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CASE REPORT

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Non-thymoma-associated exfoliative dermatitis in a European shorthair cat: A case report

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Abstract

The current case report presents a case of non-thymoma-associated exfoliative dermatitis in an 8-year-old European Shorthair female cat. The animal displayed extensive alopecia and excessive peeling of the epidermis. There were no other apparent disorders, except for the skin lesions. Roentgenographic and sonographic examinations, complete blood count and blood serum chemistry analyses, and skin biopsy were performed. The histopathological investigation revealed hyperkeratosis of the epidermis and the infiltration of lymphocytes and macrophages at the dermal-epidermal junction around the hair follicles and sebaceous glands. Moreover, edema of the basal layer and melanin migration from the epidermis to the dermis were observed. The patient underwent treatment with immunosuppressive doses of prednisolone, antibiotic therapy, and baths in anti-seborrheic shampoos and displayed resolution. However, recurrence was observed after one month. Consequently, the patient received cyclosporine A, in addition to the aforementioned treatment and the lesions resolved without relapse.

KEYWORDS
exfoliative dermatitis, feline, thymoma

1 | INTRODUCTION

Feline exfoliative dermatitis is a disease that mainly affects middle-aged and elderly cats. It is described as a disorder characterized by the formation of large scales that strongly adhere to the skin and cover significant areas of the body with extensive alopecia (Miller et al., 2012). Most cases of the aforementioned disease are associated with non-pruritic paraneoplastic syndromes with the highest incidence associated with thymoma (Parker & Casey, 1976, Turek, 2003, Scott et al., 1995, Carpenter & Holzworth, 1982, Kasabalis et al., 2017, Rottenberg et al., 2004, Cavalcanti et al., 2014). Previous literature has reported the relationship between exfoliative dermatitis and the occurrence of thymic neoplasms, which was demonstrated through the disease remission in animals after the surgical removal of the tumors (Cavalcanti et al., 2014, Singh et al., 2010, Forster-van Hijfte et al., 1997). The exact explanation pertaining to the paraneoplastic syndrome phenomena in thymic tumors remains unknown. However, several mechanisms have been proposed to explain the development of the disease. A thymoma may generate certain compounds that activate cytotoxic T cells, leading to the development of an autoimmune reaction (Rottenberg et al., 2004). Another probable explanation is the occurrence of an abnormal immune response to the tumor that results in the production of antibodies that cross-react with the antigens of the epidermis (Rottenberg et al., 2004, Forster-van Hijfte et al., 1997). Apart from the cases associated with thymic tumors, the syndrome has also been reported in cats without the aforementioned neoplasia. In addition, other neoplasms, drug reactions, and nutritional factors have been reported as syndrome-triggering agents (Pascal-Tenorio et al.,

1997, Gross et al., 2005, Declercq, 2000). Moreover, literature has described numerous cases of the disease without the identification of the factors that could be responsible for the development of dermatitis (Linek et al., 2015, Combarros et al., 2020). Regardless of the etiology, the syndrome displayed concurrent histopathological features.

The main features associated with the syndrome include orthokeratotic epidermal hyperkeratosis, extensive desquamation, hydropic degeneration of the basal keratinocytes, the presence of apoptotic cells throughout the epidermis, and cell-poor to cell-rich CD3+ lymphocytic interface dermatitis. Furthermore, some cases display interface-mural folliculitis involving the infundibular and isthmic parts of the hair follicle. Sebaceous glands are severely affected or even completely absent. Pigmentary incontinence and *Malassezia* colonization have also been reported (Gross et al., 2005). In addition to the dermatological lesions, cats with thymoma exhibit general symptoms such as weakness, cough, dyspnea, ataxia, and a megaesophagus (Scott et al., 1995, Carpenter & Holzworth, 1982, Kasabalis et al., 2017, Rottenberg et al., 2004, Cavalcanti et al., 2014)

