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CHYLOTHORAX AND IMMUNE MEDIATED PLEURAL EFFUSION – PART I AND II

CHYLOTHORAX

In most animals, abnormal flow or pressures in the thoracic duct (TD) are thought to lead to exudation of chyle from intact but dilated thoracic lymphatic vessels (a condition known as thoracic lymphangiectasia). These dilated lymphatic vessels may form in response to increased lymphatic flow (caused by increased hepatic lymph formation), decreased lymphatic drainage into the venous system as a result of high venous pressures, or both factors acting simultaneously to increase lymph flow and reduce drainage. Any disease or process that increases systemic venous pressures (i.e., right heart failure, mediastinal neoplasia, cranial vena cava thrombi, or granulomas) may cause chylothorax. Trauma is an uncommonly recognized cause of chylothorax in dogs and cats because the thoracic duct heals rapidly after injury, and the effusion resolves within 1 to 2 weeks without treatment.

Possible causes of chylothorax include anterior mediastinal masses (mediastinal lymphoma, thymoma), heart disease (cardiomyopathy, pericardial effusion, heartworm infection, foreign objects, tetralogy of Fallot, tricuspid dysplasia, or cor triatriatum dexter), fungal granulomas, venous thrombi, and congenital abnormalities of the thoracic duct. It may occur in association with diffuse lymphatic abnormalities, including intestinal lymphangiectasia and generalized lymphangiectasia with subcutaneous chyle leakage. The underlying etiology is undetermined in most animals (idiopathic chylothorax) despite extensive diagnostic workups. Because the treatment of this disease varies considerably depending on the underlying etiology, it is imperative that clinicians identify concurrent disease processes before instituting definitive therapy.

Diagnosis

Signalment. Any breed of dog or cat may be affected; however, a breed predisposition has been suspected in the Afghan hound for a number of years. Recently, it has been suggested that the Shiba Inu breed may also be predisposed to this disease. Among cats, Oriental breeds (i.e., Siamese and Himalayan) appear to have an increased prevalence. Chylothorax may affect animals of any age; however older cats may be more likely than young cats to develop it. This finding was believed to indicate an association between chylothorax and neoplasia. Afghan hounds appear to develop this disease in middle age, but affected Shiba Inus have been less than 1 year old. A gender predisposition has not been identified.

History. Coughing often is the first (and occasionally the only) abnormality until the animal becomes dyspneic. Many owners report that coughing began months before presenting the animal for care; therefore, animals that cough and do not respond to standard treatment of nonspecific respiratory problems should be evaluated for chylothorax. Coughing may be due to irritation caused by the effusion or may be related to the underlying disease process (i.e., cardiomyopathy, thoracic neoplasia).

Diagnostic Imaging

CT lymphangiography may be able to quantify branches of the thoracic duct more accurately than standard radiographic lymphangiography; however, I have not found this technique to be clinically useful.

Laboratory Findings

Fluid recovered by thoracentesis should be placed in an EDTA tube for cytologic examination. Placing the fluid in an EDTA tube rather than a clot tube allows cell counts to be performed. Although chylous effusions routinely are classified as exudates, the physical characteristics of the fluid may be consistent with a modified transudate. The color varies depending on the dietary fat content and the presence of concurrent hemorrhage. The protein content is variable and often inaccurate because of interference with the refractive index by the high lipid content of the fluid. The total nucleated cell count usually is below 10,000/ul and consists primarily of small lymphocytes or neutrophils with lesser numbers of lipid-laden macrophages.

Chronic chylous effusions may contain low numbers of small lymphocytes due to the body's inability to compensate for continued lymphocyte loss. Nondegenerative neutrophils may predominate with prolonged loss of lymphocytes or if multiple therapeutic thoracenteses have induced inflammation. Degenerative neutrophils and sepsis are uncommon findings because of the bacteriostatic effect of fatty acids

but can occur iatrogenically as a result of repeated aspiration. To help determine if a pleural effusion is truly chylous, several tests can be performed, including comparison of fluid and serum triglyceride levels; Sudan III staining for lipid droplets; and the ether clearance test. The most diagnostic test is comparison of serum and fluid triglyceride levels. Chylous effusions have a higher triglyceride concentration than simultaneously collected serum.

