Chylous Effusion in the Canine Patient

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Introduction

Chylous effusions are a relatively rare but debilitating disease in canines, which result largely from derangements of the lymphaticovenous system. Chylothorax is by far the most common presentation of chylous effusion in the dog, with the vast majority of cases being identified as idiopathic. Chylopericardium and chyloperitoneum are possible but less common presentations of chylous effusions. Unlike chyloperitoneum, chylothorax and chylopericardium are life-threatening conditions. Diagnosis of chylous effusion should be followed by a thorough diagnostic workup in order to rule out concurrent disease processes. Presentation, treatment, and prognosis vary greatly depending on the underlying etiology, chronicity of the effusion, location of the effusion, and metabolic status of the patient. In dogs, medical management of chylous effusion is rarely successful alone. Surgical intervention is indicated when there is a lack of response to medical management or when uncontrollable disease is present. A variety of different procedures can be performed; however, performing a combination of procedures yields the highest chance for resolution. Chronic chylous effusions can result in serious complications such as fibrosing pleuritis and/or pericarditis, metabolic derangements, and immune dysfunction and, therefore, should be addressed in a timely manner.

History and Presentation

Chylous effusions typically affect middle aged to older animals.[1] Breed predispositions have been found in Afghan Hounds and Shiba Inus.[1,3,26] However, no sex predilection exits. It has been hypothesized that there may be a genetic component to this disease process; however, this has yet to be proven.[4] The most common clinical signs associated with chylous effusion include: weight loss, anorexia, depression, and respiratory difficulty.[1,3] A cough is often noticed by owners, which could be present well before presentation. The cough is thought to be caused

by the effusion or by the underlying disease process itself (such as cardiac disease or thoracic neoplasia) leading to irritation of the pleural structures.[3] Other clinical signs can include abdominal enlargement (with chyloperitoneum) or exercise intolerance (with underlying cardiac disease or chylopericardium).

Upon initial physical exam, vitals may be within normal limits. Temperature is not typically elevated unless there is an underlying inflammatory cause.[3] Depending on the level of respiratory difficulty, an increased respiratory rate may be observed with or without the presence of dyspnea or shallow breathing. Heart sounds may be muffled ventrally during thoracic auscultation. Increased bronchovesicular sounds have been reported in 45% of dogs with chylothorax.[26] Other abnormalities that may be appreciated during thoracic auscultation include the presence of murmurs or arrhythmias.[3]

Pathophysiology

Chyle is composed of lymphatic fluid (predominantly consisting of lymphocytes) and chylomicrons (comprised of fat and protein).[6] Chyle is absorbed through the intestinal lacteals and travels to the cisterna chyli. The cisterna chyli is a dilated lymphatic sac located just medial to the hilus of the left kidney in most dogs.[25] From here, chyle is carried cranially where it empties into the thoracic duct.[22] The thoracic duct originates from the right dorsal border of the abdominal aorta and the ventral border of the azygous vein.[3,23] It continues cranially to about the level of the sixth thoracic vertebrae where it diverges to the left side of the mediastinum. From here it continues cranially to empty its contents into the venous system at the jugulocaval angle.[3,23]

Although chylous effusions are relatively rare in veterinary medicine, chylothorax is the most common presentation seen in dogs. Chylothorax can result from any process that either

increases lymphatic flow, decreases its drainage due to an obstruction or an increase in venous pressures, or any combination of these.[2,3,12] This includes: heart disease, congenital cardiac anomalies, pericardial effusion, heartworm disease, cranial mediastinal masses such as lymphoma or thymoma, fungal granulomas, lung lobe torsions, thrombosis of the cranial vena cava, and congenital abnormalities of the thoracic duct itself.[1,3,12] When no underlying disease processes has been found despite an extensive diagnostic work-up, as is most cases, a diagnosis of idiopathic chylothorax can be made.[1,2,3]

