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Primary Hypoparathyroidism in a Miniature Schnauzer Dog

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Abstract : A 7-year-old intact female, Miniature Schnauzer dog was presented with an acute seizure episode and tremors. Fever and panting were noted when presented. Physical examination revealed apparent forelimb muscle rigidity, fasciculations and stiff gait. Characteristic laboratory findings in this dog were severe hypocalcemia with hyperphosphatemia. The low serum concentration of intact parathyroid hormone and ionized calcium levels were consistent with the diagnosis of primary hypoparathyroidism. In addition, there were increased urinary excretion of calcium and decreased urinary excretion of phosphorus in this case. Urgent treatment was initiated with 10% calcium gluconate. The dog remained healthy with vitamin D analogue and oral calcium supplementation. A transient hyperphosphatemia was controlled well with sevelamer hydrochloride. To the author's knowledge, this is the first case report describing the clinical and laboratory characteristic features of canine primary hypoparathyroidism and its clinical outcome in Korea.

Key words **:** hypocalcemia, primary hypoparathyroidism, dog.

Introduction

Calcium plays an essential role in intracellular and extracellular metabolic process. Therefore, calcium homeostasis is accurately regulated through the action of parathyroid hormone (PTH), vitamin D and calcitonin (1). Primary hypoparathyroidism is a relatively rare disease in dogs and cats (1-3). In dogs, it is most commonly caused by immune-mediated destruction of the parathyroid glands, which decreased absolute or relative production of PTH (2,3). The diagnosis of primary hypoparathyroidism was based on the neurologic and neuromuscular abnormalities, the concurrent hypocalcemia and hyperphosphatemia, the low serum concentration of intact PTH with an low serum ionized calcium concentration, and the resolution of the clinical signs following the administration of a 10% calcium gluconate solution (1,4,5).

The following case report describes the clinical and laboratory features of primary hypoparathyroidism and treatment outcomes. This is the first case report of canine primary hypoparathyroidism in the dog in Korea.

Case

A 7-year-old intact female, Miniature Schnauzer dog was admitted for evaluation of seizure like episode, muscle twitching and forelimb stiffness. Initial treatment by the referring veterinarians consisted of diazepam. When presented, the dog was mildly depressed, but was alert and responsive. Mentation and cranial nerve examination were normal. Physical examination revealed apparent forelimb muscle rigidity, fasciculation and stiff gait. Fever and panting were also noted. No other abnormalities were noted on the physical examination.

Hematological and serum biochemical tests revealed hypocalcemia (total calcium; 4.4 mg/dL, reference range, 9.3-12.1), low ionized calcium (0.73 mmol/L; reference range, 1.15-1.35 mmol/L), and hyperphosphatemia (7.4 mg/dL, reference range, 1.9-5.0 mg/dL). Alanine aminotransferase (ALT) (113 U/L, reference range; 17-78 U/L), aspartate transferase (AST) (96 U/L, reference range; 17-44 U/L), alkaline phosphatase (ALP) (326 U/L, reference range; 0-142 U/L) and creatine kinase (CK) (> 2000 U/L, reference range; 49-166 U/L) were all elevated. Results of radiologic examination and urinalysis were not remarkable. An electrocardiogram (ECG) produced no abnormalities. The laboratory examinations suggested that severe hypocalcemia were the cause of these clinical signs. In this dog, the albumin, blood urea nitrogen and creatinine concentrations were normal, ruling out hypocalcemia as hypoalbuminemia, renal failure and intestinal malabsorption, are common conditions associated with hypocalcemia. Historically, ethylene glycol toxicity, phosphate enemas and nutritional secondary hyperparathyroidism were also ruled out. Primary hypoparathyroidism was strongly suspected and further examinations were performed to confirm this condition. Serum was tested for intact parathyroid hormone (PTH), serum lipase and magnesium concentrations. Low serum PTH concentrations (0.156 pmol/L; reference range, 2-13 pmol/L) were noted. However, serum lipase (55 U/L; reference range, 13-60 U/L) and

