Pancreatitis in canines – acutely painful or chronically frustrating?

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Recent advances in point-of-care tests have increased our awareness of pancreatitis as a differential diagnosis in dogs presenting to a clinic with a variety of clinical signs. However, it remains a frustrating disease to diagnose and treat in many cases.

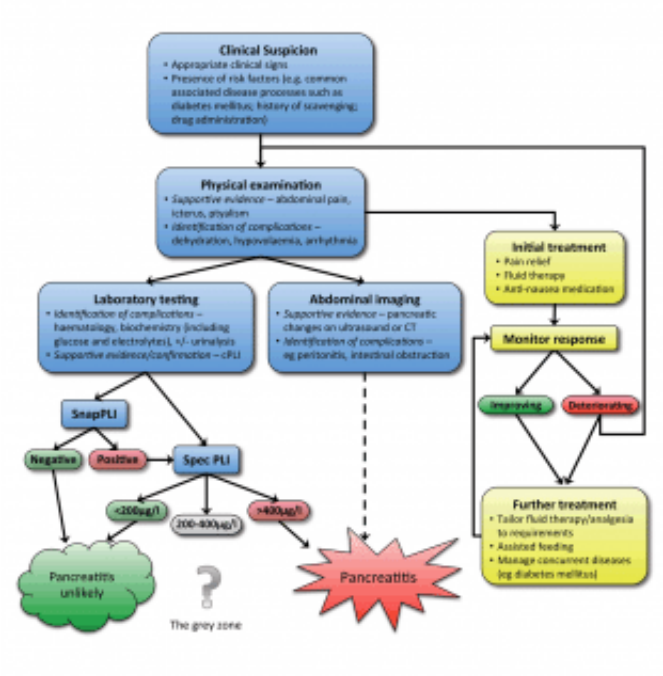

Figure 1. Basic guide to management and treatment of canine acute pancreatitis.

Clinically, canine pancreatitis is most commonly diagnosed as an acute disorder with chronic disease less frequently recognised, which is in contrast to the situation in cats[1].

This article will cover the basics of canine pancreatitis, suspected causes and risk factors, the variety of clinical signs reported, and management recommendations.

Pancreatitis describes inflammation of the exocrine pancreas, which occurs when premature activation of digestive enzymes overwhelm local and systemic defences – leading to tissue

necrosis and activation of inflammation[2]. In turn, this inflammation and necrosis leads to the clinical signs we recognise, such as abdominal pain and gastrointestinal upset (nausea, inappetence, vomiting and diarrhoea). In severe cases this inflammation can lead to systemic, potentially fatal, complications.

Gold standard classification of acute versus chronic pancreatitis requires histological analysis; however, this is rarely performed in clinical cases as it does not alter treatment recommendations.

Where histopathology has been performed in dogs with fatal acute pancreatitis, 40% had changes consistent with chronic pancreatitis in addition to acute changes[3], while a third of dogs in a large necropsy study had evidence of chronic pancreatitis in the absence of reported clinical signs[4].

Acute pancreatic changes have the potential for complete recovery, while chronic pancreatic changes are progressive and may lead to diabetes mellitus (DM) or exocrine pancreatic insufficiency. In one study of acute pancreatitis, 36% had concurrent DM[5], while 71% of dogs presenting with diabetic ketoacidosis had elevated canine pancreatic lipase immunoreactivity (cPLI)[6].

Causes and risk factors

Potential risk factors for acute episodes of pancreatitis are detailed in **Table 1**, but confirmation of causality remains elusive in many cases and many dogs are considered to have idiopathic disease.

Table 1. Potential risk factors for acute canine pancreatitis

Risk factor	Examples of increased risk
Breed	Miniature schnauzers, spaniels, terriers and dachshunds (dogs at decreased risk include miniature poodles and Labrador retrievers).
Neuter status	Neutered.
Body condition	Excessive.
Age	Middle to older.
Diet	Scavenging (for example, bin raiding), acute dietary change (for example, Sunday roast).
Adverse drug reactions	Those implicated include azathioprine, potassium bromide (as an adjunct to phenobarbital), organophosphates, L-asparaginase, sulphonamides, clomipramine and zinc.
Trauma	Hit by car.
Ischaemia	Hypoperfusion under anaesthesia, severe anaemia, immune-mediate haemolytic anaemia, congestive heart failure, gastric dilatation-volvulus.
Surgery	Partial pancreatectomy (for example, insulinoma excision).
Pancreatic duct obstruction	Local mass effect (for example, neoplasia), intestinal foreign body.
Acute hypercalcaemia	
Hyperlipidaemia	Breed-associated (miniature schnauzers), secondary to endocrinopathy (for example, diabetes mellitus, hyperadrenocorticism and hypothyroidism).

