

# **Punk'n's Petrifying Pleural Problem**

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## **Introduction**

Pleural effusions occur when there is an alteration in hydrostatic pressure, osmotic pressure, vascular permeability, or lymphatic function within the thoracic cavity resulting in a pathologic accumulation of fluid within the pleural space. Specifically, when there is leakage from the thoracic duct or decreased lymphatic drainage into systemic circulation, a modified transudate comprised of chyle or triglyceride rich lymph can develop in the thoracic cavity and is known as a chylothorax. Initial physical exam of a patient with a chylothorax will generally lead to the initial suspicion of a pleural effusion based on decreased thoracic percussion on auscultation due to gravity accumulation of pleural fluid in the ventral thorax, and some degree of respiratory distress or restrictive breathing. Interestingly, the onset of a chylothorax is often slow and subtle as most owners report coughing months before observing tachypnea, inspiratory dyspnea, and/or generalized signs of illness such as lethargy, anorexia, and weight loss. Chylothorax has also not been associated with a specific signalment in dogs and cats; however, Siamese and Himalayan cats as well as Afghan Hounds and Shiba Inu dogs seem to be overrepresented<sup>(1,2,3)</sup>. The following case report of a cat diagnosed with idiopathic chylothorax will review the history, presentation, clinical signs, diagnostic approach, pathophysiology, and treatment options of the condition in the canine and feline patient as well as the outcome of this patient, Punk'n.

## **History and Presentation:**

Punk'n is an approximately 6-year-old, spayed female domestic long hair cat who was presented to the MSU-CVM Internal Medicine Service on June 6<sup>th</sup>, 2021 for evaluation of a pleural effusion diagnosed by her primary veterinarian. Punk'n was originally presented to the

Boswell Animal Clinic on March 8<sup>th</sup>, 2021 for a history a persistent cough that was medically managed with steroid injection (Depo Medrol) in November, 2020. The owner reported that Punk'n's clinical signs improved with the initial treatment but returned approximately one month after receiving the steroid and continued to progress until March. When returning to the Boswell Animal Clinic, there were mild upper respiratory noises and tachypnea noted on physical exam by the referring veterinarian. Thoracic radiographs revealed a bilateral pleural effusion that was noticeably worse on the right side of the thoracic cavity. On March 9<sup>th</sup>, 2021, Punk'n underwent general anaesthesia for a thoracocentesis where 60 ml and 120 ml of a modified transudate was collected on the right and left side of the thoracic cavity, respectively. Analysis of the samples taken showed 6,740 cell/ul and 3.5 g/dl protein on the right, and 7,980 cell/ul and 3.7 g/dl protein on the left. The predominate cell type was small lymphocytes and had an increased number of eosinophils. These findings suggest a lymphocytic effusion that is consistent with a chylothorax, which lead to Punk'n being referred to MSU-CVM for additional diagnostics and treatment.

On presentation, Punk'n was bright, alert, and somewhat aggressive when first being handled. Punk'n presented weighing 5.3 kg, with a BCS of 7/9 (4-5 being ideal). She had a heart rate of 192 beats per minute, a respiratory rate of 60 breaths/minute. A temperature was not obtained during the initial exam due to her aggression. She had a normal haircoat with no ectoparasites noted. There was no ocular, oral, nasal, or aural discharge noted on physical exam. No murmurs or arrhythmias were noted on cardiac auscultation. Her lungs auscultated normally and there were no obvious signs of respiratory distress.

## **Pathophysiology**

When reviewing canine and feline anatomy, the thoracic duct runs dorsal to the aorta and ventral to thoracic vertebrae. In the abdomen, the cisterna chyli is the caudal extension of the thoracic duct and is in the craniodorsal abdomen. Once the cisterna chyli transverses the diaphragm, it becomes the thoracic duct and returns chyle into circulation via a lymphaticovenous anastomosis in the left external jugular or jugulosubclavian angle. Chyle is lymph rich in chylomicrons or large lipoproteins composed predominately of triglycerides, phospholipids, cholesterol, and other dietary fats. It also contains proteins, electrolytes, fat soluble vitamins, and immune cells such as lymphocytes, neutrophils, and macrophages. When there is impedance of lymph outflow into the venous system, obstruction of the thoracic duct, increased lymph flow from hepatic lymph formation, or rupture of the thoracic duct, a chylothorax can occur <sup>(1,2,5)</sup>.

