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Skin fragility in a cat presenting with pituitary-dependent hyperadrenocorticism

Lorna Hardy, Claudia Gil-Morales, Christina Maunder and Emilie Paran

Abstract

Case summary A case of skin fragility in an 8-year-old domestic shorthair cat with pituitary-dependent hyperadrenocorticism is described. The cat was referred to the Feline Centre at Langford Small Animal Hospital with a 2-month history of multiple skin wounds with no known traumatic aetiology. A low-dose dexamethasone suppression test was performed before referral, which was consistent with hyperadrenocorticism. On presentation, the cat had multiple cutaneous lacerations and patchy areas of alopecia. CT was performed, which revealed a pituitary mass most consistent with pituitary-dependent hyperadrenocorticism. Treatment with oral trilostane (Vetoryl; Dechra) was commenced and clinical improvement was observed; however, further extensive skin lesions as a consequence of her skin fragility resulted in euthanasia.

Relevance and novel information Hyperadrenocorticism is an uncommon endocrinopathy of cats; however, it is an important differential for skin thinning and non-healing wounds. Skin fragility remains an important factor in the consideration of appropriate treatment protocols and ongoing quality of life in these patients.

Keywords: Hyperadrenocorticism; Cushings; skin fragility; pituitary neoplasia

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Case description

An 8-year-old female neutered domestic shorthair cat was referred to the Feline Centre at Langford Small Animal Hospital for further investigation of skin fragility.

The cat was initially presented to the referring veterinarian 2 months before referral after she sustained three full-thickness skin wounds on the proximal aspect of the right pelvic limb, the ventral thorax and the right axilla. No traumatic event was reported, but the cat was predominantly an outdoor cat, so an unwitnessed trauma could not be excluded. She was anaesthetised for surgical debridement and repair at the referring veterinary clinic. However, she was re-presented the next day when further lacerations were noted in different anatomical locations from the original lesions. A further procedure was performed to surgically repair the additional skin wounds. Thoracic and abdominal radiographs were performed, which did not identify any internal or orthopaedic injuries. The cat was administered injectable cefovecin (8 mg/kg SC [Convenia; Zoetis]) and was dispensed non-steroidal anti-inflammatory medication (0.05 mg/kg PO q24h [Metacam; Boehringer Ingelheim]) to provide analgesia. Within 2 days of discharge, the cat experienced dehiscence of the surgical sites on the right flank and left caudal thigh. Revision surgery was performed under general anaesthesia.

One month later, the cat was re-presented with two non-healing wounds on the ventral thorax. Although the previous wounds had healed, the fur over the previously

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Table 1 Adrenocorticotropic hormone stimulation test results

Test	Results (pre-treatment) (nmol/l)	Results (post-treatment) (nmol/l)	Reference interval (RI) (nmol/l)
Cortisol – baseline	138.0	96.6	15.0–150.0
Cortisol – 1 h post ACTH	317.0	177.0	150.0–450.0
Cortisol – 90 mins post ACTH	312.0	199.0	150.0–450.0

Table 2 Low-dose dexamethasone suppression test results

Test	Results (nmol/l)	Reference interval (RI) (nmol/l)
Cortisol – baseline	162.0	15.0–150.0
Cortisol – 4 h after dexamethasone	116.0	⩽40.0
Cortisol – 8 h after dexamethasone	105.0	⩽40.0

