*VETERINARSKI ARHIV 86* (4), 591-600, 2016

# Hypoadrenocorticism in a young dwarf cat - case report

**Elisabetta Giudice[1], Francesco Macrì[2], Chiara Crinò[2], Fabio Viganò[3], and Simona Di Pietro[2]***

[1]*Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche e Ambientali, University of Messina, Messina, Italy*

[2]*Dipartimento di Scienze Veterinarie, University of Messina, Polo Universitario Annunziata, Messina, Italy*

[3]*Clinica Veterinaria San Giorgio, San Giorgio su Legnano, Milano, Italy*

**GIUDICE, E., F. MACRÌ, C. CRINÒ, F. VIGANÒ, S. DI PIETRO: Hypoadrenocorticism in a young dwarf cat - case report. Vet. arhiv 86, 591-600, 2016.**

**ABSTRACT**

A 8-month-old cat with immature appearance was referred as an emergency, showing lethargy, weakness, anorexia and dehydration. The case history reported two months of apparently neurologic disorders with behavioral changes and waxing-waning clinical course, including temporary remissions associated with parenteral fluid and/or corticosteroid administration. Clinical examination revealed hypovolemic shock, extreme weakness, severe hypothermia, and bradycardia. Laboratory profile revealed several abnormalities consistent with hypoadrenocorticism. After clinical stabilization, an adrenocorticotropic hormone (ACTH) stimulation test was performed, confirming the suspicion. The cat had a rapid decline and died. Probably, previous diagnostic errors and inappropriate treatments compromised the outcome of therapy. We emphasize the importance of early diagnosis in a disease that, although rare in this species, should not be overlooked in the differential diagnosis.

**Key words:** Addison's disease, feline, hypothermia weakness, low Na:K ratio, shock

## Introduction

Hypoadrenocorticism, also called Addison's disease, is an endocrine disorder that results from the complete or partial deficient production of glucocorticoids and/or mineralocorticoids. Most naturally occurring forms of hypoadrenocorticism affect both hormones. Cortisol, the main glucocorticoid hormone, is responsible for combating stress and helping to maintain blood sugar levels; aldosterone, the major mineralocorticoid, regulates water, sodium, potassium and chloride concentrations in the body. The disease may be classified into primary and secondary hypoadrenocorticism. The former is the

*Corresponding author:

Simona Di Pietro, DVM, PhD, Assistant Professor, Dipartimento di Scienze Veterinarie, University of Messina, Polo Universitario Annunziata, 98168 Messina, Italy, Phone: +390 903 503 509; Fax: +390 903 503 979; E-mail: dipietros@unime.it

ISSN 0372-5480
Printed in Croatia

result of adrenal cortex destruction, while the latter of a decrease in adrenocorticotropic hormone (ACTH) incretion from the pituitary gland. The first documented case in a cat was described in 1983 and only less than 50 cases have been reported, making hypoadrenocorticism a very rare disease in cats (BATTAGLIA and AGNOLI, 2012; FELDMAN and NELSON, 2004; JOHNESSE et al., 1983; REDDEN, 2005).

Currently, the pathogenesis of feline primary hypoadrenocorticism remains unknown. Immune mediated destruction of the adrenal gland tissue is thought to be the most common cause, suggested by lymphocytic infiltration of the adrenal cortex (GRECO, 2007; JOHNESSE et al., 1983; STONEHEWER and TASKER, 2001).

There have also been a few documented cases in which lymphosarcoma infiltrated the adrenal glands (FELDMAN and NELSON, 2004; GUNN-MOORE, 2005; PARNELL et al., 1999; SCOTT-MONCRIEFF, 2010) or an external trauma has been implicated (BERGER and REED, 1993; BRAIN, 1997).

Secondary hypoadrenocorticism may be due to a congenital disorder or may result from destructive lesions of the pituitary or hypothalamus, including neoplasia, inflammation, or trauma, although a spontaneously occurring form has not been reported in cats (SCOTT-MONCRIEFF, 2010).

Occasionally, secondary Addison's disease may be iatrogenic, caused by the abrupt withdrawal of steroid medications, or after progestogen administration (STONEHEWER and TASKER, 2001).

