Case Report

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Hypoadrenocorticism in a 1-Year-Old Korean Shorthair Cat

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Abstract A one-year-old spayed female Korean Shorthair cat presented to Kangwon National University Veterinary Hospital with vomiting, weight loss, lethargy, loss of appetite, and polyuria that lasted for more than two weeks. The body condition score, blood pressure, heart rate, and body temperature were abnormally low, and the physical examination findings were consistent with moderate dehydration. Hematological and biochemical tests demonstrated mild azotemia and a low Na:K ratio. Additional abdominal ultrasound imaging revealed reduced size of both adrenal glands. The adrenocorticotropic hormone (ACTH) stimulation test showed decreased post-ACTH cortisol and aldosterone levels and increased endogenous ACTH levels, confirming a diagnosis of primary hypoadrenocorticism. The cat was treated with subcutaneous injections of desoxycorticosterone pivalate (DOCP) and oral prednisolone supplementation, and subsequent electrolyte analysis showed a normal Na:K ratio. Clinical symptoms were also improved in response to treatment. Hypoadrenocorticism in cats is a very rare disease, but it should not be excluded as a potential diagnosis in favor of kidney diseases or other conditions, especially when the Na:K ratio is low. In addition, the prognosis for the disease and the response to DOCP treatment should be further evaluated in cats.

Key words hypovolemia, azotemia, desoxycorticosterone pivalate, dehydration, adrenocorticotropic hormone.

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Introduction

Hypoadrenocorticism is an endocrine disease in which glucocorticoids and/or mineralocorticoids are abnormally secreted, resulting in several clinical symptoms (2,3,10,21,23). Glucocorticoids are secreted under various stress-inducing conditions and maintain body homeostasis, whereas mineralocorticoids are hormones that regulate sodium, potassium, chlorine, and water levels through the kidneys (3,23).

Hypoadrenocorticism can be categorized as primary, secondary, or atypical depending on the type and cause of the deficiency. Primary hypoadrenocorticism is the most common, resulting from destruction of adrenal tissue by tumors, infarction, thrombosis, or mitotane or trilostane treatment (2,3,19). Secondary hypoadrenocorticism is mainly caused by destruction of the pituitary gland or hypothalamus or by a deficit of adrenocorticotropic hormone (ACTH) due to administration of exogenous glucocorticoids (2,3,6,18). Atypical hypoadrenocorticism refers to the condition in which mineralocorticoid levels are normal but glucocorticoid levels are deficient, whereas the opposite (hypoaldosteronism) is rarely observed (2,6,10).

Hypoadrenocorticism was first reported in cats in 1983. Fewer than 50 cases have been reported since then, and the exact etiology of the condition is not known (2,3,6,18,21). One of the main causes of primary hypoadrenocorticism in humans and dogs is the destruction of the adrenal cortex by autoimmune reactions, and lymphocyte infiltration in the adrenal cortex resulting from autoimmune reactions has been reported in cats (4,7,21).

As is the case with dogs, hypoadrenocorticism usually manifests during early and middle age in cats, but it can also occur later in the lifespan. It affects individuals of both sexes and of any breed (6,7,15).

Glucocorticoid deficits can cause gastrointestinal symptoms such as vomiting and diarrhea, but diarrhea does not generally occur in cats. In addition, dehydration, bradycardia, hypotension, decreased cardiac output, and weakness consistent with hypovolemia associated with aldosterone deficiency may appear, followed by decreased renal perfusion. Mild azotemia may also be present (2,6,10,13,21). Clinical symptoms are often ambiguous and can vary depending on stressors. As a result, hypoadrenocorticism may be confused with common diseases of the gastrointestinal system and the urinary tract (2,10,21). Differential diagnoses include urinary tract diseases such as acute kidney failure, necrotizing pancreatitis, acute hepatitis, diabetic ketoacidosis, and gastrointestinal inflammation, and diagnostic tests are essential to differentiate hypoadrenocorticism from these conditions (2,21). A physical examination for evaluating physical conditions associated with dehydration or hypovolemia; a complete blood count for identifying abnormalities in the blood, such as nonregenerative anemia; blood biochemistry and electrolyte analyses for identifying pre-renal azotemia and low Na:K ratio; urinalysis for differentiation of acute renal failure and evaluation of urine concentration should be performed for accurate diagnosis. Additional thoracic and abdominal X-rays, as well as abdominal ultrasound imaging, may be required (10,21). However, to confirm a hypoadrenocorticism diagnosis, it is necessary to evaluate hormonal secretion by the adrenal cortex. Measurement of cortisol levels via the ACTH stimulation test is the standard way of doing this, but the test does not distinguish between primary and secondary hypoadrenocorticism (5,10,16,20). Additional measurements of endogenous ACTH concentrations can be performed to distinguish between the two: the endogenous ACTH concentration is increased in cases of primary hypoadrenocorticism but reduced in the case of secondary hypoadrenocorticism (5,10,16,20).

