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Diagnosis of Hypoadrenocorticism in Dogs

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Canine hypoadrenocorticism (Addison’s disease) generally occurs due to atrophy or immune-mediated destruction of the adrenal cortex. Other less frequent causes of the destruction of adrenal cortex are neoplasia, metastasis, haemorrhage or adrenocorticolytic drugs. It is a relatively infrequent disease.

Depending on the clinical presentation, there are two types of adrenocorticism. The classic and more frequent form is a deficiency of mineralocorticoids and glucocorticoids which we can recognise when there is evidence of hypochortisolaemia and electrolytic imbalances (hyponatraemia and hyperkalaemia). On the other side, the atypical form (or only glucocorticoids deficiency) is characterised by hypochortisolaemia but the level of electrolytes remains normal.

Clinical diagnosis

Signalment. Hypoadrenocorticism affects primarily young adult dogs (average age of 4 to 5 years, although the range is much wider, from 1 month to 16 years). Is more prevalent in females, like other conditions of immune-mediated origin (image 1). Predisposed breeds are Great Dane, Rottweiler, Portuguese Water Dog, Standard Poodle, West Highland High Terrier and Wheaton Terrier.
Imagen 1. Signalment is a fundamental part of the diagnosis of hypoadrenocorticism. It generally affects young females (hembras). 70% of the cases are female and the majority are 2-8 years old. (machos = males)

Clinical history. The majority of these animals present with apparently inspecific symptoms which are characterised by lethargy, loss of appetite or vomition. The severity of the symptoms is variable, from fairly mild clinical signs to the onset of hypovolaemic shock (Addisonian crisis), which can eventually lead to the death of the animal.

The duration of the clinical signs in patients with only glucocorticoids deficiency tends to be more prolonged (7 months) and less severe than of dogs with the classic presentation (1 month). 85% of the dogs with classic presentation are affected by vomition, in contrast with only 54% of the dogs with mineralocorticoids only deficiency.

Due to the fact that is a relatively rare condition and with fairly inspecific clinical signs, it is probably underdiagnosed. However, some of the clinical features are characteristic and should arise clinical concern, such as the episodic nature of the disease, the deterioration in situations of stress and the excellent but transient response to inspecific treatment (hospitalisation and fluid therapy). Bradycardia on dehydration or shock is also a characteristic finding (Image 2).
3 years old female Bull Terrier with Addisons disease with a history of extreme weakness, loss of appetite, vomition and tremors. These clinical signs presented with azotaemia which had previously responded to fluid therapy but relapsed afterwards. On physical examination, the bitch presented pale, with dry mucous membranes and bradycardia.

**Laboratorial findings.** On haematology there can be mild to moderate anaemia (usually normocytic, normochromic, non-regenerative) and absence of stress leukogram. Patients with glucocorticoids only deficiency tend to present with anaemia. The biochemistry findings characteristic of hypoadrenocorticism are hyperkalaemia, hyponatraemia, azotaemia and acidosis.

Although most of the patients will present with hypercalcaemia and/or hyponatraemia, some of them will have normal levels of electrolytes at the time of diagnosis. In these cases, several samples will need to be tested at different times. Azotaemia is prerenal and usually resolves with adequate fluid replacement. Urinalysis often shows specific gravity below 1.030 even when concurrent with azotaemia.

**Radiological findings**

Most of the dogs with hypoadrenocorticism will present with one or more of the following radiographic abnormalities: reduced cardiac size (microcardia), hypoperfusion of the cranial lobe pulmonary artery, hypoperfusion of the caudal vena cava and reduced liver size. These findings are related to a reduced volaemia. Each of these abnormalities appear in a third to half of the dogs with hypoadrenocorticism.

**Electrocardiographic findings**

All animals presenting with bradycardia or severe hyperkalaemia (K+ > 6.5 mEq/L) should undergo electrocardiographic evaluation, since an abnormal cardiac conduction could have lethal consequences. Some of the findings are bradycardia, absence of P wave, prolonged QRS complexes, reduced amplitude of R wave, increased amplitude of T wave, prolonged P-R complex (Image 3). These abnormalities are not directly related to the serum potassium concentration as there are other factors such as metabolic acidosis and azotaemia which will also play a role.
**Diagnosis**

**ACTH stimulation test.** The confirmation of the diagnosis of hypoadrenocorticism in a dog with signs of the disease is by confirmation of low levels of cortisol before and after the administration of adrenocorticotrophic hormone (ACTH). There are different preparations: synthetic ACTH cosyntropin (Synachten®, Cortrosyn®) at a dose of 0.25 mg/dog IV or IM. The use of a dose calculated from bodyweight has also been proved effective (5g/kg, IV Synachten or Cortrosyn®,) and will produce similar results. Finally, we can also use nuvacthen depot (0.25 mg/dog, only IM). The samples to test cortisol levels will be taken just before and 1 hour after the administration of ACTH in both protocols.

**Basal Cortisol.** Although the test of choice for the diagnosis of hypoadrenocorticism is the ACTH stimulation test, it has been recently suggested that the basal levels of cortisol could be used to rule out Addison's disease. Basal levels of cortisol >2ugl/dl practically rule out this condition.

**Treatment**

**Treatment for Addisonian Crisis.** Acute adrenocortical deficiency (Addisonian crisis) is a potentially fatal emergency which warrants immediate intervention. We should start treatment once we have collected urine and blood samples. Fluid therapy should be initiated while the ACTH stimulation test is being carried out to confirm the diagnosis.

