

Update on the Diagnosis and Management of Feline Pancreatic Disease

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PANCREATITIS

Pancreatitis is the most common condition of the feline exocrine pancreas. Although diseases of the exocrine pancreas have been thought to occur much less commonly in cats than in humans or dogs, a retrospective study revealed significant pancreatic pathologic lesions in 1.3% of 6504 feline necropsy cases and in 1.7% of canine necropsy examinations. In addition, a recent report of 47 cats with pancreatitis documented a high incidence (59%) of concurrent fatty change in the cats' livers. The lack of sensitive and specific markers for feline pancreatitis, as well as the low index of suspicion for pancreatic disorders in cats have contributed to the relatively infrequent antemortem diagnosis of pancreatitis in this species. Chronic pancreatitis (CP) is more commonly seen in the cat and is a continuing inflammatory disease characterized by irreversible morphological change, possibly leading to permanent impairment of function.

The cause(s) for feline pancreatitis are poorly understood. Acute hypercalcemia has been shown to experimentally induce acute pancreatitis. Other risk factors include infections with Herpesvirus, *Toxoplasma gondii*, FIP, and liver flukes. Bile duct obstruction secondary to biliary calculi, sphincter spasm, tumors, or parasites can also predispose to acute pancreatitis in cats. Trauma from excessive surgical manipulation, automobile accidents, or falling from high buildings has also been associated with acute pancreatitis. Other predisposing factors include uremia and administration of cholinesterase-inhibitor insecticides.

The association of **feline hepatic lipidosis** and pancreatitis has been well documented. Pancreatitis is present in approximately 40% of cats with hepatic lipidosis and usually warrants a poorer prognosis when present. It is difficult to predict which disease occurs initially. Speculation is also increasing about the association between **feline inflammatory bowel disease** and pancreatitis. In cats with hepatic lipidosis, the signalment, history, physical examination, and clinicopathologic findings are generally indistinguishable in cats with and without pancreatitis; however, cats with pancreatitis are more likely to be underweight and have coagulation abnormalities and peritoneal effusion.

Diagnosis

The **clinical presentation** of cats with pancreatitis is vague and nonspecific. In a retrospective study of 40 cats with necropsy-confirmed pancreatitis, reported clinical signs were lethargy in 100% of the cases, anorexia in 97%, dehydration in 92%, hypothermia in 68%, vomiting in 35%, abdominal pain in 25%, palpable abdominal mass in 23%, dyspnea in 20%, ataxia, and diarrhea in 15%. In contrast, vomiting and abdominal pain are the most consistent clinical signs in dogs and in humans suffering from pancreatitis. **Hematologic abnormalities** are uncommon and nonspecific. Leukocytosis is a relatively common finding in acute pancreatitis. The patient may have a left shift or have toxic white cells if the disease is severe. Other hematologic changes reflect fluid loss and hemoconcentration. **Biochemical abnormalities** include mild to moderate elevations in ALT, ALP, and bilirubin and usually reflect concurrent hepatic disease (hepatic lipidosis or cholangiohepatitis). Azotemia is frequently observed secondary to dehydration in most cases. Hyperglycemia is far more commonly seen in cats due to concurrent stress or diabetes mellitus. Hypocalcemia is occasionally seen due to saponification of peripancreatic fat. Abdominal **radiographs** are often subtle and subjective. Decreased contrast in the anterior abdomen, dilated and gas filled small intestines, transposition of the duodenum, stomach and colon are commonly reported. **Abdominal ultrasound** may reveal a hypochoic pancreas surrounded by hyperechoic mesentery, with or without dilated bile ducts. Ascites is occasionally observed.

