Eosinophilic gastroenteritis in a domestic ferret

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Abstract — Eosinophilic gastroenteritis without peripheral eosinophilia was diagnosed histologically in a 5-year-old neutered male ferret showing acute signs of projectile vomiting, dark mucoid diarrhea, and chronic weight loss for 2 mo. The ferret was clinically normal after 4 days of treatment with parenteral fluids, antibiotics, and corticosteroids.

Résumé — Gastroentérite éosinophile chez un furet domestique. Une gastroentérite éosinophile sans éosinophilie périphérique a été diagnostiquée à l'histologie chez un furet mâle, castré, âgé de 5 ans, présentant des signes aigus de vomissements en fusée, une diarrhée mucoïde noire et une perte chronique de poids depuis 2 mois. Le furet était cliniquement normal après 4 jours de traitement comprenant fluides parentéraux, antibiotiques et corticostéroïdes.

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A 5-year-old, 1-kg, neutered male domestic ferret (*Mustela putorius furo*) with dark, scant, mucoid feces had been vomiting for 2 d and losing weight for 2 mo. The ferret had a history of surgery to remove a gastrointestinal foreign body the previous year. It was housed outside with other ferrets that were all clinically normal. The diet consisted of pelleted ferret food (Ferret Diet, Rolf C. Hagen, Montréal, Québec) and sweetened breakfast cereal (Fruitloops, Kellogg, London, Ontario).

The ferret was depressed, thin, mildly dehydrated, and infested with fleas. The axillary temperature (39.5°C) and heart rate (232 beats/min) were within normal range (1). The respiratory rate was at the high end of normal at 36 breaths/min (1). Auscultation of the heart and lungs was unremarkable. An abdominal mass was palpated and was suspected to be an enlarged organ or foreign body. The ferret exhibited vigorous projectile vomiting 3 times during the examination.

Plain radiographs of the abdomen revealed no abnormalities. Differential diagnoses at this time included gastrointestinal foreign body, eosinophilic gastroenteritis, *Helicobacter mustelae*-associated gastritis/ulceration, lymphoma, acute viral enteritis, and hepatopathy.

Balanced electrolyte solution (Lactated Ringer's Solution, Abbott Laboratories, Saint-Laurent, Québec), 25 mL/kg body weight (BW), SC, was administered. The ferret was mask-induced and maintained on isoflurane, and a ventral median exploratory laparotomy was performed. No foreign body was found and no gross lesions were evident, other than a thickened pylorus and enlarged spleen. Biopsies were taken from the greater curvature of the stomach, the antimesenteric border of the jejunum, and the quadrate lobe of the liver. A fine-needle aspirate was taken from the spleen for cytological examination. Prior to recovery, a blood sample was taken from the jugular vein. Dexamethasone (Dexamethasone 5, Vétoquinol N-A, Lavaltrie, Québec), 2.3 mg/kg BW, SC, and ampicillin (Ampicin, Bristol Laboratories, Montréal, Québec), 7.0 mg/kg BW, IV, were administered.

The hemogram demonstrated a mildly regenerative anemia with a packed cell volume of 0.35 L/L (published normal range, 0.36 to 0.50 L/L(1)); a high mean corpuscular volume of 55 fL (published normal range, 42.6 to 51 fL (2)); and low hemoglobin (107 g/L; published normal range, 120 to 163 g/L (1)). The white blood cell (WBC) count was significantly low (2.0×10^9/L; reference range, 7.7 to 15.4×10^9/L). There were 30% lymphocytes (published range, 28% to 69% (2)), with absolute lymphopenia (0.6×10^9/L; calculated range, 3.16 to 7.80×10^9/L); 5% eosinophils (published range, 0% to 7% (2)), with a normal absolute count of 0.1×10^9/L (calculated range, 0 to 0.79×10^9/L); and 2% monocytes (published range, 3.4% to 8.2% (2)), with monocytopenia (0.04×10^9/L; calculated range, 0.38 to 0.93×10^9/L). Absolute ranges were calculated by using the mean WBC and relative reference ranges reported in the literature (1).

Serum glucose was normal (4.3 mmol/L; published range, 3.5 to 7.4 mmol/L (1)). A serum biochemistry panel showed hypocalcemia (1.91 mmol/L; published range, 2.2 to 2.7 mmol/L (2)), hypoproteinemia (48 g/L; published range, 53 to 72 g/L (2)), hypoalbuminemia (26 g/L; published range, 33 to 41 g/L (2)), and increased alanine aminotransferase (ALT) (381 U/L; published range, 82 to 289 U/L (2)) and aspartate aminotransferase (AST) (306 U/L; published range, 30 to 120 U/L (1)). Venous carbon dioxide (13 mmol/L; published

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range, 20 to 28 mmol/L (2)) and serum chloride (104 mmol/L; published range, 102 to 121 mmol/L (2)) were low, to be expected after loss of gastric acid by vomiting.

