The trachea was static in size when suction was applied. A brush cytology and biopsy were taken from the tracheal mucosa. The cytology was submitted for cytology and culture, and the biopsy was submitted for histopathology. Bronchoscopy of the

lower airways was limited due to difficulty keeping the patient at appropriate anesthetic depth, but brief examination revealed no significant findings.

To confirm radiographically there was no dynamic tracheal collapse, thoracic radiographs were obtained again to measure the diameter of the trachea. These radiographs revealed minimal change in diameter, with the maximal intrathoracic tracheal diameter being 10.5 mm on inspiration and 8.5 mm on expiration. The narrowest tracheal diameter at the thoracic inlet measured 2.7 mm on inspiration and 2 mm on expiration. It is important to note that the trachea in a goat is the narrowest at the thoracic inlet, however this is still more narrow than what is considered normal[4]. These findings confirmed no evidence of dynamic tracheal collapse, and instead suggested that the tracheal narrowing was due to fixed tracheal stenosis.

Cytology of the tracheal mucosa was mostly inconclusive due to overwhelming blood contamination. Culture of the tracheal mucosa revealed light growth of *Pseudomonas aeruginosa* and no fungal growth. *P. aeruginosa* is gram-negative bacillus found in the environment[15]. It is rare for *P. aeruginosa* to cause disease in a healthy host and is therefore considered an opportunistic pathogen[15]. Kanili did not exhibit any signs of being an immunocompromised individual, so it was more likely it was able to colonize her tracheal mucosa after the mucosa had been damaged. This finding was supportive of tracheitis as a top differential diagnosis[16, 18].

Histopathology of the tracheal mucosa showed the normal ciliated pseudostratified columnar epithelium had been replaced by thick stratified squamous epithelium. The underlying lamina propria was thick with fibrous tissue, which is consistent with the bronchoscopy findings of a stenotic trachea[12]. The tissue was also infiltrated with multiple cell types including neutrophils, histiocytes, lymphocytes and plasma cells, all of which indicate chronic

inflammation[5]. Special stains were applied to the sample for additional organisms but were negative. The histopathology revealed a chronic and proliferative tracheitis with ongoing inflammation. With evidence of further maturation of fibrotic tissue, it was likely Kanili's condition would worsen[12].

Diagnosis

Based on endoscopy and histopathology, Kanili was diagnosed with a severe tracheitis of unknown origin and tracheal stenosis.

Pathophysiology

The goat trachea is smaller than what would be expected for an animal of its size[4,16]. The trachea is composed of multiple layers which include the mucosa, submucosa, cartilaginous layer, and adventitia[17]. The mucosa is composed of ciliated, pseudostratified columnar epithelium and mucus secreting goblet cells. The cilia along the tracheal lumen are necessary for removing debris and mucus out of the respiratory tract[17]. Tracheitis can have multiple causes including inhaled chemical irritants, inhaled toxins, trauma, or upper respiratory infection[1, 16, 18]. While the inciting incident of Kanili's tracheitis cannot be confirmed, the pathophysiology of the tracheal stenosis is the same.

Damage to the mucosa lining the trachea stimulates multiple mediators of inflammation including histamine, prostaglandins, cytokines and leukotrienes[14]. This results in increased blood flow, activation of neutrophils, and increased edema[10, 14]. Simultaneously, a fibrin clot will form over the injured tissue and allows for migration of fibroblasts. As the initial inflammatory response wanes, the reparative phase begins, and fibroblasts will proliferate and differentiate to

contractile myofibroblasts[12]. These myofibroblasts will begin contracting the wound. In a cutaneous wound, myofibroblasts will stop contraction once appropriate tensile strength has been reached. The myofibroblasts will then undergo apoptosis and the wound will be covered with new epithelium[12]. However, in a tubular structure such as a trachea, the myofibroblasts are not effectively inhibited as the only way tensile strength is reached is circumferentially. The result is a stricture formation[12].

The damaged epithelium must also undergo repair. In non-tubular structures, this is controlled by contact inhibition[12]. As the wound re-epithelialized, the ciliated pseudostratified columnar epithelium is replaced with squamous metaplasia and keratin. The goblet cells are lost in the transition from normal epithelium to squamous metaplasia, and thus the mucociliary apparatus is lost[5, 12]. Without the protective effects of mucociliary apparatus, the animal is prone to recurrent pneumonia[17].

Keratin, as a result of the re-epithelialization of the tracheal mucosa, can incite chronic inflammation[5]. This chronic inflammation results in a fibroblastic response within the submucosa. Repair of the submucosa can be even more detrimental if wound healing is dysregulated[5, 12]. The fibroblastic response causes excess granulation tissue formation. This leads to submucosal fibrosis, further exacerbating the stenotic trachea[12].

Treatment Options for Tracheal Stenosis

Treatment options for tracheal stenosis include tracheal resection and anastomosis, tracheal ring prosthetics, or tracheostomy tube[7]. Tracheal resection and anastomosis in goats are most commonly performed due to tracheal ruptures after dog bites[6]. Surgical management has been successful, however those goats had focal injuries. Kanili had tracheal stenosis along the

entire length of her trachea. Tracheal prosthetic rings have been successfully used in cattle and in one kid, however this was for treatment of tracheal collapse[16]. There is ongoing research in treatment of tracheal stenosis by using a 3D printed, tissue-engineered trachea as a transplant for affected patients. The experiment was performed using goats and had promising results[4]. However, this research is in its infancy and will take time before it can be used within the medical field. A tracheotomy in Kanili's situation would not have been an option. Her trachea was narrowest at the thoracic inlet, so there was not an appropriate anatomic location for a tracheostomy tube[7]. Ultimately, there were no surgical options for Kanili's tracheal stenosis.

Medical Management and Case Outcome

Due to histological evidence of severe tracheitis, medical management of the inflammation was necessary. Kanili was started on a systemic corticosteroid, dexamethasone, until she could be switched to the inhaled corticosteroid, fluticasone. Kanili was administered florfenicol at 40 mg/kg and penicillin G procaine at 40,000 units/kg for broad spectrum antibiotic coverage and was continued on her albuterol treatment.

Kanili was sent home and maintained on supplemental oxygen using bilateral nasal oxygen tubes. Kanili's owners were instructed to keep her calm, as she would be more likely to experience respiratory distress when excited. Despite medical management and rest, Kanili's condition continued to worsen, and her owners elected to have her humanely euthanized at the referral veterinary hospital.

Kanili's respiratory tract was submitted to a diagnostic lab where a pathologist confirmed the biopsy findings. Kanili had developed squamous metaplasia along her entire tracheal lumen with evidence of severe inflammation. The tracheal stenosis was confirmed, and it was found

Kanili had multifocal areas of intra-alveolar hemorrhage. The remainder of the heart and lungs were histologically normal. While the inciting incident of Kanili's severe and proliferative tracheitis can never be proven, Kanili most likely aspirated something caustic in the days or weeks prior to her showing clinical signs. This caustic substance would have set off a severe inflammatory reaction that ultimately resulted in severe tracheal stenosis.

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