CANINE ACUTE PANCREATITIS: IT DOES WHATEVER IT WANTS TO DO

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Diagnosis

History and physical examination are, as always, critically important; but, they are not that helpful for diagnosing pancreatitis. Rather, they are more useful for finding other problems that may be mimicking pancreatitis. Regarding signalment, Schnauzers and Yorkies are famous for acute pancreatitis, but these breeds get a lot of other diseases that cause vomiting. Furthermore, acute pancreatitis can be found in any breed of dog. Canine pancreatitis is classically considered to present with acute vomiting and anorexia. Abdominal pain is frequently present, but it is easy to miss during physical examination, and fever is occasionally seen. However, we are recognizing more and more and more cases in which a) vomiting is not as severe as we have come to expect, and b) in which we are initially strongly drawn to other diagnoses. To some extent, many of us are no longer sure what a "typical" case of canine pancreatitis is. Some dogs (especially those with pancreatic abscesses) may have relatively mild, intermittent, unimpressive vomiting and continue to eat a reasonable amount of food. Many of the severely ill patients may present in classic systemic inflammatory response syndrome (SIRS) which is what used to be called septic shock (until we found out that you can have the same thing occur with any cause of massive inflammation). Many dogs with very severe acute pancreatitis present as though they had an acute, septic abdomen. Some have substantial amounts of abdominal fluid. If acute pancreatitis is associated with or due to pancreatic carcinoma (rare), you may rarely see a dog that has widespread subcutaneous fat necrosis causing sterile abscesses that are typically painful and cause cutaneous discoloration. Most cases of canine pancreatitis seem to be temporally related to either ingestion of fat or lipemia associated with diabetic ketoacidosis. Trauma and drugs can also cause canine pancreatitis. Drugs that are suspected of causing pancreatitis in people and animals include azathioprine, sulfonamides, tetracycline, and potassium bromide.

CBC's often show an inflammatory leukogram, but 1) this is a very nonspecific finding and may be due to any number of problems and 2) not all animals with acute pancreatitis have a notable leukocytosis. Degenerative left shifts and substantial toxicity of circulating WBCs can be seen if the patient is in SIRS. Likewise, thrombocytopenia due to DIC is often found in severely affected patients. However, some animals with clinically severe pancreatitis have absolutely normal leukograms. There are no findings on CBC that definitively diagnose or definitively eliminate pancreatitis

Serum biochemical panels are not as helpful as we would like. Serum lipase and amylase activities are insensitive (each is about 50%) and nonspecific (again, about 50%) for pancreatitis. We no longer request them in dogs or cats. Dogs with acute pancreatitis and even pancreatic abscesses have had normal serum lipase activities. We have also identified dogs with drastically increased serum lipase activities that have intestinal foreign objects or gastritis, but no gross evidence of acute pancreatitis. Lipase is produced by the canine gastric mucosa which explains why inflammation or damage to the stomach can result in excessive serum lipase activity. Canine TLI is slightly more specific than amylase and lipase, but it is still not a sensitive test (approximately 35%). Therefore, it too has very poor negative predictive value. We have seen plenty of dogs with pancreatitis that had normal serum TLI's.

The immunoreactive canine pancreatic lipase assay (i.e., cPLI or Spec cPL) appears to be the most sensitive (approximately 80-85%) test for pancreatitis available. There are a few false negative results with this test, but it is clearly much more sensitive than any other blood test available. The real question is how specific it is for clinically important disease (i.e., lesions of the pancreas that are causing clinical disease as opposed to microscopic lesions that are clinically silent). To some extent, you can best think about cPLI like "ALT for the pancreas". The biggest advantage is that if the cPLI test is negative, it is much less likely that pancreatitis is the real problem and you need to look very hard for extra-pancreatic disease in the dog.

Blockage of the main pancreatic duct due to swelling due to generalized pancreatitis, an intrapancreatic granuloma, or an abscess that subsequently blocks the pancreatic duct may cause extrahepatic biliary tract obstruction (EHBO) with a notable increase in serum alkaline phosphatase and serum bilirubin. Pancreatitis is probably the most common cause of EHBO in the dog. Thus, while EHBO is very suggestive of acute pancreatitis (assuming that the patient does not have a mucocoele, which is usually easy to detect with ultrasound), relatively few dogs with acute pancreatitis develop EHBO. Furthermore, there are reasons for this triad of signs besides acute pancreatitis and extrahepatic biliary tract obstruction (e.g., cholangitis-cholangiohepatitis). Ultrasonographic evaluation of the abdomen (discussed below) is particularly helpful in these patients.