Cats that have been on long-term or high dose steroids should be slowly weaned off such drugs, in order to avoid this form of deficiency. Recommended doses of megestrol acetate have been shown to suppress the plasma cortisol response to ACTH, resulting in adrenal cortex atrophy in cats (GUNN-MOORE, 2005).

Although Addison's disease is extremely rare in cats, it primarily affects young to middle aged cats (PETERSON et al., 1989; REDDEN, 2005; SCOTT-MONCRIEFF, 2010).

Any breed or sex may be affected, in contrast to dogs where females and certain breeds are overrepresented (GUNN-MOORE, 2005; HOCK, 2011).

The clinical signs seen with hypoadrenocorticism are often very vague in the cat. The most common findings are lethargy, depression, weakness, shaking, dysorexia, weight loss, dehydration, hypothermia, collapse, weak pulse and bradycardia. Other less common findings in cats include vomiting, abdominal pain, polyuria and polydipsia (GRECO, 2007; GUNN-MOORE, 2005; PETERSON et al., 1989; SICKEN and NEIGER, 2013).

As these signs may mimic many other diseases, Addison's disease is often missed at the initial presentation. Common differential diagnoses include ileus, renal insufficiency, gastroenteritis, diabetic ketoacidosis, necrotizing pancreatitis and septic shock. For this reason, diagnostic tests are needed to confirm the presence of Addison's disease, and to

exclude other disorders that cause similar signs. These tests may include: complete medical history and physical examination; complete blood count (CBC), blood biochemistry profile and urinalysis; chest and abdominal radiographs and possible abdominal ultrasound, depending on the clinical signs. A definitive diagnosis of hypoadrenocorticism requires the demonstration of inadequate adrenal reserves. The ACTH stimulation test is considered the gold standard. Since this assay measures cortisol levels, it cannot differentiate primary from secondary adrenal insufficiency. An endogenous ACTH level can help determine this, as animals with primary hypoadrenocorticism have elevated endogenous ACTH levels, while animals with secondary hypoadrenocorticism have very low endogenous ACTH concentration (GUNN-MOORE, 2005; SCOTT-MONCRIEFF, 2010). An alternate approach was proposed in dogs for assessing the pituitary-glucocorticoid axis by measuring basal cortisol and plasma ACTH concentrations, and then calculating a cortisol-to-ACTH ratio. Similarly, the renin-angiotensin-aldosterone system was assessed by determining the basal plasma concentrations of aldosterone and plasma renin activity, and then calculating the aldosterone-to-renin ratio. Animals with primary hypoadrenocorticism have much lower cortisol-to-ACTH ratios and aldosterone-to-renin ratios than normal animals or animals with secondary hypoadrenocorticism, with little to no overlap in ratio values. The advantage of the use of these paired-hormone ratios is that allows for clear differentiation between the two forms in a single blood sample. Disadvantages include the expense and the difficulty of performing hormone assays, as well as the necessity of blood collection prior to any fluid or steroid treatment. In addition, it may be difficult to find a laboratory that can accurately measure hormone activities in animals (KLEIN and PETERSON, 2010).

**Case presentation**

An 8-month-old female domestic short-haired (DSH) cat was referred to authors' attention, with a 2-month history of apparently neurological disorders, with behavioral changes characterized by: excessive fear, recurrent episodes of tremors, weakness, severe hypothermia, dysorexia and pica (ingestion of sand litter), increased thirst and urination. These signs were apparently responsive to oral corticosteroids given empirically.

Past medical history stated that the cat was not growing properly, like two her brothers, one of whom died suddenly.

Extreme lethargy, severe weakness, dehydration, abdominal pain, episodic diarrhoea and hypothermia (32.5 °C) were noted two weeks earlier, when the patient was originally presented to the referring veterinarian. At this time, intestinal infection/infestation was ruled out, and radiological examination revealed small foreign bodies in the stomach, consistent with grains of litter. Intravenous fluid therapy was started, followed by a clinical improvement. The referring veterinarian initially suspected meningitis and then a porto-systemic shunt, applying the appropriate therapies with poor responses. Conversely, a

rapid increase in temperature and clinical improvement occurred after dexamethasone administration. After one week of apparent remission, the cat's condition suddenly relapsed, resulting in emergency referral for the authors' attention.