Ultimately, an abnormal pressure in the thoracic duct or cranial vena cava can lead to thoracic duct dilation or lymphangiectasia and subsequently transmural exudation of chyle into the thoracic cavity. Chronic loss of chyle into the thoracic cavity can lead to metabolic and electrolyte abnormalities such as hypoproteinemia, hyponatremia, and hyperkalemia, as well as immunocompromise from lymphocyte loss. Chyle is also a bacteriostatic fluid that irritates the pleural surface which results in a restrictive respiratory disease known as fibrosing pleuritis. Evidence that supports fibrosing pleuritis includes radiographic findings of rounded lung lobes in the presence of a small amount of pleural fluid as well as the development of a pneumothorax after performing a thoracocentesis <sup>(1,5)</sup>. Ultimately, fibrosing pleuritis is associated with a worse prognosis in both canine and feline patients who develop a chylothorax because the chronic

deposition of fibrin restricts normal parenchymal expansion and contraction even after resolution of the chylothorax.

Although most cases of chylothorax in the canine and feline patient are idiopathic, other differentials should include intramural (neoplasia or fungal granuloma) or extramural (increased intrathoracic pressure) obstructions, cranial mediastinal masses (lymphoma), cardiac diseases that increase right sided venous pressures (congenital or *Dirofilariasis*), and trauma. In humans, iatrogenic chylothorax predominates due to traumatic rupture in surgery; however, this is unlikely in the veterinary patient because the thoracic duct heals quickly, and the effusion generally resolves within 1-2 weeks <sup>(5)</sup>.

### **Diagnostic Approach**

Following Punk'n's initial physical exam, blood was collected and submitted for analysis which revealed a moderate lymphopenia (369 cell/ul), mild anemia and elevated creatinine kinase. An Idexx SNAP test for Feline Immunodeficiency Virus (FIV) antibodies and Feline Leukemia Virus (FeLV) antigens was also performed which was considered below detectable limits or negative.

Under sedation, thoracic radiographs of Punk'n were taken to determine if there were any new developments of the pleural effusion that was previous diagnosed by her primary veterinarian in March. The thoracic radiographs depicted a chronic bilateral pleural effusion that was worse on the right hemithorax. The pleural effusion was characterized by multifocal alveolar pattern which may be associated with chronic changes such as fibrosis, but parenchymal consolidation, severe aspiration pneumonia and neoplastic infiltrations are possible.

Punk'n was then put under general anesthesia where approximately 170 ml of an odorless, pink-tinged milky fluid was collected from the right hemithorax via an ultrasound guided thoracocentesis. In addition to the milky white appearance of this modified transudate, some of the characteristic features of chyle is a low protein concentration (2.5- 4 g/dl), low cellularity (<7000 cells/ $\mu$ l), and specific gravity below 1.032. Cytologic evaluation of Punk'n's pleural fluid revealed a low to moderate cellularity that was most consistent with a modified transudate and the predominance of small mature lymphocytes, which suggested a chylous effusion. This presumptive diagnosis was confirmed by comparing the triglyceride concentration in the effusion (127 g/dL) to the serum (24 g/dL). This diagnostic test is considered the "gold standard" to definitively diagnosing a chylothorax as the concentration of the pleural effusion is greater than that of the serum. It is also important to note that the lymphocytes from this sample were most consistent with a chylous effusion, but if there is any clinical concern of a small cell lymphoproliferative disorder, then other diagnostics such as flow cytometry of the fluid should be considered. To rule out an underlying bacterial infection, the sample was also submitted for aerobic and anaerobic culture and aerobic sensitivity testing, which was negative for bacterial growth after 48 hours of incubation. Punk'n also received an echocardiogram to rule out any cardiac conditions that could be associated with the chylothorax but revealed no clinically significant abnormalities other than the pleural effusion.

Finally, Punk'n's had a thoracic CT with contrast which revealed a pleural effusion, as well as a thickened, contrast enhanced parietal pleura and enlarged sternal lymph nodes, which were most likely secondary reactive changes such as fibrosis. There was also increased soft tissue attenuation of the right cranial lung lobe most consistent with atelectasis; however, infectious, or neoplastic etiologies were not excluded. If surgery is being considered, thoracic

computed tomography (CT) of the thoracic duct via mesenteric or popliteal lymphangiography is recommended preoperatively for surgical planning, and postoperatively to confirm that the thoracic and its branches were adequately ligated.

