Iatrogenic Hyperadrenocorticism in 12 Cats

Iatrogenic hyperadrenocorticism is an extremely rare condition in cats. Twelve cats with a medical history of progressive skin lesions and long-term treatment with corticosteroids were retrospectively studied. Noncutaneous signs in the cats were variable and included anorexia, lethargy, polydipsia, polyuria, and atrophy of the thigh muscles. Laboratory abnormalities included leukocytosis, elevated alanine aminotransferase levels, and hyperglycemia. Transient diabetes mellitus was a secondary complication in four cats, and transient hypothyroidism was suspected in four cats. The mean time for regression of signs was 4.9 months after corticosteroid withdrawal. **J Am Anim Hosp Assoc 2006;42:414-423.**

Yu-Hsin Lien, DVM, MVM

Hui-Pi Huang, DVM, PhD

Pen-Heng Chang, DVM, PhD

RS

From the Department of Veterinary Medicine, (Lien, Huang, Chang), National Taiwan University, No. 1, Section 4, Roosevelt Road, Taipei, 106, Taiwan; and the Azu Clinic for Animals (Lien), 92, Section 1, Kin-Shan South Road, Taipei, 100, Taiwan.

Address all correspondence to Dr. Huang.

Introduction

Iatrogenic hyperadrenocorticism (HAC) is an extremely rare condition in cats that is caused by excessive administration of corticosteroids.[1] Only four cases of iatrogenic HAC have been reported in cats.[2-5] Cutaneous abnormalities were reported in all affected cats, and most had clinical signs similar to spontaneous HAC, such as polyphagia, polydipsia, polyuria, elevated hepatic enzymes, and concurrent diabetes mellitus.[1-5]

Adrenocorticotropic hormone (ACTH) release is suppressed by exogenous corticosteroids through feedback mechanisms of the hypothalamic-pituitary-adrenocortical axis in cats.[6-8] Diagnosis of iatrogenic HAC is based on a history of corticosteroid administration, clinical and physical findings consistent with HAC, and the results of an ACTH stimulation test. The aim of this study was to retrospectively evaluate iatrogenic HAC in cats.

Materials and Methods

Medical records were reviewed of cats that were presented with a history of worsening skin disease and systemic illnesses (despite ongoing treatment) between May 1998 and November 2001 to the Azu Clinic for Animals and the National Taiwan University Veterinary Hospital. Criteria for diagnosis of iatrogenic HAC included treatment with oral, parenteral, or topical corticosteroids (for various skin disorders or other systemic illnesses) for >1 month prior to referral; cutaneous abnormalities that were consistent with feline HAC, such as progressive alopecia or thin, inelastic skin; and low cortisol levels (<2.1 µg/dL; reference range 3 to 5 µg/dL) in response to ACTH stimulation. The duration of previous treatment, administration routes, clinical presentation, and physical examination findings were recorded. Cases were included if they were followed for at least 18 months.

A complete blood cell count, biochemical profile, baseline serum total thyroxine level (T_4), and ACTH stimulation tests were performed in all cats at initial evaluation. The ACTH stimulation test was performed using synthetic ACTH[a] (0.125 mg intramuscularly). Serum cortisol samples

were collected prior to and 45 minutes after ACTH administration.[9] Cortisol[b] and T_4 levels[c] were measured using validated assays.

Results

Twelve cats met the criteria for a diagnosis of iatrogenic HAC. Breeds represented included the Persian (n=7), domestic shorthair (n=4), and Himalayan (n=1). There were seven males (one castrated) and five females (two spayed). Ages ranged from 0.8 to 8 years (mean ± standard deviation [SD] was 2.7±1.9 years). Previous diseases and treatments prescribed by the referring veterinarians are recorded in Table 1. The mean duration of treatment for skin disorders and other systemic illnesses prior to referral was 8.3 months (range 6 weeks to 48 months). All 12 cats had worsening skin lesions at the time of referral. Clinical findings for all affected cats are summarized in Table 2.