Although chylous effusions within the pericardium and peritoneal space are far less common in dogs, they also occur.[6] Chylopericardium, when found, is often in conjunction with chylothorax; however, the cause of this is largely unknown.[5] Chyloperitoneum, or chylous ascites, is thought to be a manifestation of numerous etiologies, many of which also cause disruption or impairment of the lymphaticovenous system.[19] However, unlike patients with chylothorax, dogs with chylous ascites have far less complications as chylous accumulation within the abdominal cavity is not life-threatening and appears to induce minimal inflammation. Furthermore, cases of spontaneous chylous effusion within both the pleural and peritioneal cavities have largely been associated with neoplastic disease processes. [25] Due to the composition of chyle, chronic loss into third spaces such as the pleura, pericardium, and peritoneum can lead to immunosuppression, fat depletion, hyponatremia, hyperkalemia, hypoproteinemia, and vitamin K deficiency.[24]

Diagnostic Approach and Considerations

In patients with pleural or pericardial chylous effusion, thoracocentesis and pericardiocentesis respectively are performed for diagnostic purposes as well as stabilizing the patient. Cytologic and biochemical evaluation of the effusion is arguably the most important test

in diagnosing chylous effusions.[7] Chylous effusions classically have a milky appearance; however, this can vary depending on multiple factors such as concurrent hemorrhage, chronicity, and the patient's diet and level of anorexia.[3] Chylous effusions are classified as exudates. The protein content is typically greater than 2.5 g/dL.[1] The total number of nucleated cells are between 400-10,000 /ul and consist predominantly of small lymphocytes and/or neutrophils. There may be a lesser number of macrophages present containing phagocytized lipid molecules. Degenerative neutrophils and sepsis are rare, as fatty acids are bacteriostatic in nature.[2] This typically only occurs when bacteria has been iatrogenically introduced as a result of multiple thoracocenteses.[1,3,7] As the effusion becomes more chronic, it is typical to see lower numbers of small lymphocytes due to the body's inability to compensate for continued losses. Nondegenerative neutrophils will begin to predominate as lymphocytes are lost and inflammation is incited by multiple attempts for fluid removal. Macrophages may also increase in number over time in an effort to remove the lipid rich effusion.[2] Comparison of the fluid and serum triglyceride levels in simultaneously collected samples has proven to be the gold standard for differentiating chylous effusions from non-chylous effusions. An effusion is considered chylous if the triglyceride levels are higher in the effusion than in the serum. [1,2,3]

Ultrasound is very helpful in the initial diagnosis of effusion. Echocardiography, in particular, is helpful in critically evaluating the heart and ruling out cardiogenic causes.[7] Thoracic and abdominal radiographs are recommended for diagnosing effusion and ruling out concurrent disease processes.[7] Following removal of fluid from the chest cavity, iatrogenic pneumothorax may be observed due to thoracocentesis. Depending on the chronicity of the pleural effusion, fibrosing pleuritis may also be appreciated.[3] Complete blood count, chemistry panel, and urinalysis are helpful in evaluating the overall health status of the patient.

Abnormalities such as lymphopenia and panhypoproteinemia may be noted due to ongoing losses of lymphocytes and protein.[1] Electrolyte abnormalities such as hyponatremia and hyperkalemia may also be appreciated.[3]

Lymphangiography may be used for diagnosis, pre-surgical planning, and/or post-operatively. With traditional lymphangiography, a mesenteric lymphatic vessel is canulated using a catheter and contrast material is injected. Images via fluoroscopy, radiography, or computed tomography (CT) are subsequently taken.[6,8] Placing the catheter is relatively easy and straightforward; however, maintaining its patency and appropriate positioning throughout the movement of imaging can be challenging.[8] The use of this imaging modality remains largely clinician preference, as there is no literature to date proving its effect on surgical or patient outcome. As a less invasive approach, percutaneous injection into a mesenteric or popliteal lymph node via ultrasound guidance has proven a successful alternative.[10,29,30] CT is considered a superior imaging modality over radiography, as it is more successful in identifying small thoracic duct branches.[28] CT is also useful for further investigating and ruling out concurrent disease processes as well as visualization of lymphatic structures.[8]

