Central Diabetes Insipidus

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History

A 10.5-year-old, 59.5-lb (27-kg), spayed Australian shepherd crossbreed was presented for examination for a 6-month history of persistent polyuria (PU) and polydipsia (PD) without stranguria or pollakiuria. The owner noted that large amounts of urine would leak approximately once to twice per week while the dog was asleep. Vomiting and/or diarrhea were not reported, and the patient had a normal appetite and energy level. Pollakiuria occurred once 5 months prior to presentation and was responsive to a 10-day course of amoxicillin (22 mg/kg PO q12h); urinalysis was not performed. A seasonal flea and tick preventive was the only other medication given.

Physical Examination

The dog was bright, alert, and responsive, and vital signs were within normal parameters. Dehydration was not present. Her abdomen was tense on palpation. The remainder of the physical examination was unremarkable. BCS was ideal at 5/9, and weight loss was not reported.

Diagnosis

PU/PD are nonspecific clinical signs. The potential causes for PU/PD are central diabetes insipidus (CDI), primary or secondary nephrogenic diabetes insipidus (NDI; eg, hyperadrenocorticism, hypoadrenocorticism, hyperthyroidism, liver disease, hypercalcemia, pyometra, pyelonephritis), osmotic diuresis (eg, diabetes mellitus, chronic kidney disease, Fanconi syndrome, postobstructive diuresis), low renal medullary tonicity, and psychogenic polydipsia (PP).[1]

Based on the patient's history of PU/PD and the results of laboratory diagnostics and imaging (***Table***, next page), many of the most common causes of PU/PD could be ruled out, leaving complete or partial CDI,

CDI = central diabetes insipidus
NDI = nephrogenic diabetes insipidus
PD = polydipsia
PP = psychogenic polydipsia
PU = polyuria

TABLE

LABORATORY DIAGNOSTICS & IMAGING

Diagnostic Test	Result
Blood pressure*	126/63
Mean arterial pressure*	67
CBC	Normal
Serum chemistry profile†	
Phosphorus	2.4 mg/dL (range, 2.6-7.2 mg/dL)
Albumin	4.2 g/dL (range, 2.8-4 g/dL)
Alanine aminotransferase	56 U/L (range, 14-86 U/L)
Cholesterol	379 mg/dL (range, 82-354 mg/dL)
Symmetric dimethylarginine	11 µg/dL (range, 0-14 µg/dL)
ACTH stimulation	
Basal cortisol	1.8 µg/dL (range, 1-7.7 µg/dL)
Post-ACTH stimulation	10 µg/dL (range, 6-18 µg/dL)
Bile acids (pre-/post-)	Normal
Urinalysis (cystocentesis)†	
USG	1.001
pH	6.5
Squamous epithelial cells	0-1/hpf (range, 0-3/hpf)
USG samples	1.001 (3 AM)
	1.006 (6 PM)
	1.004 (10 AM)
Urine cortisol:creatinine ratio‡	12§
Urine culture	No growth
Abdominal ultrasonography‖	Right kidney smaller than left kidney; borderline normal in size
	Bladder contained a large volume of urine; patient urinated 45 minutes prior to examination
	Bladder wall thickness was normal¶
	No masses or calculi

*Measured using Doppler. Normal systolic blood pressure is <140 mm Hg.
†All other results were normal.
‡Taken from an at-home sample
§Cushing's disease is highly unlikely in dogs with urine cortisol:creatinine ratio ≤13.
‖All other structures in the abdomen were within normal limits.
¶Normal thickness of a moderately distended bladder is 1.4 mm.

primary (rare) or secondary (more common) NDI, and PP as the most probable causes.

Clinical Signs

PU/PD is confirmed if water consumption is >100 mL/kg/day, urine production is >50 mL/kg/day, and random urine specific gravity (USG) is ≤1.012.[2] Urine from the patient's first urination of the morning (3 AM) had a USG of 1.001. In general, a USG between 1.012 and 1.018 may indicate partial CDI. Additional testing (eg, preprandial and postprandial serum bile acid concentration) may be necessary to further exclude liver disease.