Plain abdominal radiographs help eliminate other diseases which may mimic acute pancreatitis. Not finding evidence of other abdominal disease (e.g., foreign object) is helpful in eliminating obstruction and narrowing the list of differential diagnoses. Occasionally, one finds radiographic signs which specifically suggest acute pancreatitis. A sentinel loop (i.e., a dilated, air-filled segment) in the descending duodenum, and/or lack of serosal detail in the upper right abdominal quadrant, and/or lateral displacement of the descending duodenum on the ventro-dorsal projection, and/or a mass medial to the descending duodenum (on the ventro-dorsal projection) and/or a mass just behind the liver and just below the pylorus (on the lateral projection) are somewhat suggestive of acute pancreatitis. These findings are only meaningful if present; many (probably most) dogs and cats with acute pancreatitis do not have any of these radiographic findings. Probably the most greatest value of abdominal radiographs is that they help eliminate other diseases that could be causing signs similar to those caused by pancreatitis.

Abdominal ultrasonography often finds abnormalities that suggest or are consistent with pancreatitis as well as eliminate other potential causes of vomiting and abdominal pain. Ultrasonography has been suggested to be about 40-70% sensitive in finding canine pancreatitis. One may sometimes detect hypoechogenicity surrounded by hyperechoic fat in the region of the pancreas that is due to pancreatitis. At other times, a markedly thickened pancreas may be found. Both findings are very specific evidence of pancreatitis. Evidence of EHBO (i.e., dilated bile ducts, not just a big gall bladder) is very suggestive of pancreatitis. Rarely, you will find dilated bile ducts due to inflammatory biliary tract disease, but this is not nearly as common a cause as is biliary tract obstruction. Any dog with extra-hepatic biliary tract obstruction (that does not have a mucocoele) and that is vomiting/anorexic should be assumed to have pancreatitis until proven otherwise. It is very important to note that the ultrasonographic appearance of the pancreas can change dramatically within a few hours, so repeating abdominal ultrasound later on the same day or early the next day can sometimes be most revealing.

Diagnosing pancreatitis during laparotomy is the least desirable method of diagnosis. Some patients present exactly like acute septic peritonitis but are ultimately diagnosed as having non-septic pancreatitis. There is nothing wrong with doing an exploratory laparotomy in a patient in which septic abdomen is a major consideration, only to find out that the patient has non-septic pancreatitis. We very rarely have reason to biopsy a normal appearing canine pancreas, and what grossly appears to obviously be pancreatitis in the dog seldom requires a biopsy unless carcinoma is a concern. However, you should never simply look at what appears to be an obviously neoplastic mass in the pancreas and make a diagnosis of carcinoma without biopsying it, no matter how extremely terrible it appears. Pancreatitis is much more common in dogs than pancreatic carcinoma, no matter how bad the pancreas looks or how many adhesions are present. If you biopsy the pancreas, it is important to obtain a biopsy that goes deeper than the superficial necrotic surface or adhesions. Cytology can be useful for making a presumptive diagnosis; however, I have seen at least one case in which cytology of a pancreatic mass was read out as carcinoma by two accomplished cytologists and yet multiple biopsies all came back as necrotic pancreatitis. Anecdotally, there appears to be more risk of causing iatrogenic pancreatitis with surgery in the dog than in the cat. Maintaining excellent mesenteric perfusion during anesthesia and performing the surgical biopsy with reasonable care and good technique minimizes the risks. Laparoscopic biopsy of the pancreas might be safer than surgical biopsy, but that is just anecdotal at this time.

