

Hyperadrenocorticism in 10 Dogs with Skin Lesions as the Only Presenting Clinical Signs

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ABSTRACT

Ten dogs that had skin lesions as the only presenting signs of hyperadrenocorticism (HAC) and as the owners' primary complaint are described. Dogs were included if the initial examination was for skin disease, there were no signs of systemic illness on initial presentation and there was a confirmed diagnosis of HAC by specific screening tests. Dogs were excluded if they had a severe disease that might interfere with screening tests for HAC or if the screening tests were not diagnostic. There were five males and five females; six dogs were intact. Nine dogs were diagnosed at ≥ 7 years. Eight dogs weighed ≤ 10 kg. Alopecia was present in nine dogs. Eight dogs had bacterial pyoderma, five had hyperpigmentation, and four had thin skin. One dog had unresolved dermatophytosis. Skin lesions resolved after treatment in eight dogs. One dog was not treated and one was lost to follow-up. This study showed that skin lesions may be the only clinical signs of HAC. The presence of the more common clinical signs of HAC, such as a non-pruritic, truncal alopecia and/or thin skin, without any systemic signs of HAC and/or the presence of poorly responsive skin infections warrant screening for this disease. (*J Am Anim Hosp Assoc* 2011; 47:419–427. DOI 10.5326/JAAHA-MS-5623)

Introduction

Hyperadrenocorticism (HAC; Cushing's syndrome) is a common endocrine disorder of dogs with a wide variety of clinical manifestations. Reported clinical signs are primarily systemic and include polydipsia, polyuria, polyphagia, lethargy, muscle atrophy, abdominal enlargement, hepatomegaly, cystitis, and uncontrolled diabetes mellitus.^{1,2} Hematologic abnormalities include relative or absolute neutrophilia, lymphopenia, and eosinopenia; biochemical abnormalities include an increase in serum values of alkaline phosphatase (ALP), glucose, cholesterol, triglycerides, and alanine aminotransferase (ALT).^{1–3} Urinalysis (UA) often reveals dilute urine and signs of a urinary tract infection.^{1,2} Skin manifestations are common and most often include hair loss (bilateral and symmetrical), with atrophy of hair follicles and sebaceous glands, thin skin, hyperpigmentation, and susceptibility to cutaneous infections. The cutaneous changes are generally nonpruritic unless associated with secondary infections or calcinosis cutis.^{3–6}

Some authors believe that unless systemic signs are present, a diagnosis of HAC is very unlikely, and treatment should not be initiated.^{1,2} Very observant owners may detect subtle changes in their dogs' hair coats before other signs develop, and skin manifestations of endocrine and other systemic diseases can precede systemic signs or be the only signs.^{6–8} The purpose of this report was to present 10 dogs that showed skin lesions as the only presenting signs of HAC (i.e., without polyuria, polydipsia, polyphagia, muscle atrophy, or abdominal enlargement) and to note that some of these skin lesions were different from the "classic" lesions of dogs with HAC described in the veterinary medical literature.

Materials and Methods

All cases included in this retrospective study presented for dermatologic examination between April 1992 and December 2005 at the dermatology department of the Veterinary Teaching Hospital at

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ACTH adrenocorticotrophic hormone; ALP alkaline phosphatase; ALT alanine aminotransferase; CBC complete blood count; HAC hyperadrenocorticism; LDDST low-dose dexamethasone suppression test; PDH pituitary dependent hyperadrenocorticism; PO per os; T4 thyroxine; TSH thyroid-stimulating hormone; UA urinalysis; US ultrasonographic

the Koret School of Veterinary Medicine. Medical records of dogs that were diagnosed with HAC were reviewed. Dogs were included in this study if the initial examination was for skin disease, there were no signs of systemic illness on initial presentation, and there was a confirmed diagnosis of HAC by specific screening tests (adrenocorticotrophic hormone [ACTH] stimulation test, low-dose dexamethasone suppression test [LDDST], or both). Dogs were excluded if they had a severe disease that could have interfered with the screening tests for HAC or if the screening tests for HAC were not absolutely diagnostic. Breed, sex, age, the presence of pruritus, and other dermatologic conditions at the time of disease onset or presentation were recorded. Results of blood tests and other diagnostic methods, treatment protocols, and response to treatment were all obtained from the patients' medical records.

