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■ Paraneoplastic exfoliative erythroderma in a cat with thymoma

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■ Παρανεοπλασματική αποφολιδωτική ερυθροδερμία σε γάτα με θύμωμα

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ABSTRACT. A 14-year-old domestic shorthair cat was admitted with a 2-month history of excessive body weight loss and generalized exfoliative dermatitis with erythroderma. Radiographic and ultrasonographic examination revealed a cranioventral cavitory mass within the anterior mediastinum. An ultrasound-guided fine needle aspiration cytology from the mass revealed numerous small mature lymphocytes intermingled with much fewer inflammatory mast cells. These findings, along with a cell-poor interface and mixed cell dermatitis demonstrated on skin histopathology, made the diagnosis of paraneoplastic exfoliative dermatitis straightforward. This uncommon case illustrates the relative value of keratoseborrheic skin disease as a useful indicator of an internal malignancy in the cat.

Keywords: cat, exfoliative dermatitis, thymoma

ΠΕΡΙΛΗΨΗ. Γάτα 14 χρονών, κοινής ευρωπαϊκής φυλής, προσκομίστηκε με ιστορικό σημαντικής απώλειας σωματικού βάρους και γενικευμένης αποφολιδωτικής δερματίτιδας με ερυθροδερμία που εμφανίστηκε τους τελευταίους δύο μήνες. Στην ακτινογραφική και υπερηχοτομογραφική διερεύνηση του θώρακα παρατηρήθηκε ευμεγέθης μάζα που εντοπιζόταν στον πρόσθιο μεσοπνευμόνιο χώρο. Η κυτταρολογική εικόνα του επιχρίσματος, η οποία πάρθηκε ύστερα από διαθωρακική παρακέντηση με λεπτή βελόνα, ήταν συμβατή με το θύμωμα, αφού παρατηρήθηκαν πολυάριθμα ώριμα λεμφοκύτταρα ανάμικτα με σαφώς λιγότερα φλεγμονικά σιτευτικά κύτταρα. Η ολιγοκυτταρική δερμοεπιδερμική δερματίτιδα, της οποίας το κυτταρικό φλεγμονικό διήθημα ήταν μικτό, ήταν ο κυρίαρχος ιστοπαθολογικός μορφότυπος στις βιοψίες που πάρθηκαν από το δέρμα, γεγονός που επιβεβαίωσε τη διάγνωση της παρανεοπλασματικής αποφολιδωτικής δερματίτιδας από θύμωμα. Με βάση αυτό το σχετικά σπάνιο περιστατικό, επισημαίνεται η αξία των κερατοσεβορροϊκών αλλοιώσεων ως κλινικού δείκτη για υποκείμενα νεοπλάσματα στη γάτα.

Λέξεις ευρετηρίασης: γάτα, αποφολιδωτική δερματίτιδα, θύμωμα

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CASE HISTORY

A 14-year-old, intact female, Domestic shorthaired cat was admitted (Companion Animal Clinic, Faculty of Veterinary Medicine, Aristotle University of Thessaloniki, Greece) with a 2-month history of significant weight loss, mild anorexia and a generalized non-pruritic dermatitis. Although there was no information of recent drug exposure, the cat had experienced a severe dyspneic episode one year prior to admission, possibly associated with the presence of a cranioventral mediastinal mass detected on thoracic radiographs. However, no further diagnostic investigation was undertaken at that time, since the respiratory problem spontaneously resolved. Apart from the poor body condition of the animal, physical examination revealed a non-compliant cranial thorax and a severe exfoliative and erythematous dermatitis extending over both pinnae, lateral thorax, abdomen, limbs, perineum and tail (Figure 1a). At closer examination, a waxy and brownish keratosebaceous debris was found to fill the ear canals and a multifocal to diffuse but non-pruritic hypotrichosis-alopecia accompanied by a moderate to severe scaling and erythema (Figure 1b) extended all over the body (generalized disease). The hair shafts and psoriasiform scales were easily epilated and peeled-off, respectively, and there was blanching of the erythematous skin upon diascopy (Figure 1b). Skin scrapings, tape strippings and ear canal mineral oil wash-outs failed to harvest any ectoparasites. Wood's light examination, direct microscopy of plucked hairs and fungal cultures (DTM and Sabouraud's) were, also, negative for dermatophytes. Diff Quick-stained cytology smears did not yield *Malassezia* spp. yeasts. Complete blood count and serum biochemistry revealed neutrophilic leucocytosis, lymphopenia and mildly increased alkaline phosphatase and alanine aminotransferase activities (Table 1). Urinalysis was unremarkable and the cat was tested negative for feline leukemia virus (FeLV) antigen and feline immunodeficiency virus (FIV) antibodies by applying an in-office enzyme linked immunosorbent assay (Snap FIV/FeLV, Idexx, USA). Survey thoracic radiography disclosed a soft tissue opacity located at the cranioventral mediastinum, displacing the trachea dorsally and cranial lung lobes caudolaterally (Figure 2). On thoracic ultrasonography, the mediastinal mass was found to be of mixed echogenicity with hypoechoic zones; abdominal ultrasonography was unremarkable.