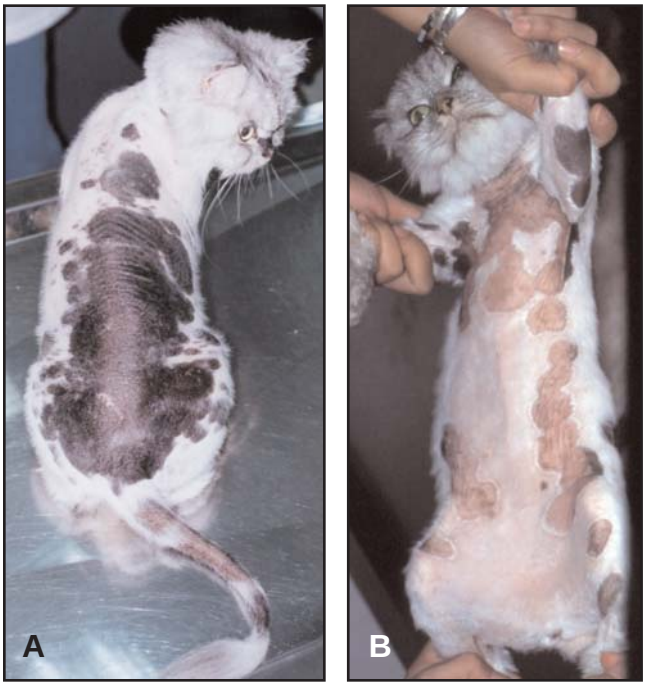
Localized or generalized hair loss along the dorsal and ventral trunk were the most apparent dermatological abnormalities. Alopecia occurred bilaterally and was mainly present on the temporal region of the head, pinnae, and trunk. One cat that had received only topical medication had mild cutaneous lesions characterized by bilateral alopecia of the pinnae, chest, and ventral abdomen. In cats medicated with systemic corticosteroids or where topical ointment had been applied (n=2), affected skin was thin, fragile, and exhibited poor healing. No evidence of calcinosis cutis was palpable in the cats. Poor cutaneous elasticity was found in three cats.

Leukocytosis and monocytosis were the most predominant hematological findings [Table 3]. The remaining hematological parameters were unremarkable. The most common biochemical abnormalities were elevations of alanine aminotransferase (ALT, n=6; range 29 to 238 U/L, median 62 U/L, mean ± SD 81±60 U/L, reference range 22 to 114 U/L) and hyperglycemia (n=6; range 98 to 457 mg/dL, median 214 mg/dL, mean ± SD 220±145 mg/dL, reference range 84 to 197 mg/dL). The remaining biochemical parameters were all within the reference ranges [Table 4].

All 12 cats had subnormal baseline cortisol levels and a suppressed or poor cortisol response to ACTH administration [Table 5]. The mean baseline cortisol concentration before ACTH stimulation was 0.18 µg/dL (range 0.1 to 0.5 µg/dL, reference range 0.5 to 3 µg/dL). The mean cortisol concentration 45 minutes after ACTH administration was 0.53 µg/dL (range 0.1 to 2.1 µg/dL, reference range 3 to 5 µg/dL). Administration of ACTH did not produce a change in cortisol levels in five cats, and seven cats had a suppressed response to ACTH. Baseline T_4 levels for the 12 cats were generally low, with only one cat having a T_4 concentration within the normal range [Table 5].

After diagnosis of iatrogenic HAC, all medications were stopped except in the four cats with persistent hyperglycemia. These cats were treated with isophane insulin[d] (0.5 to 1.2 U/kg subcutaneously *q* 24 hours). In these four cats, the diabetes mellitus was transient, with a mean duration of 3.8±1.5 months.

The time between corticosteroid withdrawal and clinical improvement of dermatological signs varied, depending on the severity of the cutaneous lesions. Cats with localized alopecia showed initial clinical improvement in 3 weeks, whereas cats with generalized cutaneous lesions showed improvement 8 weeks after corticosteroid withdrawal. Hair regrowth in alopecic areas did not follow a specific pattern. By 8 weeks after withdrawal of corticosteroids, hepatic enzyme levels had returned to normal in the six cats that had elevated enzymes. Four cats (case nos. 3-6) had prolonged recoveries and later developed cutaneous hyperpigmentation in alopecic areas [Figures 1A, 1B]. Skin biopsies from case no. 3 revealed epidermal hyperplasia, with increased melanin deposition and vacuolization of the erector pili muscles in the dermis [Figures 2A, 2B]. Demodex mites were seen within the follicular infundibula of the hair follicles.



Figures 1A, 1B—Generalized alopecia and pigmentation associated with iatrogenic hyperadrenocorticism and suspected hypothyroidism in a 2.5-year-old, spayed female Persian (case no. 3). **(A)** Lesions are visible on the dorsal nose, back, and tail. **(B)** Lesions also developed on the ventral chest and abdomen and medial aspects of the legs. These photographs were taken 10 weeks after withdrawal of corticosteroids.