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magnesium (2.26 mg/dl, reference range, 1.5-2.7 mg/dl) concentrations were normal. Urinary fractional excretion of calcium (F_ECa) and phosphorus (F_EP) were also measured. The F_ECa value was increased (4.7%, reference range, 0.05~0.56%) and the F_EP value was decreased (2.7%, reference range, 3.0~39.0%). This was consistent with primary hypoparathyroidism. Based on the history, clinical signs, physical examinations and laboratory findings, the present case was diagnosed as a primary hypoparathyroidism in a dog.

Treatment was initiated with the intravenous administration 10% calcium gluconate (1 ml/kg, over 10 to 30 minutes) while monitoring with an electrocardiograpy (ECG) for arrhythmias. The blood calcium level increased to 7.7 mg/dl 3 hours after injection of bolus 10% calcium gluconate solution. The forelimb rigidity and fasciculation resolved after calcium infusion but the dog still had a stiff gait. Administration of a vitamin D analogue (calcitriol, 0.04 μg/kg/day, PO; Asia Pharm, Seoul, Korea) and oral calcium supplementation (calcium carbonate 500 mg PO q 8 hrs; Bayer Korea, Seoul, Korea) were started. A constant-rate infusion of 10% calcium gluconate (1 : 4 dilutions) in sterile 0.9% saline (10 ml/kg per hour) was consecutively administered for three days with daily monitoring of serum calcium concentration (Table 1).

The clinical signs of the dog were improved over the next 3 days, although serum phosphorous concentration increased to 9.1 mg/dl. Sevelamer hydrochloride (Renagel®, 60 mg/kg/day, PO; Genzyme Corp., Cambridge, MA) was administered. The dog was discharged from the hospital on continuing calcitriol, calcium carbonate, and sevelamer hydrochloride treatment. The serum calcium and phosphorus concentration had stabilized to the normal range by 7 days following discharge. The dog remained clinically normal and serum calcium concentration remained within the reference range 5 months after admission.

Discussion

Primary hypoparathyroidism is most common in middle-aged, female dogs (1,4). Any dog breed can be affected, but it has been the most frequently reported in German shepherd and Miniature Schnauzers. (1,3). The most common clinical signs were focal of diffuse muscle tremors or twitching, generalized seizure, stiff gait, rear leg muscle pain/cramping and behavior changes such as restless, nervous, anxious, aggressive, reluctant to be touched. Decreased activity, weakness, vomiting, diarrhea, and weight loss were less commonly detected (1-5). The seven-year-old, intact female Miniature Schnauzer dog in this case had compatible signalments and clinical signs with primary hypoparathyroidism.

The cause of primary hypoparathyroidism in dogs is still unknown. However, the autoimmune process of the sporadic form of idiopathic hypoparathyroidism in humans have been well defined through the detection of antibodies against parathyroid tissue (3,7). Histological findings of lymphocytic and plasmacytic infiltration of the parathyroid glands have been identified to be relatively common in dogs (2,3,5,8). This supports the hypothesis of an immune-mediated pathogenesis of hypoparathyroidism in dogs due to circulating autoantibodies against parathyroid tissue have not been demonstrated in dogs (3,6).

In this dog, other causes of hypocalcemia concurrent with hyperphosphatemia were all excluded through historically, clinically and various laboratory examinations. The markedly low serum PTH concentrations with low ionized calcium and good prognosis following calcium supplementation supported the definite diagnosis of primary hypoparathyroidism. However, histological examination of the parathyroid gland in this dog was not performed, thus, the underlying cause was not determined and the etiology of this dog was classified as idiopathic.

