CASE STUDY
Cushing’s Disease in a 10-year-old Cocker Spaniel

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“Hudson,” a 10-year-old MC Cocker spaniel, was referred for evaluation of severe polyuria and polydipsia (PU/PD) of 3 months in duration...

1. Physical Examination

On physical examination no significant abnormalities were detected, with the exception of mild hepatomegaly. The skin and hair coat appeared to be normal.

2. History

Previous laboratory analysis, including a complete blood count and serum biochemical profile, was unremarkable, with the exception of a urine specific gravity (USG) of 1.010 and positive urine culture for Escherichia coli. The pet was treated with enrofloxacin (5 mg/kg Q 24 H) for 10 days; however, no change in the PU/PD was observed.
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An ACTH stimulation test was performed, with a resting cortisol and 1-hour post cortisol results of 2.7 and 14.8 mcg/dL, respectively. These results were considered normal for the laboratory.

3. Differential Diagnosis

Hyperadrenocorticism (HAC) was still considered to be the most likely differential cause for the PU/PD, despite the previously normal ACTH stimulation test, given the signalment, history, and clinical signs.

4. Diagnostics

A low-dose dexamethasone suppression (LDDS) test was performed following IV administration of 0.01 mg/kg of dexamethasone. The resting cortisol, 4-hour post LDDS, and 8-hour post LDDS results were 5.1 (reference range, 1.4–5 mcg/dL), 1.2, and 4.6 mcg/dL, respectively.

The elevated 8-hour cortisol (reference range, < 1.4 mcg/dL), in combination with greater than 50% suppression in cortisol concentrations seen at 4 hours, was diagnostic of pituitary-dependent hyperadrenocorticism (PDH), also known as Cushing’s disease.

5. Treatment Plan

Treatment options were discussed with the referring veterinarian and treatment with trilostane (Vetoryl) was recommended, starting with 2 mg/kg PO Q 24 H in the morning.

The owner was instructed to:

- Administer the medication with food to enhance gastrointestinal absorption.
- Monitor the animal’s water consumption, urination, appetite, and activity level.
- Observe for any adverse reactions, such as vomiting and diarrhea.
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A recheck examination consisting of a physical examination and ACTH stimulation test with monitoring of electrolytes was scheduled 10 days following the start of medication.

6. Follow-Up

Ten-Day Recheck
At the time of the recheck examination, the owners reported a marked reduction in the PU/PD.

An ACTH stimulation test was performed 4 hours post administration of trilostane, with pre and post ACTH cortisol concentrations 2.2 and 5.4 mcg/dL, respectively, indicating adequate adrenal suppression. Determination of electrolytes with an in-house chemistry analyzer was performed and sodium and potassium concentrations were within normal limits.

Due to the laboratory results, along with the observed improvement in clinical signs, the current dose of trilostane was continued and the pet scheduled for a recheck examination in 4 weeks.

Four-Week Recheck
During the subsequent recheck examination, the owners reported that the pet was more active, with normal water consumption and urination.

A morning urine sample collected by the owner demonstrated a USG of 1.028. Electrolytes were within normal limits. The pre and post cortisol concentrations were 1.4 and 4.8 mcg/dL, respectively, indicating continued adequate adrenal suppression.

The dose of trilostane was maintained and the pet scheduled for a recheck examination in 3 months.
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Three- and 6-Month Rechecks
Three and 6 months later the pet was clinically normal. One episode of vomiting and diarrhea had occurred at 4.5 months, but the patient responded to the use of a bland diet, and clinical signs resolved in 24 hours, with no adjustments made to the treatment protocol.

At the 3- and 6-month recheck examinations, electrolyte concentrations were within normal limits and post ACTH cortisol concentrations were less than 4.2 and 5 mcg/dL, respectively. The dose of trilostane was maintained and the pet scheduled for a recheck examination in 3 to 4 months.

7. Discussion
This case illustrates several important points regarding Cushing’s disease and its treatment with trilostane.

The referring veterinarian had 3 questions regarding this patient’s presentation and diagnostic results:

1. The lack of clinical signs of Cushing’s disease other than PU/PD.
2. The normal initial ACTH stimulation test.
3. The finding of normal serum ALP on the initial laboratory evaluation.

Clinical Signs
PU/PD may be the only clinical sign of HAC. Dermatologic abnormalities, such as bilateral symmetric endocrine alopecia and pyoderma, need not be present.

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ACTH Stimulation Test
Up to 15% to 20% of dogs with HAC have a normal ACTH stimulation test upon initial evaluation of the pituitary–adrenal axis. When faced with a patient that has clinical signs indicative of HAC but a normal ACTH stimulation test, consider LDDS to establish a diagnosis or rule out HAC. Conversely, up to 10% of dogs have an initially normal LDDS, therefore, if LDDS is used as the initial screening test and a normal test result is obtained, consider an ACTH stimulation test.

Serum ALP Results
Up to 20% of dogs do not have an elevated ALP in response to either exogenous or endogenous steroid excess, likely due to lack of the gene encoding for the steroid inducible isoenzyme.

Treatment Evaluation
The target hormonal goal for the ACTH stimulation test is considered a post ACTH cortisol of less than 9.1 mcg/dL. Together with improvement in clinical signs, this level of adrenal suppression indicates appropriate dosing with trilostane. In our hands, up to 80% of patients obtain clinical and hormonal improvement with once daily dosing.
Dr. Bruyette received his Doctor of Veterinary Medicine degree from the University of Missouri in 1984. He completed an internship at Purdue University and a residency program in internal medicine at the University of California Davis. He was a staff internist at the West Los Angeles Veterinary Medical Group, as well as a member of the Department of Comparative Medicine at Stanford University, an Assistant Professor and Head of Internal Medicine at Kansas State University, and Director of the Analytical Chemistry Laboratory at Kansas State.

In addition to his duties as Medical Director, Dr. Bruyette practices internal medicine and specializes in the hormonal system and its diseases. His interests also include adrenal disease, diabetes and thyroid disorders. Dr. Bruyette joined VCA West Los Angeles Animal Hospital in 1996.