“Pireaux’s Pleural Problems”

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Introduction:

The pleural cavity is the space between the visceral and parietal pleura of the lungs. The pleural cavity normally contains <5 milliliters of lubricating fluid that allow the lungs to move within the cavity during respiration.[9] Pleural effusion is the abnormal accumulation of fluid within the pleural cavity. The fluid that accumulates can be further classified into an exudate (<3.0 g/dl of protein, >5,000 cell/ µl nucleated cells), a modified transudate (2.5-3.5 g/dl of protein, 500-1,000 cell/ µl nucleated cells) or a pure transudate (<2.5 g/dl of protein, <1,000 cell/ µl nucleated cells). Based on the characteristics of the fluid, the pleural effusion can be further characterized into a specific disease that is affecting the pleural cavity: Pyothorax is the accumulation of purulent fluid and septic inflammation of the thoracic cavity. [9,13] The subsequent case is a review of the presentation, diagnostic and therapeutic approach, pathophysiology, treatment, and management of pyothorax in a canine.

History and Presentation:

Pireaux is a 3-year-old female black Labrador Retriever who presented to MSU-CVM Emergency Services on 1/21/21 for an approximately 1.5-month history of waxing and waning lethargy and inappetence. At the time of intake, Pireaux was performing in field trials, lived at home with a retired duck hunting dog, was up to date on her vaccines and had not had any previous health issues before December 2020 . Prior to being admitted to MSU-CVM, Pireaux had been seen multiple times by her rDVM for the same complaint.

On 12/11/20, Pireaux first presented to her rDVM for lethargy, inappetence and trembling. Blood work was performed during that visit revealed a mild pancreatitis and she was prescribed maropitant citrate, clavamox and piroxicam. On 12/29/21, Pireaux was seen again for

pale gums and inappetence. Diagnostics including abdominal radiographs, bloodwork, gastrointestinal profile, and pythiosis titers revealed no significant findings except mildly elevated globulins and amylase. At that time, Pireaux was prescribed more antibiotics. On 1/21/21, Pireaux again presented to her rDVM for malaise and inappetence. Blood work performed at that time showed a mild hyperglobulinemia at 4.4 g/dl (normal reference range: 2.0-3.6 g/dl) Thoracic radiographs revealed pleural effusion. Erlichia and Lyme antibodies and tick titers were submitted and came back negative. Pireaux was then referred to MSU-CVM for further diagnostics and treatment.

At the time of presentation to the MSU-CVM Emergency Services, Pireaux weighed 33.3 kgs and had a body condition score of 5/9. She was bright, alert, and responsive with a temperature of 100.9 °F, a heart rate of 140 beats per minute and a respiratory rate of 32 breaths per minute. The only abnormalities noted on her triage exam included pleural effusion that was diagnosed on TFAST (Thoracic Focused Assessment with Sonography for Trauma) and mildly muffled heart sounds upon ventral auscultation of her chest. Otherwise, her physical exam parameters were within normal limits.

Pathophysiology:

Pleural effusion is the result of a disruption of Starling's forces within the pleural cavity.[5,9,13] Depending on the etiology behind the pleural effusion, different forces are affected, and fluid accumulates. In the case of a pyothorax, inflammation will lead to the release cytokines and inflammatory mediators that increase endothelial damage and vascular permeability. The increase in vascular permeability allows bacteria to easily enter the pleural space.[9,13] The accumulation of fluid and bacteria within the pleural space then leads to thickened parietal pleura, thickened and inflamed tissue within the thoracic cavity (lungs, heart, mediastinum) and