Ten cats underwent testing with thyroid-stimulating hormone (TSH) using bovine TSH[e] (0.1 U/kg intravenously). This dose was used because higher doses of bovine TSH (i.e., 0.5 U/kg) in cats may induce adverse effects (e.g., vomiting, anaphylactic shock). Samples for T_4 determinations were collected prior to and 6 hours after TSH administration.[10,11] In four cats (case nos. 3-6), subnormal baseline T_4 levels and poor T_4 responses to TSH administration were found [Table 5], with a mean baseline T_4 <0.5

Table 1

Clinical Data on 12 Cats With Iatrogenic Hyperadrenocorticism

Case No.	Signalment*	Clinical Signs	Previous Diseases	Prior Corticosteroid Treatments†	Concurrent Disorders
1	4-y, M Persian	Generalized hair loss, polyphagia	Atopic dermatitis	Topical triamcinolone 1% ointment *q* 6 to 8 h; SC dexamethasone 0.1 to 0.5 mg/kg *q* 7 d for 48 mos	None
2	3-y, M Persian	Alopecia of truncal regions, anorexia, polydipsia, polyuria, muscular atrophy	Spinal problem and back pain	Topical triamcinolone 1% ointment *q* 8 h; SC dexamethasone 0.1 to 0.5 mg/kg *q* 24 h to *q* 7 d for 3 mos	Transient diabetes mellitus
3	2.5-y, SF Persian	Alopecia and hyperpigmentation of truncal regions, lethargy	Ear mite infestation, atopic dermatitis	Topical triamcinolone 1% ointment *q* 8 h; dexamethasone 0.09% ear solution *q* 8 h; SC dexamethasone 0.1 to 0.5 mg/kg *q* 24 h to *q* 7 d for 6 mos	Transient diabetes mellitus, transient hypothyroidism
4	0.8-y, CM Himalayan	Ventral alopecia and hyperpigmentation, pot-belly appearance, polydipsia, polyuria, lethargy	Atopic dermatitis	Topical triamcinolone 0.1% ointment 4 to 5 g *q* 24 h to skin lesions for 2 mos	Transient hypothyroidism
5	8-y, M DSH	Generalized alopecia and hyperpigmentation, thin and easily torn skin, polydipsia, polyuria	Feline infectious peritonitis	Oral prednisolone 2 to 3 mg/kg *q* 24 h for 12 mos	Transient diabetes mellitus, hypothyroidism
6	2-y, M Persian	Generalized alopecia and hyperpigmentation	Undiagnosed skin problem	Topical triamcinolone 1% ointment *q* 8 h; SC dexamethasone or triamcinolone *q* 24 h to *q* 7 d for 6 mos	Transient hypothyroidism
7	7-y, SF DSH	Ventral and truncal hair loss, thin and easily torn skin, lethargy, muscular atrophy	Atopic dermatitis	Topical triamcinolone 1% ointment *q* 8 h; SC dexamethasone, triamcinolone 0.1 to 0.5 mg/kg *q* 24 h to *q* 7 d for 6 mos	Transient diabetes mellitus

(Continued on next page)

Table 1 (cont'd)