The measurement of **serum lipase and amylase** activities is of **low value** in the diagnosis of pancreatitis in cats, with serum concentrations appearing quite variable. Determination of serum **trypsin-like immunoreactivity** (TLI) measures antibodies against circulating trypsin and trypsinogen. TLI is cleared by the kidney; therefore, elevations can occur with renal dysfunction. TLI values in the normal reference range do not rule out pancreatitis, and abnormally elevated TLI concentrations are not diagnostic for pancreatitis. A serum **feline pancreatic lipase immunoreactivity** (fPLI) test was recently developed and validated and preliminary findings suggest that this test is more sensitive than any other diagnostic tool for the diagnosis of feline pancreatitis. The current "gold standard" for diagnosing pancreatitis is pancreatic **biopsy** for histologic evaluation. Peripancreatic fat necrosis is a typical finding in cats with pancreatitis, with variable amounts of acinar cell necrosis and inflammation. Chronic pancreatitis is characterized by interstitial fibrosis with acinar atrophy and lymphocyte infiltrates. The disease can have a "patchy" or multifocal distribution, and pancreatic biopsies should always be procured during laparotomy even if the gross appearance of the organ appears normal.

Therapy

The clinical picture of pancreatitis in cats differs markedly from that in dogs. Most cats diagnosed with pancreatitis have a more chronic and indolent form of the disease, with vomiting or diarrhea being relatively uncommon presenting complaints. Because of these dissimilarities, therapeutic recommendations for the cat are quite different to those in the dog with pancreatitis. Many cats are anorectic, and fasting the cat for an additional 3–5 days to "rest" the pancreas will be of little to no clinical benefit. In addition, there is little clinical evidence to support excessive dietary fat restriction in cats with pancreatitis. At the University of California, Davis VMTH, cats with pancreatitis that are anorectic or have lost significant body weight undergo gastrostomy or esophagostomy tube placement for enteral feeding. Despite the dogma recommending complete "pancreatic rest" in patients with pancreatitis, we have not appreciated any clinical deterioration in these patients associated with enteral feeding. Enteral tube placement is avoided if the cat is vomiting intractably or has moderate ascites present. Jejunostomy tube feeding or total parenteral nutrition can be used in cats that are vomiting despite the administration of antiemetic therapy. Surgical placement of jejunostomy tubes is preferred over percutaneous endoscopic placement. Most cats with chronic pancreatitis can be fed a commercially obtained complete and balanced canned diet formulated for maintenance of the animal. It is unnecessary to feed human liquid formulas and liquid veterinary products that frequently contain large amounts of fat. In addition, most human liquid enteral formulas are too low in protein, are free of taurine, and deficient in arginine for the maintenance of feline patients.

The foundation of treatment for cats with severe acute necrotizing pancreatitis is similar to that in the dog with AP. These cats present with a more acute history of anorexia, vomiting, and weight loss, and many cats will be icteric due to extrahepatic bile duct obstruction. Maintenance of **fluid and electrolyte balance** is of paramount importance. Most of these cats will not tolerate intragastric feeding, and jejunostomy tube feeding or TPN should be administered. Although controversial, **antibiotic** administration is best avoided unless the cat is febrile or exhibits toxic changes on the hemogram. Most pancreatitis cats have a sterile pancreas and inappropriate antibiotic administration in cats could result in anorexia, salivation, and vomiting. If indicated, one can administer enrofloxacin (5 mg/kg IV q 12 hr) and cefotaxime (25–50 mg/kg IV q 8 hr), as these drugs penetrate well into the pancreas. **Antiemetic therapy** is indicated if the vomiting is persistent or severe. Phenothiazine derived antiemetics such as chlorpromazine work well, although prokinetic drugs such as metoclopramide as a continuous infusion (1–2 mg/kg/24 hr) may also be helpful. **Analgesic therapy** (fentanyl, buprenorphine, or butorphanol) should be given to provide relief if abdominal pain is severe. Diabetes mellitus is relatively commonly seen in cats with pancreatitis, and animals should be treated with insulin. Respiratory distress, neurological problems, cardiac abnormalities, bleeding disorders, and acute renal failure are all poor prognostic