Concurrent skin infections were diagnosed by skin scrapings, skin cytology or culture, and susceptibility tests; dogs were treated accordingly. Atopic dermatitis was diagnosed using major and minor inclusion criteria as described by Willemse and by ruling out other possible causes of the relevant clinical signs.⁹ Cutaneous food reaction was diagnosed when marked improvement of clinical signs was noted after 10–12 wk of a strict elimination diet and recurrence of clinical signs after challenge with the dog's original diet.

Complete blood counts (CBC), blood chemistry profiles, and UAs were obtained for all cases before performing specific HAC screening tests. Urine cortisol/creatinine ratios were not available. Thyroxine (T4) and thyroid-stimulating hormone (TSH) levels were evaluated in five dogs. Sampling for these analyses occurred either before or concurrently with the diagnosis of HAC. The diagnosis of HAC was made by either LDDST, ACTH stimulation test, or both.^{1–3,10,11} Serum cortisol values were determined by chemiluminescent competitive immunoassay^a. The ACTH stimulation test was performed using synthetic ACTH^b (250 µg/mg intramuscularly). Blood for serum cortisol values was collected before and 60 min after ACTH administration. The LDDST was performed using 0.01 mg/kg dexamethasone^c injected intravenously. The blood for serum cortisol values were obtained before and 4 and 8 hr after the administration of the dexamethasone. Laboratory cut-off values from the veterinary literature were used: cortisol values >1.4 µg/dL 8 hr after the administration of 0.01 mg/kg dexamethasone or >22 µg/dL 1 hr after the administration of 250 µg ACTH were considered compatible with the diagnosis of HAC.¹

Eight dogs had abdominal ultrasonographic (US) examinations. These results were used to examine the adrenal glands for enlargement or atrophy and to evaluate the liver for US changes.

After a diagnosis of HAC was established, owners were offered the option to treat their dogs with mitotane^d (o,p'-DDD); response

to treatment was monitored. Induction doses of mitotane were 12.5–25 mg/kg *q* 12 hr *per os* (PO) for 6–9 days. For most dogs, an ACTH stimulation test was performed 6–8 days after beginning induction and after 1 mo of maintenance dose. If the dog's condition was stable, ACTH stimulation test was then performed every 3 mo for the first year and every 6 mo thereafter. If the results of the ACTH stimulation test indicated a change in dose of the mitotane, and ACTH stimulation test was performed a month after the new dosage was started, the above protocol was repeated. Once the ACTH stimulation test results showed blood cortisol values that were within the range of healthy dogs (1.3–7.9 µg/dL), the dogs were subsequently administered maintenance doses of 25–50 mg/kg, divided and administered two to three times per week. The dogs in this report had only mild signs of HAC and further suppression of the adrenal glands was deemed unjustified. In the dogs diagnosed with atopic dermatitis, the mitotane treatment was subsequently managed, such that some elevation in endogenous cortisol values remained to control the atopic dermatitis. The authors' clinical experience showed that if the adrenal function was depressed, and there were normal post-ACTH levels in atopic dogs, their pruritus was not controlled, and clinical manifestation of their allergy remained. However, if some excessive blood cortisol remained, the clinical signs of atopic dermatitis were better controlled.

Dogs were re-examined to evaluate the skin lesions every month until resolution of lesions. ACTH stimulation tests were performed 1 mo after the initiation of the maintenance dose, and then every 3–6 mo during the first year of treatment and every 6–12 mo thereafter. If the maintenance dose of mitotane was changed, another ACTH stimulation test was performed 1 mo after the new dose was initiated.

