

Acute Pancreatitis

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Acute pancreatitis is one of the most difficult diseases a clinician can manage. The systemic inflammatory response syndrome can be severe in these animals. Major organ failure – refractory hypotension, liver failure, gastrointestinal failure, ARDS (acute respiratory distress syndrome), and DIC (disseminated intravascular coagulation) may develop. Only through aggressive medical management and sometimes surgical management can the clinician hope to minimize morbidity and mortality. Commonly used diagnostic tests do not necessarily correlate with severity of disease or prognosis, which means that the clinician should treat all pancreatitis patients as having potentially life-threatening disease. The ultimate diagnosis of pancreatitis is a histopathologic one which is rarely achieved. Aggressive fluid therapy, analgesia and nutritional support form the cornerstone of therapy. If patients have necrotic, abscessed or neoplastic pancreatic tissue present, the inflammatory process may not subside until the affected tissue is debrided. Surgery is rarely indicated but may be important in the management of some patients.

Pathophysiology

Multiple causes of pancreatitis have been identified but in most dogs and cats it is considered to be idiopathic. Regardless of the cause the pathophysiology is similar and ultimately is a result of activation of the pancreatic enzymes within the pancreas leading to autodigestion as well as digestion of the peripancreatic tissues and subsequent activation of the inflammatory process. If the inflammatory cascades persist unabated the systemic inflammatory response syndrome (SIRS) can result.

The systemic uptake of all of the products that are liberated during the inflammatory process can then lead to systemic inflammation and multisystem involvement. The protective plasma protease inhibitors such as α -2-macroglobulin and α -1-protease inhibitor are consumed as the necrotizing process continues. Alpha macroglobulins change the configuration of the proteases when they bind to them which allows macrophages to clear the enzymes. As the plasma protease inhibitors are depleted death can occur from acute disseminated intravascular coagulation and shock as the circulating proteolysis and cytokines activate the complement, coagulation, and fibrinolytic cascades.

Grossly pancreatitis progresses from that of edema and mild saponification and a few one millimeter sized abscesses to that of severe edema, numerous areas of saponification and many small abscesses. Then it progresses to hemorrhagic pancreatitis, localized peritonitis and edema of the surrounding tissues and advances to necrosis, larger abscesses, and the formation of very firm sections of cellulitis and pancreatitis (a phlegmon). In some cases bacteria are thought to translocate from the duodenal lumen and generalized peritonitis, bacterial abscessation, secondary biliary blockage and necrosis of the ventral aspect of the duodenum may occur. In the most severe cases the entire pancreas becomes involved. In some cases necrosis of fat that normally accumulates in the retroperitoneal space and falciform ligament may be present. Gastric and duodenal ileus are common.

Diagnosis

Animals with acute pancreatitis are usually presented because of depression, anorexia, vomiting, and in some cases, diarrhea. In severe cases shock and collapse may be present. In other cases the signs are very vague to almost nonexistent. Cats with mild pancreatitis are often presented with a vague history of being inappetent. Some animals with severe pancreatitis will exhibit signs of cranial abdominal pain and even a "praying" position. Pain may or may not be evident. Patients in shock may not show any signs of pain until perfusion is restored with fluid therapy. Occasionally the only clinical signs the patient exhibits are from systemic complications. Physical examination should include careful auscultation, palpation and visual inspection of the animal. Lack of gastrointestinal sounds is consistent with ileus, which may be localized or generalized. The right and left cranial

abdominal quadrants should be individually evaluated using palpation underneath the rib cage. Large dogs may need to have their front feet placed on a stool or chair to shift abdominal contents caudally. The umbilicus should be closely inspected since masses involving the umbilicus have been associated with pancreatic neoplasia. A rectal examination should be performed to evaluate for evidence of diarrhea as well as the presence of blood. Vomitus should also be evaluated for blood.