signs, but attempts should be made to manage these complications by appropriate supportive measures. Gastric mucosal protection with an **H2 blocker** is recommended in patients with acute pancreatitis where gastric mucosal viability is compromised. Severe pancreatitis is also associated with a marked consumption of plasma protease inhibitors as activated pancreatic proteases are cleared from the circulation. Saturation of available alpha macroglobulins is rapidly followed by acute DIC, shock, and death. Although controversial, transfusion of **plasma** or whole blood to replace alpha macroglobulin may be life saving under these circumstances. Colloid support to enhance pancreatic perfusion can be supplied with hydroxyl starch or high molecular weight dextran. Corticosteroids should be given on a short-term basis to animals in shock associated with fulminating pancreatitis, or on a long-term basis in patients with concurrent IBD or lymphocytic/plasmacytic cholangiohepatitis. We have not observed any deleterious effects of prednisone administration in cats with pancreatitis and concurrent IBD or cholangiohepatitis when prednisone was administered at a dosage of 10 mg daily. In those patients in which acute pancreatitis is confirmed at exploratory laparotomy, **removal of any free peritoneal fluid** by abdominal lavage is advisable. In some cases, pancreatitis may be localized to one lobe of the gland, and surgical resection of the affected area may be followed by complete recovery.

The use of dopamine by constant rate infusion at 5 µg/kg/min has been shown to be beneficial in preventing exacerbation to severe hemorrhagic pancreatitis in a feline model of pancreatitis. This effect is probably mediated by ameliorating increases in microvascular permeability that could promote pancreatic edema. Unfortunately, this effect was only shown when dopamine was administered within 12 hours of initiating pancreatitis in these cats. Clinical trials evaluating dopamine in cats with spontaneous pancreatitis are warranted before this drug can be uniformly endorsed. **Pancreatic enzyme supplements** may decrease abdominal pain probably by feedback inhibition of endogenous pancreatic enzyme secretion. Similarly, somatostatin and its analogues inhibit pancreatic secretions, although clinical studies have failed to show any ameliorating effects of spontaneous pancreatitis in human beings.

EXOCRINE PANCREATIC INSUFFICIENCY (EPI)

Etiology

End-stage chronic pancreatitis is a much less common cause of EPI in dogs, although it is probably the most common cause in cats. Despite the relative frequency with which feline pancreatitis occurs, EPI is relatively rare in the cat. In chronic pancreatitis both endocrine and exocrine pancreatic cells are progressively destroyed, thus EPI in cats is often accompanied by diabetes mellitus. Rare causes of EPI include congenital pancreatic hypoplasia, obstruction to the flow of pancreatic juice secondary to adenocarcinoma, and, in cats (which unlike dogs usually only have a single pancreatic duct), duct loss as a complication of proximal duodenal resection and cholecystoduodenostomy.

Pathophysiology

A lack of pancreatic digestive enzymes leads to nutrient malabsorption secondary to failure of intraluminal digestion. In addition, intestinal mucosal transport mechanisms for mono- and disaccharides, amino acids, and fatty acids are disturbed and is speculated to be due to the absence of the trophic influence of pancreatic secretions.

Clinical Signs

The clinical signs of cats with EPI are virtually identical to the dog with EPI. Polyphagia, severe weight loss, and diarrhea are the classic signs associated with EPI, although vomiting and anorexia are occasionally observed in cats with EPI. The feces are typically pale, loose, voluminous, and malodorous, although cats can also develop

watery diarrhea secondary to intestinal disease. Cats can also develop a greasy appearance to their hair coat, especially in the perianal and tail regions, secondary to the high fat content of their feces.

Diagnosis

Routine laboratory test results are generally not helpful in establishing a diagnosis of EPI. A species-specific ELISA for measurement of feline serum trypsin-like immunoreactivity (fTLI) has been developed and validated at Texas A & M University, and has replaced use of an earlier radioimmunoassay. There is no cross reactivity between canine and feline TLI. In a recent study, a serum fTLI concentration of $\leq 8.0 \mu\text{g/L}$ had a specificity of 85–100% in 20 cats with suspected EPI.