2 | CASE PRESENTATION

An eight-year-old European shorthair cat weighing 5 kg was presented for dermatologic consultation in July 2020. The individual displayed gradual hair loss commencing from the limbs three months prior to the visit. Subsequently, the condition progressed to affect the pinnae, sides of the chest and abdomen, and the back regions. Numerous scales and scabs were formed in the aforementioned areas with simultaneous alopecia. Mild pruritus was present. One month before presentation the cat underwent treatment using orally administered antibiotics (cephalexin 22 mg/kg BID and amoxicillin with clavulanic acid 25 mg/kg BID for two weeks), and glucocorticosteroids (dexamethasone 0.2 mg/kg one dosage). Moreover, monthly topical application of moxidectin (Advocate, Bayer, Germany) was performed twice. Skin scrapings and hair samples were submitted to microbiological culture, which showed a *Bacillus* sp. that was sensitive to most of the antibiotics tested. The owner reported that no additional dermatological investigations were performed.

At the time of presentation, the cat did not display any systematic symptoms. Extensive alopecia and thinning of hair on the lateral surfaces of the chest and abdomen, back, and to a lesser extent, the limbs and the head were observed (Figure 1). The remaining hair was easy to pull out and the proximal hair shaft was affixed with scales and epidermal cells. Numerous scales of varying sizes were observed in the above-mentioned areas (Figure 2). Moreover, erythema was observed, especially on the limbs, lower abdomen, and the sternal region. The cat underwent further dermatological investigations: Wood's lamp examination, microscopic examination of hair, skin scraping and cytological examination. No fluorescence was observed under the Wood's lamp light. Microscopic examination revealed the presence of sebaceous cuffs on the proximal part of the hair. However, numerous scrapings yielded negative results for parasites. Imprint cytology of the erythema affected areas revealed the presence of numerous corneocytes, single neutrophils, sparse gram-positive bacteria, and free melanin grains. Blood samples were collected from the cat, in order to analyze the complete blood count and serum chemistry (the results are shown in Tables 1 and 2, respectively). The results were not observed to deviate from the reference values, except for a slight increase in the activity of aspartate aminotransferase and minimal elevation of total protein value. The tests for feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) yielded negative results.

