Short Communications

Presumptive paraneoplastic exfoliative dermatitis in four domestic rabbits

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Introduction

A seborrhoeic rabbit is a common diagnostic challenge, and differential diagnoses include malnutrition, ectoparasites, dermatophytosis, yeast dermatitis (White and others 2003), sebaceous adenitis (Jassies-van der Lee and others 2009, White and others 2000b), cutaneous lymphoma (White and others 2000a), autoimmune hepatitis-associated (Florizoone and others 2007) and thymoma-associated exfoliative dermatitis (Florizoone 2005). The clinical observation of exfoliative dermatitis and histologic changes of lymphocytic mural and interface dermatitis and absence of sebaceous glands should prompt the clinician to search for a systemic cause with thymic neoplasia representing one of the top differentials. Our goal was to report on the historical and clinical progression, as well as the diagnostic and therapeutic alternatives used in four rabbits with exfoliative dermatitis associated with a mediastinal tumour.

Case reports

Case 1

A seven-and-a-half-year-old male castrated rabbit, 1.4 kg, was presented with a history of non-pruritic progressive hair loss, scaling, depression and weight loss over the previous 1.5 months. Dermatologic examination revealed multifocal alopecia and hypotrichosis, erythema, severe scaling and follicular casts. Multiple deep and superficial skin scrapings, acetate tape impression smears, trichograms and a fungal culture were negative for parasites, bacteria and fungi. Dermatopathological examination revealed severe epidermal orthokeratosis and mild, multifocal, lymphocytic exocytosis and a severe lymphocytic mural and interface folliculitis with absent sebaceous glands (Fig 1). Radiographs and ultrasound revealed a large mass in the cranial thorax cranial to the heart base, respectively. Cytology of fine needle aspirates showed them to contain predominantly lymphoblasts suggestive of lymphoma. The results of haematology, biochemistry and urinalysis were all within normal limits. The owner elected only symptomatic skin treatment, including an antiseborrheic shampoo (Douxo Séborrhée Shampooing; Sogeval) once weekly, followed by a whole-body neutral bath oil (Balmandol; Spirig Pharma), consisting of liquid paraffin, almond oil, tocopherols and glycine soja oil, once weekly for 10 minutes, and essential fatty acids (EFA) (Viacutan; Boehringer Ingelheim) 1–2 drops orally 24h. After five months of therapy the skin lesions improved by 70 per cent. Seven months after starting the therapy the rabbit's skin was in remission. One month later the patient died with signs of severe dyspnoea. On postmortem analysis, a $4 \times 3.5 \times 2$ cm brown mass cranial to the heart, histologically consistent with lymphoma, was found.

Cases 2–4

Table 1 presents an overview of the individual histories, clinical appearances and diagnoses, which were similar to Case 1. Additionally, all therapeutic interventions and the outcomes of each patient are described. Fig 2 shows clinical lesions of Case 4.

Discussion

We describe four cases of severe exfoliative dermatitis in rabbits with mediastinal tumours. Histopathology revealed a thymoma in two rabbits and a thymic lymphoma in one case. Unfortunately, histopathology of Case 4 was not performed, but the cytological examination pointed toward a mesenchymal tumour or thymoma.

Thymoma represents a thymic epithelial cell neoplasm occurring in various species including rabbits (Thomas and others 1999, Rottenberg and others 2004, Florizoone 2005) and is considered the most common tumour of the anterior mediastinum (Thomas and others 1999). Older individuals are usually affected (Kostolich and Panciera 1992, Day 1997, Thomas and others 1999, Florizoone 2005, Morrisey and McEntee 2005), as was seen here. Reported clinical signs include coughing, regurgitation, anorexia, exercise intolerance and dyspnoea (Kostolich and Panciera 1992, Rottenberg and others 2004, Florizoone 2005), and are similar to our cases. A tumour-induced immune-mediated process has been proposed

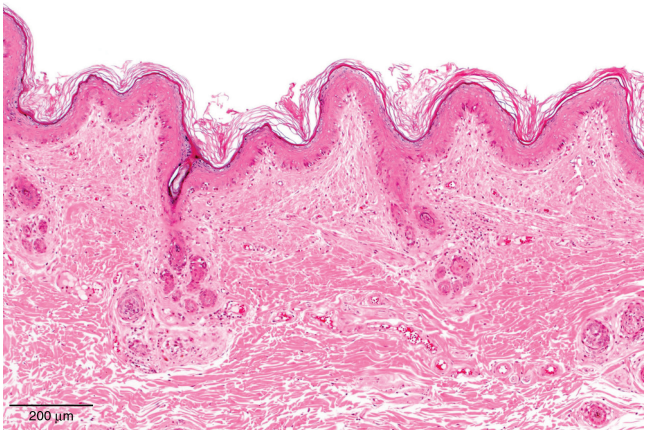

FIG 1: Case 1—severe epidermal orthokeratosis, epidermal hyperplasia and mild exocytosis. haematoxylin and eosin. Bar=200 µm

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TABLE 1: Summary of four rabbits with exfoliative dermatitis associated with a mediastinal mass