Splenic cytological evaluation revealed hematopoietic tissue, including megakaryocytes, large blasts, small lymphocytes, and cells of the myeloid and erythroid series. Histological examination revealed inflammation in the stomach, jejunum, and liver. Noticeable infiltrates of eosinophils, associated with a smaller number of lymphocytes, were seen in the depths of the gastric mucosa, but eosinophils were less prominent in the lamina propria of the more superficial mucosa. Few spiral bacteria were detected, and the mucosal surface was covered with a mature epithelium. The lamina propria of the jejunum was edematous, with a moderate infiltrate of eosinophils and smaller numbers of lymphocytes. A discontinuous band of inflammatory cells was seen at the base of the crypts. The crypt:villus ratio was within normal limits, and the villi were covered with columnar epithelial cells. No erosions were observed in the stomach or small intestine.

There was mild, predominantly periportal, inflammation in the liver, with a mixture of mononuclear cells, neutrophils, and eosinophils in the portal tracts. Scattered infiltrates of similar cells were found throughout the parenchyma, and there were foci of necrotic hepatocytes surrounded by numerous neutrophils. There was no evidence of neoplasia in any of the biopsy samples.

On the basis of these findings, eosinophilic gastroenteritis (EG) and splenic extramedullary hematopoiesis were diagnosed, with mild suppurative hepatitis attributed to an ascending bacterial infection. Extramedullary hematopoiesis is a common finding in older ferrets and is considered clinically insignificant (3).

The ferret was hospitalized for 4 d after surgery. An isotonic, balanced electrolyte solution (25 mL/kg BW, SC, q12h) and ampicillin (7 mg/kg BW, SC, q12h) were administered concurrently for 2 d. The fluid replacement dose was increased to 50 mL/kg BW on the third day. Dexamethasone, 1.9 mg/kg BW, SC, was given daily. No vomiting was observed and appetite increased to normal on the original diet of sweetened breakfast cereal and bulk ferret food provided by the owner. The ferret was discharged on amoxicillin and clavulanic acid (Clavamox, SmithKline Beecham, West Chester, Pennsylvania, USA) in strawberry syrup (15 mg/kg BW, PO, q12h) for 2 wk, and oral prednisone (Deltasone, Pharmacia & Upjohn, Orangeville, Ontario) (2.3 mg/kg BW, PO, q24h) for 1 wk, followed by a tapering of the prednisone dose for the subsequent 7 wk.

The ferret remained clinically normal and was returned to the hospital for hematologic evaluation 4 d after discharge. There was mild polychromasia. The total WBC and differential counts were estimated from counts of 20 high-power fields. The total WBC was calculated as 3.2×10^9/L, below normal but higher than at first presentation. Band cells were high (0.8×10^9/L; calculated range, 0 to 0.245×10^9/L) and neutrophils had increased but were still below normal (2.14×10^9/L; calculated range, 2.71 to 8.81×10^9/L (2)). Lymphopenia was even more profound (0.16×10^9/L). The eosinophil count had not changed.

Eosinophilic gastroenteritis has been documented in humans, dogs, cats, and horses (4,5), and was first described in ferrets in 1989 (5). It is characterized by focal or diffuse infiltration of the gastrointestinal tract with normal, mature eosinophils (6), in association with a persistent, absolute peripheral eosinophilia. Affected ferrets are usually 6 mo to 4 y old, with no sex predisposition (8). Clinical signs include chronic weight loss; anorexia; and bloody or mucoid diarrhea, or both. Episodic vomiting is occasionally observed (4,8). In one case, a ferret was presented for coughing (7), while another had a history of reproductive failure (8). Gastrointestinal signs probably depend on the segment of the gut most affected. Infiltration of eosinophils in the small intestinal mucosa may cause malabsorption and a protein-losing enteropathy with watery diarrhea, whereas infiltration of the colonic mucosa may cause bloody or mucoid diarrhea (10). Vomiting occurs as a result of eosinophilic inflammation of the gastric wall or mechanical obstruction of gastric outflow (9). In a recent study comparing 6 affected ferrets, weight loss and diarrhea occurred in 5 of the 6, and vomiting in 2, and no gastrointestinal signs were seen in 1 ferret (4).