Results

Signalment and History

Ten dogs met the criteria for this study. Eight of the 10 dogs were small breeds (≤ 10 kg). There were five males and five females, six of which were intact. Nine of the dogs were ≥ 7 yr old at the time the clinical signs and the diagnosis of HAC were made; five dogs were ≥ 10 yr. The described clinical signs of dog 8 appeared 4 yr before the diagnosis of HAC; this dog was also diagnosed with atopic dermatitis, cutaneous adverse food reaction, and hypothyroidism (Table 1).

Common Dermatologic Signs in HAC

Dermatologic signs noted on initial presentation are also listed in Table 1. Five dogs (dogs 2, 4, 5, 6, and 9) presented with non-pruritic, truncal alopecia. Dog 2 had alopecia, hyperpigmentation, and pyoderma on the dorsal trunk. Dog 4 had alopecia on the

TABLE 1**Signalment and Presenting Dermatologic Signs of the 10 Dogs Presenting with Skin Lesions as the Only Signs of Hyperadrenocorticism**

Dog	Breed	Body weight (kg)	Sex	Age of onset of clinical signs, y	Site of lesions	Alopecia	Pruritis	Pyoderma	Others
1	Miniature pinscher	6	FS	4	4 paws (Figures 2A,B)	Yes, severe	Yes, moderate pododermatitis	Yes, abdomen	Hyperpigmentation and comedones on the abdomen
2	Poodle cross-breed	7	MC	8*	Trunk (patches)	Yes	No	Yes, moderate, recurrent	Hyperpigmentation
3	Toy poodle	5	M	9	Pinnae, muzzle	Yes	Yes	Yes, mild	Thin skin on pinnae and abdomen, concurrent atopic dermatitis
4	English setter	20	F	7	Bilaterally symmetrical, over dorsum, ventral neck, and pinnae	Yes	No	Yes, severe	Thin skin and comedones on abdomen, hyperpigmentation
5	Toy poodle	5	M	10	Entire dorsum	Yes	No	No	Thin skin
6	Mix terrier	10	F	10	Entire dorsum	Yes	No	Yes, mild	Hyperpigmentation
7	Poodle cross-breed	10	MC	13	3 circumscribed lesions on the trunk, one fore and one hindlimb	Yes	No	No	<i>Microsporum canis</i>
8	American cocker spaniel	12	M	8*	4 paws, otitis externa	No	Yes	Yes, severe, recurrent pododermatitis	Concurrent atypical dermatitis, dietary hypersensitivity, otitis externa, and hypothyroidism
9	Mix breed	5	F	14	Trunk, patches (Figure 1), and tail and abdomen	Yes	No	Yes, moderate	Hyperpigmentation, mammary gland tumors
10	Mixed breed	10	FS	15.5	4 legs, paws, foot pads	Yes	Yes	Yes, severe, recurrent	Hyperpigmentation
Median $\pm$ SD		8.5 $\pm$ 4.6		9.5 $\pm$ 3.5					
Range		5–20		4–15.5					

* Dog 2 first presented 2 yr earlier, with similar clinical signs. The dog was diagnosed with "castration responsive dermatosis." Signs resolved after castration and reappeared later. Dog 8 was diagnosed with adverse food reaction and atopic dermatitis when he was 4 yr old and hypothyroidism when was 5 yr old.

F, female, intact; FS, female, spayed; M, male, intact; MC, male castrated; SD, standard deviation.

dorsal trunk, ventral neck, and pinnae, and thin skin of the abdomen with hyperpigmentation and a bacterial pyoderma at each of these sites. Alopecia and thin skin on the dorsal trunk were present in dog 5. Alopecia was noted on the dorsal and ventral abdomen in dog 6, with hyperpigmentation and a bacterial pyoderma at these sites. Dog 9 had patchy truncal alopecia (**Figure 1**) and alopecia of the tail and abdomen with hyperpigmentation and a moderate bacterial pyoderma at these sites.

Other Dermatologic Signs and Concurrent Dermatologic Diseases

Dogs 1, 3, 8, and 10 initially presented with pruritus as the owners' chief complaint. Dog 1 had a pruritic pododermatitis and a bacterial pyoderma involving all four feet with hyperpigmentation noted on the dorsal aspect of all paws (**Figures 2 A and B**). The abdomen also had thin skin and comedones.