Medical management

If an underlying disease is diagnosed, it should be treated and the chylous effusion managed by intermittent thoracentesis. If the underlying disease is effectively treated, the effusion often resolves; however, complete resolution may take several months. Surgical intervention should be considered only in animals with idiopathic chylothorax or those that do not respond to medical management. Chest tubes should be placed only in animals suspected of having traumatic chylothorax (very rare) with rapid fluid accumulation, or occasionally after surgery. Electrolytes should be monitored; hyponatremia and hyperkalemia can occur in dogs with chylothorax undergoing multiple thoracentesis. A low-fat diet may reduce the amount of fat in the effusion, which may improve the animal's ability to resorb fluid from the thoracic cavity.

Commercial low-fat diets are preferable to homemade diets; however, if commercial diets are refused, homemade diets are a reasonable alternative; the fat content of these diets is about 6% on a dry basis). Medium-chain triglycerides (once thought to be absorbed directly into the portal system, bypassing the thoracic duct) are transported via the thoracic duct in dogs; therefore, they may be less useful than previously believed. It is unlikely that dietary therapy will cure this disease, but it may help in the management of animals with chronic chylothorax. Clients should be informed that with the idiopathic form of this disease, the only surgical treatment that is likely to stop the effusion is TD ligation. However, the condition may resolve spontaneously in some animals after several weeks or months of medical management.

Benzopyrone drugs have been used for the treatment of lymphedema in human beings for years. Whether these drugs might be effective in reducing pleural effusion in animals with chylothorax is unknown; however, preliminary findings suggest that some animals treated with rutin have complete resolution of effusion 2 months after initiation of therapy. Whether the effusion resolves spontaneously in these animals or is associated with the drug therapy is unknown.

Somatostatin is a naturally occurring substance that has an extremely short half-live. It inhibits gastric, pancreatic, and biliary secretions (i.e., glucagon, insulin, gastric acid, amylase, lipase, and trypsin) and prolongs gastrointestinal transit time, decreases jejunal secretion, and stimulates gastrointestinal water absorption. In recent years analogues of somatostatin have been used to successfully treat chylothorax in humans with traumatic or postoperative chylothorax. In these patients, reduced gastrointestinal secretions may aid healing of the TD by decreasing TD lymphatic flows. It has also been reported to result in early decreased drainage and early fistula closure in dogs with experimental transection of the TD. The mechanism by which non-traumatic chylothorax may benefit from this treatment is unclear; however, resolution of pleural fluid (chyle and postoperative serosanguineous effusion) in both dogs and cats has occurred after administration of octreotide. Octreotide (sandostatin; 10 mcg/kg subcutaneously three times a day for 2 to 3 weeks) is a synthetic analogue of somatostatin that has a prolonged half-life and minimal side effects. Soft stools that resolve after withdrawal of the drug may occur. Prolonged treatment should be discouraged because people treated for longer than 4 weeks are at risk for gallstones.

Surgical treatment

Surgical intervention is warranted in animals that do not have underlying disease and in which medical management has become impractical or is ineffective. Surgical options include thoracic duct ligation plus pericardectomy (with or without mesenteric lymphangiography), passive pleuroperitoneal shunting, active pleuroperitoneal or pleurovenous shunting, pericardiectomy, omental drainage, and pleurodesis. Only thoracic duct ligation, pericardiectomy, mesenteric lymphangiography, and active pleuroperitoneal shunting are recommended by the author and are described here. The mechanism by which thoracic duct ligation is purported to work is that after TD ligation abdominal lymphaticovenous anastomoses form for transport of chyle to the venous system. Chyle bypasses the thoracic duct, and the effusion resolves. Properly performed, TD ligation results in over 80% of dogs and cats resolving their effusion. Formation of a nonchylous effusion (from pulmonary lymphatics) may occur in some animals after surgery.

