

Hyperadrenocorticism in a crab-eating fox (*Cerdocyon thous*) kept under human care

Hiperadrenocorticism em cachorro-do-mato (*Cerdocyon thous*) mantido sob cuidados humanos

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ABSTRACT: Hyperadrenocorticism is a relatively common endocrine disease affecting the adrenal glands of domestic dogs. However, there are few reports of this disease in wild canids. A crab-eating fox (*Cerdocyon thous*) kept under human care was diagnosed with the disease after detection of conformational abnormalities in the adrenal glands visualized by ultrasonography, a cortisol suppression test after low-dose dexamethasone, and the detection of proteinuria and bacteria in urinalysis. After the diagnosis, the patient was treated with trilostane with a satisfactory clinical response. This report aims to report the sonographic and laboratory findings of hyperadrenocorticism and its treatment in a specimen of the species.

KEYWORDS: Adrenal; Cortisol; Cushing's syndrome; Trilostane.

RESUMO: O hiperadrenocorticismo é uma doença endócrina que acomete as glândulas adrenais relativamente comum em cães domésticos. Porém, em canídeos selvagens, poucos são os relatos descritos dessa enfermidade. Um exemplar de cachorro-do-mato (*Cerdocyon thous*), mantido sob cuidados humanos, foi diagnosticado com a doença após detecção de anormalidades conformacionais em glândulas adrenais visibilizadas via ultrassonografia, teste de supressão de cortisol após uso de baixa dose de dexametasona, além de detecção de proteinúria e bactérias em urinálise. Após o diagnóstico, instituiu-se tratamento medicamentoso a base de trilostano com resposta clínica satisfatória. Este relato objetiva reportar os achados ultrassonográficos e laboratoriais de hiperadrenocorticismo e seu tratamento em um exemplar da espécie.

PALAVRAS-CHAVE: Adrenal; Cortisol; Síndrome de Cushing; Trilostano.

INTRODUCTION

Hyperadrenocorticism (HAC), or Cushing's disease, is a common endocrine disorder of the dog resulting from chronic exposure to excess endogenous or exogenous glucocorticoids (FELDMAN et al., 1997; BEHREND et al., 2002). HAC can be classified as pituitary dependent (HDP), adrenal dependent (ADH), or iatrogenic (FELDMAN, 2004; NELSON; COUTO, 2010). Included among the clinical signs are predominantly polydipsia and polyuria (HERRTAGE; RAMSEY, 2015), and hepatomegaly can

also occur, caused by glycogen accumulation under the effects of glucocorticoids on lipid metabolism (FELDMAN, 2004). For the HAC diagnosis, a laboratory investigation must be followed by a complete blood count, liver enzymes, cholesterol, triglycerides, and urinalysis, in addition to abdominal ultrasound and hormone tests (MARCO, 2015). In this sense, despite being a common finding in domestic dogs (HERRTAGE, 2015), no reports were found in the literature researched on individuals of *Cerdocyon thous*. Therefore, this study aims to report a case of diagnosis and

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treatment of hyperadrenocorticism in a specimen of *C. thous*, kept under human care.

CASE REPORT

A 12-year-old female crab-eating fox (*Cerdocyon thous*), weighing 7.2kg, with a dietary base of meat, feed, and calcium supplement, kept under human care as part of a zoological collection's breeding stock, underwent a preventive check-up. This procedure required chemical restraint based on ketamine (15mg/kg) and xylazine (0.4mg/kg) administered intramuscularly. During the procedure, a physical examination was performed based on the semiological inspection (FEITOSA, 2014) that revealed no noteworthy changes, with the animal being normal colored, normohydrated, with capillary refill time equal to two seconds, a physical score good for the species, and the absence of alopecia or other dermatopathies. In addition, other procedures were performed, including the collection of blood samples punctured from the cephalic vein and stored in ethylenediaminetetraacetic acid (EDTA) and dried with clot activator tubes. for hemogram and biochemistry; abdominal ultrasonography; and urine collection by the cystocentesis technique to perform urinalysis.

The sonographic findings were hepatomegaly, hepatic hyperechogenicity, left (46mm-cranial pole x 96mm-caudal pole) and right (39mm-cranial pole x 90mm-caudal pole) adrenomegaly. The other organs did not show any noteworthy changes.

