Proceedings of the 33rd World Small Animal Veterinary Congress

Dublin, Ireland - 2008

Next WSAVA Congress:

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UNUSUAL ENDOCRINE DERMATOSSES IN THE DOG AND CAT

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Alopecia X
Alopecia X is a disease of great uncertainty in veterinary dermatology. As the name implies, there are significant gaps in our understanding of the pathogenesis involved, disease diagnosis and the best treatment option in individual cases. Alopecia X is characterized clinically by a non-inflammatory, progressive bilaterally symmetric alopecia in affected dogs. This adult-onset disease has previously been referred to by many other names including:
- growth hormone-responsive dermatosis
- castration-responsive dermatosis
- pseudo-Cushing’s syndrome
- congenital adrenal hyperplasia.

The above nomenclature clearly reflects the multitude of findings when affected individuals are subjected to various hormonal test assays and therapeutic strategies. A variety of breeds are reported to be affected including Alaskan malamutes, huskies, Pomeranians, chows, keeshonds, samoyeds and miniature poodles. Although it was postulated that Alopecia X may resemble human congenital adrenal hyperplasia (a disease caused by reduced activity of a 21-hydroxylase enzyme that catalyses cortisol production in the adrenal gland), some data from a study in Pomeranians did not highlight any abnormality in the 21-hydroxylase gene (Takada et al., 2002).

The breed predisposition has led some authors to investigate a potential hereditary component to the disorder. Mausberg et al. (2007) postulated that Alopecia X may have a monogenic autosomal dominant pattern of inheritance. However, to date, the candidate genes investigated (e.g. cathepsin L2 gene) have not been significantly associated with the disease.

Signalment
Clinically, affected individuals are typically in good systemic health, with no abnormal findings on bloods (haematology/biochemistry) and urinalysis. However, cutaneous lesions include symmetrical, hyperpigmented alopecia of the body trunk. The condition is not normally pruritic unless accompanied by secondary microbial infection or seborrhoea. Lesions may start focally, but invariably progress with time. The normal age of onset is 1-4 years of age. Both males and females can be affected.

Histopathological findings in lesional biopsies may include hyperkeratosis, follicular keratosis, flame follicles, thinning of the epidermis, epidermal pigmentation and melanin aggregates within the follicular keratin.

Diagnosis
- History and clinical signs
- Biopsy of lesional skin
- Elimination of resembling endocrinopathies e.g. hypothyroidism on bloods etc.
- ACTH stimulation testing - measurement of 17-OH progesterone levels pre- and post-ACTH administration. Any increase should be interpreted in the light of either a normal or abnormal cortisol response. Some laboratories measure additional intermediate adrenal steroid hormones. An elevated 17-OH progesterone concentration post stimulation is suggestive of a diagnosis of Alopecia X.

Treatment
Neutering has often been recommended in intact male dogs; however the success rate is often only about 40% and partial/complete hair re-growth may take up to 6 months.

A wide variety of drug therapies have been advocated. The main problem for clinicians is that there is no one agent that can be recommended as the drug of choice. There is a lot of variability in response, which may reflect the difference in the underlying imbalance in adrenal hormone synthesis etc. in individual animals. Suggested therapies include:
- Mitotane
- Trilostane - inhibits 3β-hydroxysteroid dehydrogenase. Normally given at a dose rate of 3-4 mg/kg per day PO for several months. Treatment with trilostane has resulted in good hair re-growth in several studies.
- Ketoconazole
- Prednisolone - not recommended by many authors
- Growth hormone - very expensive and difficult to obtain.
- Testosterone
- Melatonin - administered normally at an initial dose of 3-6 mg twice daily (bodyweight can be a factor). Based on clinical progression over several weeks to months, the dose of melatonin may be increased.
- Alpha-tocopheryl
- Oestrogen-receptor blockers - although a regulatory oestrogen receptor pathway for telogen-anagen hair follicle transition has been described in rodents, receptor blockers such as fulvestrant have not been associated with clinical improvement of Alopecia X.

Prognosis
At first presentation, it is hard to predict which dogs will respond and which will not. In addition, even for
those cases with complete hair re-growth, on-going medication is often required.

**Gonadal sex steroid imbalances**

This is an uncommon group of dermatoses in the dog and cat. Clinically, dogs with sex steroid imbalances typically present with bilateral symmetrical alopecia affecting the groin, inguinal and flank regions. Again, the condition is usually non-pruritic unless secondary problems develop. Affected individuals may suffer from an under-production or over-production of gonadal hormones. In certain cases, the underlying pathology may involve a neoplastic process e.g. over-production of oestrogen by Sertoli cell tumours. Clinical suspicion is normally aroused when other resembling skin diseases are ruled out. At that point, the intact/neutering status of the animal is taken into account and any history of disease exacerbation during periods of hormonal peaks/troughs e.g. oestrogen surges during oestrus.

Treatment involves the removal of the offending hormone e.g. castration for hyperandrogenism, or hormonal supplementation if appropriate e.g. oestrogen or testosterone. In the latter case, it may be more appropriate not to administer treatment when one considers the side-effects of some hormonal therapies.

**Hepatocutaneous syndrome**

This uncommon dermatosis occurs in dogs with underlying significant hepatic pathology e.g. cirrhosis. Although a similar syndrome involving pancreatic pathology (usually glucagon-secreting tumour) occurs in man, most affected dogs do not have a demonstrable pancreatic lesion. Nevertheless, hyperglucagonaemia is an occasional finding and may be related to a failure of hepatic metabolism of this hormone. Affected animals usually present with severe cutaneous lesions including erythema, crusting, oozing and ulceration of the face, muzzle, genitalia, distal limbs and footpads. Hyperkeratosis and ulceration of the footpads are commonly reported. Systemic signs including weight loss, inappetance and lethargy are often present. Histopathological findings in lesional biopsies are highly characteristic and include superficial perivascular to lichenoid dermatitis, parakeratotic hyperkeratosis and a marked intra- and inter-cellular oedema limited to the upper half of the epidermis.

**Diagnosis**

- Haematology/biochemistry - hepatic enzymes elevated, particularly alkaline phosphatase
- Bile acid stimulation test - typically demonstrates elevated values
- Diagnostic imaging e.g. microhepatica if cirrhosis present
- Biopsy - liver pathology and above noted characteristic signs in lesional skin biopsies

**Treatment**

The prognosis is usually very poor as the hepatic pathology is often irreversible. Could try:

- Hepatic support diet
- Liver supplements e.g. methionine
- Anti-fibrotic agents e.g. colchicine and penicillamine
- Symptomatic treatment for skin lesions e.g. anti-microbial therapy