Figure 1 a. A cat with thymoma under sedation showing diffuse alopecia-hypotrichosis and erythroderma of the head, pinnae, neck and thorax.



Figure 1b. Closer view of the lateral thoracic wall of the cat, also, showing excessive psoriasiform scaling and an easily epilated haircoat.

Ultrasound-guided transthoracic fine needle aspiration cytology of the mass showed a large number of small mature lymphocytes intermingled with much fewer inflammatory mast cells (Figure 3). Multiple punch skin biopsies (6 mm) were, also, obtained, fixed immediately in 10% buffered formalin, routinely processed and stained with hematoxylin and eosin. The ensuing histopathology revealed a cell-poor interface dermatitis, characterized by a mixed-cell infiltrate and accompanied by orthokeratotic and segmental parakeratotic hyperkeratosis, epidermal acanthosis with neutrophilic exocytosis, sub-corneal neutrophilic pustulosis and lymphocytic mural folliculitis down to

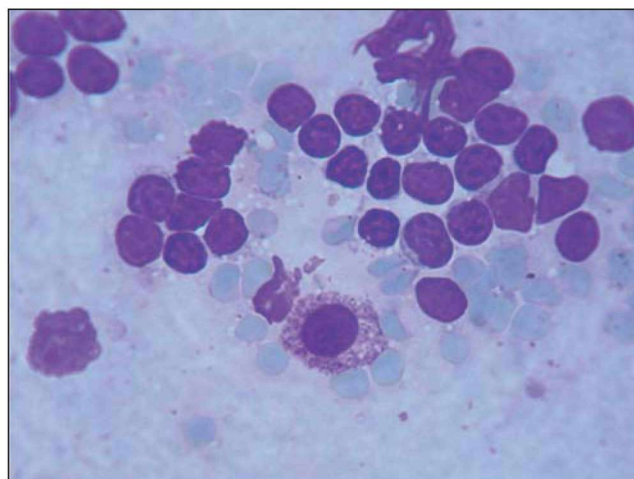
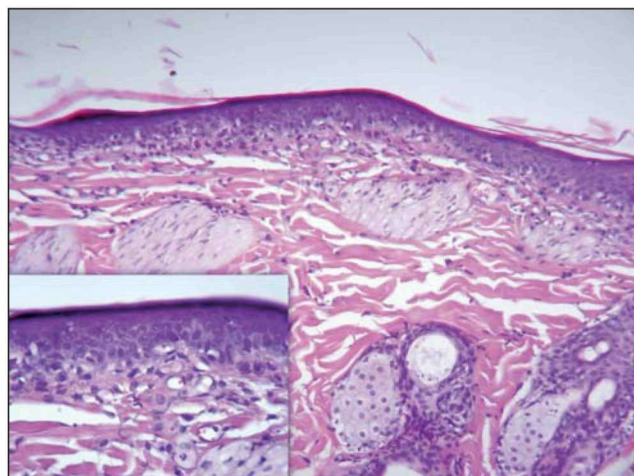
Table 1. Hematological and biochemical findings on admission in a cat with thymoma-associated exfoliative dermatitis

