Canine hyperadrenocorticism (part I)

Lorraine McDonnell RVN outlines what to look out for in patients with suspected canine hyperadrenocorticism

Canine hyperadrenocortism, or more commonly known as Cushing's disease, is becoming more frequent in practice today as patients are now living longer. Hyperadrenocorticism is caused by the adrenal glands secreting excess amount of cortisol. It is one of the most common endocrinopathy encountered in older dogs. The adrenal gland is composed of the medulla and a cortex. These are embryologically and functionally separate endocrine glands.

Unlike the medulla, the cortex is essential for life and produces three groups of hormones:

- Mineralcorticoid aldosterone is vital to regulate electrolytes and water homeostasis regulation;
- Glucocorticoids are secreted in response to a single stimulator adrenocorticotropic hormone (ACTH) from the anterior pituitary. ACTH is, itself, secreted under control of the hypothalamus, which is regulated by the corticotropin-releasing hormone (CRH); and
- Cortisol, which has negative feedback effects on the hypothalamus, thus decreasing formation of CRH and the anterior pituitary gland, which will decrease the formation of ACTH .
- These feedbacks secretions of CRH and ACTH are normally episodic and pulsatile, which result in fluctuating cortisol concentrations throughout the day (Mooney CT, Peterson ME. BSAVA Manual of Canine and Feline Endocrinology 4th edition).
- Sex hormones, androgen and oestrogen, which are usually secreted in such small amounts, play no major significance in healthy animals.

There are three causes:

- **PITUITARY-DEPENDENT HYPERADRENOCORTICISM (PDH)**
  This accounts for over 80% of dogs with naturally occurring hyperadrenocorticism. In these cases dogs have slow growing pituitary tumour called adenoma. This causes it to secrete an excess amount of ACTH. The cells in the zona fasciculata area of the adrenal glands respond to this excess ACTH by hypertrophying (enlarging) and secreting excess cortisol. It is this excess of cortisol that is circulating in the bloodstream that causes the symptoms we see in this disease.

- **ADRENAL-DEPENDANT HYPERADRENOCORTICISM (ADH)**
  The adrenal-based form of the disease is usually a result of an adrenal tumour that causes an oversecretion of glucocorticoids. Adrenal tumours are responsible for around 20% of the cases of hyperadrenocorticism.

- **IATROGENIC CUSHING**
  is the third type caused by excessive cortisol administration from prolonged use of steroids, either orally or injectable. Although the steroids were usually given for a legitimate medical reason, in this case, their excess has become detrimental. The level of cortisone that results from this use will cause the adrenal glands to atrophy. The negative feedback loop tells the brain there is plenty of cortisol in the bloodstream, so the pituitary secretes less ACTH. The pet has the symptoms of hyperadrenocorticism because cortisone is being introduced into its body, not because the adrenal glands are producing it in excess amounts.

HISTORY OF PATIENT

When talking to clients it is important to take a detailed history of the patient, as hyperadrenocorticism symptoms varies.

Patients suffering from PDH can be seen in dogs between the ages of two to 16 years but more commonly seen dogs aged seven to nine years, whereas ADH tend to be seen from four to 16 years old but frequently seen in dogs approximately 11 years of age. There is no specific breed that develops hyperadrtenocorticism, although breeds like terriers, poodles, springer, dachshund, boxers and beagles seem to be at higher risk. Clinical signs can vary between patients, with slow progression over many months or years. In the older dog, some signs can be mistaken as normal aging process so symptoms can be missed. Some cases can have quick onset and rapid progression of clinical sign.

SYMPTOMS OF HYPERADRENOCORTICISM

Polydipsia and polyuria (increased drinking and urination). Polydipsia is always noticed by client especially when consumptions exceed 100ml/kg/day. Nocturia incontinence (the need to wake and pass urine at night) is also reported by the owner;

Polyphagia (increased appetite) is very common, where some owners may see as normal healthy appetite, when it becomes more for example stealing/scavenging for food may become more concerning for owners;

Abdominal distension (potbellied) is very common. This is from the redistribution of fat to the abdomen, liver enlargement and weakness of abdominal muscles;