IMMUNE-MEDIATED PLEURAL EFUSSION and FIBROSIS

Immune-mediated pleural effusion has rarely been reported in dogs; however, in humans systemic autoimmune diseases such as SLE and rheumatoid are frequently associated with pleural effusion. One dog has been reported that had sterile nodular panniculitis, small pulmonary nodules and a resulting sterile pleural effusion that has all resolved with immunosuppressive therapy. Pulmonary biopsies and tests such as ANA and rheumatoid factor titers would be necessary to definitely diagnose the disease; however, improvement with immunosuppressive therapy may lead to a presumptive diagnosis.

Pleuritis is technically an inflammation of the linings around the lungs (the pleura). In humans, it is often used synonymously with the term "pleurisy" which denotes a sharp chest cavity pain that worsens with breathing. The differential list in humans with pleuritis is long and includes aortic dissections, autoimmune disorders such as systemic lupus erythematosus (or drug-induced lupus erythematosus), autoimmune hepatitis, rheumatoid arthritis, bacterial infections associated with pneumonia and TB, chest injuries, familial Mediterranean fever, fungal or parasitic infections, pericarditis, lung cancer, cystic fibrosis, pneumothorax, and pulmonary embolisms, to name a few. While many of these may also be rule-outs for dogs and cats with pleuritis, this discussion will focus on restrictive or fibrosing pleuritis and immune-mediated pleuritis.

Restrictive or fibrosing pleuritis

Fibrosing pleuritis is a life-threatening complication of chronic chylothorax in cats and dogs. In addition to chylothorax, pyothorax, feline infectious peritonitis, hemotho¬rax, and tubercu¬losis have been associated with the develop¬ment of fibrosing pleuritis. Although the cause of the fibrosis is unknown, it appar¬ently can develop subsequent to any prolonged exuda¬tive or blood-stained effusion. Exu¬dates are characterized by a high rate of fibrin formation and degrada¬tion. Fibrin formation probably increases because chronic inflammatory exudates, such as chylothorax and pyothorax, induce changes in mesothelial cell morphologic features, resulting in in¬creased permeabili¬ty, mesothe¬lial cell desquama¬tion, and triggering of both pathways of the coagula¬tion cas¬cade. These desquamated mesothelial cells have also been shown to produce type III collagen in cell culture, promot¬ing fibrosis. In animals with fibrosis, the pleura is thickened by diffuse fibrous tissue that re¬stricts normal pulmonary expansion. Pulmonary function testing in human patients with fibrosing pleuritis have shown a decrease in vital capacity and static compliance, necessitating greater negative intra¬pleu¬ral pressures for any given change in lung volume when compa¬red with healthy patients. Importantly, the degree of fibrosing pleuritis does not appear to warrant a poor prognosis in cats or dogs. The author has operated cats with severe fibrosing pleuritis that appear clinically normal once the effusion stops.

There are two major causes of RPE. One cause is the abnormality of the pulmonary microvessels caused by the chronic collapse. The microvasculature becomes thickened, less flexible, and more susceptible to injury. The second is mechanical stress caused by the abrupt re-expansion. For years, barotrauma had been discussed as the primary cause of this mechanical stress. However, more recent research into ventilation induced lung injury (VILI) and acute respiratory distress syndrome (ARDS) has revealed that there are multiple aspects to lung injury with barotrauma playing less of a role than initially believed.

To avoid RPE, there are two general concepts to consider. The first is slow recruitment of collapsed lung by using positive end expiratory pressure (PEEP). A PEEP of 5 to 10 helps to prevent re-collapsing of alveoli and the associated atelectrauma. The second strategy is to be very careful not to over distend healthy lungs. Glucocorticoids are of little value in treating RPE once it has occurred. A number of pharmaceutical agents are currently being investigated for the treatment of RPE, but conclusive evidence of their beneficial effects is not yet available.