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Successful Therapeutic Management of Hyperadrenocorticism in a Crossbred Bitch

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Abstract

An eight year old crossbred bitch was presented in Veterinary Polyclinic, Chengannur with a history of polydypsia, polyphagia, lethargy and skin lesions. On clinical examination all parameters were in normal range. On hemato-biochemical examination, leucocytosis, elevated ALP and serum cortisol level were observed. Based on history, clinical signs and laboratory values hyperadrenocorticism was confirmed. Therapeutic dose of Ketoconazole at 10 mg/kg (BID PO) was initiated for 30 days and advised review after 1 month. Supportive therapy with hepatonics and vitamin supplements were provided along the course of treatment. After one month of treatment animal showed improvement in conditions and treatment is being continued until complete resolution of clinical signs.

Key words: Hyperadrenocorticism, Cortisol, Ketoconazole

Hyperadrenocorticism (HAC) also known as Cushing's disease is an endocrinopathy characterized by glucocorticoid excess, which is generally caused by tumours of either the pituitary or adrenal glands. However, long term administration of exogenous glucocorticoids can also cause HAC (Hoffman *et al.*, 2018). Canine hyperadrenocorticism has been noted as one of the most commonly diagnosed endocrinopathies in the dog (BSAVA Manual of Canine and feline endocrinology, 2004). HAC commonly affects middle-aged to older dogs and affected animals exhibit polyuria, polydypsia, polyphagia, abdominal distension and endocrine alopecia. The most frequently reported dermatological changes include hyperpigmentation, thin skin, comedones, poor hair growth etc (Kahn, 2010). Routine laboratory findings for evidence of HAC include reduced urine specific gravity and proteinuria in urinalysis, elevated Alkaline Phosphatase (ALP) and stress leukogram in Complete Blood Count. Screening tests for HAC include Adrenocorticotropic Hormone stimulation test, Low Dose Dexamethasone Suppression Test and Urine Cortisol Creatinine Ratio (Behrend *et al.,* 2010). The treatment of choice depends upon several factors like cause, severity of the disease, available treatment options and clinician-client preferences.

Case History and Observations

An eight year old crossbred bitch weighing 31.3 Kg was presented in Veterinary Polyclinic, Chengannur with a complaint of increased food and water consumption since last 2-3 weeks. Owner also reported that the animal was lethargic and had increased hair fall and some skin lesions on ventral abdomen. On physical examination the animal was found to be less active and had distended abdomen with symmetrical non pruritic alopecia on ventral region. Skin was very thin with prominent veins, comedones and calcinosis cutis could also be observed (Fig 1-3). On clinical examination all parameters were in normal range. On hematobiochemical examination, leucocytosis, elevated ALP and serum cortisol level were observed. Based on history, clinical signs and laboratory findings the condition was diagnosed as hyperadrenocorticism.

Treatment and Discussion

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Table I: Haemato-biochemical values of the patient on day-1 and day-30

Parameter	Day 1	Day 30	Reference values
RBC count (millions per mm3)	7	6.9	5-7.9
PCV (%)	43	42	35-57
Haemoglobin(g/dL)	15.3	15.2	12-19
Total WBC count (cells/mm3)	20.5	14	5-14.1
Granulocytes (%)	76	74	58-85
Lymphocytes (%)	18	12	8-21
Monocytes (%)	6	4	0-9
Platelets (lakhs/mm3)	5.2	5.7	2.1-6.21
ALP (IU/L)	207	56	1-114
ALT (IU/L)	89	93	10-109
Potassium(mEq/L)	4.7	4.9	3.9-5.1
Serum cortisol (ug/dl)	6.2	3.2	≤2
Creatinine (mg/dl)	0.62	0.8	0.5-1.7
BUN (mg/dl)	14	16	8-28
Sodium(mEq/L)	148.6	145	142-152

(Reference range: The Merck veterinary Manual, 10thedn, 2010)

Treatment was initiated with Tab. Ketoconazole 200mg (@10mg/kg BID PO for 1 month) hepatotonics (Syrup Tefroliforte[a]3 tsp BID PO for 1 month)and Syrup Nutricoat[b] (3tsp BID PO for 1 month). Advised review after 1 month. Resolution of dermatological symptoms was observed after one month of treatment (Fig. 4). Improvement in condition was observed both physically as well as in serological values. Cortisol level reduced from the initial value of 6.2ug/dl to 3.2ug/dl. A marked change could be observed in ALP and leucocyte count. Also owner reported improvement in symptoms including polyphagia, polydypsia and lethargy.

Normally, the amount of cortisol in the blood is regulated by interaction between the adrenal glands, the pituitary gland, and the hypothalamus. When cortisol is needed, the hypothalamus signals the pituitary gland to release adrenocorticotropic hormone (ACTH), which prompts the adrenal glands to produce cortisol. This acts by a negative feedback loop mechanism. When a pituitary or adrenal gland is affected by a tumour, it stops responding to the signals of the feedback loop. Secondary, or iatrogenic HAC is caused by administration of high doses of exogenous cortisol which creates a physiologic situation similar to that of an adrenal tumour (Mindy Cohan, 2013). Females are slightly more predisposed than males. Poodles, dachshunds, beagles, German shepherds, and many terrier breeds are commonly affected.