Clinical Data on 12 Cats With Iatrogenic Hyperadrenocorticism

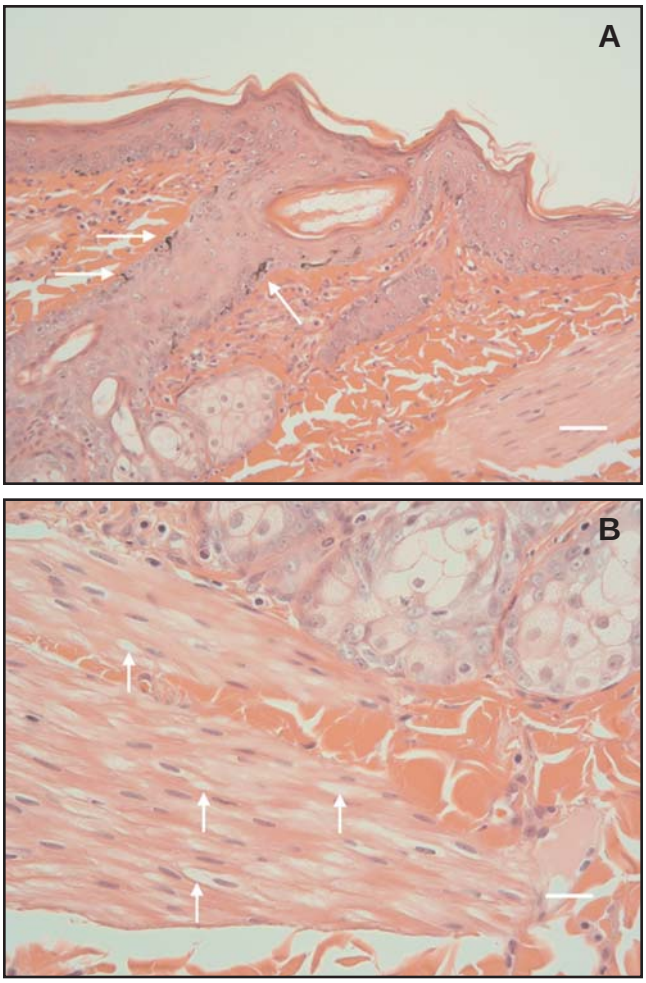
Case No.	Signalment*	Clinical Signs	Previous Diseases	Prior Corticosteroid Treatments†	Concurrent Disorders
8	3-y, F Persian	Hair loss on ventrum and temporal areas of the head	Ear mite infestation, atopic dermatitis	Topical triamcinolone 1% ointment *q* 8 h; dexamethasone 0.09% ear solution *q* 8 to 12 h; SC dexamethasone 0.1 to 0.5 mg/kg *q* 24 h to *q* 7 d for 2 mos	None
9	3-y, F DSH	Hair loss on ventrum	Undiagnosed skin problem	SC dexamethasone 0.1 to 0.5 mg/kg *q* 24 h to *q* 7 d for 7 mos	None
10	5-y, M Persian	Hair loss on ventrum and temporal areas of the head	Undiagnosed skin problem	Topical triamcinolone 1% ointment *q* 8 to 12 h; SC dexamethasone or triamcinolone 0.1 to 0.5 mg/kg *q* 24 h to *q* 7 d for 2 mos	None
11	0.9-y, F Persian	Hair loss on ventrum and temporal areas of the head	Ear mites and atopic dermatitis	Topical triamcinolone 0.1% ear solution *q* 8 h; dexamethasone 0.09% ear solution *q* 8 h; SC dexamethasone 0.1 to 0.5 mg/kg *q* 24 h to *q* 7 d for 3 mos	None
12	0.9-y, M DSH	Hair loss on ventrum and pinnae	Undiagnosed skin problem	Topical triamcinolone 1% ointment *q* 8 h; SC dexamethasone 0.1 to 0.5 mg/kg *q* 24 h to *q* 7 d for 2 mos	None

* M=male, SF=spayed female, CM=castrated male, F=female, DSH=domestic shorthair
† SC=subcutaneous

Table 2

Summary of Clinical Findings in 12 Cats With Iatrogenic Hyperadrenocorticism

Clinical Findings	No. of Cats
Chief complaints at presentation	
Anorexia, lethargy	4
Polydipsia	3
Polyuria	3
Polyphagia	1
Cutaneous lesions	
Localized hair loss	6
Localized alopecia	3
Generalized hair loss or alopecia	3
Localized or generalized hyperpigmentation	4
Skin tears	2
General physical changes	
Muscular atrophy	2
Pot-belly, distended abdomen	1



Figures 2A, 2B—Microscopic sections of a skin biopsy taken from the cat in Figures 1A and 1B, showing **(A)** epidermal hyperplasia with increased melanin deposition (arrow; Hematoxylin and eosin stain, bar=60 µm) and **(B)** vacuolization of erector pili muscles (arrows; Hematoxylin and eosin stain, bar=120 µm).

µg/dL (reference range 2 to 3.5 µg/dL) and a post 6-hour T_4 <0.5 µg/dL (reference range, doubling of baseline T_4). These results were consistent with hypothyroidism.

Levothyroxine[f] (50 µg orally *q* 24 hours) was given to these four cats for 6 weeks. New hair growth on the alopecic areas was observed 2 weeks after initiation of levothyroxine. Three years after remission of iatrogenic HAC, baseline T_4 levels were within the normal range for case nos. 3-6 (2.5, 2.3, 2.5, and 2.9 µg/dL, respectively). Stimulation tests with TSH were normal in the two cats (case nos. 3, 4) tested. In case no. 3, the pre-TSH T_4 level was 2.5 µg/dL, and the post-TSH T_4 level was 4.9 µg/dL. In case no. 4, the pre-TSH T_4 level was 2.3 µg/dL, and the post-TSH T_4 level was 5.3 µg/dL.

For six of the cats (case nos. 7-12), TSH responses were normal despite low or low-normal (case no. 9) baseline T_4 levels [Table 5]. Clinical improvement of cutaneous lesions in these six cats was good after withdrawal of corticosteroids. For all 12 cats, the mean time for complete coat recovery was 4.5 months (range 1 to 12 months).