Dog 3 had alopecia of the pinnae and muzzle, pruritus directed at the muzzle, a mild pyoderma of the muzzle, and thin skin noted on the pinnae and abdomen. This dog was diagnosed as atopic, as it had been licking its paws since 2 yr of age. The paw licking resolved at approximately the same time that the alopecia on the pinnae



FIGURE 1 Patchy alopecia and scales on the back of dog 9.

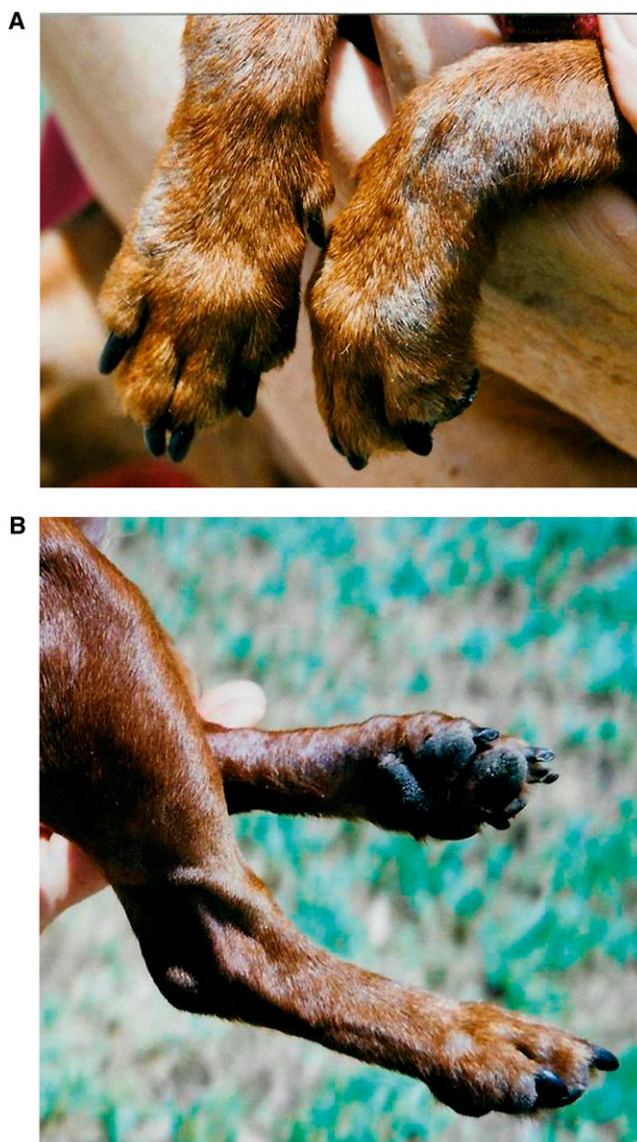


FIGURE 2 Dog 1—alopecia and hyperpigmentation on front (A) and hind (B) limbs. These lesions were caused by intense pedal pruritus.

appeared at the age of 9 yr, but recurred when the cortisol levels diminished after treatment with mitotane. A cutaneous adverse reaction to diet was ruled out via a dietary trial, but the pruritus resolved when post-ACTH levels were maintained at 8–9 $\mu\text{g/dL}$ and did not recur during the long (4 yr) follow-up period.

Dog 8 had a pruritic pododermatitis, a bacterial pododermatitis, and was concurrently atopic with a cutaneous adverse reaction to food and was receiving thyroid supplementation for hypothyroidism. The precise food allergen was not determined, as after responding to elimination dietary trial and relapsing on challenge with its original diet, the dog was maintained on the elimination diet without specific allergen challenges. This dog

was treated with glucocorticoids (prednisone at a starting dose of 1 mg/kg PO *q* 24 hr then tapered to a maintenance dose of 0.25 mg/kg PO *q* 2–3 days) for several months after the diagnosis of atopic dermatitis (made 4 yr before the diagnosis of HAC). At the time the diagnosis of HAC was made, the atopic dermatitis of dog 8 no longer required neither glucocorticoids for at least 3 yr nor antihistamines for 2 yr. T4 levels were within normal range as per post pill evaluation (2.84 µg/dL), but clinical signs of hypothyroidism had not improved.