Chronic pancreatitis (i.e., chronic pancreatitis with intermittent, relatively mild recurrences) can be challenging to diagnose. Dogs with episodic vomiting due to recurrent bouts of pancreatitis may not have any other signs of disease, and they invariably are admitted to your clinic for a work up after the last bout has run its course or is on the mend. Episodes of vomiting and anorexia due to recurrent pancreatitis can be random and unpredictable. In such patients, the previously mentioned diagnostics may be attempted, especially when acute exacerbations occur. Very rarely, upper gastrointestinal barium contrast radiographs may rarely reveal duodenal abnormalities (e.g., dilatation, stricture) which suggest that recurrent bouts of acute pancreatitis have caused scarring of the pancreas which in turn have compromised the maximum size of the duodenal lumen. Ultrasonographic changes are nice if they are present, but they can be minor making it difficult to accurately interpret them. Feeding an ultra-low fat diet for 3-4 times longer than what was previously the longest interval between episodes may sometimes be helpful in making a presumptive diagnosis. If episodic vomiting/anorexia does not recur while feeding such an ultra-low fat diet for an interval so long that you would have been sure to experience another episode, then we can often assume (rightly or wrongly) that the signs were due to pancreatitis (or perhaps some other dietary-responsive disease). Anytime you find exocrine pancreatic insufficiency (diagnosed with TLI) in a breed that is not commonly affected with pancreatic acinar atrophy (e.g., German shepherd, rough-coated Collie), then chronic pancreatitis becomes a major concern.

Pancreatic abscesses in dogs (as opposed to cats) are almost invariably sterile. Affected dogs typically can have a much more chronic, smoldering course (e.g., vomiting for a month or more, mild loss of appetite) than most dogs with more typical acute pancreatitis. We have even found a few dogs which had pancreatic abscesses that were completely asymptomatic. Abdominal pain may be present or absent. CBC and serum biochemistry findings are unpredictable. Diagnosis

requires ultrasound. Treatment may be surgical marsupialization, percutaneous ultrasonographic drainage or just observation.

Therapy

As of this writing, there is not a single, well-designed, robust, prospective, stratified study on the treatment of canine acute pancreatitis. Therefore, all any of us has is opinions, period. Nothing per os (NPO) has been the classic therapy for pancreatitis for many years. While it is true that they feed people with pancreatitis earlier than we feed dogs, you must remember that human pancreatitis is unassociated with dietary fat. People get pancreatitis from alcohol, trauma, gall stones and MOF (multiple organ failure). Canine pancreatitis is associated with dietary fat (as well as surgical trauma when poor technique is used around the pancreas). An initial study in Australia suggests that it is safe and perhaps beneficial to feed dogs with acute pancreatitis per os or with an esophagoscopy tube as soon as they can tolerate it (i.e., they do not get worse, even if they are still vomiting). I recommend that a) you feed a diet with as low a fat content as possible, and b) if the feeding is associated with worsening of the vomiting, that you stop it and either try again in a day or two, or go to jejunostomy feeding. Do not try to get full caloric intake into the patient; rather, start with small amounts to see if the patient will hold down the food. Obviously, if feeding is associated with worsening of the vomiting or general condition, stop the feeding. I generally start feeding potato or rice (i.e., no fat) and gradually work my way up to commercial diets with low fat content. Try hard to avoid parenteral nutrition.

Fluid therapy is critical, and subcutaneous administration of fluids is clearly inferior to IV fluids for all but mildly affected animals. IV fluid administration is often sufficient, even in dogs in which a pancreatic granuloma has temporarily blocked the main bile duct. Adequate pancreatic circulation is probably crucial for healing damaged pancreatic tissue; therefore, it is probably better to provide a little too much fluid rather than a little too little fluid unless the patient has congestive heart failure or oliguric renal failure. The abdominal viscera is not "first in line" to receive circulation when the patient is dehydrated (which most dogs with pancreatitis are when they come to your office). Obese and fat dogs (which describes a lot of dogs with pancreatitis) do not necessarily have skin tenting when they are dehydrated. Likewise, although you might expect dry, tacky oral mucus membranes, a nauseated animal may be salivating enough to make the mucus membranes moist even though it is dehydrated. If a vomiting dog is not eating or drinking, then it is dehydrated regardless of how well hydrated it appears on physical examination. However, if you give substantially too much crystalloid and dilute the serum protein concentrations, this could be detrimental.