Discussion

Cats are generally resistant to developing iatrogenic HAC, both clinically and experimentally.[1,6-8] Although iatrogenic suppression of the hypothalamic-pituitary-adrenocortical axis has been documented in cats, the clinical signs and clinicopathological abnormalities associated with iatrogenic HAC have been inconsistent and difficult to produce experimentally, possibly owing to the low expression of corticosteroid receptors in cats (compared with other species).[6-8] In the study reported here, iatrogenic HAC developed after at least 6 weeks of administration of parenteral, oral, or topical medications containing corticosteroids. Many of the cats had been treated by several veterinary practices prior to referral, which made obtaining a complete medical history difficult. Because corticosteroids can be obtained without prescription in Taiwan, the true frequency, dosage, and duration of administration may have been even higher than those recorded. Of the 12 cats studied here, seven were Persians, which probably reflected the popularity of the breed in the local area rather

Table 3

Hematological Results From 12 Cats With Iatrogenic Hyperadrenocorticism

Case No.	Hemoglobin (g/dL)	RBC* ($\times 10^6$/µL)	Hematocrit (%)	WBC† (/µL)	Neutrophil (/µL)	Eosinophil (/µL)	Lymphocyte (/µL)	Monocyte (/µL)
1	11.6	8.2	35.9	16,300	14,018	163	1956	163
2	12.5	7.9	32.1	12,500	8375	125	2750	1250
3	13.5	9.3	43.3	35,400	32,568	354	2124	354
4	11.9	8.1	36.6	32,400	29,160	324	1620	1296
5	8.0	5.1	37.4	38,400	36,864	384	384	768
6	15.7	10.0	50.0	16,900	13,520	1014	2028	338
7	11.1	6.3	37.0	22,200	18,870	888	2220	222
8	15	8.6	48.9	8600	6106	516	1634	344
9	12.6	7.4	43.2	22,200	20,202	222	666	888
10	12.8	8.4	40.9	9100	7735	182	910	273
11	12.2	8.1	41.6	21,600	19,440	216	1296	648
12	11.8	8.3	42.3	20,800	18,720	208	1248	624
Mean ± SD‡	12.4±1.9	8.0±1.3	40.8±5.3	21,367±9762	18,798±9856	383±288	1570±696	597±388
Median ± SD	12.4±1.9	8.1±1.3	41.3±5.3	21,200±9762	18,795±9856	273±288	1627±696	489±388
Reference range	9.7-14.7	5.2-9.4	26.2-46.2	5900-20,600	2773-18,952	59-618	236-5979	0-412

* RBC=red blood cell count
† WBC=white blood cell count
‡ SD=standard deviation

Table 4

Results of Biochemical Analyses of 12 Cats With Iatrogenic Hyperadrenocorticism

Case No.	Albumin (g/dL)	Alkaline phosphatase (U/L)	Alanine transferase (U/L)	Blood urea nitrogen (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total protein (g/dL)
1	3.5	20	29	14	1.1	101	8.3
2	3.6	65	126	18	0.9	256	6.3
3	3.8	74	43	18	0.7	405	8.4
4	3.0	38	238	18	1.0	196	6.4
5	3.5	53	44	31	1.0	457	7.4
6	3.7	54	62	14	1.2	98	7.6
7	3.6	25	40	27	1.2	415	7.3
8	3.2	42	68	13	1.2	196	5.1
9	3.7	10	62	11	1.1	145	7.6
10	4.0	20	115	15	1.1	100	7.3
11	3.0	50	112	14	1.1	109	6.8
12	3.2	35	31	18	1.5	140	7.5
Mean ± SD*	3.5±0.3	41±20	81±60	17.6±5.9	1.1±0.2	220±145	7.2±0.9
Median ± SD	3.6±0.3	40±20	62±60	16.5±5.9	1.1±0.2	214±145	7.4±0.9
Reference range	2.7-3.9	28-78	22-66	12-36	0.9-1.8	84-197	5.9-8.7

* SD=standard deviation

Table 5

Results of Adrenocorticotropic Hormone (ACTH) Stimulation and Thyroid Stimulating Hormone (TSH) Stimulation Tests in 12 Cats With Iatrogenic Hyperadrenocorticism

Case No.	Pre-ACTH Cortisol (µg/dL)	Post-ACTH Cortisol (µg/dL)	Pre-TSH T_4* (µg/dL)	Post-TSH T_4* (µg/dL)
1	0.2	1.0	0.6	NA†
2	0.1	0.1	0.7	NA
3	0.1	0.1	0.3	0.3
4	0.1	0.1	0.4	0.3
5	0.1	0.4	0.4	0.4
6	0.3	0.5	0.3	0.4
7	0.1	0.2	0.7	1.9
8	0.1	1.1	0.6	1.5
9	0.2	0.4	2.3	4.1
10	0.2	0.2	1.1	2.3
11	0.2	0.2	1.1	2.1
12	0.5	2.1	1.7	3.3
Mean ± SD‡	0.18±0.15	0.53±0.40	0.85±0.61	1.66±1.34
Median ± SD	0.12±0.15	0.60±0.40	0.65±0.61	1.70±1.34
Reference range	0.5-3	3-5	2.0-3.5	Doubling of baseline T_4

* T_4=serum total thyroxine level
† NA=not available
‡ SD=standard deviation

than a predisposition to iatrogenic HAC. No sex predilection was found.