Dog 10 had alopecia of the extremities, pruritus directed at the extremities, a pyoderma, and hyperpigmentation of legs and paws.

Dog 7 had three circumscribed areas of alopecia that were diagnosed as dermatophytosis with no response to topical antifungal treatment.

Laboratory Findings

The laboratory findings for all dogs are summarized in **Table 2**. Only one dog (dog 10) had any abnormal findings on CBC (neutrophilia and eosinopenia). Four dogs had elevated fasting values of cholesterol and triglycerides. Only in dog 5 were these elevations considered severe (675 and 1,784 mg/dL; reference ranges, 120–260 and 50–100 mg/dL, respectively). Dogs 2 and 9 had elevated triglycerides with normal cholesterol values. Seven of the 10 dogs had elevated ALP values, 5 of which were >1,500 U/L (reference range, 10–140 U/L).

Five dogs had T4 values measured, all of which were within normal limits (0.8–4 µg/dL). In one of these dogs (dog 8), hypothyroidism was diagnosed 3 yr before the diagnosis of HAC. The skin lesions in this dog had stopped responding to treatment with L-thyroxine^f, and a recurrence of otitis externa and pododermatitis prompted the clinician to look for HAC.

UAs were within normal ranges in all dogs. Specifically, the specific gravity of the urine was >1.025 (range, 1.026–1.045), and no signs of cystitis were noted.

Results of Tests for HAC and Ultrasonography

As summarized in Table 2, the LDDST was the only test performed on two dogs, the ACTH stimulation test was the only test performed on four dogs, and four dogs had both tests performed. The LDDST diagnosed HAC in all six dogs tested, whereas the ACTH test diagnosed HAC in five of the eight dogs tested. Only dog 4 was diagnosed with HAC using both methods. Three of the six dogs diagnosed with HAC by the LDDST had suppression at 4 hr after injection, which was suggestive of pituitary dependent hyperadrenocorticism (PDH).¹

Abdominal US was performed on eight dogs and was used to differentiate between PDH and an adrenal tumor.^{1,2} One of the

three dogs in which cortisol values were not suppressed at 4 hr in the LDDST (dog 4) had unilateral enlargement of an adrenal gland and was therefore suspected of having an adrenal tumor on US examination. Four dogs, including dogs 1 and 10 who had no suppression at 4 hr on the LDDST, had adrenal glands of normal size. Dogs 5, 8, and 9 had bilateral adrenal gland enlargement. Ultrasonic evidence of liver enlargement was found in all four dogs in which adrenal glands were enlarged (i.e., dogs 4, 5, 8, and 9).

Treatments and Outcomes

Responses to treatment with mitotane, when used, are summarized in **Table 3**. Nine dogs were treated with mitotane. The induction dose of mitotane used ranged between 21 mg/kg and 26 mg/kg (mean, 24.2 mg/kg). The maintenance dose of mitotane used ranged between 25 mg/kg and 50 mg/kg (mean, 35.9 mg/kg). Dog 7 did not complete the induction phase and was instead started on the maintenance dose after recovery from a heating-pad burn at a grooming parlor that had occurred immediately after beginning the induction phase. The owners of dog 4 declined surgery for the suspected adrenal tumor and instead accepted treatment with mitotane. Dog 9 was not treated for HAC because the first author and the owners decided that the mild clinical signs did not justify treatment.

Dog 5 was lost to follow up shortly after starting treatment. Dogs were followed up from 6 mo to 7 yr (mean and median ± SD, 3.2 ± 2.2).

In the eight dogs that were treated and followed, almost all skin lesions resolved after treatment, and no adverse effects to the mitotane were observed while the dogs were on the maintenance dosage. Resolution of skin lesions was noted within 1–3 mo after initiation of treatment with mitotane.