Fig. 1. Clinical case: 8-month-old female DSH cat with severe dehydration and a dull and scruffy fluffy hair coat. Note the kittenish appearance.

On physical examination, the cat was found in lateral recumbency with severe hypovolemic shock (9-10% dehydrated) (Fig. 1 and Fig. 2). The cat was hypothermic (rectal temperature 33.9 °C) and bradycardic (95 beats per minute, bpm), with a weak pulse. She weighed 0.9 kg and had a body condition score (BCS) of 1.5 out of 5, with reduced skeletal development and immature kittenish appearance (she looked like a 4-5 month-old kitten). The cat was non-ambulatory and showed severe generalized weakness.

On abdominal palpation, bladder repletion was appreciated, in contrast to the state of dehydration. An abdominal ultrasound was performed and did not reveal any abnormalities.

Due to the serious clinical condition, the cat was rewarmed and given intravenous fluid therapy (0.9% NaCl; 20 mL/kg over 15 min, twice). After the patient was stabilized, a blood sample was collected for hematological and biochemical tests, and cystocentesis was performed for urinalysis. The abnormal laboratory parameters were reported in Table 1.

Fig. 2. The cat shown in Fig. 1: frontal view

Table 1. Abnormal laboratory findings in a cat with hypoadrenocorticism

| Test | Values | Normal range |
|---|---|---|
| Mature neutrophils ($10^9$/L) | 2.85 | 3.6-13.3 |
| Lymphocytes ($10^9$/L) | 7.98 | 1.3-4.8 |
| Blood urea nitrogen (mmol/L) | 28.13 | 5.7-12.82 |
| Alanine aminotransferase (U/L) | 302 | 10-40 |
| Aspartate aminotransferase (U/L) | 60 | 10-40 |
| Sodium (mmol/L) | 113 | 141-155 |
| Potassium (mmol/L) | 5.8 | 3.6-5.6 |
| Na/K ratio | 19.48 | >27 |
| Phosphorus (mmol/L) | 1.68 | 0.81-1.61 |
| T4 (nmol/L) | 9.8 | 10-51 |
| Cortisol (nmol/L)<br>Basal<br>Post-ACTH | <br>Undetectable (<13.8)<br>Undetectable (<13.8) | <br>15-150<br>130-450 |
| Urine specific gravity (USG) | 1.014 | 1.035-1.060 |

As the clinical history, physical examination and laboratory findings were suggestive of adrenal insufficiency, an ACTH stimulation test was performed by injecting intravenously 0.125 mg synthetic ACTH, tetracosactrin (Synacthen, Biofutura Pharma, Milano, Italy).

Forty minutes after ACTH injection, the cat's condition rapidly worsened. Although an intravenous dexamethasone sodium phosphate bolus (1 mg/kg) was given, she died shortly thereafter. A blood sample was collected immediately postmortem and the very rapid onset of autolysis was observed. The owner denied permission to perform an autopsy.

The ACTH stimulation test revealed undetectable basal cortisol values that did not change after 50 min. In order to investigate the possibility of hypothyroidism and porto-systemic shunt, thyroxine (T4), bile acids and ammonia were evaluated. The thyroxine level was low-normal, thereby congenital hypothyroidism was not completely ruled out. Bile acids and ammonia were found to be in the normal range, allowing us to exclude the shunt.

**Discussion**

In the present case, in light of the diagnostic tests performed, we were able to rule out several conditions that may have led to the patient's clinical signs, such as: porto-systemic shunt, ileus, gastroenteritis, parasitosis, renal failure, diabetic ketoacidosis, necrotizing pancreatitis and septic shock.

The clinical signs that raise the index of suspicion for hypoadrenocorticism are: i) bradycardia in spite of circulatory shock; ii) response to nonspecific therapy (corticosteroids and fluids); iii) waxing and waning clinical course before the collapse (GRECO, 2007), all present in our case.

