

Case Report

Canine exocrine pancreatic insufficiency treated with porcine pancreatic extract

Ju-won Kim, Dong-in Jung, Byeong-Teck Kang, Ha-jung Kim, Chul Park, Eun-hee Park, Chae-young Lim, Hee-myung Park*

Department of Veterinary Internal Medicine, College of Veterinary Medicine, Konkuk University, Seoul 143-701, Korea

A 1.8-year-old intact female Maltese dog was presented because of a history of chronic diarrhea, polyphagia, weight loss, and coprophagia. The patient was severely emaciated and evacuated very moist and four-smelling, yellow feces. Fecal stain with Sudan III revealed numerous lipid droplets. Result of fat absorption test showed maldigestion. A definite diagnosis was made based on trypsin-like immunoreactivity assay in serum which was low enough to be diagnosed as an exocrine pancreatic insufficiency. After pancreatic enzyme supplement with porcine pancreatin powder, the clinical signs were disappeared. This case report documents clinical manifestations, diagnostic tools, treatment and efficiency of oral pancreatic enzyme replacement therapy of exocrine pancreatic insufficiency in a Maltese dog.

Key words: dog, exocrine pancreatic insufficiency, trypsin-like immunoreactivity assay

Exocrine pancreatic insufficiency (EPI) means impaired exocrine pancreatic excretion that results from severe progressive atrophy or inflammatory destruction of pancreatic acinar tissue [15]. Inadequate production of digestive enzymes-amylase, lipase, and proteases leads to a syndrome of maldigestion and malabsorption [1,10]. Typical clinical signs of EPI are weight loss, diarrhea, voluminous feces, steatorrhea, and polyphagia [7,10-14]. Feces are light in color, loose in texture, and can be quietly malodorous [7].

EPI is relatively common disease in dogs, especially in the German shepherd dogs and rough-coated Collies [7,10]. Pancreatic acinar atrophy (PAA), chronic relapsing pancreatitis, and pancreatic neoplasia were reported to cause EPI in dogs [2,10,12-14]. EPI is diagnosed on the basis of compatible clinical signs together with pancreatic function tests, such as measurement of circulating trypsin-like immunoreactivity

(TLI), which is classically low in this condition [4]. Treatment of EPI is the replacement of pancreatic digestive enzymes [8,10,12-14] and the prognosis is good if there are good responses, such as weight gain, decreased the volume of feces, and diminishment of steatorrhea [12-14].

The purpose of this case report is to present typical clinical signs and diagnostic tools of canine EPI and propose an effective enzyme replacement therapy.

A 1.8-year-old, intact female Maltese dog was referred to the Veterinary Medical Teaching Hospital of Konkuk University due to progressive weight loss, polyphagia, coprophagia, and chronic diarrhea. The duration of these problems is 3 months. On the history taking, the dog had shown no prior sign of systemic illness. She had been being fed a high-quality, commercial diet and housed indoors with her mother, and the mother was not shown those clinical signs at all. Rabies and canine distemper, hepatitis, parvovirus, parainfluenza, and leptospirosis vaccinations had been administered one month ago. The general condition of the patient was relatively normal except severe emaciation and the vital signs were normal. The hair around perineum was yellow-tinged and oily. Incompletely digested, yellow, grease, and malodorous feces were identified. On abdominal auscultation, borborygmus was detected. The hemogram revealed mild normocytic normochromic anemia and mild lymphocytosis. Serum chemistry findings were elevation of alanine aminotransferase (ALT; 121 U/l, reference range; 13-53 U/l) and alkaline phosphatase (ALP; 183 U/l, reference range; 0-142 U/l), hypoproteinemia (4.8 g/dl, reference range; 5.0-7.1 g/dl) with hypoalbuminemia (2.6 g/dl, reference range; 2.6-3.9 g/dl). There was no remarkable finding on radiographic studies.

