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Hypoadrenocorticism in Small Animals

Deborah S. Greco, DVM, PhD, DACVIM

The diagnosis and treatment of hypoadrenocorticism can be one of the greatest challenges faced by veterinary practitioners, as Addison's disease may have many faces and many presentations. Although the disease is most often diagnosed in dogs, cats may also suffer from Addison's disease. The practitioner must have a high index of suspicion to make a diagnosis of hypoadrenocorticism. This index of suspicion is based on knowledge of the common signalment, history, physical examination, and laboratory findings. Diagnosis of hypoadrenocorticism is supported by appropriate choice of diagnostic endocrine tests that are described in detail in this article. Once a diagnosis of hypoadrenocorticism has been made, expedient treatment is of foremost concern. Timely treatment using fluids, corticosteroids, and supportive care will ensure a successful outcome; the emergency treatment of Addison's is covered briefly in this article and fully in another article in this issue. The purpose of this review was to describe the clinical diagnosis and chronic treatment of hypoadrenocorticism in dogs and cats.

KEYWORDS hypoadrenocorticism, Addison's disease, feline, canine, deoxycorticosterone pivalate

Hypoadrenocorticism is a result of deficient secretion of both mineralocorticoids (aldosterone) and glucocorticoids.[1] Naturally occurring primary hypoadrenocorticism is usually caused by immune-mediated destruction of the adrenal cortex in both cats and dogs.[1-3] However, lymphomatous infiltration of the adrenals has been reported as a cause of hypoadrenocorticism in cats.[4] Secondary hypoadrenocorticism, in which the pituitary gland produces inadequate amounts of adrenocorticotrophic hormone (ACTH), can be caused by chronic steroid therapy or less commonly by tumors, trauma, or congenital defects of the pituitary gland.[1,4] Secondary hypoadrenocorticism is rare in both dogs and cats. Hypoadrenocorticism, which is glucocorticoid-deficient only, has been termed "atypical" Addison's disease.[4] Secondary hypoadrenocorticism is always atypical and primary hypoadrenocorticism is atypical in the early stages of the disease before destruction of the zona glomerulosa.

Signalment, Clinical Signs, and Laboratory Abnormalities

Canine hypoadrenocorticism is most often diagnosed in young female dogs (70%) of any breed.[1-3,5,6] However, hypoadrenocorticism has been reported in families of Leonbergers and standard poodles, suggesting a genetic basis in some breeds.[7,8] Young cats of any breed or sex can also develop hypoadrenocorticism.[4,9]

Historical findings compatible with hypoadrenocorticism include intermittent vomiting, diarrhea, weight loss, lethargy, depression, anorexia, and weakness.[1-6] There may be a history of vomiting or diarrhea responsive to nonspecific treatment, such as intravenous fluids, only to have signs reoccur several days to weeks later. Often the clinical signs come and go (waxing and waning) periodically. As the disease progresses, the animal may present with collapse, hypothermia, shaking, polyuria, and polydipsia. Hair loss and melena are unusual historical findings. Differential diagnoses for the common clinical signs consistent with hypoadrenocorticism include inflammatory bowel disease, intestinal parasitism, bilious vomiting syndrome, and renal disease. A comparison of clinical signs of hypoadrenocorticism in cats and dogs is shown in Table 1 and a comparison of typical and atypical hypoadrenocorticism in dogs is listed in Table 2.

Physical examination of animals in an acute Addisonian crisis reveals weak pulses, bradycardia, prolonged capillary refill time, severe mental depression, and profound muscle weakness.[1,2]

Clinical features that should heighten the index of suspicion of hypoadrenocorticism include *a normal or slow heart rate in the face of circulatory shock*, previous response to corticosteroid or fluid therapy, and a "*waxing and waning*" course of disease before collapse.

