AN UPDATE ON ATYPICAL HYPERADRENOCORTICISM

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Atypical hyperadrenocorticism is defined as a syndrome in which a dog appears to have hyperadrenocorticism based on history, physical examination and clinicopathologic findings but a low dose dexamethasone suppression test, urine cortisol creatinine ratio test and ACTH stimulation tests fall into the currently accepted reference range. This is an uncommon endocrine disorder, which affects middle aged to older dogs and clinically may mimic the signs of hyperadrenocorticism. This disease is thought to be a result of overproduction of estradiol, androstenedione, progesterone, and 17-hydroxyprogesterone in addition to cortisol. The disease process may be a result of adrenal hyperplasia, adrenal tumours or a functional pituitary microadenoma. It is more common to have the adrenal form of the disease; however, both forms have been documented.

Clinical signs may include polyuria, polydipsia, polyphagia, lethargy, abdominal distension, muscle weakness, or recurrent urinary tract infections. Dogs may also present with dermatological signs as their primary complaint. These dermatological abnormalities may include truncal alopecia, thin skin, comedones, bruising, cutaneous hyperpigmentation, calcinosis cutis, pyoderma, dermal atrophy, secondary demodicosis and seborrhea. Abnormalities to a dogs reproductive status may also be noted and include perianal adenoma in females or castrated males, clitoral hypertrophy in female dogs, behavioral estrus in spayed females, testicular atrophy in intact males, prostomegaly in castrated males or behavioral or physical signs of testosterone excess.

Common laboratory abnormalities include an elevated alkaline phosphatase, an elevated ALT, hypercholesterolemia, hyperglycemia, and a decreased BUN. Sterile urinary tract infections (urinary tract infections without pyuria and bacteriuria) and proteinuria may be noted on a urinalysis. Lastly, sick euthyroid syndrome may be noted.

Multiple treatment modalities are recommended for this disease process. Treatment is influenced by which intermediate adrenal hormones are elevated on the individual adrenal androgen panel. Melatonin can be used as it has anti-gonadotropic activity and will inhibit aromatase enzymes in tissue, which decreases androstenedione and testosterone conversion into estradiol. It is important to treat for at least 4 months for this treatment to be effective. Lignans can be used as they have phytoestrogenic activity and will compete with estradiol for tissue estrogen receptors with less biological effect. They will also inhibit aromatase enzyme, which lowers estradiol and inhibits the 3-beta hydroxysteroid dehydrogenase enzyme.

Lysodren therapy is very effective at suppressing cortisol, progesterone, androstenedione and 17-hydroxyprogesterone levels. Estradiol is not always suppressed by Lysodren therapy. Some research demonstrates that this is the preferential therapy for atypical hyperadrenocorticism. Ketoconazole is thought to be a good therapy in cases with both increased estradiol concentrations and elevated intermediate adrenal steroid levels. The mechanism of action is inhibition of 17-hydroxyprogesterone early in the adrenal pathway and inhibition of 11-beta hydroxylase enzyme later in the pathway.

In summary atypical hyperadrenocorticism is an uncommon endocrine disorder of dogs with clinical signs, which are suggestive of hyperadrenocorticism; however traditional ACTH stimulation test, low dose dexamethasone suppression test, and urine cortisol creatinine ratio will not yield a positive diagnosis. The specificity for adrenal panels is low, therefore it is only recommended to test for atypical HAC when moderate to severe clinical signs are present.