One should monitor the serum albumin concentration during fluid therapy in these patients. If the serum albumin concentration decreases significantly (i.e., to < 2.0 gm/dl), then the plasma oncotic pressure likewise decreases which diminishes the effective perfusion at the capillary level. Since perfusion is so critical to treating dogs with pancreatitis, one should probably become concerned whenever the serum albumin concentration falls below 2.0 gm/dl. It is very hard to administer enough plasma to significantly raise the plasma albumin concentration. Half of the albumin in the plasma that you administer will end up in the extravascular compartment instead of the intravascular compartment. Hetastarch is a better choice because it will stay in the circulation and raise the plasma oncotic pressure for much longer than plasma. Be careful with hetastarch; it occasionally is associated with worsening of clinical signs. It is best to give small

amounts repeatedly than just give a large amount. Human albumin can be used effectively, but it occasionally causes anaphylactoid reactions that can kill the patient; therefore, it is not recommended. Canine albumin is safer, but it does not last as long as hetastarch. Plasma might be more effective than hetastarch because plasma might also restore circulating protease inhibitors and replenish AT III (which is a treatment for DIC). This is a very contentious point. One retrospective study has shown that plasma did not help treat dogs with pancreatitis; however, this study suffers from the problems inherent in all retrospective studies.

If the patient cannot tolerate early refeeding (i.e., the vomiting becomes worse), then jejunostomy feeding is another option. It is safer, less expensive, and less dangerous than parenteral nutrition, and has been associated with a better prognosis. In particular, it should be considered if an exploratory laparotomy was performed when the pancreatitis was diagnosed because a J-tube can be placed at that time. Alternatively, one can place a jejunostomy tube via laparoscopy, through a G-tube, and via the nose (naso-jejunostomy).

Antiemetics are useful in patients that are vomiting repeatedly or that feel so nauseated that they feel terrible. I prefer to only use antiemetics for short periods of time because I want to see if the patient is improving enough so that it no longer needs the antiemetic to stop vomiting. However, if the patient is vomiting multiple times per day or obvious feels terrible due to the nausea, then maropitant (1 mg/kg SQ) appears to be very useful. Maropitant might also have the advantage of providing some analgesia because it blocks Substance P binding. Dolasetron (0.3-1.0 mg/kg qd) and ondansetron (0.25 mg/kg qd) can also be effective.

H-2 receptor antagonists have been used to “prevent gastric ulceration and erosion”. It is doubtful that ulceration/erosion is a common problem in all but the sickest patients. Furthermore, if one desires to protect the gastric mucosa, the proton pump inhibitors are far superior to the H-2 receptor antagonists. Pantoprazole (1 mg/kg IV qd) or omeprazole (1-2 mg/kg PO bid) are the most commonly used drugs. I suspect that they provide more benefit by being antidyspepsic in nature (thereby making the patient feel better) than they do by preventing ulcers. Currently, there is no clear evidence that they are indicated in dogs with acute pancreatitis.

Antibiotics have been used to “prevent” secondary bacterial infection of the inflamed pancreas, which is supposed to be "fertile ground" for infection. However, there is minimal evidence that bacterial infection is of any significance in routine canine pancreatitis. Antibiotics do not hurt these patients, but it is very questionable how helpful they are. However, dogs in SIRS due to pancreatitis may be a different story. Any dog in SIRS from any reason is potentially at increased risk of infection due to severely compromised mesenteric circulation.

Currently, glucocorticoids are very controversial in the treatment of pancreatitis. While they increase serum amylase and lipase activities, they do not cause pancreatitis. It is possible (this is controversial) that they may be useful in treating patients that are in Systemic Inflammatory Response Syndrome (i.e., SIRS, which used to be called “septic shock”) due to the pancreatitis. At this time, there are good data showing that it is probably reasonable to give physiologic doses because dogs in SIRS typically can have what has been termed “Critical illness related corticosteroid insufficiency” (CIRCI), that is to say that they are relatively hypoadrenal.

However, this is a very controversial statement. If steroid therapy for pancreatitis is contemplated, it should probably be reserved for the severely ill dog which is not responding to appropriate fluid resuscitation.

If DIC appears to be a major problem, aggressive administration of fresh frozen plasma to replace clotting factors and anti-thrombin III concentrations is probably more effective than heparin.

Analgesics are critically important. One must remember that dogs are clearly much “tougher” than people, and they often hide their pain well. Unless there is some good reason to the contrary, it is best to routinely assume that dogs with acute pancreatitis are in pain and will benefit from analgesic. In the very mildest of cases, butorphanol might be sufficient. In moderate cases, methodone is reasonable. As the pain becomes more severe, we progress to constant rate infusions of fentanyl. Is the most severe cases, we administer a constant rate infusion of fentanyl, lidocaine and ketamine.