MANAGEMENT OF ACUTE PANCREATITIS
AND IT’S SYSTEMIC COMPLICATIONS IN DOGS

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Acute pancreatitis is a common disease presentation for the emergency practitioner. We are all familiar with the presentation of the acutely vomiting dog with pain in the cranial abdomen. Diarrhea, especially large bowel diarrhea because of the anatomic location of the pancreas close to the colon, is also common in these patients.

Pancreatitis begins as inflammation that is localized to the pancreas, the surrounding mesentery, and the cranial part of the peritoneal cavity. The inflammation leads to focal abdominal pain and extends to the peritoneal surfaces of bowel that is anatomically close to the pancreas. Effusion of an inflammatory exudate can occur into the peritoneal cavity. Because of the inflammation, the stomach and intestine that is close to the pancreas have decreased motility and become dilated and fluid-filled. Vomiting occurs because of stretch- and inflammation-mediated stimulation of visceral afferent receptors that activate the vomiting center in the brainstem.

Pancreatitis becomes life-threatening when the inflammation is so severe that inflammatory mediators, activated pancreatic enzymes, and cytokines are released into the circulation and can have far-reaching effects on distant organ systems. Distributive shock can occur, and pulmonary, coagulation and hepatic failure are common causes of death.

Confirming the diagnosis of acute pancreatitis

Pancreatitis is often a challenging clinical diagnosis that is made by careful evaluation of the results of several diagnostic tests, taking all factors into consideration. The clinical findings are the most important, as it is difficult to support a diagnosis of acute pancreatitis in an animal that has no abdominal pain and no vomiting. Imaging is the next important strategy for diagnosis (see Dr Moon’s handout).

The complete blood count often reveals evidence of inflammation, including a left shift, leukocytosis or leukopenia. Platelet counts may be low if the systemic inflammatory response syndrome (SIRS) is resulting in disseminated intravascular coagulation (DIC), as discussed below. The chemistry panel may reveal hypoalbuminemia if protein loss is occurring into the gut lumen or into the peritoneal cavity in an effusion. Hyperglycemia is concerning as it suggests that there may be significant activation of diabetogenic stress hormones and/or severe inflammation involving the Islets of Langerhans. Azotemia that may be pre-renal or renal in origin may occur. Non-specific elevations of the liver enzymes are common. The presence of icterus is a serious sign that may indicate obstruction of the biliary tree because of pancreatic inflammation. Coagulation testing may reveal prolongations of PT and/or PTT if DIC is present. Testing serum for canine pancreatic lipase can provide terrific additional information, but is non-specific and should not be used alone to make a diagnosis of pancreatitis.
Clinical supportive care for dogs with acute pancreatitis

The most important strategy for management of pancreatitis is to avoid further stimulation of the gut, and to provide supportive care.

Avoidance of oral intake of water and food is a reasonable step in dogs that are vomiting and have abdominal pain. As long as the body condition of the patient is reasonable, food can be withheld for 3-5 days without serious consequences. If the dog is in poor body condition, especially if it has decreased muscle mass, then nutritional support may be required earlier than 3 days after the dog last ate a meal.

Pain management is the next priority. Because of concerns about visceral perfusion, NSAIDs and alpha-2 agonists should be avoided despite their efficacy for pain control. Opioids remain the most valuable analgesics, despite concerns about their deleterious effects on gastrointestinal tract motility. Buprenorphine may be useful for mild visceral pain, but is likely to be insufficient if pain is severe. Pure mu agonists such as methadone, hydromorphone (may induce vomiting however), or fentanyl can be very helpful in these patients, and can be combined with infusions of ketamine and/or lidocaine to find the optimal combination for each individual patient. Epidural analgesia requires more study but may be very helpful in selected animals.

Antiemetic drugs are advised if vomiting is ongoing and severe. Prokinetic drugs such as metoclopramide should be considered because of potential beneficial effects in animals with ileus. Additional antiemetics that can be added individually or together include maropitant, chlorpromazine, or ondansetron. Gastoprotectants that inhibit gastric acid secretion, such as famotidine or esomeprazole, should be added to the regimen.