Table 1. Potential risk factors for acute canine pancreatitis.

Fewer data are available regarding risk factors for chronic pancreatitis due to many cases being mild or subclinical. However, in one UK-based necropsy study, cavalier King Charles spaniels, collies and boxers were over-represented[4].

Based on similarities to human disease, a suspicion is English cocker spaniels are at risk of immune-mediated pancreatitis[7].

Clinical signs

No clinical signs, or combinations thereof, are considered pathognomonic for either acute or chronic pancreatitis. This is further complicated by overlap of clinical signs with concurrent disorders, or predisposing factors.

Common clinical signs of acute pancreatitis include:

- Abdominal pain – from mild abdominal discomfort on palpation, to severe abdominal pain with a hunched stance, reluctance to move and boarded abdominal wall.
- Gastrointestinal complications:
    - inappetence/anorexia
    - nausea/vomiting
    - diarrhoea
- Weight loss – through anorexia and dehydration.
- Dehydration – tacky mucous membranes and skin tenting.
- Hypovolaemia – weakness, poor pulse quality, hypotension, tachycardia, hypothermia, pallor and prolonged capillary refill time.
- Icterus.
- Pyrexia.

In severe cases with systemic complications:

- Peritonitis – with local or generalised fluid accumulations.
- Cardiac arrhythmias – associated with the systemic inflammatory state or electrolyte disturbances.
- Disseminated intravascular coagulation (bleeding tendencies with thrombocytopenia and prolonged clotting times).
- Acute lung injury – dyspnoea, tachypnoea, hypoxia.
- Death.

In chronic cases, clinical signs are typically mild and non-specific, often presenting with waxing and waning weakness, variable appetite, weight loss and intermittent vomiting. Abdominal discomfort may be appreciable.

Clinical signs relating to concurrent disease may predominate – for example, diabetic ketoacidosis with polyuria/polydipsia, vomiting, dehydration and collapse or exocrine pancreatic insufficiency with chronic weight loss and small intestinal diarrhoea.

Diagnosis

Diagnosis of pancreatitis is often presumptive, based on history, physical examination and compatible clinical signs, in combination with measurement of cPLI and/or ultrasonographic examination of the pancreas (**Figure 1**). Biopsy of the pancreas for histopathological confirmation is rarely performed because it is invasive and carries significant risk of exacerbating pancreatitis, if present.

Although haematology and serum biochemistry are not diagnostic for pancreatitis, and often reveal non-specific changes, they should be considered in all cases of sick dogs presenting with non-specific clinical signs, such as those suspected of having pancreatitis. They are most useful in identifying and monitoring systemic complications requiring intervention; for example, azotaemia due to hypovolaemia or renal insult, electrolyte disturbances due to vomiting, or diabetes mellitus.

Abdominal imaging (ultrasonography or radiography) in the first opinion setting is also most useful at assessing for concurrent disease; for example, duodenal foreign body. Limitations to the use of abdominal imaging include lack of availability, operator experience and, due to the often severe abdominal pain present, requirement for heavy sedation or anaesthesia for restraint.

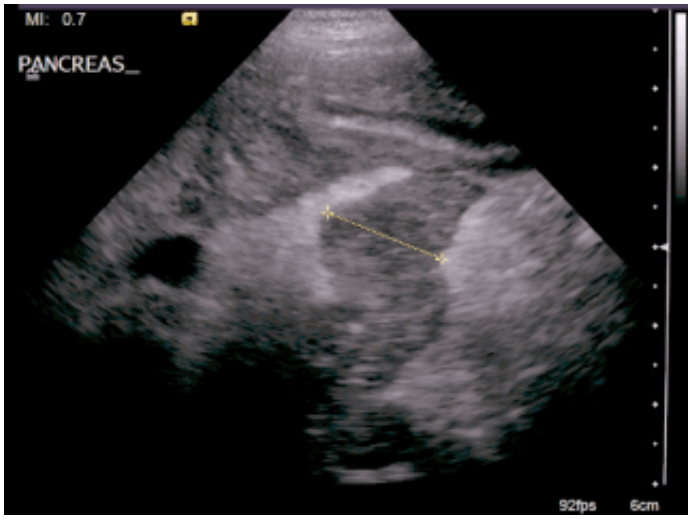

Figure 2. Ultrasonographic appearance of acute pancreatitis in a four-year-old male neutered bichon frise, with enlarged hypoechoic pancreas and surrounding hyperechoic mesenteric fat.

