Intermittent pancreatitis in a 2-year-old Chihuahua mixed breed dog

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Abstract — A 2-year-old, female, Chihuahua mixed breed was presented on multiple occasions with vomiting and diarrhea. Diagnostic tests, including blood analyses and ultrasonography, established pancreatitis as the cause of gastrointestinal irritation. Hospitalization and supportive care, followed by maintenance of a prescription gastrointestinal diet, allowed management of the disease.

Résumé — Pancréatite intermittente chez un Chihuahua de race croisée âgé de 2 ans. Une femelle Chihuahua de race croisée âgée de 2 ans a été présentée à maintes reprises pour vomissement et diarrhée. Des tests diagnostiques, dont des analyses sanguines et des échographies, ont révélé que l’irritation gastro-intestinale était causée par une pancréatite. Une hospitalisation et un traitement de soutien suivi d’un maintien sur une diète gastro-intestinale de prescription ont permis de contrôler la maladie.

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A 2-year-old intact, female Chihuahua mixed breed was presented to the small animal clinic of the Veterinary Teaching Hospital (VTH) of the Western College of Veterinary Medicine (WCVM), with speculation by the owner of a potential toxicity. The dog had a 2-day history of diarrhea and passed soft stool that had evidence of blood. The dog had also begun to vomit a clear foamy material on the previous day, thought to have occurred after eating grass. She had progressively worsening inappetance and was not drinking water. These latter signs began 4 d previously after the dog had been at a lake and had subsequently been bathed with a flea (pyrethroid permethrin) shampoo for the 1st time. The owner had administered bismuth subsalicylate (Pepto-Bismol; Procter & Gamble, Toronto, Ontario) the night before presentation, but the dog had vomited it. The owner indicated that the dog had always had a sensitive gastrointestinal tract and was being fed quality commercial dog food (Nutrience Premium; Hagen, Montreal, Quebec), supplemented with soft dog food (Cesar; Dare Foods, Kitchener, Ontario), and was not given any human food. The dog had been vaccinated 1 mo previously at her regular veterinary clinic and had just finished her estrous cycle.

On presentation, the dog weighed 2.05 kg, appeared depressed, and stood in a hunched position. During the physical examination, she did not show apparent signs of pain on abdominal palpation. She had a heart rate of 120 beats/min, a respiration rate of 24 breaths/min, and a rectal temperature of 38.8°C (the thermometer was covered with frank blood and mucus). Her mucous membranes were pink and her capillary refill time was less than 2 s. Her teeth had a moderate amount of tartar and she had a retained upper right deciduous canine tooth. She also had an open fontanelle and bilateral grade III luxating patellae. No other abnormalities were observed.

The differential diagnoses at this time were focused on the gastrointestinal tract and included inflammatory conditions, possibly from toxin ingestion and absorption; dietary indiscretions or sensitivities; infectious causes, such as parvovirus, Salmonella spp. or Coccidia; an intestinal accident, such as an intussusception or ingestion of a foreign body; liver disease; or pancreatitis. The initial diagnostic plan included blood analysis, radiographs of the abdomen, and possibly ultrasonography. In-hospital monitoring and IV fluid therapy (lactated Ringer’s solution) were begun.

Prairie Diagnostic Services, WCVM, ran a complete blood (cell) count (CBC), biochemical profile, and urinalysis. The leukogram showed evidence of a mild inflammatory response (white blood cells [WBC] 15.1 × 10^9/L; reference range, 4.8 to 13.9 × 10^9/L) with a neutrophilia (13.7 × 10^9/L; reference range, 3.0 to
10.0 \times 10^9/L), and a mild regenerative left shift (bands 0.15 \times 10^9/L; reference range, 0.0 to 0.1 \times 10^9/L). A lymphopenia (0.91 \times 10^9/L; reference range, 1.2 to 5.0 \times 10^9/L), was also present, most likely stress induced. The erythrogram was unremarkable. The urinalysis demonstrated only ketonuria and scant granular casts, the latter suggestive of mild acute renal tubular injury. The biochemical profile showed an increased amylase (3247 U/L; reference range, 343 to 1375 U/L), indicative of pancreatic injury resulting in leakage of the enzyme into the circulation, although the enzyme may originate from other sources, such as gastric and intestinal mucosa (4); a mild alkaline phosphatase elevation (97 U/L; reference range, 9 to 90 U/L), secondary to pancreatitis or indicative of hepatobiliary dysfunction. A mild panhypoproteinemia (total protein: 49 G/L; reference range, 55 to 71 G/L, albumin: 24 G/L; reference range, 28 to 38 G/L), which may have resulted from gastrointestinal bleeding, hepatic damage, or vascular and peritoneal leakage (2). Creatinine levels were low, possibly due to decreased muscle use and lethargy (16 \mu mol/L; reference range, 41 to 121 \mu mol/L). Prerenal azotemia was not apparent, but it occurs in 50% of dogs with pancreatitis from dehydration and volume contraction (2). Interestingly, the lipase levels, which are usually increased together with amylase, were within the normal range. Lipase and amylase activity does lack specificity; both lipase and amylase have a short half-life and levels are influenced by a number of other disease conditions, such as renal failure, dehydration, and hyperlipidemia (3). The most useful marker of pancreatic inflammation is a pancreatic lipase immuno-reactivity (cPLI) assay that is increasingly available and more beneficial in conclusively diagnosing pancreatitis (1,2,4).