Although a leukocytosis with a left shift is commonly observed in more serious cases there may be no changes in the white cell number or types in milder cases. Red blood cell morphology should be closely examined, especially in cats, for signs of oxidant-induced damage (suggesting depleted glutathione levels). Assays of pancreatic enzymes (amylase, lipase) do not provide any useful information in dogs and cats. Species specific pancreatic lipase immunoreactivity (fPLI and cPLI) are sensitive (85-90%) for pancreatitis but some feel they are not very specific. Both SNAP and Spec tests have been validated. Spec tests are quantitative and repeat tests may allow for trending of the disease process. Liver enzymes and bilirubin may be elevated. If the inflammatory process has progressed then albumin levels may be decreased due to third-spacing. Blood gas abnormalities will reflect the degree of perfusion abnormalities as well as any possible secondary pulmonary involvement (aspiration pneumonia, ARDS). Electrolyte abnormalities typically reflect a combination of dehydration and losses through vomiting and diarrhea. Hypocalcemia may result from calcium soap formation, intracellular shifts due to alterations in membrane function, or altered levels of thyrocalcitonin and parathyroid hormone. Ideally ionized hypocalcemia should be assessed rather than total calcium. Coagulation profiles (PT, PTT, platelet counts or estimates) are indicated in sick pancreatitis patients in order.

Radiographs often reveal increased density, diminished contrast, and granularity in the right cranial quadrant of the abdomen, displacement of the stomach, widening of the "angle" between the antrum and the descending duodenum, and displacement of the descending duodenum to the right with gas patterns in the duodenum. The subjective loss of visceral detail in the cranial abdomen is probably the most common radiographic sign observed. In cats the loss of detail associated with pancreatitis is more commonly seen on the lateral view immediately caudal to the stomach and extreme lateral displacement of the duodenum does not occur.

Ultrasonic interrogation of the cranial abdomen will be helpful but is operator dependent. The appearance of mixed echogenicity or a mass effect within the pancreas as well as cystic areas, abscesses (complex cystic regions), edema, and free intraabdominal fluid are occasionally observed. Changes in the duodenum consistent with pancreatitis include a fluid and gas-filled descending duodenum, a thick-walled duodenum and atony. Caution should be exercised in ruling out pancreatitis on the basis of a normal ultrasound exam.

Medical Management

Supplemental oxygen should be provided to all patients showing signs of shock, typically using nasopharyngeal catheters. Aggressive fluid support is indicated. This requires a continuous rate intravenous infusion of a crystalloid and often colloids. Use a replacement formula to rehydrate the animal and replace fluids and electrolytes lost secondary to vomiting, diarrhea, and third spacing and plan to rehydrate over 6 to 8 hours. Colloids should be used immediately in more critical patients (hypotensive, evidence of hemorrhagic vomiting or diarrhea, systemically ill patient, hypoproteinemic, evidence of developing coagulopathy) to improve microcirculatory blood flow and help in the prevention of endothelial, interstitial and intracellular edema.

Albumin levels should be maintained above 2 mg/dL using plasma. Not only is plasma an important contributor to oncotic pressure but albumin is important also as a free radical scavenger. Plasma provides a source of α -macroglobulin, which binds the activated and liberated proteases. In the author's opinion fresh frozen plasma should be used during resuscitation if there is any concern that a coagulopathy is present or is developing.

To ensure adequate fluids are being administered adequate urine output (at least at 1/2 ml/kg/hr in cats, 1 ml/kg/hour in dogs), central venous pressure (3-7 cm H₂O), and normal heart rate and arterial blood pressure should be maintained.

Pain kills. Analgesics should be provided immediately to patients in pain in adequate doses and at frequent enough time intervals to control the pain. Methadone and hydromorphone are effective intermediate acting pure mu agonists. Butorphanol may be indicated in very critical patients (0.05-0.2 mg/kg) and may be effective in cats, but it should be kept in mind that butorphanol may only last 20 to 60 minutes and is not very effective if pain is moderate to severe. A constant rate infusion of butorphanol may be helpful in more painful cats. Patients with severe pancreatitis may require continuous rate infusions of fentanyl. For those with intractable pain peritoneal lavage with lidocaine and bupivacaine is often very effective. Nonsteroidal antiinflammatory drugs (NSAIDs) should be avoided.