A tentative diagnosis of EPI was supported by fecal stain with Sudan III solution. Fecal cytology revealed lots of red-orange colored droplets, which indicated the feces contained inadequately absorbed lipid that was steatorrhea (Fig. 1). We performed fat absorption test (triglyceride challenge test). After 12 hours fasting, basal serum triglyceride (TG) level was measured and administrated 3 ml per kg body weight of corn oil per oral. There was no significant difference in

*Corresponding author
Tel: +82-2-450-4140; +82-2-450-3037
parkhee@konkuk.ac.kr

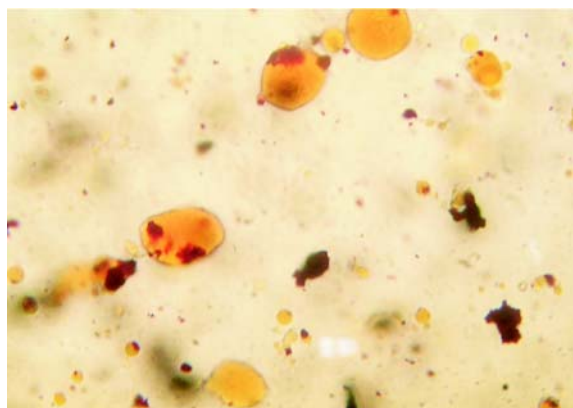


Fig. 1. Fecal stain with Sudan revealed red-orange colored lipid droplets, $\times 400$.

Table 1. Serum triglyceride levels before and after oral administration of corn oil only and corn oil plus pancreatic enzyme power (unit: $\mu\text{g/l}$)

Items	Corn oil	Corn oil + PE*
12 h fasting	41	42
1 h after administration	55	184
2 h after administration	48	164
3 h after administration	42	100

*PE; pancreatic enzyme power.

Table 2. Assay of serum cobalamin and folate

Items	Serum level
Cobalamin of EPI suspected patient	372.5 (ng/l)
Control range of canine serum cobalamin	225-660 (ng/l)
Folate of EPI suspected patient	2702 ($\mu\text{g/l}$)
Control range of canine serum folate	6.7-17.4 ($\mu\text{g/l}$)

serum TG levels before and after corn oil administration and there was no lipemia on gross examination (Table 1). When corn oil and two tea spoonful of pancreatic enzyme powder (Pancreatin; Sigma-Aldrich, Korea) were administered together, post-administration serum TG level was increased more than four-fold and lipemia was observed (Table 1). These results mean that the patient's fat absorption function was normal but fat digestive function was abnormal.

The definitive diagnosis was made on measurement of serum trypsin-like immunoreactivity (TLI) by radio-immunoassay. The serum sample was sent to Gastrointestinal Laboratory, Department of Small Animal Medicine and Surgery, Texas A&M University, USA. The result of TLI assay was $0.4 \mu\text{g/l}$ (reference range; $5\text{--}35 \mu\text{g/l}$), which was diagnostic for EPI. On assay of serum cobalamin (vitamin B12) and folate, folate level was increased far above control range, which indicated small intestinal bacterial overgrowth (SIBO) secondary to EPI (Table 2).

The goal of the treatment was relief of clinical signs and compensation of nutritional deficiencies. Pancreatic digestive

enzyme supplementation is the most important therapy [12-14]. Thus, among several products available, we used the frozen porcine pancreatic extract powder, Pancreatin. The daily maintenance volume of normal diet was determined by kg body weight, and divided into four meals. The porcine pancreatic powder was added per each meal. The initial dose was half teaspoon per each meal, and increased until there was no steatorrhea and other clinical signs were alleviated. The dosage was adjusted 3 times at 1 week interval and the effective dose was determined at one and half teaspoon per each meals. Later, the frequency of meal was decreased to three times a day.

Concurrent medication was aimed to control SIBO secondary to EPI and to correct nutritional deficiencies. Antibiotics therapy was initiated with ampicillin (30 mg/kg , PO, TID; Chong Kun Dang, Korea) and metronidazole (12 mg/kg , PO, TID; Celate Pharm Korea, Korea). Vitamin B complex (B-com; Yuhan, Korea) and vitamin E (CVS Pharmacy, USA) supplementation was continued for one month. Ferrous sulfate (Daewoong Pharm, Korea) was prescribed to correct mild anemia. Additionally, to improve liver function, Ursodeoxycholic acid (10 mg/kg , PO, SID; Korea United Pharm, Korea) and silymarin (70 mg/kg , PO, SID; Sinil Pharm, Korea) were added.

After treatment for one month, the typical clinical signs of EPI as diarrhea and steatorrhea were nearly diminished, and the body weight of the patient started to gain. The feces of the patient were decreased in volume and became solid. Fecal stain with Sudan III solution revealed few lipid droplets. After 8 weeks, the patient was good of general condition and the clinical signs were not recurrent any more. Mild anemia and elevated liver enzyme activities were corrected. Decreased TP and albumin were recovered to normal range. Antibiotics therapy was discontinued and pancreatin powder was prescribed only. After 3 months, there was no abnormal sign developed at all.