A modified water deprivation test is designed to determine whether endogenous adenosine vasopressin (AVP) is released in response to dehydration and whether the kidneys respond to this stimulus, but it can be time-consuming and is associated with risks (eg, severe dehydration, hypernatremia, death). Also, although useful in differentiating primary NDI from CDI, a modified water deprivation test may not differentiate partial CDI from PP with complete certainty. Dogs and cats with partial or complete CDI or primary NDI have an impaired ability to pass concentrated urine when dehydrated.

A desmopressin acetate trial could help determine the cause of PU/PD in this patient. Desmopressin tablets or conjunctival drops of 0.01% desmopressin human intranasal spray should be administered every 12 hours for 7 days, and the desmopressin effect should be evaluated after 5 to 7 days of treatment (required to overcome medullary washout). CDI is likely if an observable or measurable decrease in water consumption is noted and USG increases by at least 50% or exceeds 1.018.

Clinical Background

CDI, which can be congenital or secondary due to trauma[3-7] or neoplasia, is caused by any condition that damages the neurohypophyseal system (eg, infection, neoplasm, trauma, vascular disease, autoimmune hypothalamitis, cysts), destruction of the antidiuretic hormone (ADH) production site in the hypothalamus, loss of major axons that carry ADH to storage sites in the posterior pituitary, or disruption of the ability to release stores of ADH. A prolonged hypoxic event (eg, cardiac arrest) can lead to development of CDI.[4]

CDI must be suspected if there is any history of trauma. MRI or CT is recommended if neurologic signs are present and if there is suspicion of intracranial neoplasia.

NDI can be familial, which is rare, or acquired (ie, secondary to several diseases) and can lead to decreased action of AVP in the kidney. Desmopressin supplementation cannot effectively manage NDI due to lack of response of AVP receptors in the kidney or lack of AVP receptor numbers. The prognosis of primary NDI is guarded-to-poor because of limited therapeutic options.

Treatment

Treatment may not be necessary if the patient has unlimited access to water and PU/PD is not distressing to the owner.[2]

Desmopressin, a synthetic AVP analogue, can be given for partial or complete CDI; prognosis depends on the underlying cause of CDI. Desmopressin is a potent V_2-receptor agonist and has minimal effects in V_1 receptors if no hypertension is observed. The 0.01% human intranasal solution (dogs, 1-4 drops [≈1.5-5 µg/drop] q8-24h; cats, 1 drop q12h) should be administered in the conjunctival sac or nose. The injectable formulation of desmopressin (administered intravenously over 15-30 minutes and repeated as needed) in dogs and cats has a short-term effect and is best used in cases of diabetes insipidus as a diagnostic tool. Tablets can also be given (dogs, 100 µg PO q12-24h; cats, 25-50 µg PO q8-12h). Therapeutic response is variable.

Dose and frequency should be titrated to effect for each patient. Response to treatment is rapid, and PU returns quickly if treatment is discontinued.[8] Desmopressin is generally safe, and complications are uncommon.[1] The most common complications are hyponatremia and failure to decrease water intake. If the patient develops hyponatremia, desmopressin should be discontinued, then only given as needed. Close monitoring of electrolytes and USG is needed at the beginning of treatment until the appropriate individual dose is achieved.

In this patient, phenylpropanolamine (1 mg/kg PO q12h) was tried without success to manage the urinary incontinence episodes. The patient was then started on an initial trial therapy of desmopressin tablets (0.2 mg PO q12h). The tablet dosage was later increased (0.3 mg PO q12h), after which USG was concentrated at 1.022 and clinical signs resolved.

The patient did not return for a follow-up examination within the next year. At an eventual return visit, she had a USG of 1.003, but the owner chose not to resume treatment.

Conclusion

Diabetes insipidus is an important differential for PU/PD, and, although not a very common condition, it must be considered when managing a dog or cat presented with PU/PD. Other causes of PU/PD should be excluded before diagnosis of diabetes insipidus is pursued.

ADH = antidiuretic hormone
AVP = adenosine vasopressin
CDI = central diabetes insipidus
NDI = nephrogenic diabetes insipidus
PD = polydipsia
PP = psychogenic polydipsia
PU = polyuria
USG = urine specific gravity

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