Antiemetics are usually indicated, maropitant being the most effective drug in most patients. Serotonin antagonists such as ondansetron hydrochloride or dolasetron can also be used. Metoclopramide may help improve gastrointestinal motility and clinically seems to be more effective given as a constant rate infusion (2 mg/kg/d) than when given as intermittent injections. Nasogastric (NG) tubes should be placed for gastric decompression in patients that have significant gastric distention with fluid or frequent large volume vomiting.

Nutritional support ideally should begin within 12 hours of admission. Partial parenteral formulas can be given by peripheral catheter. ProcalAmine (B. Braun Medical), which is a hyperosmolar solution containing 3% amino acids, 3% glycerol and maintenance concentrations of electrolytes, is an excellent partial parenteral nutritional support product. It is given at a rate of 0.5 mL/kg/hr as a constant rate infusion. Maintenance fluids to which 3% amino acids and 3-5% dextrose are added can be used instead of commercially prepared solutions.

Enteral feeding is always preferred over parenteral. Jejunal feeding is the ideal route since feeding in this location does not stimulate pancreatic enzyme secretion and is generally well tolerated. Patients that have surgery have an advantage since a jejunostomy or gastrojejunostomy tube can be placed. Evidence also suggests that gastric feeding may be possible in some patients. It is recommended that an NG tube be placed and used for gastric decompression as well as microenteral feeding. This trickle feeding (0.1 – 0.25 mL/kg/hr) of an electrolyte solution containing an isotonic mixture of electrolytes and 3 to 5% glucose is well tolerated. This will help prevent gastric stress ulceration, help prevent the down regulation of the gastrointestinal tract that occurs when the patient is not eating, and help improve the transition to full enteral feeding. This microenteral nutrition is only continued if hourly aspirations of the NG tube reveal no accumulation of this fluid in the stomach and/or no vomiting of the material is detected.

Close monitoring is essential in patients with severe pancreatitis. Monitoring should include regular (q 1 to 4 hr) measurement and documentation of level of consciousness, temperature, heart rate and rhythm, pulse rate and strength, respiratory rate and effort, blood pressure, central venous pressure (if a jugular catheter is in place), pain/analgesia, gastrointestinal sounds, amount and characteristics of vomitus and diarrhea, and volumes of fluid suctioned via the NG tube. Blood tests are indicated at least every 24 hours including packed cell volume, total solids, albumin, glucose, creatinine, electrolytes, blood gas, and blood smear evaluation. Additional tests (complete blood counts, other blood chemistries, radiographs, fluid analysis, etc.) may be indicated based on the status of the patient. All parameters should be kept in as normal a range as possible. More critical patients or those with clinically relevant abnormalities will require more frequent monitoring.

Indications for Surgery

A decision to perform surgery is made based on history, physical examination findings, laboratory parameters, and diagnostic imaging; however, many of these findings are nonspecific, especially in cats. One study showed that there was no definitive means of determining acute necrotizing pancreatitis from chronic nonsuppurative pancreatitis. The presence of septic peritonitis based on paracentesis or diagnostic peritoneal lavage, or a mass lesion found on ultrasound consistent with an abscess is an absolute indication for surgery. Other indications are more subjective.

Surgical exploration should be considered in patients with a waxing and waning history of recurrent pancreatitis in order to procure an exact diagnosis as well as determine if resolution of the disease is possible. Patients who have been diagnosed with pancreatitis that is not responding to medical management should be explored – again to diagnose the underlying cause, debride or resect necrotic, infected or neoplastic tissue, and place an enteral feeding tube.

References available on request.