DISORDERS OF THE PITUITARY GLAND: CENTRAL DI, PITUITARY DWARFISM AND ACROMEGALY

Deborah S. Greco DVM, PhD Diplomate ACVIM
Nestle Purina Petcare

Diabetes insipidus (DI) is a disorder of water metabolism characterized by polyuria, urine of low specific gravity or osmolality, and polydipsia. It is caused by defective secretion of ADH (central DI) or by the inability of the renal tubule to respond to ADH (nephrogenic DI). Deficiency of ADH can be partial or complete. Central DI is characterized by an absolute or relative lack of circulating ADH and is classified as primary (idiopathic and congenital) or secondary. Secondary central DI usually results from head trauma or neoplasia.

Central DI may appear at any age, in any breed of dogs and cats, and in either gender; however, young adults (6 months of age) are most commonly affected. The major clinical signs of DI are profound polyuria and polydipsia (more than 100 mL/kg/day; normal range is 40 to 70 mL/kg/day), nocturia, and incontinence, usually of several months' duration. The severity of the clinical signs varies, inasmuch as DI may result from a partial or complete defect in ADH secretion or action. Other, less consistent signs include weight loss (because these animals are constantly seeking water) and dehydration.

Routine complete blood cell count and serum biochemical and electrolyte profiles are usually normal in animals with DI. Plasma osmolality is often high (>310 mOsm/L) in central or nephrogenic DI as a result of dehydration. Animals with primary polydipsia often exhibit low plasma osmolality (<290 mOsm/L) as a result of overhydration. When abnormalities, such as slightly increased hematocrit or hypernatremia, are present on initial evaluation, they are usually secondary to dehydration from water restriction by the pet owner. In DI, the urinalysis is unremarkable except for the finding of a persistently dilute urine (urine specific gravity, 1.004 to 1.012).

Diagnostic tests to confirm and differentiate central DI, nephrogenic DI, and psychogenic polydipsia include the modified water deprivation test or response to ADH supplementation. The modified water deprivation test is designed to determine whether endogenous ADH is released in response to dehydration and whether the kidneys can respond to ADH. The more common causes of polyuria and polydipsia should be ruled out before this procedure is performed. Failure to recognize renal failure before water deprivation may lead to an incorrect or inconclusive diagnosis or cause significant morbidity in the patient. Hypersecretion of vasopressin in the absence of osmotic or volumetric stimulation is called the syndrome of inappropriate antidiuretic hormone secretion. Neoplastic processes are often involved in this syndrome; ectopic tumors, often located in the lung, are the neoplasms most likely to cause SIAD.

Clinical syndromes of somatotropin deficiency and excess include pituitary dwarfism in the dog and acromegaly in the cat, respectively. Pituitary dwarfism results from destruction of the pituitary gland via a neoplastic, degenerative, or anomalous process. It may be associated with decreased production of other pituitary hormones, including TSH, ACTH, LH, FSH, and GH. Pituitary dwarfism is most common in German shepherd dogs aged 2 to 6 months. Other affected breeds include Carnelian bear dogs, spitz, toy pinschers, and Weimaraners. In German shepherd dogs, the disease is inherited.
as a simple autosomal recessive trait and occurs as a result of cystic Rathke’s pouch. The first observable clinical signs of pituitary dwarfism are slow growth, noticed in the first 2 to 3 months of life, and mental retardation, usually manifested as difficulty in house-training. Physical examination findings may include proportionate dwarfism, retained puppy haircoat, hypotonic skin, truncal alopecia, cutaneous hyperpigmentation, infantile genitalia, and delayed dental eruption. Clinicopathologic features include eosinophilia, lymphocytosis, mild normocytic normochromic anemia, hypophosphatemia, and occasionally hypoglycemia resulting from secondary adrenal insufficiency. Differential diagnoses include other causes of stunted growth such as hypothyroid dwarfism, portosystemic shunt, diabetes mellitus, hyperadrenocorticism, malnutrition, and parasitism. Diagnosis is made by measuring serum growth hormone concentrations (assay no longer commercially available) or serum somatomedin C (insulin-like growth factor 1 [IGF-1]). The advantage of IGF-1 is that it is not species-specific. There is usually a subnormal response to exogenous TSH and ACTH stimulation tests; furthermore, endogenous TSH and ACTH are decreased in affected dogs as a result of panhypopituitarism.

Acromegaly, or hypersomatotropism, is the condition resulting from chronic excessive GH secretion in the adult animal. Canine acromegaly is an extremely rare disorder observed after the administration of progestational compounds for suppression of estrus in intact female dogs. The disease is caused by excessive secretion of GH from mammary cells under the influence of exogenous progesterone. Acromegaly in cats, as in humans, is caused by a GH-secreting tumor of the anterior pituitary gland. Such tumors in cats grow slowly and may be present for a long time before the onset of clinical signs. Feline acromegaly occurs in older (8- to 14-year-old) cats and occurs more commonly in males. Canine acromegaly occurs in intact female dogs given progestational compounds for estrus prevention.

Clinical signs of uncontrolled diabetes mellitus are often observed as the first manifestations of acromegaly; therefore, polydipsia, polyuria, and polyphagia are the most common presenting signs. Net weight gain of lean body mass in animals suffering from uncontrolled diabetes mellitus is a key sign of acromegaly. Organomegaly, including renomegaly (observed in both cats and humans suffering from acromegaly), hepatomegaly, and enlargement of endocrine organs, is also observed. Some dogs and cats show the classic enlargement of extremities, body size, jaw, tongue, and forehead that is characteristic of acromegaly in humans. Some of the most striking manifestations of acromegaly occur in the musculoskeletal system; they include an increase in muscle mass and growth of the acral segments of the body, including the paws, chin, and skull. Cardiovascular abnormalities, such as cardiomegaly (as determined radiographically and echocardiographically), systolic murmurs, and congestive heart failure, develop late in the course of the disease. Azotemia develops late in the course of the disease in approximately 50% of acromegalic cats. Neurologic signs of acromegaly in humans, such as peripheral neuropathies (paresthesias, carpal tunnel syndrome, sensory and motor defects), and parasellar manifestations, such as headache and visual field defects, are not generally detected in acromegalic small animals.

Impairments in glucose tolerance and insulin resistance that result in diabetes mellitus are observed in all cats and most dogs with acromegaly. Measurement of endogenous insulin reveals dramatically increased serum insulin concentrations. Despite
severe insulin resistance and hyperglycemia, ketosis is rare in acromegalic animals. Feline acromegaly should be suspected in any diabetic cat (especially males) that has severe insulin resistance (insulin requirement > 20 U/cat/day). Hypercholesterolemia and mild increases in serum activities of liver enzymes are attributed to the diabetic state. Hyperphosphatemia without azotemia is also a common clinicopathologic finding, perhaps as a result of GH-stimulated bone growth. Urinalysis findings are unremarkable except for persistent proteinuria, probably as a result of systemic hypertension and glomerulosclerosis.

A definitive diagnosis of acromegaly requires documentation of increased plasma GH or somatomedin C concentrations. Unfortunately, feline and canine GH assays are no longer commercially available. At this time, the most definitive test for the diagnosis of acromegaly in cats is computed tomography of the pituitary region. Computed tomographic findings, coupled with the exclusion of other disorders that cause insulin resistance (hyperthyroidism, hyperadrenocorticism), in cats that exhibit clinical signs of acromegaly should lead the clinician to a diagnosis of acromegaly.