Additional monitoring and treatment depends on which body system is most severely affected by the systemic inflammatory response, as below:

Cardiovascular system and fluid therapy

In dogs, the initial stages of SIRS involve cytokine or endotoxin-mediated peripheral vasodilation. At this early stage, heart rate increases and cardiac output is high, in an attempt to maintain tissue perfusion and blood flow in spite of a decreased peripheral vascular resistance. The pulses may feel bounding, indicating an excessive difference between systolic and diastolic pressures. In SIRS, the capillary endothelia become more permeable, and fluid and albumin begin to leak into the interstitium. This ultimately can lead to hypoproteinemia and hemoconcentration, which increases blood viscosity and exacerbates sludging and stasis in peripheral capillaries. Activation and chemotaxis of neutrophils contributes to the inflammatory process, and tiny leukocyte clusters embolize capillaries, further affecting blood flow. A similar process occurs with platelets, with aggregation and adherence of platelets to damaged endothelia, and obstruction of blood flow. The endothelial damage and inflammation lead to activation of the coagulation and fibrinolytic cascades.

Fluid therapy remains the mainstay of SIRS treatment. By providing intravenous fluids, we hope to improve circulating blood volume, decrease blood viscosity, and increase venous return, thus helping to improve cardiac output and tissue perfusion. Shock boluses of replacement crystalloid
(Lactated Ringers, balanced electrolyte replacement solutions) may be required if the patient is cardiovascularly unstable at presentation. Initially, 10-30 ml/kg is delivered rapidly intravenously (over 15-20 minutes) while the animal is carefully observed for a response, or for evidence that the fluid bolus is causing a problem. This dose can then be repeated if necessary till the total shock dose has been reached. The end point of resuscitation is an improvement in tissue perfusion, which is clinically recognized by an improvement in mucous membrane color, better quality pulses, a decrease in the heart rate towards normal, and improved mentation. Packed cell volume (PCV), total solids (TS), electrolytes and blood glucose should be monitored before, during, and after each fluid bolus.

Animals with ongoing fluid losses (severe vomiting, peritoneal effusion etc) may then require high fluid volumes in order to maintain a normal heart rate, pulse quality and urine output. The rate of replacement fluid therapy is determined by clinical parameters such as heart rate, blood pressure, and urine output. Several problems may arise as a result of high crystalloid fluid replacement rates, and these problems are most severe in patients that are hypoproteinemic or those that have vasculitis. Since only about 25% of a crystalloid solution stays in the circulation in the normal state, and even less in the patient with increased vascular permeability and hypoproteinemia, interstitial fluid accumulation may occur. The lungs are the organ most severely affected, potentially limiting gas exchange.

Colloid replacement solutions such as hydroxyethyl starch, plasma or human albumin can be invaluable in the management of SIRS. Colloids are large molecules that stay within the vasculature, providing persistent volume expansion and increases in colloid osmotic pressure. Although the decreased interstitial fluid accumulation is difficult to quantify clinically, we have anecdotally seen increased survival and decreased morbidity in critical patients as our use of synthetic colloid solutions has increased. Synthetic colloid solutions should be considered in any animal that needs high rates of intravenous fluid support, particularly if hypoproteinemia is present. Current recommendations suggest that doses of synthetic colloids greater than 20 ml/kg/day not be exceeded. This maximum dose rate is based on possible adverse effects on the coagulation system and on volume overload. We have found that this dose can be greatly exceeded in critically ill dogs, without significant adverse effects. When using synthetic colloids for ongoing management of critically ill hypoproteinemic patients, it is ideal to measure colloid osmotic pressure to determine the dose requirement. Hetastarch can be administered at very rapid rates as part of a total shock bolus, if desired. Total doses of 15-20 ml/kg can be given for shock resuscitation, usually in increments of 5 ml/kg at a time. Hetastarch can then be continued at a dose rate of 1 ml/kg/hr to maintain the colloid osmotic pressure.

In addition to physical parameters, packed cell volume, total solids and indirect indicators of tissue perfusion such as serum lactate, the adequacy of cardiovascular resuscitation should be monitored using continuous EKG, measurement of arterial blood pressure and central venous pressure. Changes in CVP provide information about the intravascular volume: that is, the degree of filling of the great vessels. The CVP is usually low (0-5 cm H2O), but it may increase if the capacitance of the great vessels is exceeded. In general, intravenous fluids can be safely administered as long as there is no rise in central venous pressure, although caution should be exercised, and other parameters such as lung auscultation should also be monitored. Once a rise in central venous pressure occurs, fluid administration should be decreased or suspended.

