Juvenile Diabetes Mellitus Accompanied by Exocrine Pancreatic Insufficiency in a Dog

Ji-Houn KANG1), Ki-Jeong NA1), In-Pil MO1), Dongwoo CHANG1) and Mhan-Pyo YANG1)*

1)College of Veterinary Medicine, Chungbuk National University, Cheongju, Chungbuk 361–763, Republic of Korea
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ABSTRACT. A 6-month-old male crossbred dog weighing 0.78 kg was presented with acute bilateral immature cataracts, intermittent diarrhea and growth retardation. The clinical manifestations and laboratory findings were suggestive of concurrent juvenile diabetes mellitus (DM) and exocrine pancreatic insufficiency (EPI). Moreover, the DM was associated with a decreased level of serum insulin-like growth factor I. Histological examination revealed a markedly lower number of pancreatic islets and acinar cells. This case shows that juvenile-onset DM can occur simultaneously with EPI and result in growth retardation, acute cataract formation and a high cortisol concentration.

KEY WORDS: canine, diabetes, endocrinology.

Diabetes mellitus (DM) is a rare disease in dogs less than 1 year old [10, 11] but is one of the most common endocrine diseases in middle-aged and older dogs [8]. The recognized clinical forms of canine juvenile DM are insulin deficiency diabetes [1, 2] and insulin-dependent diabetes mellitus [17], although there are no internationally accepted criteria for classification of canine DM [6]. Recently, a case of juvenile DM similar to human type 1 DM was described in a dog [15]. The possible causes of canine juvenile DM are suggested to include congenital beta cell hypoplasia/abiotrophy, viral infection and/or autoimmunity [1, 2, 15, 16].

Exocrine pancreatic insufficiency (EPI) is a disease characterized by inadequate production of digestive enzymes from pancreatic acinar cells and is diagnosed based on clinical signs and a decrease in the circulating trypsin-like immunoreactivity (TLI) concentration [18, 21]. Canine EPI usually results from pancreatic acinar atrophy (PAA) and has been reported to be most common in the German shepherd [20]. Chronic pancreatitis is also a possible cause of EPI but is less commonly diagnosed in dogs than in humans or cats [19]. Clinical manifestations of EPI have rarely been reported in dogs less than 6 months old [20].

Since a case of PAA with EPI symptoms was described in a 3-month-old German shepherd with DM [17], clinicians have noted the possibility that EPI can occur simultaneously with canine juvenile-onset DM. However, concurrent DM is very rare in young dogs with EPI due to PAA because the endocrine portion of the pancreas in dogs with PAA is usually well preserved [6, 18]. Herein, we describe the clinical and pathological findings associated with alterations in the exocrine pancreas in a young dog with DM.

A 6-month-old male crossbred dog weighing 0.78 kg was presented with acute bilateral immature cataracts that had developed over the previous 2 days (Fig. 1). The owner reported that the dog frequently produced voluminous soft stools and that although the dog had a good appetite, his growth was very slow compared with that of his normal littermates. The dog had no history of vaccination. A physical examination showed that the dog was emaciated with mild dehydration and thin skin. The menace response was present in both eyes. Dental eruption was relatively normal, considering the dog’s poor physical condition.

The serum biochemical analyses revealed the following: hyperglycemia (18.4 mmol/l; reference interval [RI] 3.6–6.5 mmol/l), hypercholesterolemia (9.5 mmol/l; RI 3.5–7.0 mmol/l), hypertriglyceridemia (4.2 mmol/l; RI 0.2–1.3 mmol/l), hypoproteinemia (27 g/l; RI 54–71 g/l) with hypoalbuminemia (16 g/l; RI 26–33 g/l) and an elevated alkaline phosphatase value (269 U/l; RI 29–97 U/l). The anion gap was within the normal range, and serum osmolality was 322 mOsm/kg. A complete urinalysis revealed a specific gravity of 1.033 with glucosuria (15.5 mmol/l), but not ketonuria.

Fig. 1. External appearance of a juvenile dog with diabetes mellitus. Note the cataract formation in the right eye (the upper right corner of the photograph).

*CORRESPONDENCE TO: YANG, M.-P., Laboratory of Veterinary Internal Medicine, Department of Veterinary Medicine, College of Veterinary Medicine, Chungbuk National University, Cheongju, Chungbuk 361–763, Republic of Korea. e-mail: mpyang@chungbuk.ac.kr
The dog was hospitalized with close monitoring and initially rehydrated with intravenous infusion of Normosol-R (Plasma Solution A®, CJ Pharma, Seoul, South Korea) over the course of 4 hours. Blood analysis was performed again the following morning. The blood glucose concentration was decreased (9.7 mmol/l) but still higher than the reference range. Serum osmolality was 295 mOsm/kg. The diagnosis of DM was questioned due to the dog’s age and the decrease in serum glucose. A glucose tolerance test was performed to confirm the diagnosis of DM with the owner’s consent since intravenous administration of a glucose load may cause hyperosmolality. The blood glucose concentrations were outside the normal limits 3 hours after intravenous administration of a 50% dextrose solution (0.5 m/kg). The glucose concentrations of samples obtained before and 3 hours after the glucose load were 9.8 mmol/l and 13.1 mmol/l, respectively. The fasting serum insulin and fructosamine levels were 0.1 µU/ml (RI 2–21 µU/ml) and 584 µmol/l (RI 225–365 µmol/l), respectively. The serum insulin level was still at its lowest limit of detection (0.1 µU/ml) 1 hr after the 50% dextrose IV injection, and anti-insulin antibodies were not detected in the serum. The test results for insulin, anti-insulin antibodies and fructosamine only became available 9 days later because they had to be analyzed elsewhere. Moreover, the serum canine TLI value was below the normal range (2.3 µg/l; RI > 5.0–35.0 µg/l), suggesting decreased exocrine pancreatic capacity. These findings support the possibility of simultaneous occurrence of juvenile-onset DM and EPI.

