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Atypical Presentation of Hypoglycemia in a Dog

Charlie, an 8-year-old neutered male toy poodle, was referred for a 2-day history of lethargy, anorexia, and severe hypoglycemia.

History. Clinical signs appeared 1 day after the dog received annual vaccinations. No dietary changes had been made or medications administered during the past year, and the owner reported no history of recent travel. The patient had a history of multiple episodes of acute colitis associated with various stressful events but had been treated successfully with conservative symptomatic medical management.

Examination. The dog's body condition score was 3/5. Temperature, pulse rate, and respiration rate were within normal limits; systolic blood pressure was 115 mm Hg. The patient was too weak to stand and was exhibiting generalized muscle fasciculations. No other abnormalities were noted.

Laboratory Results. A random blood glucose measurement was 31mg/dL (reference range, 67–132 mg/dL) and additional diagnostics were performed (see **Table**).

Abdominal Imaging. No abnormalities were identified on abdominal radiographs. An abdominal ultrasound revealed a small (3.7 mm) right adrenal gland; the left adrenal gland was not identified. The gastric wall was slightly thickened. No pancreatic or hepatic masses were noted.

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Table. Relevant Laboratory Results

Laboratory Test	Result	Reference Interval
Blood Analysis		
Albumin (g/dL)	2.1	2.3–3.9
Ammonia (umol/L)	24.9	1–46
Blood glucose (mg/dL)	31	67–132
Cholesterol (mg/dL)	150	125–301
Sodium (mmol/L)	140	138–148
Potassium (mmol/L)	3.6 (Na:K = 38.9)	3.5–5
Insulin (mU/mL)	1.8	< 5*
Leukocytes (× 10^3/mcL)	19.2	6–17
Lymphocytes (× 10^3/mcL)	3.46	1–5
Segmented neutrophils (× 10^3/mcL)	14.78	3–12
ACTH Stimulation		
Baseline plasma cortisol (mcg/dL)	< 1	1–6
Poststimulation (mcg/dL)	< 1	7–17
Additional ACTH Testing		
Endogenous plasma ACTH (pg/mL)	713	40–50

*When blood glucose < 60 mg/dL

ASK YOURSELF ...

Which is the most likely diagnosis for this dog?

A. Primary insulinoma resulting in uninhibited release of insulin and subsequent hypoglycemia
B. Bacterial sepsis resulting in systemic consumption of glucose and hypoalbuminemia due to an acute phase response
C. Hypoadrenocorticism resulting in hypoalbuminemia and hypoglycemia due to decreased hepatic gluconeogenesis
D. Hepatic failure, leading to hypoglycemia and hypoalbuminemia due to decreased hepatic production

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FIND MORE

Read more Addison's disease cases on our website:

- Some Dogs Just Do Not Read the Same Book (May 2004)
- Weakness & Collapse in a Golden Retriever (March 2006)
- Common Gastro-intestinal Signs = Challenging Diagnosis? (October 2008)

ACTH = adrenocorticotropic hormone

CORRECT ANSWER: C. HYPOADRENOCORTICISM RESULTING IN HYPOALBUMINEMIA AND HYPOGLYCEMIA DUE TO DECREASED HEPATIC GLUCONEOGENESIS.

Hypoglycemia that is severe enough to cause neurologic manifestations is an uncommon presentation of hypoadrenocorticism. Glucocorticoid deficiency decreases hepatic gluconeogenesis and increases peripheral insulin sensitivity, resulting in hypoglycemia.

Differential Diagnoses. Other differentials for the acute severe hypoglycemia in this dog included insulinoma, sepsis, hepatic failure, and toxin exposure (eg, insulin overdose, xylitol ingestion).

Initial Diagnostics. Following a thorough physical examination, diagnostics should include complete blood count, serum biochemical panel, urinalysis, serum insulin concentration, and ACTH stimulation test. An insulinoma will typically result in normal to increased insulin concentration (reference range, 5–20 mU/mL) in the face of hypoglycemia.