Treatment and Management Options

Unfortunately, a single routine and successful treatment for idiopathic chylous effusion has not been established. As first line therapy, conservative medical management is typically pursued; however, its success is unclear. Traumatic and iatrogenic causes of chylothorax have been proven to heal on their own in a matter of days to weeks with or without intervention.[9,17,43] However, for cases of chylous effusion caused by other etiologies, a combination of periodic removal of fluid, dietary modification, and a variety of pharmaceutical and nutraceutical therapies can be implemented with varying degrees of success.[1,6]

Therapeutic thoracocentesis and/or pericardiocentesis should be performed as needed to relieve respiratory and cardiac distress respectively.[6] Patients undergoing repeated removal are at risk for developing fat soluble deficiencies, vitamin K in particular, as well as electrolyte abnormalities such as hyponatremia and hyperkalemia.[3,6] Immune dysfunction is also common as the removal of lymphocyte rich chyle depletes the body.[6] Patients with chylous ascites are at less of a risk for these complications, as fluid buildup in the abdomen is not life-threatening and typically does not require removal.[19]

Historically, low-fat diets and supplementation of medium chained fatty acids were part of the mainstay for medical management of chylous effusions in small animal patients.[1,6] In humans, medium chained fatty acids bypass the lymphatic system and are absorbed directly into the bloodstream.[1,23] However, they have been found to enter the thoracic duct in dogs and, consequently, are no longer recommended.[3,6,45] Rutin, a benzopyrone drug, has proven successful in improving and resolving human cases of lymphedema.[1,3,6] It is thought to increase macrophage activity and number, therefore increasing phagocytosis of protein within the effusion.[23,28] There have been limited reports of success in cats; however, its effectiveness in dogs has not been proven. [1,23,38] Although the benefits are likely minimal, there are no known side effects of Rutin, and it is relatively cheap. [1,3,6]

Octreotide, a somatostatin analog, is another drug commonly used in human medicine to treat chylous effusion. It is a naturally occurring substance that inhibits gastric, pancreatic, and biliary secretions.[3] By decreasing gastrointestinal secretions, the amount of lymphatic flow to the thoracic duct is also decreased allowing it time to heal.[2,3] Although experimental results showed promise, it had variable success when used in dogs with naturally occurring idiopathic chylothorax.[3,23] It is relatively expensive and prolonged treatment is discouraged, as this has

been correlated with an increased risk of gallstone formation in humans.[3] Anti-inflammatories have also been used, but they are more commonly reserved for dogs that produce non-chylous effusions after surgical intervention.[20] Cytologic analysis of these non-chylous effusions supports that an inflammatory process is involved. Resolution was found in 60% of cases treated with corticosteroids.[20]

Surgical treatment options should be considered if the patient does not respond to medical management or if clinical signs are progressing uncontrollably.[1,3] There are many different surgical procedures proposed to treat chylous effusions which further suggests that no one procedure is definitively curative.[25] Thoracic duct ligation, cisterna chyli ablation, and subtotal pericardiectomy are the most common and successful procedures performed. Currently, it is common practice to inject methylene blue dye into an abdominal lymphatic to highlight the lymphatics during these procedures.[3,20]

Ligation of the thoracic duct is the most widely accepted and commonly performed procedure for treatment of idiopathic chylothorax in veterinary medicine.[23] The thoracic duct and its subsequent branches can either be ligated individually or by using en bloc ligation. When using this method, visualization of each branch is not attempted, but rather, all tissues dorsal to the aorta and ventral to the sympathetic chain are ligated.[23] Studies that have compared these two methods have not found a statistical difference between the two.[25] This procedure alone has a 50-60% success rate for resolution.[23] By ligating the thoracic duct, new lymphaticovenous connections are stimulated to form in the abdomen allowing chyle to bypass the thorax.[3] The presence of chylous effusion after thoracic duct ligation has been proven to be the result of developing collateral lymphatic branches around the ductal ligation site, rather than

failure to ligate all branches.[42] This finding further supports the importance of using adjunctive procedures in order to decrease pressures on the thoracic duct and improve rates for resolution.