### **Treatment and Management Options:**

Chylothorax in the veterinary patient can be successfully treated with a combination of medical, surgical, and dietary management. If the underlying disease process is identified and treated, then the chylothorax may be managed with intermittent thoracocentesis. It is important to note that in severely compromised animals, the goal is to remove the amount of fluid necessary to relieve clinical signs. Rapid removal of the pleural fluid or multiple thoracocentesis can result in life-threatening sequelae such as hypoproteinemia, hyperkalemia, hyponatremia, and immunocompromise from lymphocyte depletion.

When discussing the protocol for medically managing chylothorax, one of the unique nutraceuticals that is often used is Rutin. Rutin (benzopyrone) is a pigment extracted from plants and is marketed as an over-the-counter product or nutraceutical. Although the exact mechanism of action is not fully understood, it is thought to reduce leakage from blood vessels, increase removal of protein from tissues, and enhance macrophage phagocytosis of chyle. The efficacy of this product has also not been fully determined because cats can have spontaneous resolution of their idiopathic chylothorax. However, based on previous case studies, resolution of clinical signs and of the pleural effusion without mechanical removal via thoracocentesis days after initiating rutin therapy may be associated with its efficacy rather than spontaneous resolution <sup>(4)</sup>. In Punk'n's case, rutin therapy was initiated after her surgery and she will continue to take this product until further notice. Other medications that are thought to be beneficial in treating

traumatic or post-operative chylothorax is Somatostatin or Octreotide (synthetic somatostatin analogue), which is thought to decrease lymphatic flow to allow the thoracic duct time to heal.

If the chylothorax is idiopathic or fails to resolve with medical management, then surgical intervention is necessary. Surgical resolution can be accomplished with a combination of a thoracic duct ligation (TDL) and subtotal pericardiectomy (SPC) or Cisterna Chyli Ablation (CCA). With TDL alone, there is an approximately 50% success rate; however, when combined with either a SPC and/or CCA, the success rate is about 80-85 %. A SPC is often preferred over the CCA because it eliminates the need of additional incisions. Ultimately, it is the TDL that remains the most critical procedure in surgically managing a chylothorax. It is important to note that a TDL is approached via a left lateral thoracotomy in dogs and a right lateral thoracotomy in cats over the tenth intercostal space. This is because the canine thoracic duct is on the right side of the thorax until the 5-6 thoracic vertebrae where it then crosses to the left side, whereas the TD runs along the aorta and azygous on the left side of the thorax in cats. Intraoperative visualization may be facilitated by injecting methylene blue into the ileocecal or popliteal lymph nodes which will stain the thoracic duct a deep blue making identification easier. If using methylene blue, there is dose dependent Heinz body anemia that can occur if injected intravenously, thus caution should be taken when using this technique <sup>(1,5)</sup> A noninvasive alternative to injecting the lymph nodes to allow intraoperative visualization of the thoracic duct would be to give heavy cream 1-2 hours before induction so there will be lymph flow through the duct during the procedure <sup>(1)</sup>. In Punk'n's case, the heavy cream worked well for this purpose.



The most common complication of surgery is reoccurrence of the chylothorax or development of a serosanguinous effusion. Medical management with Rutin and a low fat diet is recommended post-operatively as well as routine rechecks every few weeks. Initially, Punk'n began Rutin therapy at 250 mg orally every 8 hours, and now receives 500 mg of Rutin once daily. She was transitioned to a low fat diet. She does not have any clinical signs or radiographic features of a chylothorax, and since her surgery has returned to normal activity. It is important to note that recurrent chylothorax has been reported up to 2 years post-operatively, therefore, it is critical to continue monitoring their progress until this point to declare complete resolution <sup>(5)</sup>.

### **Conclusion:**

In summary, when there is impedance of lymph outflow into the venous system, obstruction and/or rupture of the thoracic duct, or increased lymph flow from hepatic lymph formation, a chylothorax can occur. There are numerous etiologies of chylothorax reported in veterinary literature; however, an underlying cause is rarely identified. A chylothorax is definitively diagnosed with pleural fluid analysis in which the triglyceride concentration of the pleural fluid is greater than serum triglyceride concentration. Although some cases of chylothorax can be medically managed with a low fat diet, Rutin, and somatostatin, surgery is often the treatment of choice for idiopathic chylothorax. Thoracic duct ligation with a subtotal pericardiectomy and/or cisterna chyli ablation resulted in about an 80-85% success in resolution of chylothorax in the canine and feline patient; however, recurrence has been reported up to 2 years following surgery; thus, routine monitoring every 2-3 months is critical <sup>(1,3,5)</sup>.

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