Polydypsia, polyuria (PD/PU) and pendulous abdomen are very common complaints in canine HAC. Dermatological symptoms include comedones formation, calcinosis cutis, thin skin and hyperpigmentation. Cortisol is associated with the "fight or flight" response; therefore,

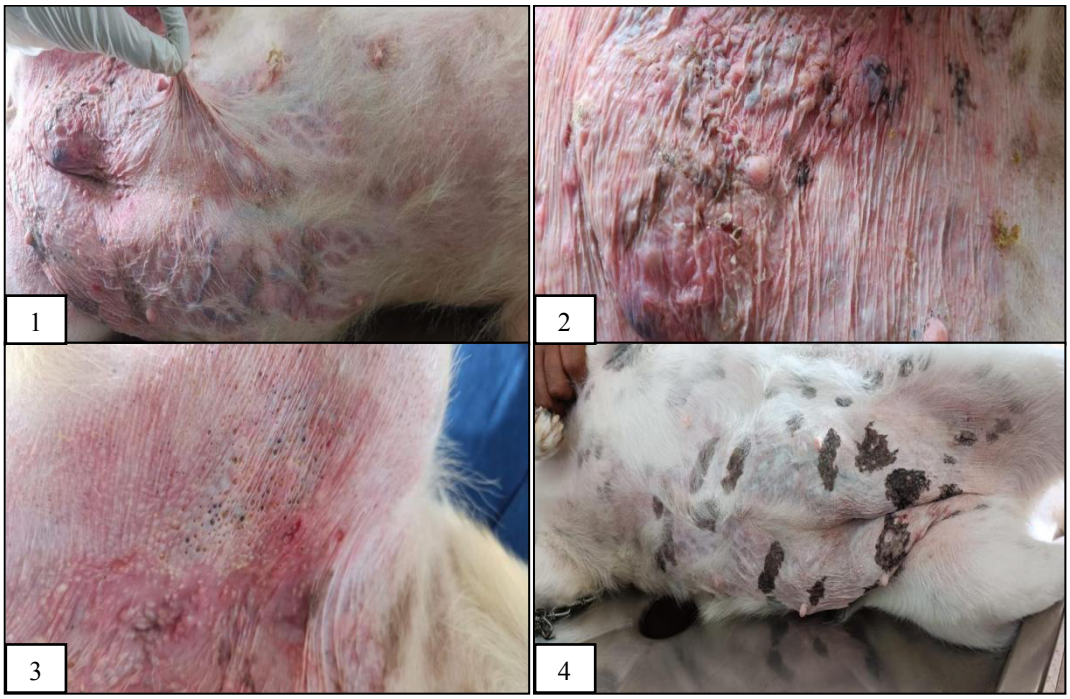

Fig 1.Thin skin, Fig 2.Calcinosis cutis, Fig 3.Comedones (Fig 1-3 on day 1), Fig 4. Day 30

patients with HAC exhibit stress leukogram in Complete Blood Count. These changes include neutrophilia, monocytosis, lymphopenia, and eosinopenia. Elevation in serum alkaline phosphatase (ALP) is the most common abnormality. The most common urine abnormality seen in dogs with HAC is a reduced urine specific gravity (Kahn, 2010).

Usually dogs with HAC will have high Urine Cortisol: Creatinine Ratio. Because of the high sensitivity and low specificity of the UC: CR, a negative result is very helpful in ruling out HAC. In Low-Dose Dexamethasone Suppression Test (LDDST) in a dog without HAC, the administration of exogenous dexamethasone causes the pituitary gland to decrease its secretion of ACTH, which in turn, decreases the adrenal glands release of cortisol. However, canine patients with pituitary-dependent HAC (PDH) are minimally affected by the administration of a low dose of exogenous dexamethasone. Analysis of blood samples taken before and 4 and 8 hours after dexamethasone administration reveals whether cortisol levels are affected by this test (Behrend and Kemppainen, 2001).

In ACTH stimulation test, exogenous ACTH is administered and the patient's cortisol response measured. Dogs with naturally occurring HAC are expected to have exaggerated cortisol production (Braddock, 2003). The advantages of this test are the short time it requires and its ability to distinguish naturally occurring HAC from iatrogenic HAC (Mack. R.E,1994). Abdominal ultrasonography can be useful in differentiating PDH from adrenal tumour, but it has limitations. Dogs with iatrogenic HAC should be slowly weaned off of exogenous steroids to allow the adrenal glands to resume normal production of glucocorticoids.

Mitotane, a derivative of the insecticide dichlorodiphenyl dichloroethane can be used to treat PDH or adrenal tumour. The initial induction phase of therapy involves a daily mitotane dose of 40 to 50 mg/kg PO with food for a period of 7-10 days (Peterson and Kintzer, 1994). Concurrent prednisolone (0.15 to 0.25 mg/kg/day PO) can help alleviate the potential side effects following mitotane administration. Once clinical signs have improved and desired results of an ACTH stimulation test are reported, maintenance dose 25 to 50 mg/kg PO divided over 2 or 3 days of the week can be given. Ketoconazole is an antifungal agent that

decreases cortisol production by inhibiting the enzymes necessary for glucocorticoid synthesis. Unlike mitotane, ketoconazole has the potential to cause a change in coat colour, elevated liver enzymes, and hepatotoxicity. Trilostane is a synthetic, hormonally inactive steroid that inhibits the production of cortisol, aldosterone, and sex hormones. As it resolves hypercortisolemia, patients may experience lethargy and a decrease in appetite (Mindy Cohan, 2013).

Summary

All endocrinopathies require timely diagnosis for fruitful therapy. Most of the time pet owners do not take care of the earlier symptoms like polyphagia, skin problems, obesity and animals may not be presented to the hospital until systemic signs start at their terminal stages. So hyperadrenocorticism goes undiagnosed in field conditions. For this animal, symptoms started months back. From symptoms, hematology and clinical biochemical analysis we could diagnose that it was a case of Hyperadrenocorticism. One month after initiation of treatment revealed improvement in condition physically as well as in serological values.

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