In dogs, cardiac output may be decreased by the onset of arrhythmias. Cardiac arrhythmias are common following shock of any etiology, and are often seen in the first 24-48 hours.
Ventricular arrhythmias are usually seen, with atrial arrhythmias much less common. In dogs with SIRS, ventricular arrhythmias usually do not represent serious primary myocardial disease. When faced with a SIRS patient that has ventricular arrhythmias, the clinician should seek to correct as many metabolic disturbances as possible, before resorting to the use of anti-arrhythmic drugs. The provision of supplemental oxygen alone can often significantly improve the cardiac rhythm, as can correction of electrolyte imbalances and careful attention to blood volume, oxygen-carrying capacity, pain management and acid-base balance. The arrhythmias seen in these patients vary a great deal in severity. The requirement for treatment depends on the extent to which the VPCs or ventricular tachycardia are affecting cardiac output and tissue perfusion. Idioventricular dissociation rhythms (ventricular tachycardia at rates < 180 bpm) are unlikely to affect perfusion. If the dog is well perfused (mucous membranes are pink, good pulses, good mentation), anti-arrhythmic drug therapy may be unnecessary, and the ventricular arrhythmias usually spontaneously resolve within 48-72 hours. Specific abnormalities that may require drug therapy include rapid ventricular rhythms (> 180 bpm), or frequent R-on-T which may be a prelude to fibrillation. In such cases, a lidocaine bolus should be administered IV (2 mg/kg), and repeated in 5 minutes if there is no response. A response to lidocaine may range from complete recovery of sinus rhythm, to slowing of the ventricular rate. If a satisfactory response is obtained, a continuous infusion of lidocaine should be started (40-80 mcg/kg/min), with another bolus of lidocaine at the time the infusion is initiated. In most cases anti-arrhythmic drugs are only required for 2-5 days.

If an animal does not respond to fluid therapy, or for those in which fluid therapy is contraindicated (eg those with severe lung disease), continuous infusions of catecholamines are an important way to support the circulation and improve tissue perfusion. Numerous drugs are available, but this author’s first-line inotropic and pressor drug is dopamine. Dopamine is well tolerated by the majority of animals and at low to moderate doses does not appear to have many negative effects. Beta receptor agonist doses (5-8 ug/kg/min CRI) are often effective and helpful, while alpha receptor agonist doses (8-15 ug/kg/min) may be needed in severely affected patients. Other catecholamines such as epinephrine or norepinephrine may be needed occasionally, but typically represent a “second line” only if dopamine is ineffective.

Monitoring of arterial blood pressure provides important information to guide catecholamine administration. Efforts should be made to maintain systolic blood pressures above 90 mmHg (normal = 110-150 mmHg), and mean arterial pressure above 70 mmHg. Addition of dopamine to patient management should be considered if:
- arterial pressures are less than 70 mmHg (mean) in spite of adequate fluid resuscitation
- mean arterial pressure is less than 70 mmHg and fluids cannot be administered fast enough to correct hypotension
- fluid administration is probably necessary, but the presence of lung disease or pleural effusion is limiting the ability to administer more fluids
- central venous pressure is greater than 5 cmH2O, and hypotension is persisting.

Dopamine is started at a rate of 5 ug/kg/min, then measurements of blood pressure are obtained every 15 minutes. The drug dose can be increased in increments of 2.5 ug/kg/min up to 15 ug/kg/min, until the blood pressure improves. Dopamine should be made up diluted in fluids, at a concentration that can be delivered at a very slow fluid rate (1-3 ml/hr), in order to prevent worsening fluid overload in small patients. The animal should be maintained on the minimum dose of dopamine required to keep
the mean arterial pressure above 90 mmHg. Dopamine is then weaned gradually based on the response of the animal and repeated measurements of blood pressure.

Respiratory system

The lungs may suffer serious injury as a result of cytokine- and neutrophil-mediated increased vascular permeability and fluid accumulation. The acute respiratory distress syndrome (ARDS) is an acute, usually fatal, complication of a number of disease states, particularly SIRS and sepsis. In SIRS, a diffuse inflammatory process initiates an avalanche of activation of many diverse inflammatory mediators, including a variety of cytokines, the complement and arachidonic acid cascades, and cells such as neutrophils and macrophages. Patients that develop respiratory failure due to ARDS are simply demonstrating a local pulmonary manifestation of SIRS.

In dogs and cats with ARDS, the initial stages of the syndrome begin as a diffuse exudative vasculitis, with infiltration of neutrophils and macrophages into the lung. Such changes are accompanied by effusion of protein-rich fluid into the alveoli, and clinical evidence of progressive pulmonary edema. As ongoing inflammation is combined with early attempts at repair by the lung tissue, we begin to see proliferation of Type II pneumocytes, formation of hyaline membranes within alveoli (organization of protein-rich fluid and cellular debris), deficiency of surfactant, and collapse and atelectasis of alveoli. This is later followed by interstitial fibrosis as the lung attempts to repair the damaged tissue. These inflammatory changes in the lung may vary in severity, and may be unevenly distributed. At times, they may be mild, and almost clinically unrecognisable. In more severely affected animals, the inflammation is profound, overwhelming, and leads to severe hypoxia.