The signs of iatrogenic HAC in the present study were variable. Historically, cats have received prednisolone (2 to 4 mg/kg) or methylprednisolone (5.5 mg/kg) once weekly for 4 consecutive weeks without producing clinical signs of HAC.[7,8] In the present series of cases, only four cats were anorexic or lethargic when admitted; three were polydipsic and polyuric. One cat had a pot-bellied appearance. In cats with spontaneous HAC, a majority (>50%) have exhibited anorexia, polydipsia, polyuria, muscular wasting, and a pot-bellied appearance.[16-29] The severity or frequency of clinical signs might have been higher in the present cases if corticosteroid therapy was more prolonged. Differences in corticosteroid treatment regimens (e.g., types of corticosteroids, dosage, frequency, duration) may also have contributed to the variation and severity of the clinical signs.

The severity of hair loss was generally related to the route of corticosteroid administration. Generally, systemic administration of corticosteroids induced more severe clinical signs. Corticosteroids induced generalized alopecia in some of the cats, which contrasted with dogs.[12] In dogs, cutaneous lesions associated with systemic corticosteroids are initially noted on the face and head and gradually extend toward the back, flanks, hind legs, and tail.[12] In the cats reported here, however, hair growth occurred on alopecic areas randomly.

Cutaneous hyperpigmentation of alopecic areas after >8 weeks of corticosteroid withdrawal has not been reported previously. All four of the cats with hyperpigmentation had very low baseline T_4 levels and no response to TSH stimulation. Hyperpigmentation and alopecia resolved completely after a short course of levothyroxine. Only a few cases of spontaneous, adult-onset feline hypothyroidism have been reported, and descriptions of the clinical signs and cutaneous histopathology are limited.[13,14] Hypothyroidism in cats resembles the disease in dogs, where the predominant clinical signs are dry hair coat, scaliness, poor hair growth,

and asymmetrical or bilateral alopecia.[14,15] The cats reported here had a dry hair coat, poor hair growth, and mild scaliness, as well as cutaneous hyperpigmentation, which has not been previously reported with feline hypothyroidism. Whether the hyperpigmentation was secondary to iatrogenic HAC or hypothyroidism remained unclear.

In one cat (case no. 3), cutaneous histopathological findings supported a diagnosis of concurrent or secondary hypothyroidism.[13,14] Although iatrogenic HAC was initially diagnosed in this case, epidermal atrophy was not found in the skin biopsies. Epidermal hyperkeratosis has been seen in a case of spontaneous, adult-onset feline hypothyroidism, and hypothyroidism could explain the absence of epidermal atrophy.[13] In the case reported here, the skin biopsies were taken at least 10 weeks after the corticosteroids were withdrawn. At the time skin biopsies were taken, the major clinical manifestations associated with HAC had resolved, and hepatic enzymes were normal, which might explain why no epidermal atrophy was found in the skin biopsies.

Transient hypothyroidism was observed in four cats, and these cats had normal T_4 levels and normal TSH stimulation tests 3 years after remission of the iatrogenic HAC. Suppressed pituitary secretion of TSH also occurs in chronic canine HAC (both spontaneous and iatrogenic), and approximately 70% of dogs with spontaneous HAC have decreased serum baseline T_4 levels.[16,30] The proposed mechanism for this suppression is negative feedback by exogenous corticosteroids on the pituitary gland, leading to down-regulation of TSH release.[16,30] By comparison, normal baseline T_4 levels have been found in most cases of spontaneous feline HAC, and <5% of affected cats have had low baseline T_4 levels.[18-20] No associated clinical signs were described in those cases.[18-20] In the present study, most cats (91.7%) initially had subnormal T_4 levels. Six cats showed good clinical improvement and later had normal responses to TSH stimulation, while four cats that developed hyperpigmentation at alopecic sites and did not improve had no responses to TSH stimulation. The exact mechanism for the development of hypothyroidism in cats with iatrogenic HAC is unclear.