Six dogs received appropriate antibiotics for superficial pyodermas for periods of 3–4 wk, except dog 8, which had severe pododermatitis and needed a longer treatment period. For the other five dogs, the skin lesions did not resolve upon resolution of the pyoderma, but did resolve upon treatment with mitotane.

Pyodermas did not reoccur in these dogs during the follow-up period. Dog 7 (diagnosed with dermatophytosis) was treated topically with 2% miconazole cream^e *q* 12 hr. In this dog, the skin lesions resolved, but the fungal culture was still positive when the ACTH stimulation test revealed normal values of cortisol 2 mo after initiating mitotane treatment. A negative culture was achieved 2 mo later (i.e., 4 mo after starting mitotane).

Discussion

Ten dogs were diagnosed with HAC between April 1992 and December 2005. Although this small number of cases cannot be

TABLE 2

Results of Key Serum Biochemistry Tests, the Low-Dose Dexamethasone Suppression Test (LDDST), ACTH Stimulation Test, and Abdominal Ultrasound Findings (US) in 10 Dogs

Dog/test (reference range)	ALP (10–140 U/L)	ALT (8–50 U/L)	AST (9–50 U/L)	GGT (1–10 U/L)	Cholesterol (120–260 mg/dL)	TG (50–100 mg/dL)	Glucose (85–110 mg/dL)	T4/TSH (0.8–4.0 μg/dL/0.02–0.4 nmol/L)	LDDST 0/4 hr/8 hr	ACTH 0/60 min	US
1	71	37	35	NP	346*	348*	80	NP/NP	7.5/3.1/2.3	8.7/18.7	No abnormal findings
2	2,168*	23	22	1.0	152	145*	NP	1.1/NP	NP	6.9/28.2	NP
3	46	52	44	4.7	245	79	107	2.2/0.38	6.9/1.5/7.8	2.0/18.0	NP
4	2,516*	416*	35	133*	295*	112*	NP	NP/NP	34.3/21.0/16.0	15.8/>50	Echogenic and enlarged liver, enlarged left adrenal gland, right not detected
5	1,536*	514*	85	17.4*	675*	1,784*	NP	1.7/0.1	NP	3.5/32.8	Enlarged liver and both adrenal
6	543*	104*	29	2.9	200	123	NP	NP/NP	3.8/<1/38	NP	No abnormal findings
7	47	56	28	2.5	186	NP	94	NP/NP	9.40/1.77/3.13	3.57/14.8	No abnormal findings
8	3,869*	82*	61*	18*	304*	145*	NP	2.84 [†] /0.07 [†] <0.05 [§] /0.45 [§]	NP	5.50/34.0	Enlargement of both adrenal glands; enlarged liver
9	658*	156*	46	NP	212	146*	NP	1.59/0.13	NP	7.20/34.1	Enlargement of both adrenal glands; enlarged liver
10	1,660*	65	29	5	231	55	NP	NP/NP	4.27/7.48/4.42	NP	No abnormal findings

* Abnormal value

[†]The values of T4 and TSH were measured while receiving L-thyroxine 20 μg/kg PO q 12 hr (5-hr "postpill" value), at the time the HAC was diagnosed.

[§]The values measured when hypothyroidism was diagnosed 3 yr previous.

Normal resting cortisol, 1.3–7.9 μg/dL; cutoff point/value for suppression of cortisol, 1.3 μg/dL; stimulated cortisol level indicative of HAC ≥ 22 μg/dL, "gray zone", 17–21 μg/dL.² NP, not performed; TG, triglyceride.

TABLE 3**Response to Treatment with Mitotane (o,p'-DDD)**

Dog	Response	Time until first response (wk)	Longest follow-up (yr)
1	Skin lesions resolved	6	4
2	Re-grew hair	10	7
3	Re-grew hair on pinnae	8	4
4	Full hair re-growth	4	0.5
5	Lost to follow-up		
6	Started treatment 7 mo after diagnosis when systemic signs appeared, re-grew healthy coat later	10	1
7	Started treatment with maintenance dose. Two months later full hair re-growth at lesion sites but still had positive culture to <i>M. canis</i> , which resolved after another 2 mo	8	5
8	Dermatitis of paws resolved, improvement of otitis externa	Difficult to determine; multifactorial	2.5
9	No treatment. (signs were not severe enough to justify treatment with mitotane)		
10	Pyoderma resolved, re-grew hair	4	1.5
Median $\pm$ SD		8 $\pm$ 2.5	3.2 $\pm$ 2.2
Range		4–20	0.5–7