Addison's Disease. Hypoadrenocorticism (Addison's disease) is most commonly associated with deficiencies of both mineralocorticoids and glucocorticoids. Aldosterone (mineralocorticoid) deficiency results in hypotension, hyponatremia, and hyperkalemia, all of which are hallmark abnormalities for this disease. Two other forms of Addison's disease, however, do not result in mineralocorticoid deficiency:

- **Glucocorticoid-deficient primary "atypical" hypoadrenocorticism** is characterized by glucocorticoid deficiency in the face of increased circulating ACTH, with preservation of mineralocorticoid production and release. As many as 30% of Addisonian dogs are estimated to have the atypical form of hypoadrenocorticism.
- **Secondary hypoadrenocorticism**, which is far less common, is characterized by decreased production or release of ACTH from the pituitary gland that results in adrenal gland atrophy. Mineralocorticoid production and release may be diminished but remains adequate to maintain electrolyte balance. This condition can be idiopathic, caused by a destructive lesion within or adjacent to the pituitary gland, or (more commonly) by prolonged drug-induced pituitary suppression.

ACTH = adrenocorticotropic hormone

TAKE-HOME MESSAGES

- A wide range of clinical signs may be observed in dogs with Addison's disease. For dogs with unexplained hypoglycemia, an ACTH stimulation test is an appropriate first-line diagnostic test.
- Between 10% and 30% of dogs with hypoadrenocorticism will have glucocorticoid deficiency alone (serum sodium and potassium concentrations will be normal).
- Mineralocorticoid supplementation is not needed for treatment of secondary hypoadrenocorticism and atypical Addison's disease; physiologic doses of glucocorticoids will suffice.
- Measurement of endogenous ACTH will allow differentiation between the forms of hypoadrenocorticism and assist in guiding therapy and long-term follow-up; samples for measurement must be collected before glucocorticoid administration.

Although mineralocorticoid-deficient hypoadrenocorticism is the most common presentation of hypoadrenocorticism, clinicians should be aware of these less common presentations. Normal serum electrolyte values, lack of a stress leukogram, and a plasma cortisol value of < 2 mcg/dL after ACTH stimulation are diagnostic for atypical or secondary hypoadrenocorticism. Measurement of endogenous ACTH will allow differentiation of the 2 forms of the disease.

Because progression to mineralocorticoid deficiency does not occur in secondary hypoadrenocorticism, continued monitoring of electrolytes is not necessary. With atypical Addison's disease, serum electrolytes should be monitored regularly (at least every 3–6 months) because mineralocor-

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ticoid deficiency may develop in some dogs. Initial therapy for atypical Addison's disease does not involve mineralocorticoid therapy, but treatment modifications may be necessary if the disease progresses to include mineralocorticoid deficiency.

Charlie's Case. The presented case describes an example of glucocorticoid-deficient atypical Addison's disease. The plasma cortisol concentration of < 1 mcg/dL after ACTH stimulation confirms the diagnosis of hypoadrenocorticism, and the increased endogenous ACTH (713 pg/mL) confirms primary hypoadrenocorticism.

In secondary hypoadrenocorticism, endogenous ACTH concentration will typically be < 5 pg/mL, although some dogs may have a concentration within the normal reference range (40–50 pg/mL). Clinicians should remember that any exogenous corticosteroid administration will affect the ability to interpret endogenous ACTH levels because the negative feedback from glucocorticoids causes a rapid decrease in ACTH production.

See Aids & Resources, back page, for references and suggested reading.

TX AT A GLANCE

Atypical Addison's Disease

- Glucocorticoid therapy with prednisone, 0.1–0.2 mg/kg Q 24 H, will result in resolution of clinical signs and laboratory abnormalities once the initial crisis has been managed.

  The dose may be tapered to the minimum dose necessary to control clinical signs. The maintenance dose can be doubled before anticipated stressful events.
- As long as serum electrolyte values are within normal limits, mineralocorticoid therapy is unnecessary.