Hematology	Reference interval	Diseased cat
Hematocrit (%)	25-45	38.8
White blood cells (/μl)	5,500-19,000	24,500
Segmented neutrophils (/μl)	2,500-12,500	23,520
Lymphocytes (/μl)	1,500-7,000	980
Monocytes (/μl)	0-850	0
Eosinophils (/μl)	0-700	0
Platelets (/μl)	200,000-700,000	200,000
Serum biochemistry		
Total proteins (g/dL)	6-7.8	6
Albumins (g/dL)	2.7-4.3	3.2
Creatinine (mg/dL)	0.5-1.6	1.3
Blood urea nitrogen (mg/dL)	14-40	25
Glucose (mg/dL)	75-140	110
Alkaline phosphatase (U/L)	28-157	237
Alanine aminotransferase (U/L)	12-60	88
γ-Glutamyltransferase (U/L)	1-7	1
Creatine kinase (U/L)	49-580	497
Phosphorus (mg/dL)	2.2-6	5.3
Calcium (mg/dL)	8-11	8
Potassium (mEq/L)	3-4.3	4.1
Sodium (mEq/L)	133-154	148

**Figure 2.** Lateral thoracic radiograph of the cat with thymoma demonstrating a soft tissue mass located cranial to the heart and displacing of the trachea dorsally.

the level of isthmus. No apoptotic keratinocytes could be found where the sebaceous glands looked normal (Figure 4).

The clinical manifestations along with the radiographic, ultrasonographic and cytological features of the anterior mediastinal mass and skin histopathology were strongly suggestive of a thymoma-associated

**Figure 3.** Transthoracic ultrasound-guided fine needle aspiration in a cat with thymoma. In a slightly bloody background, the majority of the cells are small lymphocytes. Occasional mast cells are also seen (Giemsa, 1000x).**Figure 4.** Skin histopathology of a cat with thymoma-associated exfoliative dermatitis, demonstrating cell-poor interface dermatitis and epidermal hyperplasia (Haematoxylin and Eosin, x100). Inset: Closer view of the same histo slide showing the mixed-cell inflammatory infiltrate and the vacuolated basal keratinocytes (Haematoxylin and Eosin, x400).

exfoliative dermatitis. A few days later, and pending the surgical excision of the mass, the still clinically stabilized cat died unexpectedly, but unfortunately no permission for necropsy was granted by the owner.

DISCUSSION

Exfoliative dermatitis in the cat has mainly been associated with thymoma (Rottenberg et al. 2004). However, of as many as 100 feline thymomas retrieved by the authors in a literature review, only 16 had exfoliative dermatitis (Loveday 1959, Dubielzig and

DeLaney 1980, Willard et al. 1980, Carpenter and Holzworth 1982, Bonnard and Drazek 1992, Gores et al. 1994, Scott et al. 1995, Forster-van Hijfte et al. 1997, Day 1997, Godfrey 1999, Riviere and Olivry 1999, Smith et al. 2001, Smits and Reid 2003, Rottenberg et al. 2004, Lara-Garcia et al. 2008, Fidel et al. 2008, Spadavecchia and Jaggy 2008, Zitz et al. 2008, Singh et al. 2010). Apart from exfoliative dermatitis, myasthenia gravis is a well-known paraneoplastic condition in cats with thymoma, appearing alone or in combination with the former dermatitis (Scott-Moncrieff et al. 1990, Singh et al. 2010); polymyositis and granulocytopenia may, also, develop but far less commonly (Moore and Ogilvie 2001, Fidel et al. 2008). In humans, many paraneoplastic conditions of putative immunologic basis are, also, seen in conjunction with thymomas. Thymoma-associated exfoliative dermatitis and pancreatic/hepatobiliary carcinoma-associated alopecia characterized by a glistening skin are the main paraneoplastic syndromes at the feline skin (Turek 2003). The paraneoplastic nature of the former disease has been proven by the regression of clinical signs after the surgical removal of thymoma (Foster-Van Hijfte et al. 1997, Riviere and Olivry 1999).

Thymomas usually occur in middle-aged to older, domestic shorthaired and FeLV/FIV negative cats (Moore and Ogilvie 2001), as was the animal of this report. Dyspneic bouts and/or coughing can be attributed to the space-occupying effect and/or secondary pleural effusion (Moore and Ogilvie 2001); apparently, the latter condition did not develop in our cat. Exfoliative dermatitis, also appearing with the other clinical and/or paraneoplastic manifestations of thymoma, may be the sole presenting complaint (Bonnard and Drazek 1992, Scott et al. 1995, Forster-van Hijfte et al. 1997, Rottenberg et al. 2004, Singh et al. 2010), as it was the case in this cat. Typically, it is a progressive and non-pruritic dermatitis, the lesions of which start from the head and ear pinnae, to spread eventually all over the body (Scott et al. 1995, Forster-van Hijfte et al. 1997, Rottenberg et al. 2004). Similar to this case, a heavy accumulation of scales and crusts is a common occurrence (Scott et al. 1995).

