

A Case of Canine Gastrinoma

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ABSTRACT. The dog of this case was a 10-year-old Shih Tzu with refractory vomiting, diarrhea and anorexia. Endoscopy revealed an unclear at gastric angle, a stenosis at pyloric antrum and congestion in duodenal mucosa. Since abnormal shadows of irregular echo-levels were disclosed by pancreas ultrasonography, serum gastrin level was determined with a suspect of gastrinoma. And an increase of serum gastrin was demonstrated. In addition, postmortem histological examination revealed that the pancreatic cells were positive for gastrin. Based on these findings, the dog was diagnosed as pancreatic gastrinoma.

KEY WORDS: canine, gastrinoma, Zollinger-Ellison syndrome.

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Gastrinoma or Zollinger-Ellison syndrome was first reported as a tumor and a syndrome in human medicine in 1955 [10]. Gastrinoma is a malignant endocrine tumor, that is mainly characterized by hypersecretion of gastrin derived from D cells in pancreatic Langerhans islets [1, 3, 6]. The clinical symptoms of gastrinoma in dogs and cats are usually severe vomiting, melena, anorexia, depression and weight loss caused by gastric hypersecretion due to hypergastrinemia [1–3, 5–9]. Iron-deficiency anemia due to gastrointestinal hemorrhage and anemia with upper gastrointestinal tract chronic inflammation sometimes occur [2, 5, 7, 9]. These symptoms are intractable, and gastric hypersecretion often causes ulceration in the stomach and duodenum, followed by perforation resulting in peritonitis [7]. As a diagnostic approach to gastrinoma, the observation of clinical symptoms [2, 9] and the determination of serum gastrin concentrations [1, 2, 9] as well as the performance of a biopsy [5, 9] and CT imaging [1, 9] with a radioisotope have been reported, but there is no report about a combined use of these methods for the diagnosis of gastrinoma in dogs. We report a case diagnosed as gastrinoma based on the clinical course, endoscopic findings, echograms and hematological findings in life, and the clinical diagnosis was confirmed by the postmortem examination.

A 10-year-old castrated male Shih Tzu, weighing 5.2 kg (6.3 kg at the first visit for the medical examination 4 months ago) was presented with a one-month history of persistent anorexia and frequent vomiting after meals despite being vigorous. The dog had a previous history of eye diseases including conjunctivitis and traumatic inflammation of the cornea.

The dog presented with marked emaciation and rough hair coat. Physical examination showed a body temperature of 38.5°C, no abdominal tenderness and pink mucous membrane. There was no abnormal bowel sound or cardiac murmur. Hematological examination revealed an increase in

WBC with increased Band and Seg. and a decrease in lymphocytes. Blood biochemical examination demonstrated a decrease in TP and K (Table 1).

Plain radiography showed no abnormality in the abdomen. Ultrasonography of the stomach and surrounding organs approached through the xiphoid process confirmed the retention of excessive gastric fluid and highly irregular contour of the gastric mucosa. In addition, a mixed echo pattern containing low and high echo levels was demonstrated from the greater curvature of the stomach to the pancreas region around the lower pyloric part (Fig. 1). Endoscopic examination of the stomach and duodenum

Table 1. Results of blood tests

Item	Unit	First	7 month
RBC	$\times 10^6/\mu\text{l}$	7.28	4.68
HGB	g/dl	14.3	12.2
PCV	%	45.7	32.7
MCV	fL	64.9	69.8
MCHC	g/dl	40.3	37.3
WBC	$\times 10^3/\mu\text{l}$	24.3	31.8
Band	$\times 10^3/\mu\text{l}$	3.14	0.32
Seg	$\times 10^3/\mu\text{l}$	17.98	26.38
Eos	$\times 10^3/\mu\text{l}$	3.3	0.95
Bas	$\times 10^3/\mu\text{l}$	0	0
Lym	$\times 10^3/\mu\text{l}$	0.25	1.91
Mon	$\times 10^3/\mu\text{l}$	0.38	2.54
BUN	mg/dl	14.1	15.5
Crea	mg/dl	0.4	0.2
ALT	IU/l	58	14
AST	IU/l	50	14
TP	g/dl	4.2	4.4
GLU	mg/dl	82	120
T-cho	mg/dl	132	115
Na	mmol/l	155	135
K	mmol/l	2.7	5.7
Cl	mmol/l	117	90