Classic electrolyte abnormalities, such as hyponatremia, hyperkalemia, hypochloremia, and sodium-to-potassium ra-

Nestle Purina Petcare, St. Louis, Missouri.
Address reprint requests to Deborah S. Greco, DVM, PhD, DACVIM, Nestle Purina Petcare, One Checkerboard Square, St. Louis, MO 63164. E-mail: Deborah.greco@rdmo.nestle.com

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Table 1 Clinical Signs and Abnormal Laboratory Findings in Dogs and Cats with Primary Hypoadrenocorticism (Addison's Disease)[1,9]

	Cats (%) (n = 10)	Dogs (%) (n = 225)
Clinical signs		
Lethargy	100	95
Anorexia	100	90
Weight loss	100	50
Dehydration	88	45
Weakness	75	75
Slow capillary refill	63	30
Weak pulse	50	20
Vomiting	25	75
Polyuria/polydipsia	25	25
Bradycardia	13	18
Diarrhea	—	40
Waxing/waning course	—	40
Previous response to therapy	—	35
Hypothermia	—	35
Shaking	—	27
Melena	—	15
Painful abdomen	—	8
Hair loss	—	5
Laboratory findings		
Hyperkalemia	100	95
Hyponatremia	100	80
Hypochloremia	100	40
Azotemia	100	85
Hyperphosphatemia	88	85
Metabolic acidosis	—	40
Elevated ALT/AST	—	30
Hyperbilirubinemia	—	20
Hypercalcemia	13	30
Hypoglycemia	—	17
Anemia	25	25
Eosinophilia	20	13
Lymphocytosis	38	10
Urine specific gravity <1.030	—	75

tios of less than 20 to 1, are highly suggestive of primary hypoadrenocorticism.[1,2] However, gastrointestinal disease, acute renal failure, postrenal azotemia, and abdominal/thoracic effusions are additional differential diagnoses. Azotemia and hyperphosphatemia also attend primary hypoadrenocorticism, making it difficult to differentiate from acute renal failure. Azotemia associated with hypoadrenocorticism may be prerenal as a result of dehydration, hypovolemia, or gastrointestinal hemorrhage.

Hypercalcemia may be observed in up to 30% of dogs with hypoadrenocorticism as a result of hemoconcentration.[10] Metabolic acidosis results from decreased hydrogen ion secretion in the renal distal tubule, increased generation of acids secondary to reduced tissue perfusion, and renal retention of organic acids.[9] Animals with glucocorticoid deficiency only will not show classic electrolyte imbalances but may present with hypoglycemia as a result of impaired gluconeogenesis and glycogenolysis.[1,5]

Hematological findings include mild normocytic normochromic (nonregenerative) anemia; however, if the animal is dehydrated, the underlying anemia may be masked. The absence of a stress leukogram is a subtle but important feature of atypical hypoadrenocorticism.[5] The presence of a normal or elevated eosinophil or lymphocyte count in a stressed animal should be viewed with suspicion for hypoadrenocorticism, particularly atypical Addison's disease. Eosinophilia and lymphocytosis are seen in 20 and 10% of dogs with primary hypoadrenocorticism, respectively.[1-6]

Urine-specific gravity is frequently low and is attributed to

Table 2 Comparison of the Clinical Features of Typical and Atypical Hypoadrenocorticism

Typical Hypoadrenocorticism	Atypical Hypoadrenocorticism
Pathogenesis	
Primary adrenal insufficiency—late	Primary adrenal insufficiency—early
	Secondary adrenal insufficiency (ACTH deficiency)
Signalment	
Young (<5 y)	Young (<5 y)
Dogs: female, cats either sex	Dogs: female
Standard poodles, Leonbergers	Any breed
Clinical signs	
Weakness	Anorexia
Lethargy	Lethargy
Depression	Vomiting
Vomiting	Depression
Diarrhea	Chronic diarrhea
Anorexia	Waxing and waning course
Previous response to therapy	Previous response to therapy
Collapse	Hair loss
Shock	
Hypothermia	
Shaking	
Polydipsia/polyuria	
Painful abdomen	
Melena	
Hair loss	
Laboratory findings	
Lack of stress leukogram	Lack of stress leukogram
Eosinophilia	Eosinophilia
Hyponatremia	Lymphocytosis
Hyperkalemia	Hypoglycemia
Hypochloremia	
Na/K ratio <27	
Azotemia	
Hypercalcemia	
Metabolic acidosis	
Hypoglycemia	
Endocrine testing	
Decreased cortisol before and after ACTH	Decreased cortisol before and after ACTH
High endogenous ACTH	Secondary: low endogenous ACTH