ARDS is recognized clinically by the development of pulmonary edema in an animal with a predisposing cause of an inflammatory response, such as pancreatitis. Animals that have ARDS are in severe respiratory distress, and are usually cyanotic. Auscultation reveals harsh lung sounds that rapidly progress to crackles. They may expectorate pink foam, and if intubated, sanguinous fluid may drain out of the endotracheal tube. Arterial blood gases usually reveal hypoxia and hypocarbia, and metabolic acidosis may be present. These animals usually have diffuse bilateral pulmonary alveolar infiltrates throughout all lung fields on thoracic radiographs.

Most dogs and cats with ARDS show little response to oxygen supplementation, and remain severely dyspneic. If placed on a ventilator, the lungs are found to have very poor compliance, and extremely high peak airway pressures (> 40 cm H₂O) may be seen, even if the tidal volume is small. Positive end expiratory pressure is usually required to achieve adequate oxygenation.

Unfortunately, few options are available for definitive management of ARDS, apart from treatment of the underlying disease. In humans, there is a very high mortality rate, and even those who survive require positive pressure ventilation for several weeks. Because of the variety of inflammatory cascades and cells that mediate inflammatory response in ARDS, specific anti-inflammatory drugs such as corticosteroids are largely ineffective for treatment, and may cause immunosuppression that can exacerbate sepsis. Advances such as synthetic surfactant therapy, inhaled nitric oxide, and other new drugs, which have begun to be useful in human medicine, have not yet been evaluated in dogs with naturally occurring disease.
Renal function

The kidneys, with their high oxygen demands, are affected early in SIRS. Initial decreases in blood flow are associated with vasoconstriction, ADH and aldosterone release, and decreased urine output in an attempt to preserve blood volume. Increased vessel permeability and severely curtailed oxygen supply can then lead to tubular damage and acute tubular necrosis. Since the kidneys have a great deal of reserve, clinical renal failure is an uncommon complication that is most commonly seen in older patients that had some degree of renal insufficiency before the traumatic episode. In the presence of persistent hypotension, however, decreased urine output may represent the beginning of acute tubular necrosis and acute renal failure. Acute renal tubular damage may be exacerbated by use of aminoglycoside antibiotics or non-steroidal anti-inflammatory drugs.

Urine output should be monitored carefully in all critically ill patients, and if there is doubt about its adequacy, a urinary catheter should be placed and attached to a closed collection system. The onset of oliguria (<0.5 ml/kg/hr) is one of the earliest signs that renal perfusion may be inadequate, signaling that renal failure may be imminent. If oliguria occurs, a fluid volume challenge should be considered. Arterial blood pressure should be measured to ensure that the mean arterial pressure is sufficient for glomerular filtration (> 70 mmHg). Drugs such as mannitol (0.5-1 g/kg IV), dopamine in dogs (2-5 mcg/kg/min CRI), or furosemide (0.1-2 mg/kg IV) should be considered if urine output remains inadequate.

Coagulation system

Since diffuse endothelial injury is often present in patients that have SIRS due to pancreatitis, it is not surprising that disseminated intravascular coagulation (DIC) is a common sequela. Release of tissue factors, poor blood flow through tissues, and inflammation all cause activation of both the coagulation and fibrinolytic systems. Diffuse activation of these systems leads to consumption of coagulation and fibrinolytic factors. Depletion of these factors may be further exacerbated by dilution as a result of fluid and colloid therapy, and by intravenous catheters that lead to further vascular endothelial damage. The end result may be the syndrome of DIC, which may manifest either as hemorrhage or thrombosis, depending on which system is most depleted. Since both can be disastrous in the critically ill patient, it is important to monitor carefully for the presence of DIC, in order to detect it at its earliest stages, when therapy may be most successful.

If there is any evidence of excessive hemorrhage or thrombosis, or if the patient has SIRS or severe pancreatitis and is therefore deemed to be at risk for DIC, a coagulation panel should be evaluated, including platelet count, PT/PTT, D-dimers, and screening of a blood smear for the presence of red blood cell fragments. If such studies are not available, a great deal of information can be obtained from an ACT and a blood smear estimate of platelet numbers. If early signs of DIC are recognized (decreased platelet count, prolongation or shortening of PT/PTT, increased D-dimers, etc), aggressive therapy should be instituted. Therapy should include definitive management of the cause of DIC, fluid therapy to promote tissue perfusion, factor replacement via plasma or fresh whole blood, and may or may not include heparin.

REFERENCES AVAILABLE ON REQUEST