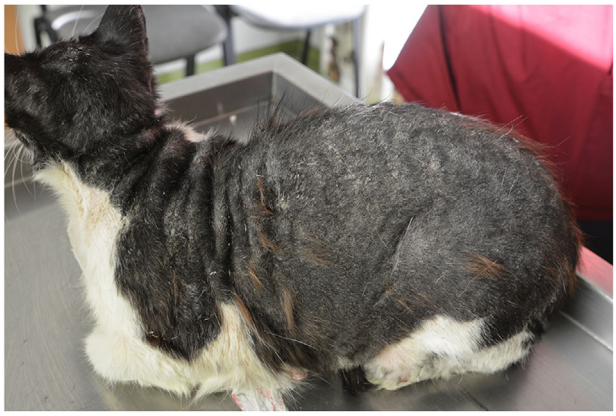

FIGURE 1 Generalized alopecia and scaling on the thorax and abdomen

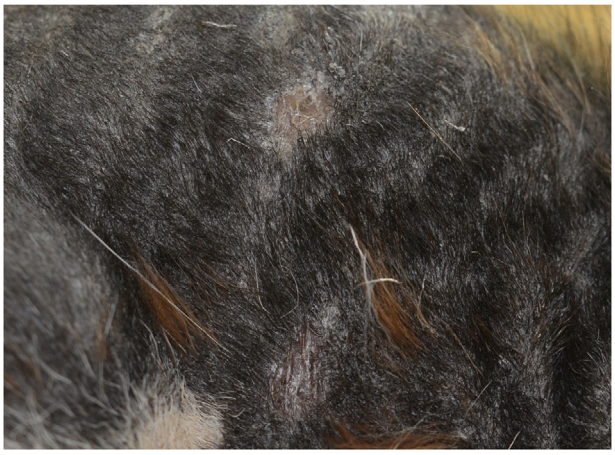

FIGURE 2 Close view of the lateral thorax with large, whitish adherent scales

Subsequent to the administration of local anesthesia with 1% lignocaine and sedation using dexmedetomidine (40 μg/kg IM), a single 6 mm punch biopsy specimen was taken from a macula located on the dorsal surface of the thorax. The sample for histopathological examination was collected and fixed using 10% formalin buffered to a pH of 7.2. Subsequently, the sample was routinely processed for hematoxylin and eosin (HE) staining. The microscopic image revealed hyperkeratosis of the epidermis with inflammatory infiltration consisting of lymphocytes and macrophages at the dermal-epidermal junction (Figure 3) and around the hair follicles and sebaceous glands (Figure 4). Additionally, the microscopic examination revealed swelling of the basal layer and melanin migration from the epidermis to the

TABLE 1 Results of the serum chemistry analysis of the eight-year-old European Shorthair cat

Parameter	Unit	Value	Reference range
AST	U/l	60.1 (H)	6-44
ALT	U/l	64.2	20–107
ALKP	U/l	43	15–92
GGT	U/l	5.01	0–10
Total Protein	g/dl	8.02 (H)	6–8
Albumin	g/dl	2.84	2.3-3.4
Total bilirubin	mg/dl	0.1	0.1-1.2
Creatinine	mg/dl	1.25	0.1-1.8
BUN	mg/dl	67.2	25–70
Total bile acids	µmol/l	0.15	0.1-25
Cholesterol	mg/dl	87	77.4-201
Triglycerides	mg/dl	36.6	17.7-159.4

AST, aspartate transaminase; ALT, alanine aminotransferase; ALKP, alkaline phosphatase; GGT, γ-glutamyl transferase; BUN, blood urea nitrogen.

TABLE 2 Complete blood count of the 8-year-old European Shorthair cat

Parameter	Unit	Value	Reference range
Leukocytes	10^3/µl	14.85	5.5-19.5
Basophils	10^3/µl	0.01	0-0.12
Neutrophils	10^3/µl	10.62	3.12-12.58
Eosinophils	10^3/µl	0.74	0.06-1.93
Lymphocytes	10^3/µl	3.06	0.73-7.86
Monocytes	10^3/µl	0.42	0.07-1.36
Erythrocytes	10^3/µl	9.99	4.6-10.2
Hemoglobin	g/dl	12.6	8.5-13.3
MCV	µm^3	39.4	38–54
MCH	Pg	12.7	11.8-18
MCHC	g/dl	32.1	29–36
RDW-CV	%	18.8	15–23
Hematocrit	%	39.4	26–47
Platelets	10^3/µl	434	100–518
MPV	µm^3	13	9.9-16.3

MCV, mean corpuscular volume; MCH, mean cell hemoglobin; MCHC, mean cell hemoglobin concentration; RDW, red blood cell distribution width; MPV, mean platelet volume.

dermis. Furthermore, the cat underwent radiographic (thoracic radiographs) and sonographic examinations of the abdominal cavity. The roentgenographic examination revealed moderate cardiomegaly, non-dilated lobar pulmonary vessels, and moderate interstitial densities; the mediastinal lymph nodes were not observed to be enlarged. The sonographic examination of the abdominal cavity revealed echogenic areas in the normal echostructure of the liver, slightly thickened wall of the gallbladder, non-dilated echo-negative bile ducts, normal structure of the stomach and small intestine, hypoechoic, coarse-grained, non-

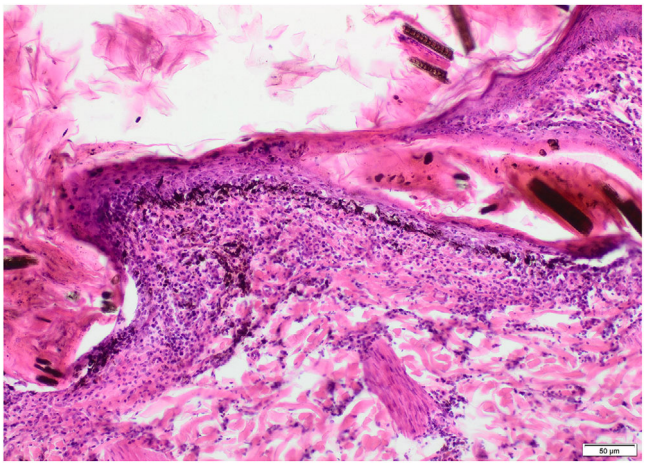

FIGURE 3 Representative image of the hematoxylin and eosin-stained slide of the specimen obtained through punch biopsy. Visible inflammatory infiltration on the border of the epidermis and dermis with melanin migration from the epidermis. Magnification: 100×

