

Hypoadrenocorticism: Diagnosis, Treatment and Management of Complications

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Introduction

Primary hypoaldosteronism (Addison's disease) is an endocrine condition characterized in most cases by a lack of glucocorticoids and mineralocorticoids which is most often caused by immune-mediated destruction of the adrenal cortex. Although often diagnosed in middle-aged purebred dogs, hypoaldosteronism (HA) has also been reported in young, older, and cross-bred dogs, as well as in cats. HA manifests itself by vague clinical signs such as inappetence, weight loss, weakness, lethargy, or waxing and waning gastrointestinal signs. Some dogs do not present the typical combination of hyponatremia and hyperkalemia. These cases are called "atypical hypoadrenocorticism". However, the name "eunatremic, eukalemic hypoadrenocorticism" is now suggested. In fact, although hypocortisolism alone exists, dogs can have a deficiency in both hormones without having electrolyte imbalances. This would be due to the presence of compensatory mechanisms protecting against changes in natremia and kalemia. Only the measurement of aldosterone allows differentiation of the two.

Diagnosis

Hypoadrenocorticism is quickly suspected in the absence of a stress leukogram, and in the presence of a decreased Na/K ratio, hypoglycemia, hypercalcemia, and signs of shock, when the animal is in Addisonian crisis. The diagnosis is then confirmed by the demonstration of low baseline and post-ACTH stimulation cortisol ($< 1 \mu\text{g/dL}$ [$< 28 \text{ nmol/L}$]). However, because the disease manifests itself with vague and varied signs and electrolyte imbalances are not always present, the challenge is to decide whether to test a patient or not. A baseline cortisol $> 2 \mu\text{g/dL}$ ($> 55 \text{ nmol/L}$) is often used as a screening test to rule-out HA. Although studies have shown alterations in urinary sodium concentration and in urinary sodium and potassium fractional excretions, assessment of urinary electrolytes does not appear, currently, to provide any utility in the diagnosis of HA. However, measurement of the urine cortisol-to-creatinine ratio would seem to be a good screening test. It has even been suggested that it could be used to confirm the diagnosis of HA, for example when ACTH stimulation is not possible, but this remains to be supported with larger studies. Finally, machine-learning tools that consider objective clinicopathological data have recently been developed and evaluated to aid in the decision to test or not a patient.

Acute Management

When the patient is presented in an Addisonian crisis, acute treatment consists of correction of hypovolemia and signs of shock, hypoglycemia, hyperkalemia and its consequences, and acid-base disturbances. In general, balanced isotonic fluids are good

choices because they allow improvement of metabolic acidosis and have a lower sodium concentration than 0.9% NaCl, thus reducing the risk of overly rapid correction of natremia. Glucocorticoids should be promptly administered during stabilization of the patient. Only dexamethasone does not interfere with the ACTH stimulation test and is therefore the drug of choice in the absence of a definitive diagnosis. Once the tests have been performed, hydrocortisone or prednisolone can be used. In general, mineralocorticoids are given only after the diagnosis is confirmed. In addition, since fluids help normalize electrolytes, administering mineralocorticoids too rapidly could lead to a sudden and undesirable increase in sodium.

Complications

As mentioned above, rapid sodium changes must be avoided. Indeed, this could lead to the development of myelinolysis, which is characterized by neurological signs. Another complication that can occur in hypoadrenocorticism is acute kidney injury most likely secondary to the shock and hypotension seen in Addisonian crisis. Case reports have also described episodes of third-degree atrioventricular block, systolic ventricular dysfunction, non-cardiogenic pulmonary edema, and very severe intestinal hemorrhage requiring blood transfusions in dogs treated for HA. Veterinarians must be aware of these possible complications to be able to recognize and treat them accordingly.

Chronic Management

Long-term quality of life is unaffected or minimally affected in most dogs diagnosed with hypoadrenocorticism. However, its management requires a high level of commitment from the owner, and costs can be considerable. It is important for the veterinary team to discuss with the client about the various long-term options for mineralocorticoid supplementation, including the choice between DOCP and fludrocortisone and the associated costs. In a Western European survey, veterinarians seem to prefer DOCP for mineralocorticoid supplementation because it provides better electrolyte control and patient response than fludrocortisone. It is also important to note that a DOCP dose of 1.1 mg/kg, which is lower than the manufacturer's recommended dose, is generally safe and effective.

References available upon request.