fibrin deposition. [5] The overarching etiologies leading to a pyothorax are bacterial, fungal, and viral. Bacterial etiologies include migrating foreign bodies (inhaled grass awns), penetrating bite wounds, penetrating trauma, parasitic migration (Spirocerca lupi), and progression of discospondylitis, neoplasia, parapneumonic spread, and introduction iatrogenically secondary to thoracocentesis. [5,9] Literature suggests that hunting/working dogs are at a higher risk of developing Actinomyces-associated pyothorax because of inhalation of a migrating foreign body.[12] Some literature suggests that the bacteria that are present in a pyothorax originate from normal oropharyngeal flora that is aspirated.[9] Bacteria that have been associated with canine pyothorax include E. coli, Nocardia, Actinomyces, Bacteroides, Enterobacter, Klebsiella, Corynebacterium, Staphylococcus and Streptococcus, Peptostreptococcus anaerobius, Prevotella and Porphyromonas.[1, 9,12,14] Cryptococcus, Blastomycoses dermatitis and Candida albicans are all fungal organisms that have been associated with pyothorax.[9]

Diagnostic Approach:

Diagnosis of pleural effusion, more specifically pyothorax can be made based on a combination of clinical signs, thoracic radiographs and ultrasound, bloodwork, and pleural fluid analysis. However, literature suggests that a definitive diagnosis is based on results of cytology of pleural effusion and aerobic and anaerobic culture results.[13] In Pireaux's case, all the aforementioned diagnostics and more were pursued. Clinical signs of pleural effusion can be both specific (tachypnea, inspiratory dyspnea, muffled heart and lung sounds, exercise intolerance, coughing, cyanosis) or non-specific (lethargy, anorexia, weight loss). [5,7,9] Based on her history and physical exam upon presentation, Pireaux experienced lethargy and had muffled ventral heart sounds indicative of the presence of fluid.

When visualizing pleural effusion on thoracic radiographs, the accumulation of abnormal amounts of pleural fluid around the lungs will cause them to appear scalloped and as if they are "floating" within the pleural cavity. [9] The scalloped appearance is due to the accumulation of fluid between the different lung lobes causing interlobar fissures. [9] The "floating appearance is due to the accumulation of fluid between the lungs and sternum. [9] Furthermore, the accumulation will cause border effacement of the cardiac silhouette and the diaphragmatic border in some cases.[9] Thoracic radiographs are also used to evaluate for bilateral and/or unilateral pleural effusion or pulmonary and/or mediastinal masses.[9] In Pireaux's case, thoracic radiographs revealed small volume pleural effusion indicated by border effacement of the cardiac silhouette and widened pleural fissures. Abdominal radiographs were also performed and revealed no abnormalities.

Ultrasonography and CT are other imaging modalities that are used to support the diagnosis of pleural effusion and pyothorax.[9] Unlike thoracic radiographs, CT allows a clinician to detect small volume pleural effusion, foreign bodies, lung abscesses and the ` of the pyothorax (small versus large volume pleural effusion, foreign body).[14] Ultrasound is used to detect the volume of effusion, the nature of the pleural fluid and can be used to detect lung abscesses as well as act as an aid for other diagnostic approaches (thoracocentesis, aspiration, biopsy, etc.).[2,14] Pireaux's abdominal ultrasound revealed a hypoechoic liver. An ultrasound guided fine needle aspirate of her liver was performed as well as an ultrasound guided fine needle thoracocentesis of her pleural space. Cytology of the liver aspirate revealed mild hepatic lipidosis. Cytology of the pleural fluid revealed septic suppurative inflammation indicated by degenerate and non-degenerate neutrophils and intracellular rods and cocci and aerobic and anaerobic cultures were negative. The thoracic CT revealed fibrin or abscesses within the pleural space, unstructured and

structured interstitial pulmonary patterns indicating fungal or bacterial infections, pulmonary bullae within the left caudal lung lobe and sternal and tracheobronchial lymphadenopathy. An echocardiogram was performed and confirmed bilateral pleural effusion and fibrinous exudate as well as abnormal mediastinal fat and thickened parietal pleura. Based on the results of the thoracic radiographs, CT, echocardiogram, and the ultrasound guided fine needle thoracocentesis, pyothorax was diagnosed.