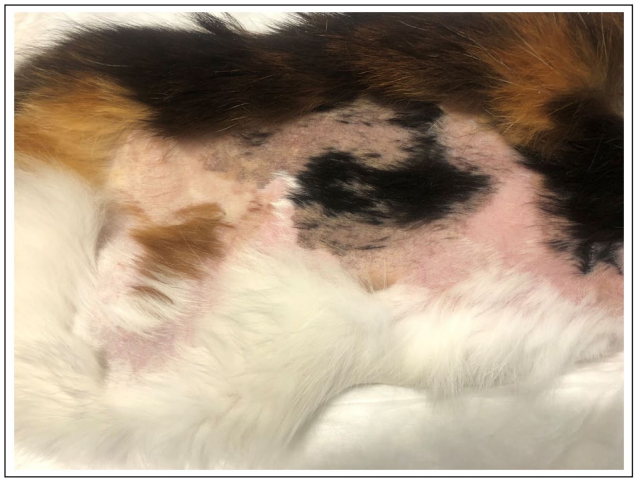

Figure 1 Patchy alopecia on the right trunk and flank

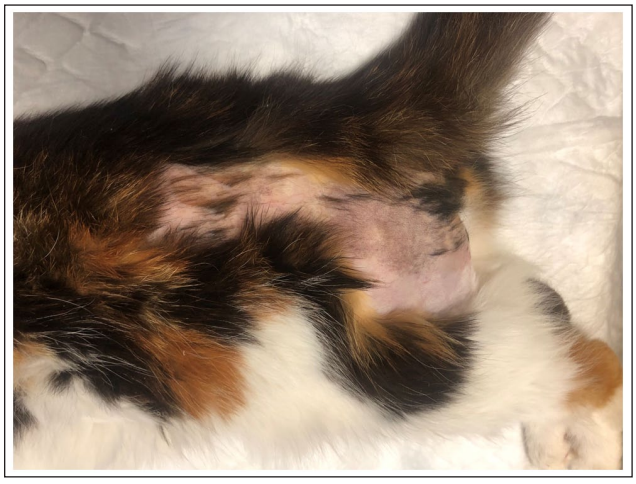

Figure 2 Patchy alopecia on the caudal left flank and proximal hindlimb

clipped surgical sites had not regrown. The owners had noted an increase in her appetite and thirst and altered vocalisation.

The referring veterinarian performed an in-house feline immunodeficiency virus/feline leukaemia virus (FIV/FeLV) SNAP test, which was negative. Haematology revealed components of a stress leucogram (mild lymphopenia 0.87×10^9/l [reference interval (RI) 0.92–6.88]), mild eosinopenia (0.10×10^9/l [RI 0.17–1.57]), as well as a mild thrombocytopenia (115 K/µl [RI 151–600]). Biochemistry revealed mild hyperglycaemia (14.93 mmol/l [RI 4.11–8.84]), mildly low urea (5.3 mmol/l [RI 5.7–12.3]) and creatinine (61 µmol/l [RI 71–212]). Fructosamine measurement was not supportive of diabetes mellitus (295 µmol/l [RI 191–349]). Total thyroxine was within normal limits at 14 nmol/l (RI 10–60). Urinalysis revealed proteinuria, glucosuria and ketonuria. No abnormalities were detected on sediment examination.

An adrenocorticotropic hormone (ACTH) stimulation test was performed, and serum cortisol was within normal limits at 60 and 90 mins after tetracosactide injection (5 µg/kg IV [Cosacthen; Dechra]) (Table 1). A low-dose dexamethasone suppression test was subsequently performed, which was consistent with inadequate suppression at 4 and 8 h after administration of dexamethasone (0.1 mg/kg IV [Dexadreson; MSD Animal Health]) (Table 2).

On presentation to the Feline Centre, the cat was bright and mentally alert. A full-thickness skin wound was observed on the right lateral thorax, and patchy alopecia was present at the previous clip sites on the dorsum, thorax, neck and flanks (Figures 1–3). The cat had a lean body condition score and a weight loss of 0.55 kg was noted since its initial presentation at the referring veterinary clinic.

Haematology (Table 3) revealed a persistent mild lymphopenia (0.537×10^9/l [RI 2–7.2]), and eosinopenia (0.17×10^9/l [RI 0.3–1.7]). Thrombocytopenia (95×10^9/l [RI 156–626]) was documented on the automated count, but adequate platelets noted on blood smear evaluation. The main finding on biochemistry (Table 4) was a moderate hyperglycaemia (15.9 mmol/l [RI 3.5–5]). In the light of this, fructosamine was measured and was 262 µmol/l (RI 191–349), which did not indicate persistent hyperglycaemia. Urine was obtained via ultrasound-guided cystocentesis for urinalysis (Table 5), which confirmed glucosuria; however, no ketonuria was detected. The urine protein: creatinine ratio (UPCR) was consistent with borderline proteinuria.