In the blood count tests performed on an automated device with differential counting in microscopy and biochemical tests performed on the Humastar[®] analyzer with the bioclin[®] kit, it was possible to observe a decrease in the red series with eosinophilia, lymphocytosis, anisocytosis, mild polychromasia, and rare reactive lymphocytes, and a slight increase in serum creatinine, liver enzymes alanine aminotransferase (ALT), and aspartate aminotransferase (AST), as described in the table 1.

The result of alkaline phosphatase was 34 IU/L, and its reference range found in domestic canines was only 12 to 121 IU/L (BAIN, 2013).

The results of the physical examination showed a turbid aspect in the urinalysis (table 2). The chemical exam showed the moderate and discrete presence of occult blood protein; and in the sedimentoscopy results, the moderate and discrete presence of RBCs, leukocytes, and granular cylinders and bacteria were observed, in addition to an increased urinary protein/urinary creatinine (UP/UC) ratio.

As a screening test, basal cortisol dosage was requested along with a cortisol suppression test after the use of low-dose dexamethasone. For previous preparation with a 12-hour fasting period for basal cortisol measurement, a blood sample was collected from the cephalic vein and placed in a dry biochemistry tube with a clot activator (red). Then, for the suppression test,

Table 1. Results and references of blood count and biochemistry of the crab-eating fox (*Cerdocyon thous*).

	Results	References (GOMES, 2007)
Blood count		
Erythrocyte	3.7x10 ⁶ /μL	4.31 - 6.77x10 ⁶ /μL
Hemoglobin	10.7g/dL	12.96 - 16.88g/dL
Globular volume	31%	38 - 49%
Leukocytes	12,000 cels/μL	8,100 - 13,900 cels/μL
Rods	0 cels/μL	0 -133 cels/μL
Segmented	7,986 cels/μL	5,758 - 0.387 cels/μL
Eosinophils	1,452 cels/μL	189 - 1,336 cels/μL
Lymphocytes	2,541 cels/μL	1,062 - 2,357 cels/μL
Total Protein	6.8 g/dL	5.47 - 7.09 g/dL
Biochemistry		
Serum Creatinine	1.2mg/dL	0.37 - 1.11mg/dL
Urea	64 mg/dL	22.46 - 71.84 mg/dL
ALT	74 UI/L	11 - 52UI/L
AST	56 UI/L	19 - 54UI/L

Table 2. Results and references of the urinalysis of the crab-eating fox (*Cerdocyon thous*).

	Results	References (SINK; FELDMAN, 2004)
Physical exam		
Aspect	Turbid	Clear to slightly turbid
Density	1.028	1.015 - 1.040
Chemical Examination		
Protein	++ (100 mg/dL)	Negative to traces (Up to 50mg/dL)
Hidden Blood	+	Absent
pH	6.0	5.5 - 7.5
Sedimentoscopy		
RBCs	15 to 18 per field	0 to 3 per field
Leukocytes	2 to 4 per field	Negative
Bacteria	+	Absent
Cylinders	Granular +	Absent
UP/UC	1.37	Up to 0.2

0.015 mg/kg dexamethasone sodium phosphate was applied intravenously, and after four and eight hours, new blood samples were collected from the jugular vein, also packed in the dry tube with a clot activator. As a result, the basal cortisol level was 14.12μg/dL (reference: 0.6 to 6μg/dL), cortisol level after four hours of dexamethasone was 7.25mcg/dL

(reference: $<1.4 \mu\text{g/dL}$), and the cortisol level after eight hours was dexamethasone 8.93mcg/dL (reference: $<1.4 \mu\text{g/dL}$) by the radioimmunoassay method with a domestic canine reference value (ANDREWS, 2013).

After exclusion of the differential diagnoses and indication by the cortisol test, CAH was suspected, and a treatment with trilostane at a dose of 6mg/kg , SID, continuous use, via oral, was instituted soon after the diagnosis date. The capsule was supplied inside a ground beef cake in the morning, which was consumed in front of the veterinary team to ensure its consumption.

After one year and five months of treatment, the patient was submitted to physical restraint for a new blood sample collection for a screening test of the treatment efficacy. The ACTH stimulation test was then performed, with an initial sample collected in a dry biochemistry tube with a clot activator, and the application of ACTHEL 25 IU (Hhub) at a dose of 0.08mL/kg , intramuscularly, and another sample collected one hour later. As a result of the basal cortisol dosage, 15.3ng/mL was obtained, with a reference range of 6 to 60ng/mL , and post-ACTHEL 73ng/mL , with a reference range of 55 to 200ng/mL (ANDREWS, 2013).