Typical ultrasonographic changes in acute pancreatitis are mass lesion with hypoechoic pancreas and hyperechoic surrounding mesenteric fat (**Figure 2**).

Serum cPLI is the most sensitive and specific test available for pancreatitis, when compared to serum lipase, amylase and trypsin-like immunoreactivity[8]. However, it must be remembered no diagnostic test is 100% sensitive and specific for pancreatitis, and sensitivity is lower for the more chronic and milder cases.

A negative SnapPLI result is unlikely in acute pancreatitis, therefore this is a good point-of-care test to rule out pancreatitis in suspect dogs. However, as with all tests it must be interpreted in a holistic manner, as elevations may be present in the absence of clinical signs or where the pancreatitis is not the primary underlying problem (for example, duodenal foreign body).

Positive SnapPLI results should always be followed up with SpecPLI for confirmation. Newer assays – for example, 1,2-o-dilauryl-rac-glycero-3-glutaric acid-(6'-methylresorufin) ester lipase activity – have been validated for the diagnosis of pancreatitis in dogs. However, further studies are required before their routine use is adopted.

A sensitive diagnostic non-invasive test for chronic pancreatitis remains illusive. In one study, only a quarter of cases had a positive cPLI (when using a low cut-off value of more than 200µg/L), while just more than half had abnormal ultrasound findings[9].

Management

As in the cat, no treatment will resolve inflammation in the pancreas and only a paucity of studies exists on treatment in dogs and cats. Management is, therefore, symptomatic and supportive (**Figure 1**) – addressing both the pancreatitis (replacing fluid losses, maintaining blood pressure, controlling nausea, providing pain relief, and early enteral nutrition) and concurrent complications (for example, DM)[10]. Where the pancreatitis is suspected to have been triggered by drug administration (for example, azathioprine), this should be withdrawn and avoided in the future. Common drug dosages are given in **Table 2**.

Replacing fluid losses

Table 2. Common drugs used in the management of acute pancreatitis

Use	Drug	Dose	Route	Frequency
Analgesia* – severe pain	Methadone	0.1mg/kg to 1mg/kg	IV, IM, SC	q2hr to 4hr
	+/- ketamine	5µg/kg/minute to 20µg/kg/minute	Constant rate infusion	As required (see text)
	+/- lidocaine†	25µg/kg/minute to 50µg/kg/minute	Constant rate infusion	As required (see text)
Analgesia* – mild pain	Buprenorphine	0.01mg/kg to 0.04mg/kg	IV, IM	q6hr to 8hr
	Tramadol†‡	3mg/kg to 5mg/kg	PO	q6hr to 12hr
Antiemetic	Maropitant	1mg/kg	SC, PO	q24hr
Gastric acid suppression	Omeprazole†	0.5mg/kg to 1mg/kg	IV, PO	q12hr
Appetite stimulation	Mirtazapine†‡	0.6mg/kg	PO	q24hr (as required)

*Titrate dose and frequency to effect. †Not to be administered concurrently. ‡Unlicensed.

Table 2. Common drugs used in the management of acute pancreatitis.

Hypovolaemia from vomiting, diarrhoea, and anorexia may contribute to the perpetuation of pancreatitis through reduced blood flow, and, therefore, should be aggressively managed. Rates are calculated to correct any hypovolaemia and dehydration present and to account for ongoing losses (for example, renal losses and vomiting). Frequent reassessment and rate adjustment is necessary.

In severe cases where oncotic support is required, a low dose bolus of dextrans or hetastarch could be considered. However, no benefit of plasma transfusion has been proven in the absence of prolonged coagulation times. Electrolyte disturbances should be corrected where present and, theoretically, lactated Ringer's solution is better than saline, due to the former's alkalising properties.

Analgesia

All dogs with acute pancreatitis should be considered painful, and many dogs will present with acute, often severe, cranial abdominal pain. This pain is mediated through a variety of local and central pathways; therefore a multimodal approach to treatment is recommended. Initially, in cases of acute pancreatitis – where hypovolaemia, dehydration and inappetence are likely present – opioid analgesia is a good first choice, particularly as dose and frequency can be escalated or de-escalated based on response. Pain scoring is recommended to monitor response to treatment – particularly in a busy clinic where multiple clinicians could be caring for individual cases.