CT of the head and abdomen was performed, which revealed an enlargement of the pituitary gland (Figure 4) measuring 6.0 mm (width) × 5.2 mm (height) × 3.3 mm (length) (reported reference interval: 5.20 × 3.10 mm [width × height] in normal cats,[1] and 3.09 ± 0.26 mm, 4.73 ± 0.31 mm and 4.88 ± 0.30 mm for pituitary gland height, width and length, respectively, for a mesocephalic cat).[2] Both adrenal glands were subjectively round at their cranial pole, but remained elongated with a normal shape. They measured 12–18 mm in length for the right (Figure 5) and left (Figure 6) adrenal glands, respectively, and 6.2 mm at the maximum height (reported reference range: length 11.6 ± 2.1 mm and height 6.1 ± 1.3 mm in normal cats).[3] Bilateral chronic renal changes (slight asymmetry and undulated margin) were also noted that were suggestive of chronic kidney disease. From the results of these diagnostic tests, a diagnosis of pituitary-dependent hyperadrenocorticism (HAC) was made.

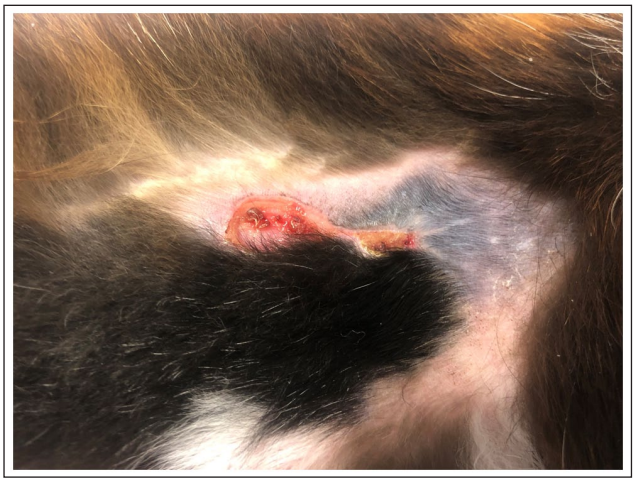

Figure 3 Full-thickness skin wound with visible subcutaneous fat and fascia on the right thorax

Treatment was commenced with oral trilostane (10 mg PO q24h [Vetoryl; Dechra]). Gabapentin (50 mg PO q12h [Gabapentin; Summit]) was also prescribed to reduce the stress associated with being kept indoors for management of the skin wounds. At reassessment with the referring veterinarian 3.5 weeks later, the owners had observed an improvement in the polyphagia and polydipsia, and the skin lesions had healed. An ACTH stimulation test was repeated, which revealed that serum cortisol remained within the reference interval at both time points after the administration of tetracosactide (5 µg/kg IV [Cosacthen; Dechra]). However, the values showed an improvement when compared with the initial ACTH stimulation test (Table 1). Fructosamine had increased to 373 µmol/l (RI 191–349), which raised concern for developing diabetes mellitus; however, treatment was not pursued at this time due to concerns regarding the difficulty of insulin administration in this cat.

Sadly, the cat re-presented to the referring practice 2 weeks later, having sustained a large full-skin-thickness

Table 3 Haematology results

Test	Result	Reference interval (RI)
Haemoglobin (g/dl)	11.50	8.1–14.2
Haematocrit (%)	34.7	27.7–46.8
Red blood cell ($\times 10^{12}$/l)	7.20	6–10.1
Mean cell volume (fl)	48.2	41.3–52.6
Mean cell haemoglobin (pg)	16.0	12–16
Mean cell haemoglobin concentration (g/dl)	33.2	27–32.8
Platelets ($\times 10^9$/l)	95	156–626
White blood cells ($\times 10^9$/l)	6.32	6.3–19.6
Neutrophils ($\times 10^9$/l)	5.38	3–13.4
Lymphocytes ($\times 10^9$/l)	0.53	2–7.2
Monocytes ($\times 10^9$/l)	0.24	0–1
Eosinophils ($\times 10^9$/l)	0.17	0.3–1.7
Basophils ($\times 10^9$/l)	0.01	0–0.1

Table 4 Biochemistry results

Test	Result	Reference interval (RI)
Creatinine (µmol/l)	59	133–175
Urea (µmol/l)	5.6	6.5–10.5
Total protein (g/l)	66.8	75–88
Albumin (g/l)	25.5	24–35
Globulin (g/l)	41.30	21–49
Albumin:globulin ratio	0.62	0.4–1.3
Total bilirubin (µmol/l)	1.2	1–8.5
Alanine aminotransferase (U/l)	52	15–45
Alkaline phosphatase (U/l)	14	15–60
Gamma-glutamyl transferase (U/l)	0	0–2
Sodium (mmol/l)	149.2	149–157
Potassium (mmol/l)	4.25	4–5
Chloride (mmol/l)	110	115–130
Calcium (mmol/l)	2.49	2.3–2.5
Phosphorus (mmol/l)	1.48	0.95–1.55
Glucose (mmol/l)	15.9	3–5