To the best of our knowledge, there were no reports of feline hypoadrenocorticism in South Korean veterinary medicine. This case study describes the diagnosis and treatment process of hypoadrenocorticism in cats.

Case Report

A one-year-old spayed female Korean Shorthair cat (*Felis catus*) presented to Kangwon National University Veterinary Hospital with symptoms that included vomiting, weight loss, lethargy, loss of appetite, and polyuria, lasting for more than two weeks. The cat had been raised indoors since its owner brought it from the wild, and there were no other cats housed at the same home. There was no specific medical history, and vaccinations had been completed. Ingestion of foreign substances or dietary allergies were the potential reasons offered by the owner to explain the vomiting, and a loss of appetite and vitality had been noticed since the onset of the symptom.

The physical examination yielded a weight of 4 kg, a body temperature of 37.7°C, and a respiratory rate of approximately 30 breaths/min. The blood pressure was as low as 30 mmHg, and the heart rate as low as 100 beats/min. A slightly degraded body condition score was recorded (3/9). Dehydration was estimated to be approximately 6-7%, the mucous membrane was dried, and the skin turgor was also reduced, resulting in a delay in the capillary refill time. The cat's mental state was acceptable; however, it was difficult to handle due to fear. There was no abnormal lung sound or

heart murmur on stethoscopy, no lymph node enlargement throughout the body, and no obvious abdominal pain during abdominal compression. Blood samples were collected for hematological and biochemical tests, and urinalysis was performed. Abnormal laboratory parameters are listed in Table 1. Regarding the urinary system, the results of the symmetric dimethylarginine (SDMA) test were slightly above the normal values (15.2 μg/dL, reference: ≤14 μg/dL), and the urine specific gravity test yielded a value of 1.019, corresponding to minimally concentrated urine.

Considering that the cat was originally wild, feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV) tests (SNAP FIV/FeLV Combo Test, IDEXX Laboratories, Westbrook, Maine, USA) were also performed to exclude infectious diseases, and the results were negative. The results of the feline pancreatic lipase immunoreactivity (Vcheck fPLI, V200 Analyzer, Bionote, South Korea) test to exclude pancreatitis related to vomiting were within the normal range (1.9 ng/mL, reference value: ≤3.5 ng/mL). Thyroxine (T4) levels were also measured to exclude the possibility of hypothyroidism, and the results were normal (2.55 μg/dL, reference range: 0.8-4.7 μg/dL). Thoracic and abdominal radiography and ultrasonography failed to show any suspected foreign bodies in the gastrointestinal tract. The boundary of the right kidney was heterogeneous. A cyst was found in the cortex of the caudal pole. The size of the left adrenal gland was measured with 1.3 mm of cranial pole and 1.4 mm of caudal pole, and the size of the right adrenal gland was measured with 2.1 mm of carnial pole and 2.0 mm of caudal pole (Fig. 1). According to Hematological examination and imaging evaluation of abdominal organs, the presence of foreign matter in the gastrointestinal tract was discarded as a possible cause for the vomiting and dehydration, but kidney diseases were considered. Hypoadrenocorticism was also suggested by the abdominal ultrasound images showing small sizes of both adrenal glands and clinical symptoms consistent with abnormal electrolyte levels and hypovolemia. The cat received treatment for hypovolemia, and electrolyte correction was performed using Ringer's lactate solution (20 mL/kg/h). After receiving intravenous fluid therapy for one day, another round of blood tests to evaluate dehydration, electrolyte levels, and kidney function were performed the following day. Calcium and phosphorus levels were still mildly increased, but blood urea nitrogen (BUN), creatinine, and electrolyte levels were normalized. An additional blood sample was required to conduct the ACTH Stimulation Test for adrenal function evaluation, and since the cat was very uncooperative, it was judged that it could cause a cortisol load, and for an accurate test, it was right to proceed in a stable state next time. After hypovolemia was improved by intravenous fluid treatment, the cat improved its physical condition, did not vomit, and did not prescribe any medication because its owner did not want to feed it unnecessary medication.

