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SHORT COMMUNICATION

Steroid induced hyperadrenocorticism in dogs- A Short study

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ABSTRACT

The present study screened ten dogs with the history of prolonged exogenous glucocorticoid administration. The dogs were subjected to detailed clinical examination and special diagnostic procedures to study the clinicopathological changes associated. The most common signs observed were thinning of skin and asymmetrical alopecia. Serum alkaline phosphatase, alanine aminotransferase, triglyceride and cholesterol were elevated. The adrenal glands were found to be atrophied on ultrasonography. The cortisol levels were within normal range in Low Dose Dexamethasone Suppression Test LDDST. Iatrogenic hyperadrenocorticism was diagnosed in these dogs and were advised withdrawal of steroid. Initial improvement of clinical signs was observed at 8 weeks after corticosteroid withdrawal.

Keywords: Exogenous corticosteroids, skin lesions, atrophied glands, withdrawal

Iatrogenic hyperadrenocorticism (IHAC), a form of Cushing's syndrome is induced by excessive administration of glucocorticoids through oral, parenteral or topical medications which are used for the treatment of a variety of allergic, autoimmune or inflammatory diseases. The development of clinical signs depends on the dosage and duration of the glucocorticoid exposure. The effects also vary among animals owing to inter individual differences in cortisol sensitivity. Exogenous corticosteroid causes sustained suppression of the hypothalamic-pituitary-adrenocortical axis (HPA axis) and thus there is less secretion of adrenocorticotrophic hormone (ACTH) (Peterson, 2007). Depending on the dose and the intrinsic glucocorticoid activity of the corticosteroid, the schedule and duration of its administration and the preparation or formulation, this suppression may exist for weeks or months after cessation of the corticosteroid administration (Kooistra and Galac, 2010). The purpose of this study is to describe the clinicopathological changes, diagnosis and outcome of dogs with Iatrogenic HAC.

MATERIALS AND METHODS

Design of Study

Ten dogs presented to Madras Veterinary College Teaching Hospital, Chennai with the history of skin disorders and treatment with oral, parenteral or topical corticosteroids for more than one month were selected for the study. These dogs were subjected to detailed clinical examination, laboratory examination (hematology, serum biochemistry and urine analysis), radiography, ultrasonography and endocrine tests like Urine Cortisol – Creatinine Ratio (UCCR) and Low Dose Dexamethasone Suppression Test (LDDST).

Special diagnostic tests procedure

Ultrasonographic examination of adrenal glands was done to assess the size and shape with ultrasound scanner (Esaote, Italy) using high frequency probe (7.5- 10MHz) as per standard procedure suggested by Hoffmann (2003). For LDDST, a basal blood sample was collected for

determination of serum cortisol and then dexamethasone was injected at the dosage of 0.01mg/kg body weight intravenously once. Additional serum samples were collected at 4th and 8th hour post dexamethasone injection. The samples were stored at -20^0 C till evaluation (Greco *et al.,* 1999). For UCCR, morning urine samples were collected on two consecutive days were stored at -20^{0}C till evaluation (Zuegswetter *et al.,* 2010). Quantitative estimation of cortisol in dog serum and urine was done by enzyme immune assay using Canine Cortisol ELISA kit (Ginel *et al.,* 1998).

RESULTS AND DISCUSSION

Present study showed that the period of steroid administration in these dogs was six months to two years. Oral route was the most common route of exogenous steroid administration which was recorded in nine dogs while only one dog was treated topically. Affected dogs were in the 5-10 years age group. Male animals were affected more commonly than female animals (7:3)**.** Though Huang *et al.* (1999) recorded similar finding, yet no study has established that there is sex predisposition for IHAC. Labradors (40 percent) and Dachshunds (30 percent) showed high incidence among the other breeds such as German shepherd and Spitz presented during the study period. This overrepresentation of affected breed was presumed to reflect its popularity in the study area. Polyuria, polydipsia and polyphagia were reported in 20 per cent cases. This was found to be in contrary with the findings of Glaze *et al.* (1988) and Huang *et al.* (1999) who reported that these were the common signs. This might be due to ignorance of owners to differentiate polyuria and polydipsia from normal process.

On physical examination, cutaneous lesions were found to be the predominant findings (Table1). The most common dermatological manifestations were thinning of skin which was due to protein catabolism (Scott *et al.*, 2001) (Figure1) followed by asymmetrical or patchy alopecia and comedones (Figure2). Nuttal *et al*. (2009) observed that thinning of the hair coat leading to bilaterally symmetrical alopecia was frequently seen with hyperadrenocorticism and occurred because of the inhibitory effect of cortisol on the anagen or growth phase of the hair cycle. But, in this study symmetrical alopecia was noticed in three dogs only (Figure3). Nonsymmetrical and nontruncal alopecia have been reported by White *et al.* (1989) which supports the asymmetrical alopecia finding in this study. Comedones are dilated hair follicle filled with corneocytes and sebaceous material (Herrtage, 2004).