Fig. 1. Ultrasonographic findings of the stomach and peripheral organs approached from the xiphoid process of the sternum (HITACHI EUB-525 5.0 MHz 10R convex). A large amount of stagnated gastric fluid (bold arrows), stagnant due to anorexia and irregular gastric mucous, are demonstrated. In the pancreatic region from the greater curvature of the stomach to the lower pyloric part, an echo-pattern consisting of a mixture of low and high echo levels is depicted (arrow).



Fig. 2. Endoscopic findings at 8.1 mm external diameter and 1,100 mm effective length. An obstruction of the pyloric antrum and petechial bleeding at the same site.

revealed ulcer and cicatrization at the gastric angle, pyloric stenosis and petechial hemorrhage. Congestion of mucosa in the duodenum was also observed (Fig. 2).

At this point, the dog was suspected of having severe chronic gastritis, hypertrophic pyloric stenosis and chronic pancreatitis based on the clinical symptoms and diagnostic imaging by means of ultrasound and endoscope, and was treated with hydration therapy, H₂ blockers and metoclopramide hydrochloride. As a result, the symptoms were gradually improved in several days. Three months later, however, the dog was presented again with gastrointestinal symptoms, such as frequent vomiting. He was suspected of having helicobacter infection since gastric ulcers were observed. Concomitant treatment with amoxicillin and metronidazole was therefore conducted for one week as well as the same treatment as that used at the previous visit. The symptoms were temporarily improved, but the dog experienced alternately repeated aggravation and improvement of the symptoms. We then, determined fasting serum gastrin concentrations by using a radioimmunoassay that had been reported to be used in dogs [4]. The gastrin concentration was 410 pg/ml (RIA-Kit, ABBOTT, Japan), being remarkably higher than the 10–40 pg/ml (RIA-Kit, Becton and Dickinson, NY) [2], 27–85 pg/ml (no measurement system is described) [9] and 45–98 pg/ml (RIA-Kit, Becton and Dickinson) [4] reported as the normal values in dogs. We therefore provisionally diagnosed the condition as gastrinoma, a gastrin-producing tumor. Since exploratory laparotomy could not be conducted to confirm the tumor, only

symptomatic treatment was conducted. The disease gradually proceeded with repeated improvement and aggravation of symptoms alternately, resulting in death 7 months after the first visit.

One week before death, the dog weighed 4.7 kg with a body temperature of 37.9°C and had lost his vigor and appetite. The visible mucosa was slightly pale. Hematological examination revealed normocytic anemia, an increase in WBC with increased Seg. and an increase in monocytes. Blood biochemical test showed low TP and T-Chol values, decreases in Na and Cl and increases in K, but the blood glucose levels changed within the normal range throughout the clinical course (Table 1).

Macroscopic findings included the retention of about 100 ml of yellow intestinal fluid in the abdominal cavity and pyloric stenosis in the stomach, but the ulcers and erosion were improved. Many ulcerative lesions were observed in the duodenum, and some of them perforated the intestinal wall, resulting in peritonitis. Enlargement and congestion of the pancreas with increased hardness were observed, and it was partly discolored to yellow-brown.

Histopathological examination revealed solid or alveolar clusters of atypical tumor cells similar to islet cells in the right lobe of pancreas adjacent to the ulcers in the duodenum. These atypical cells had round to oval nuclei with narrow, eosinophilic granulated cytoplasm and had invaded the acinar cells of the exocrine pancreas (Fig. 3). The atypical cells had also invaded adipose tissues around the pancreas, and vascular inversion infiltration of the tumor cells was observed in the lymphatic vessels of the pancreas. Based on these findings, the dog was diagnosed with islet cell carcinoma. Immunostaining (DAKO, Carpinteria, CA) by means of an avidin-biotin-peroxidase complex method (gastrin, pancreatic peptide, insulin, glucagons and somatostatin) revealed that the majority of the tumor cells were positive for gastrin (Human/Rabbit/DAKO) (Fig. 4), partly