Muscle weakness or wastage. Cortisol is needed for proper muscle action, however, too much can lead to muscles atrophy. This is due to its catabolic effect, which causes the body to break down the amino acids in the muscle fibres. Cortisol does this in a complex mechanism that involves the liver resulting in the muscles become smaller. When this occurs at the abdominal muscles, the abdomen appears pendulous, also muscle mass is decreased over spine, limbs and over temporal region;

Hyperadrenocorticism causes atrophy of hair follicles and

sebaceous glands, leading to thinning of the haircoat. Bilaterally, symmetrical alopecia (hair loss) is seen frequently. Alopecia is non-pruritic and effects mainly flanks, ventral abdomen, perineum and neck. The coat colour will often become lighter than normal;

The disruption in the elastic tissue of the skin can also cause calcium changes in the skin. This might lead to areas where calcium builds up in small nodules. Calcinosis cutis appears as a firm slightly elevated, white/cream plaque surrounded by a rim of erythema. Theses can crack causing secondary infections;

Excessive panting is the main abnormality associated with respiratory signs. In rare cases pulmonary thromboembolism may be related to glomerular protein loss, resulting in decreased antithrombin lll concentrations;

Hypertension occurs on less than 50% of dogs with untreated hyperadrenocorticism. In the majority of cases, a moderate degree of hypertension is not associated with clinical signs;

Neurological signs are uncommon at the time of presentation. A minority of cases will develop these signs mainly associated with a large functional pituitary tumour. Signs include dullness, depression, disorientation, loss of learnt behaviour, head pressing.

Figure 1: Abdominal distension.

Figure 2: Calcinosis.

CLINICAL SIGNS OF HYPERADRENOCORTICISM

On clinical exam we must look at each symptom individual as some signs maybe as a result of another disease:

- The main observation is most likely abdominal distension – however this symptom could also be due to fluid buildup from cancer or cardiac disease;
- If lymph nodes are enlarged they could be due to secondary bacterial infections or spread of an adrenal tumour;
- An enlarged liver (hepatomegaly) might be palpated, along with smaller muscle mass (atrophy) in general;
- Skin infections and wounds that do not heal or recur after antibiotics are stopped;
- Alopecia that is symmetrical, along with thinning skin, poor hair coat, and calcium deposits under the skin. Many skin conditions have similar symptoms, so numerous diseases have to be kept in mind. They include hypothyroidism, skin allergies, sarcoptic mange, demodectic mange, and ringworm;
- Blood pressure might be elevated. This might cause a detached retina, picked up by an ophthalmic exam;
- Bruising (haematoma) might be observed under the skin, or following a venous sample, regardless of the care taken or pressure applied. As cortisol is essential for the integrity of the lining of the blood vessel, it can lead to the thinning of these vessels and leads to excessive bruising following venous puncture;
- On routine haematology and biochemistry. Haematology's most consistent finding, is stress leucogram with relative and absolute lymphopenia (<1.5 x 109/L) and eosinopenia (<2 x 109/L). A mild to moderate neutrophilla and monocytosis may also be found. Platelet count may also be increased. On biochemistry alkaline phosphatase (ALP), activity is increased in >90% of cases, commonly five to 50 times the upper range of the reference. Alanine aminotransferase (ALT) is elevated, however, only mild. Urea and creatnine is usually normal or decreased due to the continual urinary loss associated with glucocorticoid-induced dieresis. Cholesterol and triglyceride concentrations are increased due to glucocorticoid stimulation of lipidlysis. Bile acids

Figure 3: Alopecia.

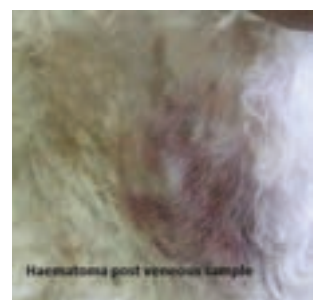

Figure 4: Haematoma.

resting and postprandial serum will show mild to moderate increase in some cases of hyperadrenocorticism due to steroid hepatopathy. Specific gravity is usually <1.015 and urine is often hyposthenuric <1.008 provided water is not withheld. It is important to culture urine as urinary tract infections (UTI) occurs in 50% of cases of hyperadrenocorticism. The sample needs to be obtained by cyctocentesis.