The suspicion was confirmed by dynamic testing. The presence of low basal cortisol levels with no or minimal response to stimulation with exogenous ACTH is considered diagnostic for the disease (FELDMAN and NELSON, 2004; PETERSON and KEMPPAINEN, 1992; SPARKES et al., 1990).

Although many authors suggest taking a blood sample 60-180 min after ACTH injection (TASKER et al., 1999), others consider 45 min post-stimulation (REDDEN, 2005) or 30 and 60 min after ACTH injection (GRECO, 2007) the right time of sampling. In the present study, due to the cat's death, the cortisol was assayed 50 min after ACTH injection, therefore according to these latter authors.

The cat showed lethargy and weakness, signs commonly seen in the course of hypoadrenocorticism in different species, including humans (FELDMAN and NELSON, 2004; HERRTAGE, 2010; SCOTT-MONCRIEFF, 2010).

In a study in which ten cases of feline hypoadrenocorticism were described, all the cats showed significant lethargy and weakness (PETERSON et al., 1989).

The extreme weakness may be confused with neurological disorders, as suspected by the referring veterinarian both in this and in other cases (TASKER et al., 1999).

Other clinical signs reported with high frequency by PETERSON et al. (1989) are: anorexia, weight loss, dehydration and hypothermia. Less frequent signs are: vomiting, polyuria/polydipsia and bradycardia.

This cat exhibited all these signs, except for vomiting. There was abdominal pain, rarely described (FELDMAN and NELSON, 2004; SICKEN and NEIGER, 2013), and diarrhea, quite common in dogs (PETERSON et al., 1989), but not in cats, in which a case of constipation was reported instead (KASABALIS et al., 2012). However, in our case, diarrhea and abdominal pain could be also attributed to litter ingestion.

Cats with hypoadrenocorticism usually have significant abnormalities in their laboratory profile.

The cat in this report exhibited mild azotemia without hypercreatininemia, severe hyponatremia, mild hyperkalemia, low Na:K ratio (<20:1), and slight hyperphosphatemia.

Most cats suffering from Addison's disease show mild to severe prerenal azotemia, hyperphosphatemia, hyponatremia, and a reduced sodium/potassium ratio. A ratio less than 27:1 strongly suggests hypoadrenocorticism (PETERSON et al., 1989; TASKER et al., 1999), although decreased Na:K ratios frequently occur in cats with diseases other than hypoadrenocorticism, which were excluded in this cat (BELL et al., 2005; THOMPSON and CARR, 2002). In the present case, the cat had prerenal azotemia probably due to severe dehydration.

The cat also showed marked and mild increases in alanine and aspartate aminotransferase, respectively. An elevation of hepatic transaminases has been previously observed in only one cat (KASABALIS et al., 2012), although it has been described in dogs (PETERSON et al., 1996). However, in our case, elevated enzymes could be related to the previous therapy.

The haematological pattern showed slight neutropenia, as described in humans (BAEZ-VILLASENOR et al., 1948), marked lymphocytosis, frequently reported in humans (BAEZ-VILLASENOR et al., 1948), and also in cats (PETERSON et al., 1989; TASKER et al., 1999), and a normal eosinophil count. A normal or increased lymphocyte and eosinophil count is significant, because the expected response to stress in a chronically and critically ill patient would be lymphopenia and eosinopenia (FELDMAN and NELSON, 2004).

Finally, impaired urinary concentrating ability, despite severe dehydration was also present, as already described in hypoadrenocorticism both in cats and in other species (TASKER et al., 1999). The loss of renal medullary solutes, particularly sodium, is

believed to result in impaired renal concentrating ability, and possibly also interferes with vasopressin release (SCOTT-MONCRIEFF, 2010).

The cat in this report was adopted at about 5 months of age and showed signs of illness shortly after. This is a relatively young age for the onset of adrenal insufficiency. In the series reported by PETERSON et al. (1989) the age of affected animals ranged from 1.5 to 14 years, with a median of 4 and a mean of 5.8 years.