Fecal proteolytic activity (FPA) can be measured using an azoalbumin, azocasein, or radial enzyme diffusion based method. Most cats with EPI have undetectable FPA levels. This test is somewhat labile and false positive results can occur due to inappropriate sample handling. The test is also impractical in that at least 3 stool samples collected over consecutive days should be evaluated. Feces needs to be frozen immediately and shipped on ice to prevent any loss of FPA in the samples.

Recently, a radioimmunoassay for the measurement of feline pancreatic lipase immunoreactivity (fPLI) has been developed and validated at the GI Laboratory at Texas A & M University. Preliminary results have revealed that the test is more sensitive and specific than the fTLI for diagnosing feline pancreatitis; however, the fTLI is superior for diagnosing EPI.

A number of tests for assessing exocrine pancreatic function have been described, but are highly discouraged because of their poor sensitivities and specificities. These tests include the microscopic examination of feces for evidence of undigested food, the quantitative assessment of fecal fat output, and determination of plasma turbidity (lipemia) after oral administration of fat.

Treatment

Enzyme Replacement

Many different preparations of pancreatic enzymes are commercially available; however, powdered formulations have been shown to be most effective in cats. Tablets, capsules and enteric-coated preparations are less effective than powdered extracts and are not recommended. Enzyme replacement using an initial dose of one teaspoon per meal is generally effective in most cats. Animals that do not show an optimum response to this dose do not usually benefit by increasing the amount of extract. The extract should be mixed with food immediately prior to feeding. It is not necessary to pre-incubate the enzyme powder in the cat's food before feeding. It is easier and cheaper to train the cat to be meal fed, as the cat can be fed twice daily with supplementation at each meal. The diarrhea and polyphagia should resolve within 2–3 days. As soon as clinical improvement is apparent, owners can determine a minimum effective dose of enzyme supplement that prevents return of clinical signs.

Dietary Modification

Fat absorption does not return to normal despite appropriate enzyme replacement therapy in dogs with EPI. Patients usually compensate by increasing their caloric intake, necessitating an increase of approximately 20% above their calculated maintenance requirements. Although fecal fat decreases when a fat-restricted diet is fed, excessive dietary fat restriction could decrease the absorption of fat, fat-soluble vitamins, essential fatty acids, and cholesterol. It has also been shown that a fat-restricted diet does not ameliorate signs of EPI. In fact, the feeding of a high-fat and high-protein diet in combination with porcine-lipase maximized fat absorption in one experimental study in dogs with EPI. Studies in human patients also reveal that certain fiber sources (e.g., wheat bran, pectin) impair pancreatic enzyme activity, therefore, high-fiber diets should be avoided. Most cats with EPI do well when

fed regular commercial maintenance diets. Fat absorption will not be improved by pre-incubation of the food with pancreatic enzymes, administration of antacids, or by addition of bile salts.

Vitamin Supplementation

Serum concentrations of cobalamin (vitamin B₁₂) are often markedly decreased in cats with EPI and do not necessarily increase in response to treatment with enzymes, even though the clinical response may otherwise be excellent. Vitamin E in the form of alpha-tocopherol should be supplemented at a daily dose of 100-150 IU per cat given in the food for 1 month. Serum cobalamin should be administered subcutaneously at a dose of 500 µg per cat once weekly for 6 weeks, with the dosing schedule decreased to once every 2 months depending on serum cobalamin concentrations. Cats appear highly susceptible to cobalamin deficiency, partly as a result of the very rapid turnover of this vitamin compared with humans. Cases of vitamin K deficiency-responsive coagulopathies have occasionally been documented in cats with EPI and severe IBD. Parenteral vitamin K₁ (2.5 mg/kg) followed by oral vitamin K₁ at 0.25 to 2.5 mg/kg q12 hours should be given when there is clinical or laboratory evidence of a coagulopathy.

Failure of the cat to respond to the abovementioned therapeutic measures warrants further work-up for other causes of diarrhea. An important consideration in these patients is concurrent lymphocytic-plasmacytic gastroenteritis, which is usually responsive to glucocorticoid therapy.

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