Case Report

Feline urticaria pigmentosa in three related Sphinx cats

CARLO B. VITALE,* PETER J. IHRKE,† THIERRY OLIVRY‡ and ANTHONY A. STANNARD†

Veterinary Medical Teaching Hospital, †Department of Medicine and Epidemiology, School of Veterinary Medicine, University of California, Davis, California 95616, USA

(Received 17 October 1995; accepted 14 March 1996)

Abstract A pruritic maculopapular eruption with clinical and histological features similar to urticaria pigmentosa of humans is reported in three related Sphinx cats. All cats shared the same grandsire, had a juvenile onset of disease, and demonstrated similar historical, clinical and histological findings. Physical examination revealed widespread bilaterally symmetrical, erythematous, partially coalescing, crusted macules and papules on the trunk, limbs, neck and head. A few macules exhibited a dark brown pigmentation. Dermatographism could not be elicited in any of the cats. Histological examination of papules revealed the presence of a perivascular to diffuse dermal and subcutaneous infiltrate of well-differentiated mast cells. In one cat where systemic involvement was pursued, evidence of internal disease was not found.

Keywords: cat, mastocytosis, urticaria pigmentosa.

INTRODUCTION

Mastocytosis is a heterogeneous group of diseases defined as an abnormal proliferation of mast cells in various organs including skin, liver, spleen, kidney or gastrointestinal tract.1-5 The infiltrating mast cells may exhibit a benign or malignant behaviour. The symptoms of mastocytosis are related to the release of mast-cell mediators in various organs.4,6 In humans, these symptoms may include vomiting, diarrhoea, nausea, abdominal pain, flushing, pruritus, headache and dizziness.3

The classification of mastocytosis in animals and humans is based upon specific clinicopathological findings.1-3,7 In humans, mastocytosis is divided into the following syndromes: indolent disease, mastocytosis associated with blood or bone marrow involvement, aggressive disease associated with lymphatic involvement, and mast cell leukaemia. Currently, there is no generally accepted classification to categorize mastocytosis in animals, as classification systems have focused on mast cell tumours. This report describes a unique skin disease in three related Sphinx cats resembling a subset of human indolent mastocytosis, termed urticaria pigmentosa (UP).

CASE REPORTS

Cats 1 and 2

A 1.5-year-old intact grey and white female Sphinx cat (cat 1) was presented to the University of California Veterinary Medical Teaching Hospital (VMTH) with an approximately 1-year history of pruritic papular lesions. Previous corticosteroid therapy resulted in partial reduction of pruritus and a decrease in the number of papules. Overall improvement was not noted with previous flea control or an elimination diet.

Physical examination revealed an otherwise healthy cat with generalized, symmetrical hypotrichosis characteristic of this breed. The hairs, where present, were fine and located predominately on the head and distal limbs. Multifocal, partially symmetrical erythematous, partially coalescing macules and occasional crusted papules were present on the ventrum, extremities, head and neck (Fig. 1). Some of the macules exhibited a dark-brown pigmentation. Differential diagnoses for these skin lesions included allergic skin disease (flea, atopy, food, contact), scabies, bacterial folliculitis, drug reaction, cheyletiellosis, neoplasia, xanthoma and pemphigus foliaceus.

Deep skin scrapings for ectoparasites and a dermatophyte culture were negative. Dermatographism could not be elicited with vigorous stroking of the skin. A complete blood count (CBC) was performed and revealed neutrophilia (19 840 μL⁻¹) [Normal 2500–11 300 μL⁻¹], eosinophilia (1488 μL⁻¹) [Normal 0–1400 μL⁻¹], and basophilia (992 μL⁻¹) [Normal 0–100 μL⁻¹]. All parameters in a serum biochemistry profile and urinalysis were within established.
reference values. Feline leukaemia (ELISA) and feline immunodeficiency virus tests were negative. Skin biopsy specimens of papules were obtained from the trunk and fixed in 10% neutral buffered formalin, routinely processed, and stained with haematoxylin and eosin.

Histopathology of the skin demonstrated a moderate to severe perivascular to diffuse infiltrate in the superficial and deep dermis (Fig. 2). The infiltrate was comprised mainly of a homogenous population of large mononuclear cells, with smaller numbers of eosinophils and neutrophils. A few large mononuclear cells were present in the panniculus. Giemsa stain revealed these mononuclear cells to be metachromatically staining mast cells (Fig. 3).

Cat 2, a 2.5-year-old castrated male Sphinx, and sibling of cat 1, was presented on the same day with a 2-year history similar to cat 1. Physical examination revealed multifocal, erythematous macules and occasional crusted papules similar to cat 1. Some of the macules were pigmented dark brown. Multiple papules were present in a strikingly bilaterally symmetrical, linear pattern on the lateral thorax and abdomen (Fig. 4).

Dermatographism could not be elicited with vigorous stroking of the skin. Deep skin scrapings for ectoparasites and a dermatophyte culture were negative. A complete blood count revealed neutrophilia (26.892 × 10⁹ L⁻¹) and basophilia (972 × 10⁹ L⁻¹). Results of a serum biochemistry profile and urinalysis were within established normal limits. Feline leukaemia (ELISA) and feline immunodeficiency viral tests were negative. Skin biopsy specimens taken from the papular lesions on the trunk were fixed in 10% neutral, buffered formalin, routinely processed, and stained with haematoxylin and eosin.