The family history of the cat is interesting. All three brothers showed harmonious growth deficiency, consisting with pituitary dwarfism. Although very rare in cats, congenital polyendocrinopathy, such as panhypopituitarism, cannot be excluded (HERRTAGE, 2010). This condition is associated with low production of pituitary hormones, including the growth hormone (GH), thyroid-stimulating hormone (TSH), ACTH and gonadotropins, which can lead to slow growth, proportionate dwarfism, persistence of puppy coat, impaired thermogenesis, stress intolerance, sexual immaturity, etc.

In this case report, hypoadrenocorticism could be secondary to pituitary ACTH deficiency, resulting in adrenal gland hypotrophy/atrophy. The low-normal level of T4 reinforces the suspicion of pituitary involvement, but the levels of this hormone may decrease due to several factors, such as extra-thyroid problems or drugs (PETERSON, 2013). The death of the cat and the lack of consent to perform a necropsy did not allow further investigation.

The treatment of the acute disease, the so-called "Addisonian crisis", requires aggressive intravenous fluid therapy to replace circulating blood volume and correct the electrolyte imbalance, in addition to glucocorticoid and mineralocorticoid administration, as evidenced in several cases (PETERSON et al., 1989; SICKEN and NEIGER, 2013; STONEHEWER and TASKER, 2001; TASKER et al., 1999). With appropriate management, cats with adrenocortical insufficiency should have a normal life expectancy (BATTAGLIA and AGNOLI, 2012; PETERSON et al., 1989; REDDEN, 2005; TASKER et al., 1999).

In the present case, although an initial response to the intensive therapy was observed, the cat died within a short time. Probably, previous diagnostic errors and inappropriate treatments compromised the outcome of therapy.

In conclusion, we emphasize the importance of early diagnosis of a disease that, although rare in this species, should not be overlooked in the differential diagnosis.

**References**

BÁEZ-VILLASEÑOR, J., C. E. RATH, C. FINCH (1948): The blood picture in Addison's disease. Blood 3, 769-773.

BATTAGLIA, L., C. AGNOLI (2012): Due casi di ipoadrenocorticismo felino. Veterinaria 26, 43-49.

BELL, R., D. J. MELLOR, I. RAMSEY, C. KNOTTENBELT (2005): Decreased sodium:potassium ratios in cats: 49 cases. Vet. Clin. Pathol. 34, 10-14.

BERGER, S. L., J. REED (1993): Traumatically induced hypoadrenocorticism in a cat. J. Am. Anim. Hosp. Assoc. 29, 337-339.

BRAIN, P. H. (1997): Trauma-induced hypoadrenocorticism in a cat. Aust. Vet. Pract. 27, 178-181.

FELDMAN, E. C., R. W. NELSON (2004): Hypoadrenocorticism (Addison's disease). In: Canine and Feline Endocrinology and Reproduction (Feldman, E. C., R. W. Nelson, Eds.). WB Saunders Co, Philadelphia, pp. 394-439.

GRECO, D. S. (2007): Hypoadrenocorticism in small animals. Clin. Tech. Small Anim. Pract. 22, 32-35.

GUNN-MOORE, D. (2005): Feline endocrinopathies. Vet. Clin. North Am. Small Anim. Pract. 35, 171-210.

HERRTAGE, M. E. (2010): Endocrine disorders. In: Clinical Medicine of the Dog and Cat (Schaer, M., Ed.) Manson Publishing, London, pp. 451-504.

HOCK, C. E. (2011): Atypical hypoadrenocorticism in a Birman cat. Can. Vet. J. 52, 893-896.

JOHNESSEE, J. S., M. E. PETERSON, S. R. GILBERTSON (1983): Primary hypoadrenocorticism in a cat. J. Am. Vet. Med. Assoc. 183, 881-882.

KASABALIS, D., E. BODINA, M. N. SARIDOMICHELAKIS (2012): Severe hypoglycaemia in a cat with primary hypoadrenocorticism. J. Feline Med. Surg. 14, 755-758.

KLEIN, S. C., M. E. PETERSON (2010): Canine hypoadrenocorticism: Part II. Can. Vet. J. 51, 179-184.