**Fluidtherapy.** Rapid intravenous administration of isotonic saline solution is essential in the treatment of dogs with adrenal crisis because it will help restore volemia, hyperkalaemia and acidosis. The circulating concentration of potassium will be reduced simply by the effect of dilution as well as by an improved renal perfusion and glomerular filtration. Normal saline solution (0.9% NaCl) is the fluid of choice, since it does not contain potassium. The initial rate of fluid therapy should be 20-40 ml/kg/hour during one or two hours. Over the following 24 hours, we should administer 60 ml/kg of saline solution. Fluid therapy will be maintained until hydration, electrolytes and azotaemia are normalised, which usually happens after 2 or 3 days of hospitalisation.

**Glucocorticoids.** The administration of intravenous glucocorticoids is also considered essential in dogs with adrenal crisis. Fast acting glucocorticoids are recommended, such as sodium phosphate dexamethasone (0.5 mg/kg). This glucocorticoid can be used during the ACTH stimulation test as dexamethasone is the only glucocorticoid which will not produce a cross-reaction with the measurement of serum cortisol. When the animal does not vomit and tolerates oral medication, we will start a maintenance dose of prednisone or prednisolone of 0.2 mg/kg/day.

**Mineralocorticoids.** There is currently no fast-acting parenteral mineralocorticoid available in the market to correct hyperkalaemia. However, the administration of intravenous fluids and glucocorticoids will rectify the most potentially serious complications (hyperkalaemia, hypovolaemia, hypotension, etc.)
Once vomition and anorexia are over, oral mineralocorticoid supplementation can be started with the use of fludrocortisone at doses of 0.1-0.02 mg/kg/day.

**Treatment of acidosis.** Mild to moderate metabolic acidosis is common in dogs with adrenal crisis and will generally resolve with the administration of fluids and glucocorticoids. Although less frequently, dogs can develop severe metabolic acidosis (pH<7.15) which will require treatment with sodium bicarbonate. The total dose can be calculated by the following formula: deficit in mmol/L = bodyweight in kg x 0.5 x base deficit (22-TCO2). One quarter of the calculated dose of bicarbonate will be administered with intravenous saline solution over the first 6-8 hours when we will then reassess the acid-base status.

**Treatment of hypoglycaemia.** Mild to moderate hypoglycaemia is relatively frequent in dogs with hypoadrenocorticism and can be treated by adding dextrose to the saline solution to achieve a 2.5-5% dextrose concentration. Severe hypoglycaemia should be treated with a slow 50% intravenous dextrose injection at a dose of -.5-1.0 ml/kg followed by dextrose infusion of 2.5-5% to maintain normoglycaemia.

**Treatment of severe hyperkalaemia.** In the majority of dogs with hypoadrenocorticism, the rapid administration of intravenous fluids is sufficient to decrease the concentration of serum potassium within 1 or 2 hours. However, if the myocardial toxicity is considered potentially fatal and in severe cases we can use regular intravenous insulin (0.25-0.5 IU/kg) and glucose (2-3 grams per unit of insulin administered) to reduce the concentration of potassium. Half of the glucose will be administered in bolus and the rest with the intravenous saline solution over the next 6-8 hours. In these cases hypoglycaemia must be monitored, since hypoadrenocorticism will increase the hypoglycaemic effect of insulin.

**Maintainance Treatment.** The majority of the dogs affected with hypoadrenocorticism present though a chronic progressive disease and do not require hospitalisation. The maintainance treatment consists of the long life supplementation of mineralocorticoids, generally together with a replacement glucocorticoid therapy. The response to treatment is excellent in most of the cases. (Image 4).
**Image 4.** French Bulldog with a history of loss of appetite, weakness, lethargy, collapse and weight loss at the time of diagnosis. 3 weeks after the onset of treatment, the clinical signs had resolved and was gaining weight.

**Mineralocorticoids.** There are two available alternatives for the treatment with mineralocorticoids: oral therapy with fludrocortisone or injections of desoxycorticosterone pivalate (DOCP, not available in Spain).

Fludrocortisone will be administered at an initial doses of 0.01-0.02 mg/kg/day divided in two doses and the daily dose will be the adjusted according to clinical response and the levels of urea and electrolytes (sodium and potassium). We will monitor initially on a weekly basis till they return to normal range. Over the following 3 to 6 months we will perform monthly checkups to then proceed with six-monthly controls. The majority of dogs will stabilise at a dose of 0.02 to 0.03 mg/kg/day. The adverse effects (polyuria and polydipsia) or an inadequate control of the disease despite normal or higher dosages may deem necessary a change from fludrocortisone to DOCP.

Treatment with DOCP is started at doses of 2.2mg/kg IM/SC administered at intervals of approximately 4 weeks. Serum electrolytes are determined 2, 3 and 4 weeks after the initial injection to establish the efficacy and duration of the drug. Once the levels of electrolytes as stable, we will check the electrolytes prior to every injection. The dose and frequency of DOCP will be adjusted to a minimal effective dose. Although most dogs need injections every 3-4 weeks, some others might need them as frequently as every 2 weeks. This protocol usually controls most cases in a satisfactory manner and does not present adverse effects.

**Glucocorticoids-** the treatment with glucocorticoids (prednisone 0.2 mg/kg/day or hydrocortisone 0.5-1.0 mg/kg/day) is added to the therapy of mineralocorticoids. Due to the partial glucocorticoid activity of the fludrocortisone, we can try to reduce progressively the dose of glucocorticoids. 50% of the dogs will not need glucocorticoids but it is recommended to administer glucocorticoids in periods of stress (journeys etc).

**Prognosis**
In general, the prognosis for dogs with controlled hypoadrenocorticism is excellent. The mean survival time is approximately of 5 years and is not affected by the type of mineralocorticoids administered, the cause of hypoadrenocorticism, age, sex or breed of the patient.

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