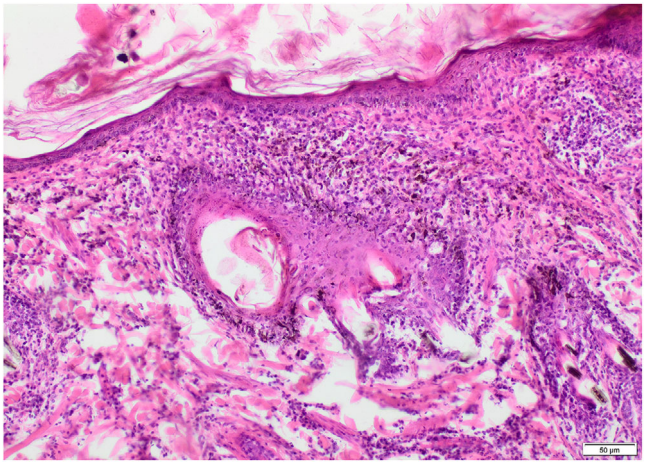

FIGURE 4 Visible epidermal hyperkeratosis and inflammatory infiltrates around the hair follicles and sebaceous glands. Hematoxylin and eosin (H&E), Magnification: 100×

enlarged pancreas, and a slightly enlarged (sedative effect), homogeneous spleen. The renal lengths were 3.1 cm (right) and 3.4 cm (left) with a hyperechoic, thickened, cortical layer, and non-dilated renal pelvis. The adrenal glands were normal in size and shape.

On the basis of the clinical picture and the results of the histopathological and radiographic examinations, a diagnosis of exfoliative dermatitis not associated with the presence of thymoma was established.

The patient was treated using immunosuppressive doses of prednisolone (4 mg/kg body weight once a day for 4 weeks and next every alternate day). Moreover, the patient received baths in anti-seborrheic shampoos and antibiotic therapy (amoxicillin with clavulanic acid 25 mg/kg BID) for 2 weeks. After 2 weeks, the skin condition displayed significant improvement and the hyperkeratosis was no longer present (Figure 5). The hair was almost completely regrown after 2 months

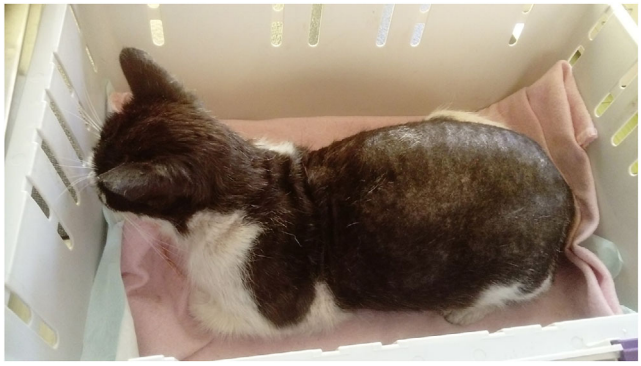

FIGURE 5 Cat after 2 weeks of treatment; visible reduction in the areas of exfoliation

FIGURE 6 Hair regrowth in alopecic areas after 2 months of treatment

from the onset of treatment (Figure 6). Unfortunately, 3 months after the onset of treatment symptoms such as the thinning of hair recurred in the lateral thoracic and abdominal areas and the scales reappeared. Consequently, the patient received cyclosporine A (7 mg/kg, once a day), in addition to the aforementioned prednisolone and antibiotic treatment. The hyperkeratosis resolved after two weeks of medication and hair regrowth was observed after another 2 months.