In most published cases, lymphopenia was the major abnormality in the leukogram of cats with spontaneous HAC (40%).[16-29] In the present study, the major finding was leukocytosis; lymphopenia was not detected in any cat. Approximately 50% of published cases of feline spontaneous HAC have had elevated hepatic enzymes.[16-29] Elevated levels of alkaline phosphatase were not found in the cats reported here, and the reason was unclear. In the present cases, elevated ALT levels were the only abnormality found in the hepatic enzyme analyses. Elevated ALT levels might have been associated with hepatic lipidosis, which is commonly reported in feline spontaneous HAC.[27]

Diabetes mellitus may be associated with feline HAC.[16-29] Corticosteroids increase gluconeogenesis, act as an insulin antagonist, and can induce a diabetic state.[16] More than 75% of feline spontaneous HAC cases have concurrent diabetes mellitus.[16-29] Diabetes mellitus was found in four cats in the present study. The diabetes was transient and occurred less frequently compared with spontaneous cases, but more cats might have developed the condition if corticosteroid therapy had been continued for longer time periods.

In the study reported here, the mean time for clinical signs of iatrogenic HAC to develop was 8.3 months. Although clinical signs associated with HAC have been difficult to induce experimentally using weekly prednisolone or methylprednisolone, one dose of systemic prednisolone or methylprednisolone can suppress the hypothalamic-pituitary-adrenocortical axis in cats.[7,8] In dogs, topical application of corticosteroids rapidly suppresses the hypothalamic-pituitary-adrenocortical axis, with plasma cortisol concentrations becoming significantly depressed within 7 hours after the first treatment.[31] Repeated topical applications of corticosteroids continue to suppress plasma concentrations of ACTH and cortisol and to reduce responses to exogenous ACTH.[31] In the cases reported here, suppression of the hypothalamic-pituitary-adrenocortical axis may also have been exacerbated by the oral intake of topical corticosteroids (owing to the grooming nature of cats). Future studies are needed to substantiate the suppression of the hypothalamic-pituitary-adrenocortical axis following the application of topical corticosteroids in cats. Based on the present study, 6 weeks of topical corticosteroids may suppress the response of the adrenal gland to exogenous ACTH and produce clinical manifestations consistent with HAC in cats.

Gradual withdrawal of corticosteroids after chronic administration is recommended in animals.[32] In the cats reported here, corticosteroids were discontinued immediately after referral, and no consequences developed, consistent with some reports in humans and dogs.[12,32] The clinical effects of abrupt corticosteroid withdrawal remain unclear in cats.

Conclusion

Iatrogenic HAC was diagnosed in 12 cats. Cutaneous lesions were the most apparent clinical abnormality and were found in all cats. In four cats, development of cutaneous hyperpigmentation in alopecic areas after corticosteroid withdrawal was suspected to be associated with transient hypothyroidism. The mechanism for development of the transient hypothyroidism was unclear and warrants further study.

---

[a] Cortrosyn; Organon, Oss, The Netherlands
[b] ACS:180 Cortisol +E; Bayer HealthCare, Tarrytown, NY 10591
[c] ACS:180 T4 +A; Bayer HealthCare, Tarrytown, NY 10591
[d] Insulatard HM; Novo Nordisk A/S, Bagsvaerd, Denmark
[e] Thyrotropic hormone; Sigma Chemico Co., St. Louis, MO 63178
[f] Eltroxin; GlaxoWellcome, Taipei, Taiwan

Acknowledgment

The authors are grateful to Dr. Neil A. McEwan for his helpful criticism and suggestions in the writing of this paper.