Abdominal radiographs were unexceptional, revealing a gas-filled colon and cecum, empty small intestine and stomach, and no evidence of a foreign body. In this case, ultrasonographs did not confirm pancreatitis, even though ultrasonography is considered the “gold standard” (1,5). The only abnormality observed was a greater than normal variability in thickness and a lack of discrimination in the layers of the gastric wall. These changes were not severe enough to suggest gastric neoplasia, such as lymphosarcoma, leiomyoma, or leiomyosarcoma. Fecal analysis showed a negative zinc sulfate fecal flotation but significant growth of unspecified Clostridium perfringens on culture. Specifically, the C. perfringens Type A form is a normal intestinal inhabitant, but at normal levels, it can produce serious enterotoxemia and enteropathy, and has been implicated in causing canine hemorrhagic gastroenteritis (6).

Pancreatitis and possibly colitis were the primary diagnoses, although liver lesions, including portosystemic shunting, were a differential diagnosis. Pancreatitis develops by a self-perpetuating autodigestion of the pancreatic tissues from premature zymogen activation within the acinar cells (2–4). Normally, the zymogens are segregated intracellularly from the enzyme containing lysosomes. This initially causes a mild edematous pancreatitis and may progress to a hemorrhagic or necrotic pancreatitis with multisystem involvement from the active pancreatic enzymes and inflammatory mediators released into the blood vessels. Vascular collapse can occur from fluid loss, due to vomiting and diarrhea, release of vasoactive substances, release of cardiodepressant substances, or fluid sequestration within the abdominal cavity (5). Acute pancreatitis is considered a potentially devastating disease, where hypovolemic shock and disseminated intravascular coagulopathy can develop; thus, it should be treated aggressively (2,3). The colitis may be secondary to pancreatitis, as the transverse colon passes dorsal to the pancreas and is susceptible to local inflammation (1).

Goals of treatment include the following: removing the inciting cause, if possible; restoring and maintaining intravascular volume and pancreatic perfusion; decreasing pancreatic secretion; relieving pain; managing complications that may delay recovery; and providing nutritional support (2). The initial treatment plan involved correction and maintenance of the fluid, electrolyte, and acid-base balances, while the pancreas was rested by administering nothing per os (NPO). Intravenous lactated Ringer’s solution was administered at a rate of 3 times maintenance (15 mL/h) for 2 h and continued at 10 mL/h.

During the first 48 h of hospitalization, the dog became more bright, alert, and responsive (BAR). Vital signs remained stable, but the animal continued to have bile-like vomitus and loose, blood-stained, mucoid feces. Recent reports indicate the need for analgesia, even in the absence of apparent signs of pain (4), as in this case. Pain was managed by administering oxymorphone (oxymorphone HCL; Dupont Pharma, Mississauga, Ontario) 0.05 mg/kg bodyweight (BW), IM, as required, not to exceed q4h. On day 3 of hospitalization, the vomiting resolved, but the dog continued to have mucoid hematochezia, with intestinal casts of mucosa. Associated straining during and postdefecation was also suggestive of colitis.

The CBC, biochemical profiling, and urinalysis were repeated. The leukogram continued to show an ongoing inflammatory response (WBC 19.3 \times 10^9/L) with a neutrophilia (15.4 \times 10^9/L) and a mild regenerative left shift (bands 0.39 \times 10^9/L). The urinalysis indicated only mild ketonuria. The biochemical profile results now showed a normal amylase (661 U/L). A panhypoproteinemia was still apparent (total protein: 42 G/L; albumin: 19 G/L), possibly due to the ongoing gastrointestinal bleeding or administration of IV fluids. Creatinine levels remained low (14 \mu mol/L). In the morning of day 4, the dog’s condition had improved to the point that water was given and then a small amount of food, low in fat and protein (Hill’s Prescription i/d; Hill’s Pet Nutrition, Topeka, Kansas, USA). No induction of vomiting or diarrhea was observed.