DISCUSSION

Hepatomegaly and especially adrenomegaly are characteristic sonographic findings of HAC (HERRTAGE; RAMSEY, 2015), which could be confirmed by knowing that in dogs, the gland length and caudal pole width are respectively 10.7 to $50.2\text{mm} \times 1.9$ to 12.4mm on the left and 10 to $39.3\text{mm} \times 3.1$ to 12mm on the right (FARROW, 2003). Since the adrenal hyperplasia is bilateral, a case of pituitary-dependent HAC can be hypothesized (BIRCHARD; SHERDING, 2008), given that the increased ACTH leads to bilateral adrenocortical hyperplasia (HERRTAGE; RAMSEY, 2015). Furthermore, there is no presence of tumorization of the glands, which would characterize an ADH, and also no history of prolonged or heavy corticosteroid use, a common cause of iatrogenic HAC.

Confirming the HDP diagnosis would require advanced imaging tests such as CT or MRI of the skull to identify pituitary tumors, especially when they are large (MEUTEN, 2015), or postmortem tests such as immunohistochemistry, considering the possibility of tumors with very small diameters (HERRTAGE; RAMSEY, 2015).

Although increased alkaline phosphatase activity occurs in more than 90% of cases of dogs with HAC (MEUTEN, 2015), in this case, the result obtained was within the reference parameters. However, the result of a domestic dog was used due to a lack of data, which does not exclude the possibility of HAC (HERRTAGE; RAMSEY, 2015). The ALT and AST levels, on the other hand, were mildly elevated, as they were mild to moderate in most dogs (MEUTEN, 2015).

Urinalysis is a test of paramount importance for the follow-up of suspected HAC given that alterations found are described in dogs positive for the syndrome, such as proteinuria, which can be seen in roughly 75% of cases, and an elevated UP/UC ratio (MEUTEN, 2015). In addition, the presence of bacteria and leukocytes indicates a bacterial infection that can be due to the immunocompromised condition of dogs with HAC due to the effect of corticosteroids (MEUTEN, 2015). Although there are no specific reference values for *Cerdocyon thous*, the reference values for domestic dogs were used since it is the species with the greatest phylogenetic proximity that has the described parameters.

In the screening test case, although the reference value is also from a domestic canine, it was prioritized considering the phylogenetic proximity and the discrepancy in the values obtained from the reference values. This test in animals that have HAC does not show a decrease in the cortisol rate after dexamethasone administration, which is excellent for differentiating normal dogs from those with HAC (MEUTEN, 2015). Thus, the absence of cortisol suppression, considering that its value remained above $1.4\mu\text{g/dL}$, allows HAC diagnosis, although the patient did not show clear clinical signs.

Thus, from the changes visualized in ultrasonography, biochemical tests, urinalysis, and screening tests, it was possible to corroborate the altered functionality of the adrenal, and hyperadrenocorticism could then be diagnosed. Thus, treatment was stipulated with Trilostane, a synthetic steroid that acts as a competitive inhibitor of 3- β -hydroxysteroid dehydrogenase, whose mechanism blocks the adrenal synthesis of glucocorticoids, mineralocorticoids, and sex hormones (HERRTAGE; RAMSEY, 2015) and has excellent clinical efficacy ($>80\%$) (NELSON; COUTO, 2014).

To confirm the effectiveness of the treatment with the drug, the animal was subjected to the ACTH stimulation test, the best test to monitor the effectiveness of hyperadrenocorticism therapy (FELDMAN; KERSEY; NELSON, 2004). The result obtained within normal levels demonstrates the control of comorbidity and thus the efficacy of the treatment and indicates that the ACTH and cortisol hormone levels were, consequently, maintained within normal values.

CONCLUSION

The present report highlights the fact that the patient had not shown previous clinical signs, and the disease was investigated based on changes found in complementary exams of preventive handling. Thus, we pointed out the control of HAC in a *Cerdocyon thous* with the use of trilostane at a dose of 6mg/kg , with the absence of perceptible side effects and increased survival of the patient. Moreover, it was shown that diagnostic techniques for HAC used in dogs were effective for the individual reported here, which may contribute to endocrine studies in *C. thous* or even wild canids.

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