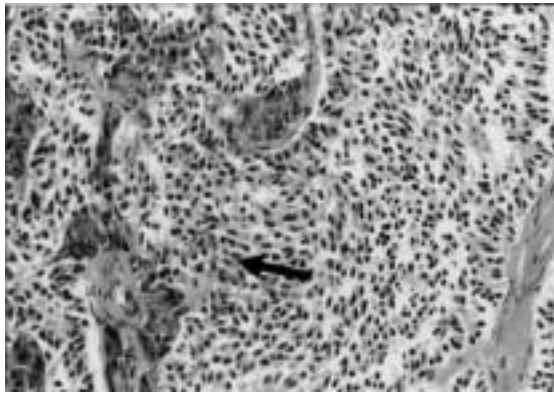


Fig. 3. The tumor cells of the pancreas are elliptic to cylindrical, with chromatin-rich nuclei. The cytoplasm is narrow with eosinophilic fine granules, and the border of the cytoplasm is obscure (arrow). (HE)

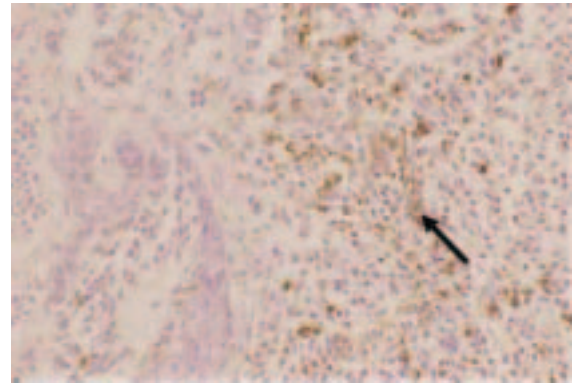


Fig. 4. Immunostaining with anti-gastrin antibody as the primary antibody (avidin-biotin-peroxidase complex method). Many gastrin positive tumor cells (arrow) are found in the pancreatic neoplasm.

positive for pancreatic peptide (Human/Rabbit/DAKO), partly positive for insulin (Swine/Gunia pig/DAKO) and negative for glucagons (Porcine/Rabbit/DAKO) and somatostatin (Human/Rabbit/DAKO). Pancreatic tumors mostly consist of one kind of hormone producing cells, although other kinds of hormone producing cells can sometimes be admixed in the neoplastic tissue [8], and this tumor was diagnosed as a pancreatic gastrinoma.

It is known that gastrinoma in dogs is a rare endocrine tumor [1, 2, 5, 9]. It occurs in dogs of middle to advanced age. There may be no difference in the incidence among breeds and between sexes. The prognosis is mostly poor since the tumor has already spread to the other organs including lymph nodes and liver at the time when the animal is diagnosed [2, 5, 9]. It has been reported that the life expectancy of dogs and cats treated with surgical and/or medical procedures was one week to 18 months (mean 4.8 months) [7]. The present dog survived for 7 months after the first examination. As medical treatments, histamine H₂ receptor antagonists, gastrointestinal protective agents including scalfate and prostaglandin E₁ analogues can decrease the gastric acidity, resulting in temporarily improvement of QOL in general [1, 2, 5]. We used histamine H₂ receptor antagonists, antiemetic drugs and hydration therapy and the symptoms were temporarily improved, but the reaction to these treatments became poor with time, and the general condition was gradually aggravated. As a result, peritonitis, due to intestinal perforation after duodenal ulcers occurred, resulting in death. The provisional

diagnosis of gastrinoma was made based on the clinical symptoms and the various test results, but it could not be confirmed in life. It has been known that definite diagnosis at the earliest possible time and surgical resection of the tumor are important in gastrinoma [2, 5, 9]. From the present results, pancreatic gastrinoma should be considered as one of the differential diagnoses in refractory gastritis of dogs.

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