3 | DISCUSSION

The current case report describes a case of exfoliative dermatitis that was not associated with thymoma, which is extremely rare in cats; thus far, only a few cases have been reported in literature (Linek et al., 2015, Combarros et al., 2020). The diagnosis was established on the basis of the clinical picture and the results of the histopathological examination. Although roentgenographic examinations cannot exclude the presence of small neoplastic tumors with absolute certainty, the effectiveness of the immunosuppressive treatment with a long monitoring period (8 months at the time of publication) indicates that paraneoplastic origin is extremely unlikely. Furthermore, the absence of any other symptoms during the monitoring period also affirms the diagnosis. In the present case, initial treatment with immunosuppressive doses of glucocorticosteroids was observed to be successful, which was followed by the equally effective cyclosporine A therapy to treat recurrence. In the cases reported and discussed by Linek et al., treatment using prednisolone, methylprednisolone, or dexamethasone was reported to be effective in feline patients (Linek et al., 2015). Apart from glucocorticosteroids, cyclosporine (at a dose of 7 mg/kg body weight/day) was also used in the treatment as a sole therapeutic agent (Combarros et al., 2020) or in combination with the glucocorticosteroids (Linek et al., 2015). In the current case, the symptoms did not resolve after monotherapy using prednisolone. Consequently, additional administration of cyclosporine A was introduced into the treatment. Only the simultaneous application of the pharmacotherapeutic agents was observed to be effective, which is consistent with the cases reported by Linek et al. Generally, improvement in exfoliative dermatitis is observed after several months of therapy (Linek et al., 2015, Combarros et al., 2020). Occasionally, the disease resolves after the use of antibiotics, shampoo therapy, or spontaneously (Linek et al., 2015).

Exfoliative dermatitis presents histopathological findings that are similar to the features of the autoimmune and immune-mediated skin disorders: lupus erythematosus (LE) and erythema multiforme (EM). Nonetheless, the typical lesions in lupus erythematosus are erosions and ulcerations located on the face, especially on the nose. Furthermore, in cats LE incidence rate is reported as “extremely rare” (Wilhelm et al., 2005) and EM incidence is reported only as “rare” (Hnilica, 2011). Erythema multiforme usually develops over the dorsum, with lesions occurring acutely and diffusely with well-demarcated serpentine margins. Main symptoms are characterized by macules, papules or plaques spreading peripherally, producing “bulls-eye” lesions. The current case did not exhibit the aforementioned symptoms. Hence, LE and EM were excluded as possible diagnoses. The most important clinical symptom reported in previous case studies was generalized or, less frequently, localized exfoliation with local or generalized alopecia (Combarros et al., 2020). The histopathological findings in the present case were consistent with the findings reported in previous literature, namely, orthokeratotic hyperkeratosis, lymphocytic interface dermatitis, mural folliculitis with the presence of apoptotic cells, and sebaceous adenitis (Linek et al., 2015, Combarros et al., 2020).

Diagnostic imaging (radiography) is a crucial element in the diagnostic process of exfoliative dermatitis, allowing for visualization of the mediastinum to confirm or refute the diagnosis of thymoma. This would diametrically change the treatment protocol towards surgical management if thymoma is confirmed (Cavalcanti et al., 2014). Surgical removal of the tumor leads to the resolution of the lesions in

thymoma-associated cases, although certain postoperative complications, such as myasthenia gravis, have been reported in literature (Singh et al., 2010).

The present case study shows that during the diagnosis of feline exfoliative dermatitis, causes unrelated to thymoma should also be taken into account. In the scenarios where no thymoma is present, there is a possibility for effective treatment with immunosuppressive agents, which in this case achieved complete remission of the lesions within several months.

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PEER REVIEW

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AUTHOR CONTRIBUTIONS

Conceptualization, formal analysis, investigation, project administration, visualisation and writing - original draft: Marcin Szczepanik, Methodology: Piotr Wilkołek; Methodology, Writing – review & editing: Grzegorz Kalisz; Methodology, Visualisation, Writing – review & editing: Anna Śmiech.

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