The predominant clinical manifestation was obesity due to fat distribution to the abdomen, shoulder and lumbar areas (Herrtage, 2004). Less common signs recorded were seborrhoea, anestrus and testicular atrophy. Secondary infections such as demodicosis and dermatophytosis were also recorded in two cases each.

Table1. Dermatological and clinical manifestations in IHAC dogs

Signs	Percent
Dermatological manifestations	
Thinning of skin	80
Asymmetrical alopecia	70
Symmetrical alopecia	30
Comedones	70
Telengectasis	20
Seborrhoea	10
Clinical manifestation	
Obesity	50
Pendulous abdomen	20
Anestrus	10
Testicular atrophy	10

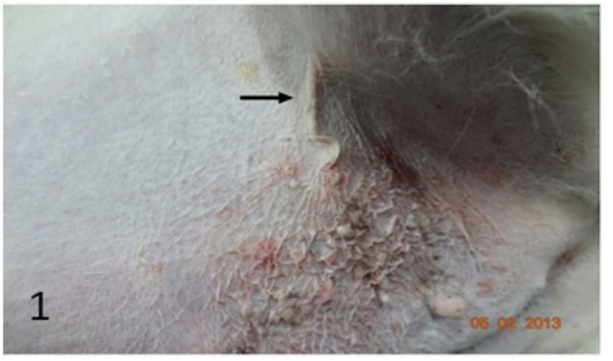

Figure1. Thinning of ventral abdominal skin (arrow mark).

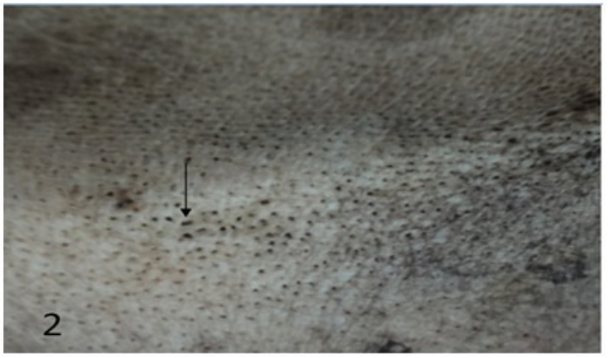

Figure 2. Comedones on ventral abdomen (arrow mark).

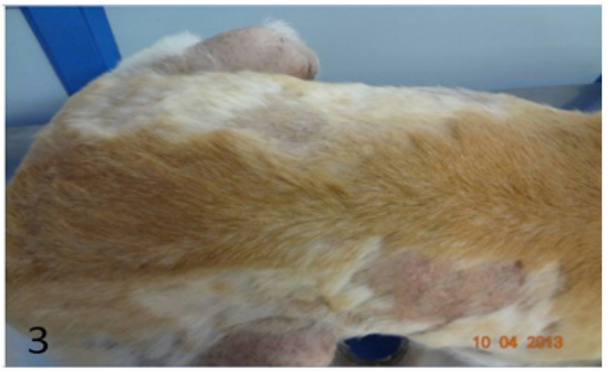

Figure 3. Symmetrical alopecia in a dog with iatrogenic hyperadrenocorticism.

Haemogram was found normal in all dogs. Leukogram was found to be in high normal range (Table 2). Biochemical studies showed elevation in serum alkaline phosphatase, alanine aminotransferase, triglyceride, cholesterol and glucose (Table 3). Huang *et al.* (1999) observed similar clinical signs and haemato biochemical parameters in dogs under prolonged exogenous steroid administration.

Visualization of left and right adrenal glands was 50 per cent and 30 per cent respectively with ultrasonography. The adrenal glands were hypoechoic (compared to adjacent kidney and spleen) and homogenous. The visualisation percentage in the present study was lesser when compared to Nyland and Mattoon (1995) who reported that currently normal adrenal glands of 85 to 90 per cent are visualized by an experienced sonologist. This may be due to the atrophy of adrenal glands due to exogenous glucocorticoids as opinioned by Pey *et al.*

Table 2: Mean ± S.E values of hematological parameters in IHAC dogs

Parameters	IHAC dogs	Reference laboratory values (Marsh *et al.*, 1965)
Haemoglobin (g/dl)	13.03 ± 0.63	12.0-18.0
PCV (%)	37.2 ± 1.61	37-55
Total erythrocyte (×106/ cumm)	5.55 ± 0.18	5.5-8.5
Platelets (×105)	2.36 ± 0.29	2.0-5.0
Total leukocyte (×103/ cumm)	12.86 ± 0.57	6-17
Neutrophils (×103/ cumm)	10.05 ±0.52	3.0-11.5
Lymphocytes (×103/ cumm)	2.1 ± 0.85	1.0-4.8
Monocytes (×103/cumm)	0.35 ± 0.06	0.15-1.35
Eosinophils (×103/ cumm)	0.19 ± 0.04	0.1-1.25