The results of the skin biopsy demonstrated similar histological changes to those seen in cat 1 (Fig. 5). Giemsa stain revealed many metachromatically staining mast cells diffusely and perivascularly in the dermis.

Based upon the clinical features and histopathological findings, a tentative diagnosis of feline urticaria pigmentosa was made for both cats. The owner of cats 1 and 2 was reluctant to pursue further diagnostic testing. Homeopathic therapy was initiated by the owner and the cats were subsequently lost to follow-up.
Feline urticaria in three related Sphinx cats

Figure 3. Geimsa stain highlighted the perivascular mast cells (Geimsa × 610).

Figure 4. In cat 2, coalescing papules spanned the lateral thorax and abdomen in a linear pattern.

Figure 5. High magnification of the perivascular mast cells from cat 2 (H & E × 610).

Cat 3
An 8-month-old intact female Sphinx cat was presented to the VMTH with a 1-month history of pruritic papular lesions. This cat had the same grandsire as cat 1 and 2. Historically, simultaneous treatment with oral amoxicillin and oral prednisolone had diminished the number of papules and lessened the pruritus.

Physical examination revealed generalized bilaterally symmetrical, erythematous and brownish macules and erythematous papules, primarily confined
to the ventrum. A diffuse red-brown patch was located on the ventral neck and chest (Fig. 6). The clinical similarity of the lesions to those observed in cat 2 was striking (Fig. 7).

Deep skin scrapings and dermatophyte cultures were negative. Dermatographism could not be elicited with vigorous stroking of the skin. A CBC revealed neutrophilia (12,852 µL⁻¹), eosinophilia (1020 µL⁻¹) and basophilia (1020 µL⁻¹). All parameters in a serum biochemical profile and urinalysis were within established reference values. Feline leukaemia (ELISA) and feline immunodeficiency viral tests were negative. Due to the presence of eosinophilia and basophilia, an occult heartworm antigen test was performed and was negative. In an attempt to evaluate the possibility of systemic involvement, a buffy coat examination, partial thromboplastin time, prothrombin time, thoracic and abdominal radiographs, abdominal ultrasound, and splenic aspirate were performed and were within normal limits. Skin biopsy specimens taken from papules on the trunk were fixed in 10% neutral buffered formalin, routinely processed, and stained with haematoxylin and eosin.

The skin histopathology revealed findings similar to those seen in cats 1 and 2. Additionally, a minimal eosinophilic infiltrate within areas of mast cells and several discrete dermal lymphocytic nodules were noted. A Giemsa stain highlighted the perivascular and diffuse mast cells. A tentative diagnosis of feline urticaria pigmentosa also was made for cat 3.

Symptomatic treatment was initiated which included oral hydroxyzine (2 mg kg⁻¹) three times daily and every-other-day bathing with a colloidal oatmeal-based shampoo. Ten days later, the macular and papular lesions were partially resolved but pruritus, although reduced, was still significant. Prednisone therapy was initiated at 0.5 mg kg⁻¹ given twice daily. Within 2 weeks, there was virtually complete resolution of the lesions and the pruritus was markedly diminished. Based upon beneficial response, the prednisone dosage was reduced to 0.25 mg kg⁻¹ twice daily and the hydroxyzine dosage was maintained as before. The dose of prednisone was gradually tapered to 1 mg kg⁻¹ every other day and the dose of hydroxyzine was reduced to 2 mg kg⁻¹ once daily. Occasional recrudescence of the papules was noted.
Six months later, the pruritus exacerbated coincident with the onset of oestrus. Physical examination revealed a few small, erythematous papules on the ventral chest and abdomen. The macules and the linearly arranged papules seen previously had not recurred. Dermatographism again could not be elicited upon vigorous stroking of the skin.

The results of a CBC, buffy coat examination, serum biochemistry profile, and urinalysis were within normal limits. An ovariohysterectomy was recommended. The surgery was uneventful and direct visual examination of abdominal organs did not reveal abnormalities. An attempt 2 months after ovariohysterectomy to decrease further the dosage of prednisone or hydroxyzine resulted in the return of the pruritus and the skin lesions. The skin disease in this cat has been managed effectively for 2½ years since diagnosis with prednisone and hydroxyzine at a dosage of 1 mg kg⁻¹ every other day and 2 mg kg⁻¹ every day, respectively.

DISCUSSION

In veterinary medicine, ample controversy exists concerning the biological behaviour and classification of mast cell disease, particularly in the cat. This controversy reflects the difficulty in distinguishing feline mast cell hyperplasia from mast cell neoplasia. Mast cell tumours are the most common form of mast cell disease in the cat. The tumours occur most frequently in the skin and viscer.a Diseases resembling urticaria pigmentosa in humans have been reported in dogs and a foal. Brown and Chalmers reported a cat with diffuse mastocytosis, a disease resembling a subset of human mastocytosis but clinically distinct from urticaria pigmentosa. Finally, Scott briefly mentioned three young cats with a disease resembling urticaria pigmentosa (UP), but further details concerning treatment and follow-up were not given. Information is not available concerning behaviour of diffuse mastocytosis in cats.