In human literature, the urinary excretion of calcium, phosphorus, and hydroxyproline was diminished in the case of concurrent hypocalcemia and mild hyperphosphatemia (9). Normally, F_ECa and F_EP were expected to be increased and decreased, respectively, in dogs with hypoparathyroidism (5). However, veterinary literature showed high of F_ECa values (in the upper half of the reference range) and low of F_EP values (in the lower end of the reference range), which was considered as diminished extracellular calcium concentrations and subsequent reduced renal excretion or unidentified mechanisms (5). In this case, the F_ECa value was increased (4.7%, reference range, 0.05~0.56%) and the F_EP value was decreased

Table 1. Laboratory findings in a dog with a primary hypoparathyroidism

	Interval after first examination								
Parameters	0	3 H	1 D	2 D	3 D	5 D	10 D	28 D	Reference Range
Total Serum Calcium (mmol/L)	4.4	7.7	5.9	5.8	8.5	12.1	11.2	11.4	9.3-12.1
Ionized Calcium (mmol/L)	0.73	ND*	ND	ND	ND	ND	ND	ND	1.15-1.35
Serum Phosphate (mmol/L)	7.4	7.9	7.1	6.6	9.1	6.6	4.5	4.2	1.9-5.0
Intact PTH (pmol/L)	0.156	ND	ND	ND	ND	ND	ND	ND	2-13

*ND : not done. H : hours, D : days

(2.7%, reference range, 3.0~39.0%). Thus, it was consistent with the expected results in primary hypoparathyroidism, supporting the diagnosis of primary hypoparathyroidism.

The therapeutic goal of primary hypoparathyroidism is to increase serum calcium concentrations and maintain them just below or at the low end of reference range (1). Using vitamine D analogues and calcium supplements were ideal treatment options; however hyperphosphatemia was a common complications (1,10). This dog showed hyperphosphatemia all along because the lack of PTH increased the serum phosphorus concentration (1,9). Furthermore, the hyperphosphatemia worsened on third day due to the vitamin D analogue which increased both serum calcium and phosphorous levels. Sevelamer hydrochloride is an oral phosphate binder preferred in the treatment of chronic kidney disease because of fewer adverse effects (11). The dog in this report had a good response to this oral phosphate binder.

In this case report, we described the first case of canine primary hypoparathyroidism in Korea.

In conclusion, this case demonstrates that the appropriate treatment including correcting electrolytes imbalances could be crucial in controlling this endocrine disease, based on the characteristic clinical signs and laboratory results of primary hypoparathyroidism.

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미니어처 슈나우저에서 발생한 원발성 부갑상선기능저하증

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요 약 : 7연령의 암컷 미니어처 슈나우저견이 갑작스런 발작과 근육 떨림 증상을 주증으로 내원하였다. 내원 당시 발열과 헐떡임이 두드러졌으며, 신체검사 상에서 현저한 앞다리 근육 강직증상, 근육부분수축과 뻣뻣한 걸음걸이가 관찰되었다. 실험실 검사에서 심각한 저칼슘혈증과 함께 고인혈증이 특징적으로 관찰되었다. 이와 더불어 관찰된 낮은 농도의 부갑상선 호르몬과 이온화된 칼슘농도, 뇨중 칼슘과 인의 배설 량 측정을 통하여 원발성 부갑상선기능저하증이 진단되었다. 이 환축은 10% 글루콘산칼슘 투여를 통한 초기 치료에 반응이 좋았으며, 비타민 D 유사체와 칼슘 보조제를 통한 유지 치료에 의해 잘 관리 되고 있다. 부작용으로 일시적인 고인혈증이 나타났으나, 이 역시 경구용 인 흡착제인 sevelamer hydrochloride를 이용한 치료에 의해 안정화 되었다. 결론적으로 본 증례의 경우 개에서 나타나는 원발성 부갑상선기능저하증의 임상증상과 특징적인 실험실 검사 결과 그리고, 치료 반응에 대한 국내 첫 증례보고이다.

주요어 : 저칼슘혈증, 원발성 부갑상선기능저하증, 개.