	Case 1	Case 2	Case 3*	Case 4
Signalment	7.5 years, male castrated, 1.4 kg	6 years, male castrated, 2.6 kg	4 years, male castrated, 1.4 kg	6 years, female, intact, 974 g
Clinical signs	Cachexia, depression	Cachexia, depression, nasal discharge, dyspnoea	Initially none; finally anorexia and dyspnoea	Initially none; finally dyspnoea
Dermatological signs	Multifocal alopecia, erythema, follicular casts and seborrhea	Multifocal alopecia, erythema, follicular casts and seborrhea	Multifocal alopecia, erythema, follicular casts and seborrhea	Multifocal alopecia, erythema, scaling, follicular casts and crusting
Histological description skin	Orthokeratosis, lymphocytic exocytosis, lymphocytic mural and interface folliculitis, absent sebaceous glands	Orthokeratosis, lymphocytic exocytosis, lymphocytic mural and interface folliculitis, absent sebaceous glands	Orthokeratosis, lymphocytic mural folliculitis, absent sebaceous glands	Orthokeratosis, lymphocytic exocytosis, lymphocytic mural and interface folliculitis, absent sebaceous glands
Thoracic radiograph	Mass in anterior mediastinum	Mass in anterior mediastinum	No mass on initial exam, not repeated radiographs	Mass in anterior mediastinum
Thoracic ultrasound	Cystic structures within mass located cranial to base of the heart	Cystic structures within mass located cranial to base of the heart	Not performed	Non-cystic mass located cranial to base of the heart
Cytological description mass	Predominantly lymphoblasts with scattered eosinophils and macrophages	Predominantly small lymphocytes and few activated macrophages	Not performed	Lymphocytes and clusters of spindle cells
Histological description mass	Consistent with lymphoma: large number of lymphoblasts with signs of atypia	Consistent with thymoma: predominantly polygonal epithelial cells intermingled with small lymphocytes	Consistent with thymoma: predominantly polygonal epithelial cells intermingled with small lymphocytes	Not performed
Treatment				
Topical	Oil soak, shampoo, aloe vera spray	Oil spray (1:100 with water), shampoo	Propylene glycol	Propylene glycol
Systemic	Essential fatty acids	EFA	Cyclosporine, Mygliol 812†, EFA	Cyclosporine, Mygliol 812†, EFA
Outcome	Complete resolution within 5 months, euthanasia after 8 months	Worsening, euthanasia after 7 months	Complete resolution within 2 months, euthanasia after 14 months	Worsening, euthanasia after 5 months

*This case has partly been described previously (Jassies-van der Lee and others 2009)
†Mygliol 812 – a medium-chain triglyceride solution
EFA Essential fatty acids

FIG 2: Case 4—severe alopecia, scaling and erythema predominantly in the neck region

in thymoma-associated exfoliative dermatitis in the feline species (Turek 2003), and suspected in one rabbit (Florizoone 2005). In cats, skin lesions disappeared after surgical tumour removal of the thymoma (Rottenberg and others 2004), suggesting a causative relationship between thymoma and the exfoliative dermatitis. A T-cell-mediated abnormality was suggested to play a strategic role in the pathogenesis of this paraneoplastic phenomenon (Rottenberg and others 2004), but further studies are needed. Thymoma is a well-recognised disease in the rabbit (Greene and Strauss 1949, Morrisey and McEntee 2005, Guzman Sanchez-Migallon and others 2006), but there are only scarce reports on concurrent paraneoplastic skin lesions. This is in contrast with human beings, where 30 per cent of thymoma patients experience myasthenia gravis (Okumura and others 2008).

In all cases, an abscess, one of the main differentials, could be ruled out by cytological examination. Thymoma exhibited mostly well-differentiated lymphocytes, as described previously (Day 1997, Withrow 2004, Florizoone 2005). These results were in concordance with histopathologic findings. The cytologic findings of a suspected mesenchymal tumour in Case 4 were unfortunately not confirmed by pathological and immunohistological examinations, and therefore, a final diagnosis was not made.

To the author's knowledge, this is the first report of thymic lymphoma in the rabbit associated with exfoliative dermatitis and interestingly, the clinical and pathohistologic skin changes resemble those seen in thymoma. There are a limited number of reports on thymic lymphoma in rabbits (Mayer-Koebnick and others 1997, Pilny and Reavill 2008). The cytologic and histologic findings exhibited a large number of lymphoblasts with signs of atypia and are in concordance with the literature (Gomez and others 2002, Withrow 2004).

These cases showed consistency in dermatohistopathologic changes consisting predominantly of lymphocytic mural and interface dermatitis with absent sebaceous glands. We propose that the term, sebaceous adenitis, as it was defined previously in similar cases (White and others 2000b, Florizoone 2005), should be reserved only for cases with clear immunological targeting of sebaceous glands without interface changes.

Surgical resection is the treatment of choice in dogs and cats. with a good long-term postoperative survival (Zitz and others 2008); it has also been reported in the rabbit (Clippinger and others 1998). Other treatment option are radiation therapy (Morrisey and McEntee 2005) and chemotherapy (Strobel and others 2010) such as L-asparaginase (Lavine and Dicintio 1980), steroids (Morrisey and McEntee 2005) and doxorubicin (Huston and Quesenberry 2004). All owners refused surgery, chemotherapy and radiation due to possible fatal side effects, therefore, symptomatic treatment with protocols for canine sebaceous adenitis were initiated (Lortz and others 2010). Complete resolution of dermatological signs was achieved in Case 1, using topical treatment and EFA, and in Case 3, using systemic cyclosporine (CsA) combined with neutral oils and topical propylene glycol. We took into consideration that CsA is suspected to increase the risk for lymphoproliferative cancer, but on the other hand, it was shown that CsA does not facilitate tumour progression and it partially inhibits tumour growth (Rafferty and others 2012). We hypothesised that CsA reverses the immune-mediated events in the skin and to some degree could suppress the tumour growth.

The lack of clinical efficacy of the therapies in Cases 2 and 4, and the fatal tumour expansion are explained by the fact that the underly-

ing cause of the disease was not addressed. Therefore, in similar cases, a targeted treatment approach focusing on the neoplasia, such as radiation therapy, surgery and chemotherapy should be discussed with the owner.

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