used for statistical analysis, most dogs were old (≥ 7 yr) and of small breeds. No dogs had dilute urine or any signs of cystitis. This finding was unexpected because dilute urine is the most common finding in UA in dogs with HAC.^{1,2} This might be explained by a lack of excessive drinking during the hospital visit.² Seventy percent of the dogs in this report had elevated ALP, as is common in dogs with HAC.^{1,4} Although secondary hypothyroidism and lower values of the thyroid hormones are common in chronic hypercortisolism,^{1,2} none of the five dogs in which thyroid values were measured had low T4 values. This includes dog 8, which had been diagnosed with hypothyroidism several years before the diagnosis of HAC. Its postpill T4 levels were within normal ranges when the diagnosis of HAC was made. Abdominal US in three of eight dogs showed enlargement of both adrenal glands. This is a nonspecific sign and only slightly suggestive of PDH.¹ One study found a very high sensitivity and specificity of adrenal US and endogenous ACTH determinations to identify the cause of HAC.¹² Unfortunately, the measurement of endogenous ACTH was not available for the cases reported here.

Four of the dogs (dogs 1, 3, 8, and 10) had nontruncal, nonsymmetrical alopecia. Nontruncal alopecia was found in 13% of the dogs with HAC in a previous study.⁸

The common dermatologic signs present in the dogs in this study (i.e., pyoderma, hyperpigmentation, thin skin, comedones) were similar to the incidence in another report of 60 dogs.⁸

The least expected sign in HAC is pruritus because of the endogenous hypercortisolism.^{1,3} Nonetheless, pruritus, including

pedal pruritus, was a major clinical sign in four of the dogs in this study. Pedal pruritus in dogs 3 and 8 could be explained by concurrent atopic dermatitis, and it might also be hypothesized that the atopic signs would have been more severe without the concurrent HAC. Such a hypothesis would not apply to dog 1. In dog 1, the pedal pruritus resolved after treatment with mitotane, but not after antibiotics (cephalexin⁸ at 25 mg/kg PO q 12 hr for 30 days) or an elimination diet. Limb pruritus and hair chewing in a dog that was suspected of having HAC, and in which the pruritus responded to treatment with mitotane, was previously reported.¹³ These authors hypothesized that the limb pruritus and hair chewing might have been associated with neurosis or psychosis as noted in people with HAC.¹⁴

Other causes of pruritus in dogs with HAC include calcinosis cutis (not found in this study) and bacterial infections secondary to the immunoin sufficiency associated with HAC.⁷ Pruritus was associated with pyoderma in four dogs, but in only dog 10 did the pedal pruritus resolve when the pyoderma was successfully treated; in dog 1 the pedal pruritus resolved when the HAC was controlled. In dogs 3 and 8, the pruritus was controlled when their allergies were controlled.

Dog 3 had lesions on its muzzle that were thought to be associated with its concurrent atopic dermatitis, as they did not resolve with mitotane treatment. Facial dermatosis as the only skin lesion in dogs with HAC was previously described.¹⁵ That report described four dogs all with facial dermatosis that had normal CBC results but with blood chemistry that revealed elevations of ALP, ALT, and cholesterol.

Dermatophytosis was the only presenting sign in dog 7. Concurrent HAC with *Trichophyton mentagrophytes* infection was described recently in a miniature schnauzer that responded very well to treatment with mitotane and terbinafine.¹⁶ An older report documented a dog with HAC and *Trichophyton mentagrophytes* in which the dermatophytosis failed to respond to systemic antifungal treatment until the HAC was treated with mitotane.¹⁷ In dog 7 in the present study, topical treatment was sufficient in resolving clinical signs of dermatophytosis once the HAC was controlled. HAC as an underlying cause for bacterial infection, dermatophytosis, and demodicosis is well described.^{3–6,18} Thus, clinicians should consider HAC as an underlying cause in spontaneously occurring infections in apparently healthy adult dogs.