References

1. Scott DW, Reimers TJ. Iatrogenic Cushing's syndrome in the cat. Fel Pract 1982;12:30-36.
2. Greene CE, Carmichael KP, Gratzek A. Iatrogenic hyperadrenocorticism in a cat. Fel Pract 1998;23:7-12.
3. Schaer M, Ginn PE. Iatrogenic Cushing's syndrome and steroid hepatopathy in a cat. J Am Anim Hosp Assoc 1999;35:48-51.
4. Ferasin L. Iatrogenic hyperadrenocorticism in a cat following a short therapeutic course of methylprednisolone acetate. J Fel Med Surg 2001;3:87-93.
5. Smith SA, Freeman LA, Bagladi-Swanson M. Hypercalcemia due to iatrogenic secondary hypoadrenocorticism and diabetes mellitus in a cat. J Am Anim Hosp Assoc 2002;38:41-44.
6. Crager CS, Dillon AR, Kemppainen RJ, *et al.* Adrenocorticotropic hormone and cortisol concentrations after corticotrophin-releasing hormone stimulation testing in cats administered methylprednisolone. Am J Vet Res 1994;55:704-709.
7. Middleton DJ, Watson DJ, Howe CJ, *et al.* Suppression of cortisol responses to exogenous adrenocorticotropic hormone, and the occurrence of side effects attributable to glucocorticoid excess, in cats during therapy with megestrol acetate and prednisolone. Can J Vet Res 1987;51:60-65.
8. Scott DE, Kirk RW, Bentinck-Smith J. Some effects of short-term methylprednisolone therapy in normal cats. Cornell Vet 1979;69: 104-115.
9. Peterson ME, Kemppainen RJ. Comparison of intravenous and intramuscular routes of administering cosyntropin for corticotrophin stimulation testing in cats. Am J Vet Res 1992;53:1392-1395.
10. Mooney CT, Thoday KL, Doxey DL. Serum thyroxine and triiodothyronine response of hyperthyroid cats to thyrotropin. Am J Vet Res 1996;57:987-991.
11. Kemppainen RJ, Mansfield PD, Sartin JL. Endocrine responses of normal cats to TSH and synthetic ACTH administration. J Am Anim Hosp Assoc 1984;20:737-740.
12. Huang HP, Yang HL, Liang SL, *et al.* Iatrogenic hyperadrenocorticism in 28 dogs. J Am Anim Hosp Assoc 1999;35:200-207.
13. Rand JS, Levine J, Best SJ, *et al.* Spontaneous adult-onset hypothyroidism in a cat. J Vet Intern Med 1993;7:272-276.
14. Scott DW, Miller WH, Griffin CE. Feline hypothyroidism. In: Muller's & Kirk's Small Animal Dermatology. 6th ed. Philadelphia: WB Saunders, 2004:865-866.
15. Feldman EC, Nelson RW. Feline hypothyroidism. In: Canine and Feline Endocrinology and Reproduction. 3rd ed. Philadelphia: WB Saunders, 2004:143-151.
16. Feldman EC, Nelson RW. Hyperadrenocorticism in cats. In: Canine and Feline Endocrinology and Reproduction. 3rd ed. Philadelphia: WB Saunders, 2004:358-393.
17. Meji BP, Voorhout G, Van Den Ingh TSGAM, *et al.* Transsphenoidal hypophysectomy for treatment of pituitary-dependent hyperadrenocorticism in 7 cats. Vet Surg 2001;30:72-86.
18. Watson PJ, Herrtage ME. Hyperadrenocorticism in six cats. J Small Anim Pract 1998;39:175-184.
19. Duesberg CA, Nelson RW, Feldman EC, *et al.* Adrenalectomy for treatment of hyperadrenocorticism in cats: 10 cases (1988-1992). J Am Vet Med Assoc 1995;207:1066-1070.
20. Peterson ME, Steele P. Pituitary-dependent hyperadrenocorticism in a cat. J Am Vet Med Assoc 1986;189:680-683.
21. Rossmeisl Jr JH, Scott-Moncrieff JCR, Siems J, *et al.* Hyperadrenocorticism and hyperprogesteronemia in a cat with an adrenocortical adenocarcinoma. J Am Anim Hosp Assoc 2000;36:512-517.
22. Moore LE, Biller DS, Olsen DE. Hyperadrenocorticism treated with metyrapone followed by bilateral adrenalectomy in a cat. J Am Vet Med Assoc 2000;217:691-694.
23. Elliott DA, Feldman EC, Kooblik PD, *et al.* Prevalence of pituitary tumors among diabetic cats with insulin resistance. J Am Vet Med Assoc 2000;216:1765-1768.
24. Schwedes CS. Mitotane (o,p'-DDD) treatment in a cat with hyperadrenocorticism. J Small Anim Pract 1997;38:520-524.
25. Daley CA, Zerbe CA, Schick RO, *et al.* Use of metyrapone to treat pituitary-dependent hyperadrenocorticism in a cat with large cutaneous wounds. J Am Vet Med Assoc 1993;202:956-960.
26. Furuzawa Y, Une Y, Nomura Y. Pituitary dependent hyperadrenocorticism in a cat. J Vet Med Sci 1992;54:1201-1203.
27. Nelson RW, Feldman EC, Smith MC. Hyperadrenocorticism in cats: seven cases. J Am Vet Med Assoc 1988;193:245-250.
28. Zerbe CA, Nachreiner RF, Dunstan RW, *et al.* Hyperadrenocorticism in a cat. J Am Vet Med Assoc 1987;190:559-563.
29. Swift GA, Brown RH. Surgical treatment of Cushing's syndrome in the cat. Vet Rec 1976;99:374-375.
30. Peterson ME, Ferguson DC, Kintzer PP, *et al.* Effects of spontaneous hyperadrenocorticism on serum thyroid hormone concentrations in the dog. Am J Vet Res 1984;45:2034-2038.
31. Zenoble RD, Kemppainen RJ. Adrenocortical suppression by topically applied corticosteroids in healthy dogs. J Am Vet Med Assoc 1987;191:685-688.
32. Romatowski J. Iatrogenic adrenocortical insufficiency in dogs. J Am Vet Med Assoc 1990;196:1144-1146.