Table 5 Urinalysis results for cystocentesis sample

Urinalysis	Result
Colour	Yellow
Ketones	Negative
Blood	Negative
Glucose	3+
Urine protein: creatinine ratio	0.30
White blood cells	Scant
Red blood cells	Scant
Fat droplets	+
Debris	Scant
Specific gravity	1.041
pH	7.4

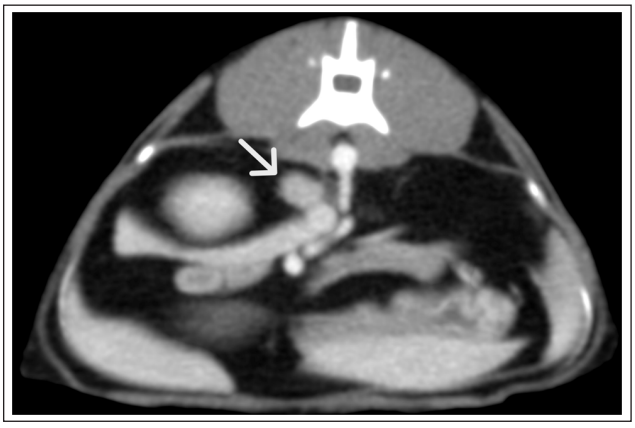

Figure 5 Right adrenal gland (white arrow)

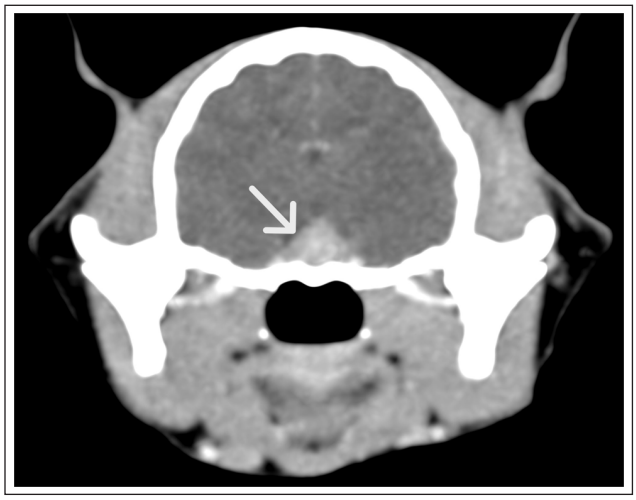

Figure 4 CT image of the enlarged pituitary gland, marked by the white arrow

laceration to the left flank region (Figure 7) and, owing to concerns for its ongoing quality of life, the cat was subsequently euthanased.

Discussion

HAC is an uncommon endocrine disease of cats and can be characterised as either primary or secondary (iatrogenic).[4] Similar to canine HAC, the majority of feline cases (approximately 80%) are pituitary-dependent HAC, with pituitary adenomas occurring most commonly.[5] The remaining 20% are adrenal-dependent, of which 50% are adenomas and 50% carcinomas.[5]

Feline HAC is a disease of middle-aged to older cats with a mean age of 10 years.[4,5] Clinical signs that have been reported include polyphagia, polyuria and polydipsia, muscle wastage, abdominal distension, poor hair coat and skin fragility. The majority of feline patients with HAC have weight loss, with a minority

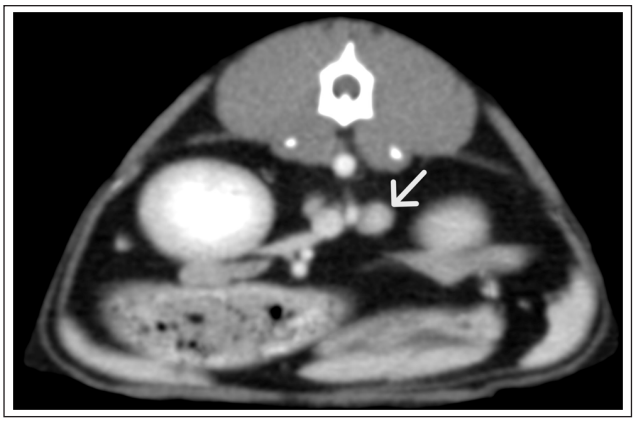

Figure 6 Left adrenal gland (white arrow)