Ablation, or roughing, of the cisterna chyli elicits deterioration which, similarly, stimulates the formation of new lymphaticovenous connections within the abdomen decreasing pressure on the thoracic duct.[15,21,31] Formation of these new connections takes time, and subsequently, chylous ascites is a common complication. However, the abdomen is exponentially more tolerable of chylous accumulations.[21] When performing cisterna chyli ablation in conjunction with thoracic duct ligation, success rates improve to 83-87% in dogs.[20,23]

Due to chronic exposure and irritation from chylous effusions, fibrous material forms on its outermost layers of the pericardium.[14,20,44] This thickening is thought to cause an increase in right-sided venous pressures, thus impeding the flow of chyle into the cranial vena cava and further increasing flow through the thoracic duct.[3,14,40] In performing a subtotal pericardiectomy, a portion of the pericardium is removed which is thought to decrease venous pressures, thus allowing the effective re-routing of lymphatic fluid.[3,25] Success rates improve to 60-100% when this procedure is performed in combination with thoracic duct ligation.[25] Subtotal pericardiectomy has also shown potential for use in refractory cases where effusion continues despite medical and surgical intervention.[14,20]

Other procedures

Several other procedures have been attempted exclusively and in conjunction with the methods mentioned above. Omentalization was proposed as a mechanism to absorb chyle and act as a seal over the thoracic duct and/or cisterna chyli.[23,25] However, its use was controversial as omentum contains lymphatics, which in turn empty into the thoracic duct system.[11] Embolization techniques using cyanoacrylate glue have been attempted to prevent forward flow of chyle to the

thoracic duct but were largely unsuccessful.[16,23,27] Pleurodesis, or the creation of adhesions between the visceral and parietal pleural layers, was also attempted.[23] However, complication rates were high and complete abolishment of the pleural space was not achieved.[25,35,36] Pleuroperitoneal and pleurovenous shunts have been implemented with some short-term success; however, obstruction of the tubing is common.[3,23,39] Additionally, the PleuralPort has been used as a cost effective and minimally invasive palliative treatment for recurrent cases as it allows the owner to manage the discomfort and respiratory compromise associated with chylothorax at home.[13,23]

Expected Outcome and Prognosis

The outcome and prognosis of canine idiopathic chylothorax is highly variable but is often deemed guarded.[1,32] There are too few cases of idiopathic chyloperitoneum in veterinary literature to provide an accurate prognosis.[19] However, cases of spontaneous chylothorax with concurrent chylous ascites are often associated with neoplastic processes and, therefore, hold a grave prognosis.[25]

By far, the most common complication following surgical intervention is persistence of effusion and is reported in up to 40% of cases.[1,3,6,23] The post-operative time required for the resolution of chylous effusion is unknown but has been reported to occur anywhere from one day up to five months.[23] Recurrence of chylous effusion is also common and has been reported to occur up to five years post-surgical intervention.[23] The presence of non-chylous or serosanguinous effusion following surgical intervention has been reported in up to one-third of veterinary patients.[23] Although very rare, another complication that may be observed following thoracic duct ligation is accumulation of chyle within the subcutaneous tissues.[41] This would occur if the dog was unable to develop new lymphaticovenous connections.[41]

Conclusion

The pathogenesis of chylous effusion remains poorly understood in veterinary medicine. Despite the relative ease of diagnosing chylous effusion, a thorough workup is warranted to successfully rule out concurrent disease processes. Medical management is often unrewarding, and surgical intervention is indicated in most cases. Although surgery has the potential to be curative, management of chylous effusions is often time-consuming, expensive, and difficult, as there are still a lot of unknowns about this disease process, effective treatment options, and long-term outcomes. Dishearteningly enough, a large number of patients are euthanized due to a lack of response to medical or surgical intervention further complicating the investigation of this disease.[3]

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