Hematologic and biochemical abnormalities seen with pyothorax include an inflammatory leukogram, hypoalbuminemia, hyperglobulinemia, and mildly elevated liver enzymes. [5,7,9] In Pireaux's case, the blood work performed at MSU-CVM, pre-operatively revealed neutrophilia at 23054.7 (3100-11800) , lymphopenia at 991.6 (1100-4800) , decreased plasma proteins at 5.2 g/dl (5.5-8) , mild hypoalbuminemia at 2.1 g/dl (2.5-3.9) as well as well as other mild electrolyte abnormalities (decreased calcium at 8.6 mg/dl (8.8-11.2), magnesium at 1.6 mg/dl (1.7-2.4), elevated CK at 315 U/L (50-300)). The fungal, anaerobic, and aerobic cultures of her pleural and Blastomycosis antigen tests all revealed no growth. Operative diagnostics were pursued including biopsies, cytology and further aerobic and anaerobic cultures.

Treatment and Management:

Treatment of pleural effusion and pyothorax can be based on medical and/or surgical management.[5,7,9] Medical treatment includes long-term antibiotics, intermittent or continuous pleural drainage and pleural lavage.[9,13] Antimicrobial therapy is based on broad spectrum antibiotics to cover as many potential organisms at possible.[9] Common antibiotic choices include penicillins, cefoxitin, enrofloxacin, and trimethoprim-sulfonamide.[8,9,12] However, there are no definitive guidelines on how long antimicrobial treatments should be but the standard in

veterinary medicine is treatment for 2 weeks past resolution of clinical signs.[13] All antibiotic choices should be based on results from a culture and sensitivity test of pleural fluid and pleural tissue. In Pireaux's case, she was placed on Trimethoprim-Sulfonamide at 15 mg/kg twice daily and Clavamox 30 mg/kg three times per day despite negative culture results.

Thoracocentesis is used for pleural drainage and as a means of diagnosis.[1,7,9] When performing a thoracocentesis, as much pleural fluid should be removed as possible, but it is not recommended that it be performed repeatedly due to the iatrogenic risks associated with it: hemothorax, pneumothorax, organ laceration, infection and pulmonary edema.[9] A better means for complete removal of pleural fluid is via thoracostomy tubes. The placement of thoracostomy tubes is based on the amount of fluid present as well as if one or both sides of the pleural cavity are affected.[9,13] The dog is sedated or placed under general anesthesia and a skin incision is made in the dorsal third of the thoracic cavity, the tube is advanced caudodorsal to cranioventral and is sutured into place.[9] Proper placement of thoracostomy tubes should be verified via thoracic radiographs. Pleural drainage via thoracostomy tubes is done every 2-6 hours depending on the amount and character of the of fluid present at the time of drainage.[9] Risks associated with thoracostomy tubes include pneumothorax, clogging, nosocomial infections, organ damage, removal, or malposition. [9,13] Thoracic lavage with sterile isotonic saline can be done via thoracostomy tubes.[1] After initial drainage of pleural fluid, 10-20 ml/kg of isotonic saline is flushed into the pleural space and allowed to sit for 5- 10 minutes and then 75% of the fluid should be removed.[9,13] Risks associated with pleural lavage include an inability to remove all the fluid that was introduced and introduction of a nosocomial infection. [9,13]

Surgical management is considered when medical management has failed to improve the patient's status within 48-72 hours or if the patient continues to deteriorate. [9] However, the

decision to pursue surgery is ultimately made by the clinician as there is not a set criterion for when to transition from medical management to surgery.[13] A thoracotomy is commonly performed when medical management has failed, when mediastinal or pulmonary lesions are present or if Actinomyces is suspected.[12] The preferred approach for a thoracotomy is a median sternotomy because it allows the surgeon to visualize and have access to both sides of the thoracic cavity. [7,9,12] During a thoracotomy, any fluid, necrotic tissue and/or foreign material should be removed, and the pleural cavity should be lavaged.[5,7] It is common for a foreign body to not be able to be identified within the pleural cavity at the time of surgery due to size, inflammation or degradation of the foreign body within the pleural cavity.[7,12] Any tissue that appears thickened should be collected and submitted for culture and histopathology. In some cases, thickened lungs and pericardium require that a lung lobectomy or pericardiectomy be performed.[9] Thoracostomy tubes should be replaced concurrently. Thoracoscopy is another surgical tool that has been recommended but not yet widely used in cases of pyothorax in veterinary medicine.[9]