Table 3: Mean ± S.E values of biochemical parameters in IHAC dogs

Parameters	IHAC dogs	Reference laboratory values (Marsh *et al.*, 1965)
Blood Urea Nitrogen (mg/ dl)	14.07 ± 0.93	10.0-28.0
Creatinine (mg/dl)	0.82 ± 0.05	0.5-1.5
Serum Alkaline Phosphatase (IU/L)	300.1 ± 78.06	20.0-156.0
Alanine aminotransferase (IU/L)	125.10 ± 9.24	21.0-102.0
Serum cholesterol (mg/dl)	194.80 ± 18.85	100.0-135.0
Serum triglycerides (mg/ dl)	108.30 ± 11.13	20.0-110.0
Glucose (mg/dl)	133.30 ± 7.81	65.0-118.0

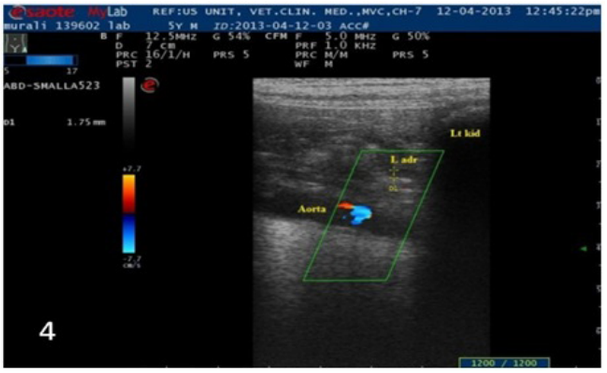

Figure 4. Ultrasound picture of atrophied left adrenal gland (marked as D1 – L. adr) in a dog with iatrogenic hyperadrenocorticism.

(2012). He further stated that there was reduction in length and height of the cranial and caudal pole of adrenal glands after 4 months of glucocorticoid administration. This was confirmed in the present study too where the width of left and right adrenal glands decreased and ranged from 2.1-4.5mm and 1.25 – 3.2mm respectively (Figure 4) . The normal glands range in thickness from 3 to 5 mm, upto 7 mm in large dogs (Hoffmann, 2003). Radiograph showed no significant changes in this study.

Mean ± S.E value of urine cortisol creatinine ratio (UCCR) was 192.91 ± 37.36 × 10^{-6}. This is in accordance with Stolp *et al*. (1983) who suggested that in hyperadrenocorticoid dogs urine cortisol creatinine ratio was more than 10 × 10^{-6}. In low dose dexamethasone suppression test (LDDST) the mean ± S.E values of serum cortisol at basal and at four and eight hours post intravenous dexamethasone administration were 7.45 ± 0.63 µg/dl, 7.16 ± 0.48 µg/dl and 6.86 ± 0.66 µg/dl respectively. In a healthy dog, because the corticotrophin system is based on negative feedback, administration of exogenous glucocorticoids suppresses the corticotrophin system, resulting in lowered cortisol measurements. However, in an affected patient, the low dose of steroid fails to suppress the HPA axis, resulting in elevated cortisol measurements. Therefore, LDDST results showing failure to suppress at 4 and 8 hours after administration are diagnostic of hyperadrenocorticism (Liss, 2012). In these dogs the cortisol level remained the same at four and eight hours and where taken as iatrogenic hyperadenocorticism based on the history of exogenous steroid administration. ACTH stimulation test is a gold standard for confirmation of IHAC (Peterson, 2007 and Liss, 2012). However, ACTH stimulation test was not included in the study because of cost constraint.

All the dogs were advised to discontinue the glucocorticoid medications administered either orally or topically. Remission of clinical signs was noticed eight weeks after glucocorticoid withdrawal. Regrowth of hair was noticed as an initial sign. Huang *et al*. (1999) recorded similar results in his study. Complete recovery of the affected dogs was observed after 4 months of glucocorticoid withdrawal.

CONCLUSION

Ten dogs with IHAC were recorded based on the exogenous steroid administration. The clinical signs exhibited where similar to those dogs with spontaneous hyperadrenocorticism. Characteristic signs were not seen in all dogs. Ultrasonographic examination showed atrophied adrenal glands. Regrowth of hair was noticed as an initial sign eight weeks after glucocorticoid withdrawal.

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