Other findings typical of EG in ferrets include enlarged mesenteric lymph nodes, thickened intestine, thin body condition, and dehydration (8). Similar presenting signs are seen in dogs (11). Cats and humans tend to have more diverse organ involvement, such as heart, lung, and skin (6). The multisystemic form of the disease is less common but has been identified in ferrets (4,7).

Peripheral eosinophilia is considered diagnostic for EG (3,5,8), although one study reported 1 out of 3 affected ferrets with no increase in circulating eosinophils (5). Persistent, severe eosinophilia is a consistent finding in cats (10). In dogs, peripheral eosinophilia is considered a necessary finding for diagnosis (11), but an increase in circulating eosinophils is not found in every case (10). Anemia may also be noted in dogs (9), and leukocytosis has been observed in affected cats (6) and dogs (9,11). Leukocytosis was reported in 1 case of multisystemic eosinophilic syndrome in a ferret (7). Hypoproteinemia and hypoalbuminemia (3,8) are common findings in ferrets.

A definitive diagnosis of EG requires microscopic examination of tissue biopsies. Exploratory laparotomy is usually warranted, as clinical signs resemble those of foreign body ingestion. Often, gross lesions are noted, such as thickened intestine and stomach wall, and enlarged mesenteric lymph nodes (8). Abscesses may be found in multiple organs (12). The intestinal mucosa is infiltrated with large numbers of eosinophils and smaller numbers of other inflammatory cells, such as lymphocytes and macrophages (5). Inflammation may extend to the serosa, causing serositis (8). Reactive fibrous tissue, common in cats, is not observed in ferrets (8); however, biopsies of the mesenteric lymph nodes of ferrets may reveal Splendore-Hoeppli (SH) material. The SH phenomen is an eosinophilic granulomatous reaction in the form of concentric rings or clubs, often found surrounding helminths, bacteria, or fungi (5,8). No organisms have been observed in association with the SH phenomenon in ferrets with EG (4), and SH has not been documented in other species with EG (8).

Although there is no known etiology, an allergic mechanism is suspected (4,7). In species other than ferrets (8), peripheral eosinophilia is characteristic of an atopic or dietary allergic response (7) or a parasitic infection, especially in association with SH material. Eosinophilic gastroenteritis is not a neoplastic disease: the eosinophils are mature and neither atypical nor mitotic (6).

Treatment for EG consists of supportive care and immune suppression. Supportive care should include SC fluids (60 mL/kg BW, q24h) and a high-calorie diet (200–300 kcal/kg BW, q24h) (8). Corticosteroids are recommended to reduce the eosinophilic inflammation. Response to steroids is generally good for dogs and ferrets, although some may require medication for life (3,7). The recommended dosage is 1.25 to 2.5 mg/kg BW, PO, q24h, gradually tapering to q48h (3). Steroid treatment is generally ineffective in cats and humans (6), and prognosis is poor (4,6). Drugs used to treat humans include cyclophosphamide, vincristine, dapsone, and hydroxyurea (6). Alternative therapies reported in ferrets included ivermectin in one ferret (7,8) and surgical removal of a granulomatous lymph node in another (5).

In this case, the ferret displayed many of the characteristics of EG described in the literature. However, there were significant differences, most obviously the vigorous projectile vomiting, which has not been reported previously. In a study of 6 ferrets with EG, mesenteric lymph nodes were enlarged in all but one, which was not examined (4). However, the only gross lesions in this ferret were an enlarged spleen and a thickened pylorus.

Another significant difference was the lack of eosinophilia. This ferret had a normal relative and absolute eosinophil count, despite a heavy flea infestation. The cause of the leukopenia and monocytopenia is unknown. The neutrophilia and pronounced lymphopenia after treatment began was attributed to the effect of the corticosteroids. The concurrent increase in band cells and polychromasia are characteristic of hematopoietic regeneration.

Suppurative periportal inflammation in the liver is characteristic of an ascending bacterial infection. Localized erosions in the pylorus or the mesenteric border of the jejunum (which was not biopsied) may have been responsible for an ascending bacterial infection that caused suppurative hepatitis. Projectile vomiting may have been caused by gastric obstruction due to pyloric inflammation. Hypoalbuminemia and hypocalcemia were attributed to intestinal protein loss.

Eosinophilic gastroenteritis should be a differential diagnosis in a ferret with vomiting, weight loss, and anorexia, regardless of the peripheral eosinophilic count. An exploratory laparotomy is recommended to differentiate EG from gastrointestinal foreign bodies and other diseases with similar clinical signs. Supportive therapy with fluids and a high-calorie diet is essential. Immune suppression with corticosteroids may be effective in controlling the disease in ferrets.

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