On day 3, endocrine tests were performed to investigate the potential mechanisms involved in growth retardation as well as to rule out other endocrine disorders that cause growth retardation [10]. As shown in Table 1, the serum insulin-like growth factor I (IGF-I) concentration was very low, but the total T4 and canine thyroid stimulating hormone values were within the normal ranges. Anti-T4 antibodies were not detected in the serum. However, the low-dose dexamethasone suppression test unexpectedly failed to suppress serum cortisol.

The owner did not consent to medical treatment of the dog and ultimately requested euthanasia; the dog subsequently underwent a post-mortem examination. The pancreas was much smaller than normal. A histological examination revealed that the pancreatic islets were markedly reduced both in number and size and that there was no inflammation, indicating atrophy of the pancreas. Disorganized acinar cells with reduced zymogen granules were prominent (Fig. 2). There was no specific histopathological change in either the pituitary or adrenal glands. In addition, the canine distemper virus (CDV) was not detected by a nested polymerase chain reaction assay using a sample prepared from the pancreas tissue.

The clinical manifestations and laboratory findings indicated that the dog had suffered from juvenile DM and that EPI might occur simultaneously although a single TLI measurement was only performed. Moreover, although immunohistochemical testing of the pancreas was not performed, the histopathological findings indicated that there was an insufficient number of islet cells and a loss of acinar cells. These changes in the pancreas were consistent with the findings of a case of concurrent DM and EPI reported previously [17]. There are a few published reports of histopathological study of young dogs with DM [1, 2, 16]. In one study of four dogs [1], pancreas samples were characterized by mild to severe diffuse atrophy of acinar cells and congenital beta cell aplasia. An inherited, early-onset form of diabetes characterized by islet hypoplasia has also been reported in the Keeshond [16]. In another study, seven of eleven dogs diagnosed with DM had no recognizable islets, and acinar atro-
phy was detected in four of these dogs [2]. In these reports [1, 2, 16], however, TLI was not measured, and the various complications, such as cataract formation, were also not reported. In the present case, no inflammatory changes, such as lymphocytic infiltration, were observed in the pancreas, which is similar to cases of juvenile-onset DM reported previously [1, 2, 16, 17]. Lymphocytic infiltration of pancreatic islets has been suggested to occur in only a portion of dogs with adult-onset DM [2, 6], but recently one case of lymphocytic insulitis in a juvenile dog with DM has been reported [15].

Concurrent DM and EPI may be due to simultaneous damage of the endocrine and exocrine pancreatic tissue, which could be caused by viral infection. Evidence of virus-induced DM has been presented in humans and animals [14]. It has been proposed that canine distemper virus may particularly be involved in the pathogenesis of juvenile DM [11]. However, the results of nested polymerase chain reaction assay for the present case, performed to detect CDV using histologic sections of the pancreas, were negative. This finding suggests that CDV was not the cause of DM and EPI, but it cannot be excluded that other viruses not tested in this case may have caused the syndrome.

Uncontrolled DM can cause additional complications in young dogs. In the present case, the serum IGF-I concentration was very low and growth was retarded. Because both insulin deficiency and nutritional deprivation caused by DM can alter the growth hormone-insulin-like growth factor axis, which leads to decreased IGF-I synthesis [4, 13], growth retardation can be observed in dogs with juvenile-onset DM. Moreover, deficient nutrient intake due to concurrent EPI may further retard growth. In the present case, the dog also exhibited hypoproteinemia associated with hypoalbuminemia, indicating most likely that protein malabsorption caused by exocrine pancreatic dysfunction had occurred.

Besides juvenile DM, growth retardation in young dogs can result from pediatric endocrine disorders including juvenile-onset hypothyroidism, juvenile-onset hyperadrenocorticism and hypopituitarism [10]. The endocrine test results and clinical signs of the present case were not consistent with these disorders, although the IGF-I level was very low, which could have resulted from the DM as mentioned above [4, 13]. However, this dog had a high serum cortisol concentration, which was not suppressed by the low-dose dexamethasone suppression test, despite normal pituitary and adrenal glands. We believe that the dog had hypercortisolism due to uncontrolled DM, but not true hyperadrenocorticism [7, 8].

The young dog also had acute bilateral cataracts. Cataracts in dogs younger than 6 months are usually congenital or hereditary, although inflammation, nutrition, toxins and traumatic events may also cause cataracts [9, 12]. Cataract formation is a common complication in adult dogs with DM [3, 12] but its development in young dogs has rarely been reported. However, the fact that bilateral cataracts have been reported previously in only one 18-month old dog with DM [5] is not very surprising, considering the low number of reported cases.

In conclusion, the case reported here demonstrates that juvenile-onset DM can occur simultaneously with EPI and result in growth retardation and acute cataract formation. Routine TLI measurement in symptomatic dogs may identify previously undiagnosed cases of EPI in dogs with juvenile-onset DM.

REFERENCES