The dog was sent home later that afternoon with the advice that the dog was not fully recovered but showing signs of improvement. The owner was asked to keep her quiet, stress-free, and warm, and to monitor for lethargy, soreness, vomiting, and diarrhea. Mild diarrhea was anticipated for only a few days longer. A restricted diet of frequent small meals of the diet low in fat and protein was prescribed for 8 to 9 d while the intestinal inflammation resolved, followed by an option to transfer back to her previous regular diet. A phone interview 4 d later.
revealed that the dog was doing well with no vomiting or diarrhea and was eating well with a normal activity level. The owner declined antibiotic therapy for the *C. perfringens* infection but had decided to continue with the low fat and protein diet to help prevent future episodes of inflammation.

A month later, the dog returned to the VTH with reports of stomach pains at night, irregular eating patterns, and frequent constipation. No new abnormalities were detected on a physical examination and body weight was maintained (2.09 kg). The differential diagnoses at this time was recurring pancreatitis, selective appetite, or irritable bowel disease. The owner declined blood analysis and decided to take the animal home and try changing to a low fat diet (Medi-Cal Gastro Formula; Medical/Royal Canin Veterinary Diet, Guelph, Ontario; Waltham Royal Canin low fat formula; Royal Canin Veterinary Diet, Guelph, Ontario).

Four months later, the dog was readmitted to the VTH after vomiting 5 to 6 times that afternoon. During the previous week, the owner had started to supplement the dog’s diet with a bone and raw food (BARF) diet (hamburger patty and ground bone). The owner believed that the dog had just gone into heat, as she had seen her licking at her swollen vulva. On physical examination, the dog’s abdomen appeared to be nonpainful and her weight was stable at 2.11 kg. Based on her previous history, it was speculated that the change in diet and ingestion of a high level of protein and fat in the raw food had caused a recurrence of the pancreatitis. The dog was hospitalized and IV fluids were administered. Diagnostic tests carried out included blood analyses, and ultrasonography was planned.

The leukogram indicated only a mild monocytosis (1.48 × 10^9/L; reference range, 0.08 to 1.0 × 10^9/L), indicating a peripheral demand for macrophages with a mild established inflammatory response. The erythro-gram was unremarkable. The biochemical profile showed an elevated amylase (8600 U/L) and an elevated lipase (3190 U/L; reference range, 52 to 305 U/L). The pathologist noted that an absence of a concurrent inflammatory leukogram is abnormal, but it can occur. Cholesterol levels were elevated (7.86 mmol/L; reference range, 2.70 to 5.94 mmol/L), probably resulting from acute pancreatic necrosis, postprandial sampling, or a high fat diet. Ultrasonography showed a pancreas that was small with fibrotic changes (hyperechogenicity), likely due to chronic inflammation.

The dog continued to receive nothing by mouth and remained bright, alert, and responsive with no diarrhea, but she continued to vomit a bile-like material. Antibiotics, ampicillin (Novo-Ampicillin; Novopharm, Toronto, Ontario), 22 mg/kg BW, IV, q8h, was administered to prevent secondary infection. Heparin (Heparin Sodium; LEO Pharma, Thornhill, Ontario), 70 units/kg BW, SC, q12h, was administered to prevent thromboembolic tendencies and disseminated intravascular coagulopathy (DIC), but this treatment has yet to be critically evaluated (2), because disseminated intravascular coagulopathy may occur from consumption of plasma protease inhibitors, such as α-macroglobulins, that prevent enzymes from entering the intravascular space (1). On day 3, the dog vomited only once but became increasingly depressed, had abdominal pain, and was reluctant to go on walks. Oxytetracycline (Numorphan; Bristol-Myers Squibb Canada, Montreal, Quebec), 0.06 mg/kg BW, IM, q4h as required, was administered. Doses of the gastric acid inhibitor famotidine (Pepcid; Merck Frosst CAN, Kirkland, Quebec), 0.5 mg/kg BW, SC, q24h, were initiated to prevent ulceration, gastritis, and esophagitis (6). Plasma acquired from VTH blood donors, 1.3 mL/h for 24 h, was transfused to provide plasma protease inhibitors to prevent DIC and further digestion of the pancreas (1), and supply plasma proteins to help maintain blood pressure (4). Optimally, clotting would be monitored regularly by an activated clotting time (ACT), but due to the large blood volume required and small size of the dog, only clinical signs were assessed. A CBC was repeated and now showed a moderate inflammatory response (WBC 25 × 10^9/L) with a neutrophilia (20.8 × 10^9/L) and a marked regenerative left shift (bands 2.0 × 10^9/L). A lymphopenia (0.5 × 10^9/L) and mild monocytosis (1.75 × 10^9/L; reference range 0.08 to 1.0 × 10^9/L) were also present.