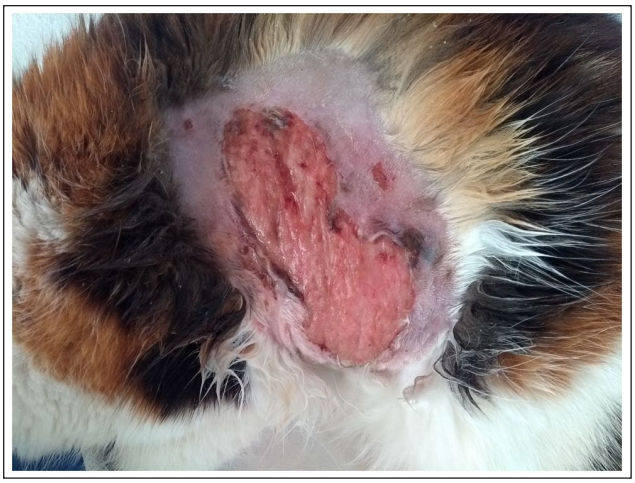

Figure 7 Extensive full-thickness skin wound on the left flank

experiencing weight gain.[4] These cases can prove challenging to identify and diagnose in clinical practice due to the similarity in presenting signs with other feline endocrine diseases.[4] Furthermore, up to 90% of cats with HAC have concurrent disease, including diabetes mellitus, hepatic lipidosis and chronic renal disease.[6]

Dermatological abnormalities are a common feature observed in HAC.[7,8] Skin fragility is not a clinical sign typically associated with canine HAC, but has been reported in >50% of cases of HAC in cats.[5–7] The pathogenesis of skin fragility relates to the inhibition of normal collagen synthesis by chronic excess cortisol. As a result, the skin becomes thin, with reduced elasticity, and it readily bruises and tears with normal handling or minimal trauma.[4,9] On histopathology and electron microscopy, this manifests as a thin epidermis and atrophy of the dermis, with disorganised collagen fibres that consist of loosely packed and variably sized fibrils.[9,10] Furthermore, chronic elevated cortisol can result in delayed wound healing.[4] Underlying mechanisms include the downregulation of proinflammatory mediators, reduced fibroblast and keratinocyte proliferation, and suppression of the immune system leading to wound infections.[11] Alopecia, hyperpigmentation, comedones and recurrent abscessation have also been observed in cats with HAC.[6] Other conditions that have been associated with skin fragility in the cat include hyperprogesteronism, hepatic diseases including hepatic lipidosis, cholangiohepatitis and cholangiocarcinoma, multicentric lymphoma and feline infectious peritonitis.[9] A reversible form of skin fragility has also been described in three cats that developed malnutrition and cachexia secondary to different aetiologies.[9] Skin biopsies are indicated for histopathology to aid in diagnosis. However, these are challenging to obtain due to the extreme thinness of the skin and difficulties in closure of the biopsy sites, which are susceptible to secondary infection and further delayed wound healing.[12] Therefore, as the results of the diagnostic tests were strongly supportive of skin fragility secondary to primary HAC in this case, skin biopsies were not pursued.

A combination of diagnostic tests is considered most effective in the approach to feline HAC. The ACTH stimulation test, routinely used for diagnosis in dogs, has a lower sensitivity in cats, with 44% of cats with HAC producing a normal result.[6] The low-dose dexamethasone suppression test (LDDST) is considered superior. However, it should be noted that cats require 10 times the dose of dexamethasone than the recommended canine protocol to achieve effective suppression in healthy cats (0.1 mg/kg IV).[6] This was demonstrated in this case, where the cat produced a normal ACTH result but subsequently produced an abnormal LDDST result that supported the diagnosis of HAC. The urine cortisol-to-creatinine ratio can also be utilised as a high-sensitivity screening test and provides a means of negating the impact of stress induced by visits to the veterinary clinic by collecting the samples in the home environment.[4]