Three weeks later, the cat visited the hospital again with clinical symptoms that included hypovolemia, vomiting, loss of appetite, and decreased vitality. It had lost 0.5 kg since the last visit. Intravenous fluid treatment was administered again, and after the cat was stabilized, an ACTH stimulation test was performed to exclude hypoadrenocorticism. Tetracosac-

Table 1. Abnormal laboratory findings in a cat with hypoadrenocorticism

Parameter	Values	Reference range
Lymphocytes (10^3/μL)	7.77	0.92-6.88
Aspartate aminotransferase (U/L)	52	12-46
Creatinine (mg/dL)	2.8	1.0-2.2
Blood urea nitrogen (mg/dL)	35.2	18.0-33.0
Glucose (mg/dL)	181	73-134
Calcium (mg/dL)	13.8	7.6-11.0
Phosphorus (mg/dL)	6.9	3.2-6.3
Amylase (U/L)	1904	550-1800
Na+ (mmol/L)	136	146-159
K+ (mmol/L)	5.5	3.8-5.3
Cl– (mmol/L)	103	108-130
Na/k ratio	24.7	>27

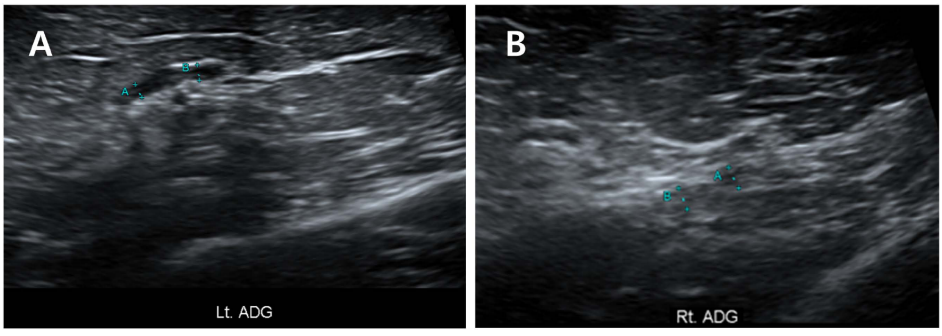

Fig. 1. Adrenal glands (longitudinal axis view), cat. The individual was diagnosed with primary hypoadrenocorticism. Notice the reduced size of both glands. (A) Left adrenal gland measured with cranial pole 1.3 mm and caudal pole 1.4 mm. (B) Right adrenal gland measured with cranial pole 2.1 mm and caudal pole 2.0 mm. These figures are ultrasonographic finding.

tide (0.125 μg), a synthetic ACTH, was injected intravenously, and pre-ACTH cortisol and aldosterone, post-ACTH cortisol and aldosterone, and endogenous ACTH concentrations were measured. Despite the injection of ACTH, the cortisol concentration showed a post-ACTH value of 1.73 μg/dL (reference range: 4.5-15 μg/dL) that was only marginally higher than the pre-ACTH value (1.55 μg/dL, reference range: 0.4-4.0 μg/dL). Aldosterone had a pre-ACTH value of 0.97 ng/dL (reference range: 7.14-14.0 ng/dL) and a post-ACTH value of 2.13 ng/dL (reference range: 10.0-26.0 ng/dL). The endogenous ACTH concentration after stimulation was 201.4 pg/mL (reference range: 0-60 pg/mL). Based on these results for adrenal function, the cat was diagnosed with primary hypoadrenocorticism. Desoxycorticosterone pivalate (DOCP; Zycortal, Dechra Pharmaceuticals) with a dosage of 2.2 mg/kg was injected subcutaneously, and prednisolone (0.25 mg/kg) was administered orally twice daily.