In Pireaux's case she was first treated via medical management. She was prescribed Trimethoprim-Sulfonamide at 15 mg/kg twice daily and Clavamox 30 mg/kg three times per day . After being placed on these antibiotics, Pireaux's pleural effusion began to decrease. However, after her CT confirmed bilateral pleural effusion and revealed thickened pleura, lymphadenopathy, and several pulmonary nodules, Pireaux had bilateral thoracostomy tubes placed. Following placement of her thoracostomy tubes, pleural fluid was aspirated, and her pleural cavity was lavaged with 10 ml/kg of 0.9% sodium chloride. After having the thoracostomy tubes in place for three days, a significant amount of pleural fluid was still being

removed from her pleural cavity. Due to a inability of medical management to completely resolve the pyothorax, a thoracotomy was pursued on 1/28/21.

The approach used for her thoracotomy was a median sternotomy. Upon visualization of Pireaux's thoracic cavity, her mediastinum was thickened, tan and covered in friable nodules. Samples of mediastinal tissue were collected for culture, cytology, and histopathology. No gross abnormalities were noted in her lungs, but a partial lung lobectomy of the right cranial lung lobe was performed, and collected for culture and histopathology. After collecting all the necessary tissue samples, her chest was lavaged with sterile saline. After closing, only her right thoracostomy tube was replaced. Post-surgical care included thoracic radiographs to confirm tube placement, continual drainage of pleural fluid from the right thoracostomy tube with a goal of 1-2 ml/kg/day of fluid, monitoring of the incision site and monitoring for any signs of respiratory distress or systemic illness. Approximately 2 hours after her procedure, Pireaux had an episode of tachypnea that was resolved with the administration of IV Acepromazine. Two days post-operatively, Pireaux developed subcutaneous edema near her manubrium. Blood work was performed and revealed a mild hypoalbuminemia and decreased total protein. No treatments were pursued to correct the edema and it spontaneously resolved within two days.

Case Outcome:

Following the thoracotomy, Pireaux's pleural effusion continued to decrease and her right thoracostomy tube was removed on 2/2/21. The cultures of her mediastinum, thorax, and pulmonary tissue showed no growth. The histopathology of the mediastinum and lung revealed an inflammatory process, but no organisms were identified. Cytology of the mediastinal and lung tissues supported the diagnosis of macrophagic and neutrophilic inflammation but again no other organisms were identified. Pireaux was discharged on 2/2/21 after fourteen days in the hospital

and at this time her physical exam parameters were within normal limits; her pleural effusion had significantly decreased, and her incision was healing appropriately. Client instructions included activity restriction, incision care and administration of medications. Pireaux was prescribed Tylenol 4 at 2 mg/kg three times daily for 5 days, Clavamox at 15 mg/kg twice daily for fourteen days, Trimethoprim-sulfonamide at 15 mg/kg twice daily for fourteen days and Trazadone at 5 mg/kg three times daily for thirty days. At the time of discharge, it was recommended that Pireaux return in 2 weeks from the time of her surgery to recheck her status. Her owner elected to schedule weekly rechecks with her rDVM and at the time of contact, rDVM radiographs revealed no pleural effusion. Based on the nature of Pireaux's pleural effusion, her role as a field trial dog and the results of her various diagnostic tests, Pireaux was given a presumptive diagnosis of pyothorax due to a bacterial infection involving Actinomyces or Nocardia.

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