Otitis externa was diagnosed in dog 8. This condition was not necessarily related to the HAC because this dog was also diagnosed with hypothyroidism, atopic dermatitis, and cutaneous adverse reaction to food, all of which are more common primary or predisposing causes for otitis externa. In addition, this dog was a cocker spaniel that could have had a genetic structural or cornification disorder of the ear canal as predisposition for its otitis.^{19,20} Interestingly, the ear infection improved better with treatment of HAC and concurrent otic preparations than with otic preparations alone.

Supporting the diagnosis of HAC was the fact that the eight dogs that were treated with mitotane treatment had an excellent response to treatment with regard to their skin lesions. In addition, their blood cortisol values normalized after treatment based on repeat ACTH stimulation tests. Dogs with adrenal hyperplasia are more sensitive to the destructive effects of mitotane, whereas healthy dogs are more resistant.¹ Although mitotane is more commonly used in the treatment of PDH, it has been used in the treatment of adrenal tumors, which might explain its success in dog 4 despite the fact that the dose was not higher than the recommended dose for PDH.¹

The treatment of choice in this report was mitotane. It is possible that other medications such as trilostane or L-deprenyl could have been used. Trilostane administration controlled PDH in 29 of 30 dogs in one study, and skin lesions improved in 9 of 11 dogs with HAC when treated with trilostane in another study.^{21,22} However, one recent report did not find any significant differences in the survival times between dogs treated with either mitotane or trilostane.²³ Trilostane was also found to be beneficial in controlling clinical signs and normalized serum chemistry in a dog with HAC due to a functional adrenal tumor.²⁴ Trilostane was reported to be very safe in these studies, although in one study the dosage had to be reduced or the drug temporarily discontinued

due to iatrogenic hypoadrenocorticism.²¹ In another case report, trilostane treatment of HAC caused adrenal necrosis and clinical signs of hypoadrenocorticism.²⁵ L-deprenyl was not recommended as a sole treatment of canine pituitary dependent HAC in one study; however, another author suggested that the drug's safety justified its use in mild and slowly progressing cases.^{26,27} It could be argued that all the dogs in this report were mild cases because of the lack of systemic signs, and that trilostane and L-deprenyl could have been considered as initial treatments (except these drugs were not available at the time most of the dogs in this study were treated).

This study demonstrated that skin lesions might be the only clinical manifestation of HAC, as mentioned previously.⁶ The reasons for this might be due to the observation skills of the owners or the stage of the disease.³ None of the other "classic" signs of HAC (i.e., including polyuria, polydipsia and polyphagia, lethargy, muscle atrophy, and abdominal enlargement) were noted in these dogs. In a survey of internists and dermatologists, only 26% of the respondents indicated they would screen a dog for HAC if the dog had only a few laboratory abnormalities consistent with HAC and no clinical signs consistent with the disease.²⁸ The cases presented here, however, suggest that HAC should be considered a differential diagnosis of unresolved skin problems in adult dogs, even if classic signs of HAC are absent.

Conclusion

This study showed that skin lesions might be the only clinical signs of HAC. The presence of the more common clinical signs of HAC, such as a nonpruritic, truncal alopecia and/or thin skin, without any other systemic signs of HAC, warrants screening for this disease. In addition, the presence of poorly responsive skin infections also warrants such screening. ■

FOOTNOTES

- ^a Immune2000 Cortisol; DPC, Los Angeles, CA
- ^b Synacten; Novartis, Basel, Switzerland
- ^c Dexacort; Teva, Petach-Tikva, Israel
- ^d Lysodren; Bristol Laboratories, Syracuse, NY
- ^e Daktarin; Janssen, Beerse, Belgium
- ^f Eltroxin; GlaxoSmithKlein GmbH&Co, Singen, Germany
- ^g Cephoral; Teva, Petach-Tikva, Israel

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