The major clinical disadvantage of opioid administration in acute pancreatitis is their negative effect on gastrointestinal motility and appetite. In the clinic, methadone could be considered in severe cases, with buprenorphine for milder cases. Where milder or recovering cases are managed as outpatients, tramadol could be considered, although individual response to treatment is variable.

In dogs with severe pain, a continuous infusion of lidocaine and ketamine could be considered as an adjunct to opiate analgesia, while, in cases of intractable pain, seeking specialist advice is recommended as epidural analgesia or additional agents may be necessary.

Antiemetic

Administration of antiemetic medication is recommended – even in absence of actual vomiting – to promote early voluntary food intake. Maropitant is an ideal first choice, as it acts both centrally and peripherally and may provide additional benefits by reducing visceral pain and lung injury. Theoretically, dopaminergic antagonists – for example, metoclopramide – should be avoided. Serotonergic antagonists, such as ondansetron, could be considered instead, but their expense could be prohibitive.

Other drugs

The use of gastric acid suppression has not been proven in dogs with acute pancreatitis, although their use could be considered in cases with clinical signs consistent with gastric ulceration or oesophagitis – for example, haematemesis, melaena or regurgitation. Where required, oral omeprazole administered twice-daily is considered more effective than H2 blockers.

Antibiotics are not routinely indicated as acute pancreatitis is typically considered a sterile process. Exceptions include where evidence exists of bacterial translocation from the intestinal tract or pancreatic abscessation.

Similarly, corticosteroids are not routinely indicated and may be contraindicated – for example, where hyperglycaemia is present.

Nutrition

Non-vomiting dogs should be tempted to eat – for example, by intermittently offering small amounts of highly palatable, warmed food in a low-stress environment. The addition of mirtazapine to stimulate appetite has the advantage of providing additional antiemetic support (not to be used concurrently with tramadol due to potential for serotonin syndrome). In anorexic cases, early enteral intervention is preferable to total parenteral nutrition.

Intervention in dogs with mild pancreatitis is recommended after five days of anorexia. In contrast, dogs with severe pancreatitis should have a feeding tube (for example, naso-oesophageal or oesophageal) placed as soon as possible, even if the administration of full nutritional requirements is initially not tolerated.

As many dogs with acute pancreatitis have hyperlipidaemia, selection of a low-fat diet is preferable, albeit clinically unproven; however, this may be difficult to achieve with some narrow-bore feeding tubes.

Complications

Acute pancreatitis can be rapidly fatal, with mortality rates in excess of 50% in some referral centre studies[10]. Causes of death or euthanasia include development of intractable pain, acute kidney injury secondary to hypovolaemia and ischaemia, intravascular coagulopathy, acute lung injury and multiple organ failure. However, these mortality rates are likely to represent the most severe, and potentially include cases where cost was a factor in the owner’s decision.

Acute worsening of cases may be associated with the development of fluid accumulations associated with the inflamed pancreas. Supportive management of clinical signs or ultrasound-guided percutaneous drainage have been recommended in preference to surgery[10], which has been associated with a very high mortality. These fluid accumulations uncommonly develop into pancreatic abscesses, which are ideally managed with antimicrobials (selected on the basis of

culture and sensitivity) prior to surgical debridement, if possible. However, mortality remains high, even in the referral setting[11].

Dogs may suffer from recurrent acute episodes of pancreatitis, which can be expensive and frustrating to owners. Management during acute episodes is unchanged, while in the longer term, management of potential risk factors – for example, hyperlipidaemia – should be attempted.

Owners should also be warned regarding the potential to develop exocrine pancreatic insufficiency or DM, or both, which can complicate diagnosis and management of all three disorders. Maintaining diabetic control can be difficult, as pancreatic inflammation waxes and wanes, leading to these cases being termed “brittle”, and could account for the increased mortality in affected dogs[12].

Take home messages

- Clinical signs/history often non-specific – have it on your differential list.
- No diagnostic test is 100% sensitive or specific.
- Rule out concurrent complications – it does not have to happen in isolation.
- Manage acute cases aggressively with fluid therapy, analgesia, antiemetics and early nutritional support.
- Chronic cases can be frustrating to diagnose, difficult to manage and may result in exocrine pancreatic insufficiency and/or DM.
- Please note some drugs in this article are used under the cascade.

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