Twelve days after DOCP administration, overall physical health, electrolyte levels, and kidney function were again evaluated. The physical examination results were good: the cat exhibited significantly improved vitality, had recovered appetite, walked around well, and had no clinical symptoms consistent with hypovolemia or gastrointestinal symptoms such as vomiting. Electrolyte tests showed that sodium levels were normal (154 mmol/L, reference range: 146-159 mmol/L), and potassium levels were slightly elevated (5.6 mmol/L, reference range: 3.8-5.3 mmol/L), but the Na:K ratio was normal at 27.5 (reference value: >27). BUN and creatinine levels were also within the normal range, and calcium and phosphorus levels that were initially high had also decreased to the normal range.

Another electrolyte analysis performed on day 25 after DOCP administration yielded a value of 151 mmol/L for sodium and 4.8 mmol/L for potassium, both within the normal range. The Na:K ratio was also normal at 31, and therefore DOCP and prednisolone were prescribed again at the same dose.

Discussion

Hypoadrenocorticism is a rare endocrine disease in cats (2,3). According to previous reports (2,3,6,19), primary, secondary, and atypical forms of the disease can occur in cats. The case presented here exhibited typical primary hypoadrenocorticism with reduced post-ACTH cortisol and aldosterone levels and increased endogenous ACTH concentrations.

Neutropenia and lymphocytosis were observed in humans affected by hypoadrenocorticism, and lymphocytosis has also been reported in cats diagnosed with the condition (1,15,22). We also observed mild lymphocytosis in the present case, with normal neutrophil levels. In cases of hypoadrenocorticism, neutropenia and lymphocytosis are presumed to be a consequence of adrenal insufficiency (1). Previously, hypercalcemia was observed in one cat with hypoadrenocorticism (15) and the cat in this case also showed slightly increased calcium levels. In this regard, neoplasia or hyperparathyroidism needed to be excluded, but calcium levels returned immediately to their the normal range after DOCP treatment. The cause of hypercalcemia in cats with hypoadrenocorticism is not well understood (9,15).

Hypoglycemia has also been reported in cats with hypoadrenocorticism, and in relation to cortisol secretion disorders in the adrenal gland, it may be caused by a decrease in glycogenolysis and gluconeogenesis in the liver. However, glucose levels were above the normal range in this cat (8,14). In previous reports on cats diagnosed with hypoadrenocorticism, hepatic transaminase levels, including aspartate aminotransferase, were increased in only one case, and the aspartate aminotransferase levels were also slightly increased in this cat (8,17).

Because the cat was deficient in both glucocorticoids and mineralocorticoids, it was treated with subcutaneous injections of DOCP and oral prednisolone. It is known that the response to treatment is slower in cats than in dogs, but this individual showed noticeable clinical improvement within two days after hormone supplementation (11,15).

In terms of prognosis, dogs suffering from hypoadrenocorticism are expected to have a normal lifespan when the hormonal deficits are appropriately managed by supplementation, but cats are known to have a poorer prognosis (12).

Conclusions

In conclusion, hypoadrenocorticism in cats should not be excluded as a potential diagnosis in favor of kidney diseases, such as acute renal failure, or other conditions, especially when the Na:K ratio is low. This case study showed clinical symptoms associated with hypovolemia and features relatively well matched with hypoadrenocorticism, such as mild azotmia and electrolyte disorders. In addition, clear adrenal insufficiency was confirmed through the ACTH simulation test, and it was found that it responded relatively well to the resulting DOCP prescription.

However, there is a lack of comparison between clinical symptoms and hematological indicators compared to hypoadrenocorticism in dogs, as well as responses and survival rates to treatments including DOCP, and further studies are needed.

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Conflicts of Interest

The authors have no conflicting interests.

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