On skin histopathology, the interface dermatitis along with the lymphocytic infiltrate, also observed in this cat, are suggestive of an immune-mediated process leading to the production of cytotoxic T-lymphocytes from the affected thymus that subsequently attack

keratinocytes (Rottenberg et al. 2004). The aberrant activity of the affected thymus, which may precipitate other immune-mediated conditions, such as myasthenia gravis and polymyositis, supports this theory (Turek 2003). Although the source of anti-epithelial T-lymphocytes between thymoma-induced exfoliative dermatitis and erythema multiforme or graft-versus-host disease is different, their immunopathogenesis (cytotoxic T-cell attack on keratinocytes) is most likely similar (Gross et al. 2005). Although the histopathology of all these three skin diseases is characterized by the presence of apoptotic keratinocytes closely surrounded by lymphocytes (satellitosis), no such features could be seen. Of notice, in some cases, the predominance of interface dermatitis makes the identification of the keratinocyte apoptosis difficult (Gross et al. 2005). Histologically, thymoma-associated exfoliative dermatitis looks similar to lupus erythematosus, erythema multiforme and graft-versus-host disease, although in the two latter diseases the transepidermal apoptosis is more pronounced (Affolter et al. 1998, Rottengerg et al. 2004).

Although the temporal association between the appearances of skin lesions and thymoma is not always straightforward (Godfrey 1999), there have been observed a few cases with a very similar exfoliative dermatitis that was not secondary to thymoma (Gross et al. 2005). Indeed, a similar exfoliative dermatitis may, also, be seen in primary sebaceous adenitis or in idiopathic mural folliculitis of the cat (Gross et al. 2005), the histopathologic features of which could be demonstrated in every skin biopsies of feline thymoma cases (Rottenberg et al. 2004). In our cat, lymphocytic mural folliculitis was, also, demonstrated in the infundibulum and isthmus of some hair follicles, in contrast to the normally appearing sebaceous glands. Other clinical differentials could be drug eruption, superficial demodicosis, cheyletiellosis, dermatophytosis and some viral (feline leukemia and feline immunodeficiency virus dermatitis), immune-mediated (systemic lupus erythematosus, erythema multiforme) or neoplastic (epitheliotropic T-cell lymphoma) dermatoses (Forster-van Hijfte et al. 1997, Scott et al. 2001), which were primarily ruled out with the aid of historical clues, physical examination and cutaneous histopathology.

Since thymoma is not commonly accompanied by clinicopathological abnormalities (Young 2000), the

hematological abnormalities detected (mature neutrophilia, lymphopenia, eosinopenia and monocytopenia) in this cat would be attributed to the stress imposed by the chronic disease (Stockham and Scott 2002). In addition, the explanation of the mild elevation of liver enzyme activities could be the hepatocellular fatty vacuolation that may appear secondarily to a systemic illness (Scherk and Center 2010). Metastatic hepatopathy was ruled out due to the lack of relevant ultrasonographic findings within the hepatic parenchyma and the very low metastatic potential of thymoma (Moore and Ogilvie 2001).

The confirmation of thymoma in this case was actually based on the aspiration cytology of the mass. Although no thymic epithelial cells could be detected in the FNA smears, the predominance of small mature lymphocytes intermingled with fewer inflammatory mast cells was highly suggestive of thymoma and, particularly, of its lymphocyte-predominant form (Day 1997, Raskin 2001). Thymic lymphoma in the cat

is usually of the lymphoblastic or histiocytic morphologic type and it does not feature a mast cell infiltrate (Day 1997). However, differentiating a lymphocyte-predominant thymoma in the absence of epithelial or mast cells from a small-cell lymphoma on a cytological basis may be challenging, warranting histopathological examination to evaluate the tissue architecture (Day 1997, Rogers 2001). In the current case, the old age of the cat, the negative FeLV status, the cavitary ultrasonographic appearance of the mass and the exfoliative erythroderma were strongly in favour of a thymoma as opposed to a mediastinal lymphoma (Foster-van Hijfte et al. 1997, Young 2000, Moore and Ogilvie 2001).

The fatal outcome of this cat still remains unresolved because no permission for necropsy was granted; nevertheless, a severe dyspneic crisis of the intermittently attended cat could be a reasonable explanation for this (Moore and Ogilvie 2001).

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