It has been reported that the serum activity of alanine aminotransferase (ALT) and alkaline phosphatase (ALP) may occasionally be mildly or moderately elevated in untreated EPI dogs [6]. Similarly, in this case, ALT and ALP were elevated and the other serum chemistry profiles were in normal range except serum protein level.

The measurement of serum canine TLI by radio-immunoassay is a sensitive and specific test of pancreatic acinal atrophy [14]. The concentration of serum TLI was recently determined to be markedly subnormal in dogs with EPI [3]. Serum TLI is species and pancreas specific [2]. Normal serum TLI values for dogs are 5 to $35 \mu\text{g/l}$. TLI values less than $2.5 \mu\text{g/l}$ are diagnostic for EPI, and values between 3.5 and $5 \mu\text{g/l}$ may reflect subclinical pancreatic disease [2,5,7,10,13,14]. Values between 2.5 and $3.5 \mu\text{g/l}$ are rarely associated with clinical signs due to EPI. Otherwise, serum TLI values above $50.0 \mu\text{g/l}$ are consistent with either acute or chronic pancreatitis or decreased renal

excretion due to severe renal insufficiency. In this case, the patient's serum TLI value was sufficiently low to be diagnosed for EPI.

Fat absorption test may be an alternative diagnostic tool for EPI but not considered sufficient for definitive diagnosis. The post-corn oil serum triglyceride (TG) values would be similar to the fasting values in dogs with EPI [13]. When the test is repeated with pancreatic enzyme powder supplemented to the corn oil, the post-corn oil serum TG values rise at least twofold over baseline, a tentative diagnosis of EPI can be made [13].

Serum cobalamin and folate assays are strongly recommended in cases of suspected EPI because serum vitamin abnormalities and secondary SIBO are common in dogs with EPI. The control range of canine serum cobalamin is 249-733 ng/l. Low serum cobalamin values below the reference range are seen in the patients with EPI, bacterial overgrowth in the upper small intestine, or diseases affecting the distal small intestine. Cobalamin deficiency has been identified in 36% to 76% of dogs with EPI. In the other hand, the control range of canine serum folate is 6.5-11.5 µg/l. Values above the control range are consistent with SIBO.

In several studies, German shepherd dogs compromise two-thirds of the cases identified to PAA, which is the most common cause of canine EPI and onsets before 2 years of age. Most of other reported cases are large breeds [10]. We can not identify the etiology of EPI in this case, but the time of onset was 1.7 years of age and the patient did not demonstrate no clinical sign associated pancreatitis. So the cause of EPI in this case is suspected PAA although Maltese breed dog is rarely reported to be identified EPI. To differentiate the cause of EPI, cytologic examination is needed following pancreatic tissue biopsy. But diagnosis of EPI is accomplished clearly by serum TLI assay so difficult and dangerous pancreatic biopsy examination is not required for routine diagnosis for canine EPI.

Dietary change such as low fat diet is indicated to improve clinical signs in the cases of no response to enzyme replacement therapy [13,14]. But in this case, a single frozen porcine pancreatin powder was enough effective, no subsidiary method was necessary and the clinical signs were almost completely diminished.

Client education was very important to achieve satisfactory response of treatment to adjust the volume and frequency of meal and enzyme powder. We had had sufficient discussions and continuous communication with owner so the owner did not give up the treatment and had maintained proper patient management.

Rare instances of dogs losing their requirement for pancreatic enzyme supplementation have been reported. In this case, discontinuation of enzyme supplementation promoted relapse of clinical signs so pancreatic enzyme supplementation will be required for the patient's whole life.

In conclusions, pancreatic enzyme supplement with porcine pancreatin powder and the treatment of SIBO were very effective in this case. The feces improved in appearance and volume immediately and the patient gained weight progressively. This report demonstrates that frozen porcine pancreatin powder can be used in management of EPI in dogs.

Acknowledgments

Special thanks are given to Dr. D.A. Williams and Dr. J.M. Steiner, Gastrointestinal Laboratory, Department of Small Animal Medicine and Surgery, Texas A&M University, USA and staffs of Cham Animal Hospital.

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