PARNELL, N. K., L. L. P, OWELL, A. E. HOHENHAUS, A. K. PATNAIK, M. E. PETERSON (1999): Hypoadenocorticism as the primary manifestation of lymphoma in two cats. J. Am. Vet. Med. Assoc. 214, 1208-1211.

PETERSON, M. E., D. S. GRECO, D. N. ORTH (1989): Primary hypoadrenocorticism in ten cats. J. Vet. Intern. Med. 3, 55-58.

PETERSON, M. E., R. J. KEMPPAINEN (1992): Comparison of intravenous and intramuscular routes of administering cosyntropin for corticotropin stimulation testing in cats. Am. J. Vet. Res. 53, 1392-1395.

PETERSON, M. E., P. P. KINTZER, P. H. KASS (1996): Pretreatment clinical and laboratory findings in dogs with hypoadrenocorticism: 225 cases (1979-1993). J. Am. Vet. Med. Assoc. 208, 85-91.

PETERSON, M. E. (2013): Diagnostic testing for feline thyroid disease: hypothyroidism. Comp. Cont. Educ. Pract. 35, E1-E6.

REDDEN, B. (2005): Feline hypoadrenocorticism. Comp. Cont. Educ. Pract. 27, 697-706.

SCOTT-MONCRIEFF, J. C. R. (2010): Hypoadrenocorticism. In: Textbook of Veterinary Internal Medicine Diseases of the Dog and Cat. (Ettinger, S. J., E. C. Feldman, Eds.), Elsevier, Amsterdam, pp. 1847-1857.

SICKEN, J., R. NEIGER (2013): Addisonian crisis and severe acidosis in a cat: a case of feline hypoadrenocorticism. J. Feline Med. Surg. 15, 941-944.

SPARKES, A. H., D. T. ADAMS, J. A. DOUTHWAITE, T. J. GRUFFYD JONES (1990): Assessment of adrenal-function in cats - response to intravenous synthetic ACTH. J. Small Anim. Pract. 31, 1-4.

STONEHEWER, J., S. TASKER (2001): Hypoadrenocorticism in a cat. J. Small Anim. Pract. 42, 186-190.

TASKER, S., A. D. MACKAY, A. H. D. SPARKES (1999): A case of feline primary hypoadrenocorticism. J. Feline Med. Surg. 1, 257-260.

THOMPSON, M. D., A. P. CARR (2002): Hyponatremia and hyperkalemia associated with chylous pleural and peritoneal effusion in a cat. Can. Vet. J. 43, 610-613.

Received: 28 June 2015
Accepted: 22 March 2016

**GIUDICE, E., F. MACRÌ, C. CRINÒ, F. VIGANÒ, S. DI PIETRO: Hipoadrenokorticizam u patuljastog mačeta - prikaz slučaja. Vet. arhiv 86, 591-600, 2016.**

**SAŽETAK**

Osmomjesečno mače bilo je zaprimljeno kao hitan slučaj sa znakovima letargije, slabosti, anoreksije i dehidracije. U povijesti bolesti naznačeno je da su se neurološki poremećaji javili prije dva mjeseca zajedno s poremećajima u ponašanju i ispadima bijesa s povremenim smirivanjem kliničkih znakova nakon parenteralne primjene tekućine i/ili kortikosteroida. Kliničkom pretragom ustanovljen je hipovolemijski šok, izrazita slabost, teška hipotermija i bradikardija. Laboratorijski je ustanovljeno nekoliko poremećaja karakterističnih za hipoadrenokorticizam. Nakon kliničke stabilizacije, za povrđivanje sumnje bio je primijenjen test stimulacije adrenokortikotropnim hormonom (ACTH). Mače je naglo slabilo i uginulo. Prijašnje dijagnostičke pogreške i neodgovarajuće liječenje vjerojatno su pogoršali ishod bolesti. Naglašava se važnost rane dijagnostike bolesti, koju se, premda rijetku u mačaka, ne bi smjelo previdjeti u diferencijalnoj dijagnostici.

**Ključne riječi:** Addisonova bolest, mačka, hipotermija, nizak odnos Na:K, šok