The treatment options for pituitary-dependent HAC include medical treatment with trilostane, radiotherapy or surgical treatment by hypophysectomy. Trilostane is a reversable competitive inhibitor of 3-β-hydroxysteroid dehydrogenase, the enzyme utilised for steroid synthesis.[5] A study of 15 cats with HAC treated with trilostane observed an improvement in clinical signs and ACTH stimulation test result in 87% of cats.[13] It should be noted that, although an ACTH stimulation test was utilised for monitoring in this case, a recommended protocol for monitoring and interpretation of this test in cats has not been determined.[4] Hypophysectomy was not considered in this case due to the owner preference to avoid an invasive procedure. Furthermore, surgical intervention poses a risk for further iatrogenic skin trauma. This cat showed good initial clinical improvement with medical management, but the unpredictable nature of the skin fragility meant that this cat's quality of life was significantly compromised. Although a predicted time frame for the resolution of skin fragility has not been determined, it has been observed that dermatological manifestations of the disease have

taken longer to resolve than other clinical signs.[13,14] There is no specific treatment for skin fragility itself; recommendations for the prevention of lesions have included keeping affected cats strictly indoors, as was advised in this case, careful handling, utilisation of collars and bandaging or vests to protect the skin and prevent excoriation, and antimicrobial use where indicated for secondary infections.

Conclusions

This case brings to attention the importance of HAC as a differential for cats with skin fragility and non-healing wounds. It also highlights the limitation of the ACTH stimulation test in the diagnosis and monitoring of HAC in cats.

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Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognised high standards ('best practice') of veterinary clinical care for the individual patient were always followed. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*.

Informed consent Informed consent (verbal and written) was obtained from the owner or legal custodian of the animal described in this work for the procedure(s) undertaken. No animals or people are identifiable within this publication, and therefore additional informed consent for publication was not required.

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References

1 Nadimi S, Molazem M, Jarolmasjed S, et al. **Volumetric evaluation of pituitary gland in dog and cat using computed tomography.** *Vet Res Forum* 2018; 9: 337–341.
2 Häußler TC, von Pückler KH, Thiel C, et al. **Measurement of the normal feline pituitary gland in brachycephalic and mesocephalic cats.** *J Feline Med Surg* 2018; 20: 578–586.
3 Mallol C, Altuzarra R, Espada Y, et al. **CT characterisation of feline adrenal glands.** *J Feline Med Surg* 2020; 22: 285–291.
4 Boland LA and Barrs VR. **Peculiarities of feline hyperadrenocorticism: update on diagnosis and treatment.** *J Feline Med Surg* 2017; 19: 933–947. Erratum in: *J Feline Med Surg* 2018; 20(8).
5 Feldman E. **Hyperadrenocorticism in cats.** In:Feldman E, Nelson R, Reusch C, et al. (eds). *Canine and feline endocrinology*. 4th ed. London: Elsevier, 2015, pp 452–484.
6 Scott D, Miller W and Griffin C. **Endocrine and metabolic diseases**. In: Danny W, Scott DW, Miller WH, et al. (eds). Muller & Kirk's small animal dermatology. 6th ed. London: W.B. Saunders, 2001, pp 780–885.
7 Valentin SY, Cortright CC, Nelson RW, et al. **Clinical findings, diagnostic test results, and treatment outcome in cats with spontaneous hyperadrenocorticism: 30 cases.** *J Vet Intern Med* 2014; 28: 481–487.
8 Cook AK and Evans JB. **Feline comorbidities: recognition, diagnosis and management of the cushingoid diabetic.** *J Feline Med Surg* 2021; 23: 4–16.
9 Furiani N, Porcellato I and Brachelente C. **Reversible and cachexia-associated feline skin fragility syndrome in three cats.** *Vet Dermatol* 2017; 28: 508–e121.
10 Regnier A and Pieraggi MT. **Abnormal skin fragility in a cat with cholangiocarcinoma.** *J Small Anim Pract* 1989; 30: 419–423.
11 Schäcke H, Döcke WD and Asadullah K. **Mechanisms involved in the side effects of glucocorticoids.** *Pharmacol Ther* 2002; 96: 23–43.
12 Kunder D and Foster JD. **Cutaneous manifestations of internal disease.** In: Little S (ed). August's consultations in feline internal medicine. Vol. 7. St. Louis, MO: Elsevier, 2016, pp 282–294.
13 Mellett Keith AM, Bruyette D and Stanley S. **Trilostane therapy for treatment of spontaneous hyperadrenocorticism in cats: 15 cases (2004-2012).** *J Vet Intern Med* 2013; 27: 1471–1477.
14 Skelly BJ, Petrus D and Nicholls PK. **Use of trilostane for the treatment of pituitary-dependent hyperadrenocorticism in a cat.** *J Small Anim Pract* 2003; 44: 269–272.