On day 5 postadmission, the dog became more BAR and had not vomited since day 3. Her weight had decreased to 1.8 kg, likely due to a prolonged period of not being fed by mouth. On day 6, a CBC revealed an attenuation of the inflammatory response (WBC 14.1 × 10^9/L) with a persisting left shift (bands 0.85 × 10^9/L) and mild monocytosis (2.3 × 10^9/L). Amylase (8767 U/L) and lipase (148 U/L) had returned to normal levels. Water and a small amount of a balanced diet for dogs with acute and chronic gastrointestinal problems (Medi-Cal Gastro Formula; Medi-cal/Royal Canin) were given without vomiting. The dog was discharged on day 7 following steady improvement in activity and appetite. The owner was instructed to administer amoxicillin and clavulinate potassium (Clavamox; Pfizer, Kirkland, Quebec), 16 mg/kg BW, PO, q12h for 10 d, and was strongly recommended to feed a prescription gastrointestinal diet for life. Suggestions were also made for the dog to undergo ovariohysterectomy and deciduous canine tooth removal. For the next 2 y, the dog did not have a recurrent episode of pancreatitis while being maintained exclusively on the balanced diet for acute and chronic gastrointestinal problems. On one occasion, the dog was hospitalized 1 h after ingesting 2 entire pieces of fried chicken, with severe gastrointestinal distension (abdominal radiographs) and discomfort; vomiting was induced and the dog recovered without further adverse effects.

The pivotal component in management of an animal with either acute or chronic pancreatitis or colitis is dietary adjustments (1–4). The goal is to decrease pancreatic stimulation but still provide adequate nutrient levels (1). Initially a food with high carbohydrate content such as rice, pasta, potatoes, can be given, as protein and fat are more potent stimulators of pancreatic secretion and will increase the likelihood of relapse (4). Then an exclusive low-fat gastrointestinal maintenance diet (Hill’s Prescription i/d, Medi-Cal Gastro Formula, or Waltham’s/Royal canin low fat) should be introduced gradually and fed for life. Such a diet contains more easily digested protein and carbohydrate sources, is supplemented with omega-3 and -6 fatty acids, and antioxidants, such as...
vitamin E. One of them (Medi-Cal Gastro Formula) also has added fructo-oligosaccharides and digestive enzymes that are stated “to improve digestion, maximize nutrient benefit and reduce the likelihood of diarrhea.” If hyperlipidemia or obesity should be a contributing factor, a diet with a fat content below 10% dry matter (DM) is recommended. The composition of protein, lipid, and fiber in these diets are compared in Table 1.

Pancreatitis is the predominant exocrine pancreatic disease that occurs commonly in dogs (4). Acute pancreatitis is reversible, with removal of the inciting cause, whereas chronic pancreatitis results in irreversible histopathological changes, such as atrophy and fibrosis occurring from the persistent inflammation. The following causative factors of pancreatitis have been identified but are in no way comprehensive. Hyperlipidemia (as may occur idioopathically in miniature schnauzers and Shetland sheepdogs), genetics, viruses such as Canine parvovirus, Mycoplasma, parasites, drugs, cholinesterase inhibitor insecticides and cholinergic agonists, scorpion stings, zinc toxicosis, and hypercalcemia have all been implicated with causing pancreatitis (1–4). Partial or complete obstructions of the pancreatic ducts, surgical manipulation, reflux of duodenal juice into the pancreatic ducts, for example, with vomiting, and blunt abdominal trauma are also possibilities. Whatever the trigger, ischemia has been implicated as a causative or exacerbating factor (4).

The exact inciting etiology of each individual case is usually unidentified despite the extensive list of potential risk factors. A history of a dietary indiscretion commonly precedes clinical symptoms of vomiting, weakness, abdominal pain, depression, and diarrhea. Episodes can be very unpredictable in their occurrence and severity. Pancreatitis can affect an animal of any age or body condition, but it is primarily seen in the middle-aged (5 y) or older dogs, and more frequently in females (2,4,5). It has been suggested that the disease is more prevalent in obese animals (43% in a recent report [1]), less severe in lean animals, and there is evidence that a high fat-diet induces pancreatitis (4). Thus, nutrition appears to be both an important component of predisposing individuals to pancreatitis, as well as being integral in its prevention.

### Table 1. Comparison of nutritional factors in canine gastrointestinal diets (expressed as % dry matter). Modified from Hands et al (3)

<table>
<thead>
<tr>
<th>Product</th>
<th>Protein</th>
<th>Fat</th>
<th>Fiber</th>
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</thead>
<tbody>
<tr>
<td>Hills Prescription Diet i/d</td>
<td>26.4</td>
<td>13.6</td>
<td>1.2</td>
</tr>
<tr>
<td>Iams Eukanuba Low-Residue</td>
<td>25.4</td>
<td>10.6</td>
<td>2.1</td>
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<tr>
<td>Medi-Cal Gastro Formula</td>
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<td>11.7</td>
<td>2.0</td>
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<td>Purina CNM EN-Formula</td>
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<td>11.7</td>
<td>1.1</td>
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<tr>
<td>Waltham/Pedigree Low Fat</td>
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<td>5.4</td>
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### References