Classification of feline cutaneous mast cell tumours has been infrequent and controversial and is based upon clinical morphology and histology. Wilcock et al. reported two histologically distinct tumours described as mast cell-type and histiocytic-type. The histiocytic-type mastocytomas primarily affected young Siamese cats and resembled the Siamese kittens reported by Chastain et al. In both tumour types, the mast cells were morphologically abnormal. Alternatively, Holzinger reported two histological types described as compact or diffuse. The Sphinx cats presented in this report are clinically and histologically distinct from the cats described by both Holzinger and Wilcock.

Traditionally, the classification of mastocytosis in humans has been subdivided into paediatric and adult based upon age of onset. The paediatric forms are further subdivided on a clinical and histological basis into UP, solitary mastocytoma, diffuse mastocytoma/mastocytosis, and telangiectasia macularis eruptiva perstans. Recently, an alternative classification scheme proposed by Metcalfe divides mastocytosis into four groups: indolent disease, mastocytosis associated with blood or bone marrow involvement, aggressive disease associated with lymphatic involvement, and mast cell leukaemia. Urticaria pigmentosa, the cutaneous form of indolent mastocytosis, is the most common subtype both in children and adults.

Urticaria pigmentosa is the most common variant of paediatric mastocytosis in humans and comprises 80% of all paediatric cases of cutaneous mastocytosis. Urticaria pigmentosa in children usually develops early in life (less than 6 months of age). Approximately 50% of the cases resolve spontaneously by puberty. The disease in humans is characterized by pruritic red-brown macules and papules which often coalesce. These lesions are found most often on the trunk but may appear anywhere, including the mucous membranes.

Urticaria pigmentosa in humans is believed to be familial and the mode of inheritance is thought to be autosomal dominant with incomplete penetrance. A study by Anstey et al. describes a mother and daughter with diffuse cutaneous mastocytosis with demonstrable dermatographism and identical mast cell immunophenotypes. Three generations of people with UP were described by Clark et al. with one member of the family showing typical histological features of UP but no clinical evidence of lesions. The three Sphinx cats presented in this report all share the same grandsire. However, according to the breeder, the grandsire of these cats did not have clinical evidence of skin disease.

Darier's sign (erythema and/or urtication upon physical trauma to the skin), a type of dermatographism, can be a hallmark of UP. However, Muller et al. and Caplan reported four out of 33 and eight out of 72 UP cases with negative Darier's sign, respectively. The clinical configuration of linear, coalescing papules seen in cats 1 and 3 may have been induced by self-trauma. It is possible that the cats scratched or licked the trunk in such a manner as to induce mast cell degranulation and thus produced the striking linear patterns. This resembles the Koebner phenomenon described with some human dermatological diseases (psoriasis, lichen planus and vitiligo).

The histological appearance of UP in children can be variable. Skin biopsies typically reveal mast cell hyperplasia throughout the dermis. Mast cells have also been reported to infiltrate perivascularly and within appendages. Perivascular mast cells was a common histological finding in all three cats reported here. The skin biopsy of cat 3 demonstrated prominent lymphoid nodules. These aggregates of dermal lymphocytes is somewhat similar to previous descriptions of lymphoid accumulations in feline mast cell tumours. One author (A.A.S.) has noted these
nodular accumulations of lymphocytes in both feline and equine mast cell tumours, however, their significance is not known. It is conceivable that cytokines released from mast cells (interleukin 4, 5, 6 and tumour necrosis factor-a) recruit lymphocytes allowing their trafficking into areas of mast cell infiltrates. Dermal lymphoid aggregates have not been reported as a histological finding of UP in humans. Finally, eosinophils were rarely seen in the skin biopsies of the Sphinx cats. This finding is similar to the paucity of eosinophils observed in the skin biopsy specimens from children with UP.

In humans, approximately 10% of all paediatric cases of UP progress to systemic involvement. In the cases that do not progress, about half resolve spontaneously by puberty. It appears that adult-onset UP and childhood UP persisting into adult hood renders a poorer prognosis with mast cell infiltration to other organs seen commonly, particularly to the bone marrow. A bone marrow biopsy is not performed in children unless there is evidence of bone pain, radiographic evidence of bone pathology, or haematological abnormalities. In children lacking systemic mast cell proliferation, complete blood counts are normal. Buffy coat examinations in children with UP rarely reveal mast cells. Plasma histamine levels are consistently high in skin biopsy specimens from children with UP.

In the cats reported here, there was no evidence of bone pain, clinically relevant blood dyscrasias and, in cat 3, absence of systemic involvement. Although clinical evidence of abdominal organomegaly was not noted in any of the three cats, the abdominal ultrasound and cytology of a splenic aspirate was performed in cat 3 to evaluate for the presence of occult visceral disease. The presence of peripheral eosinophilia and/or basophilia in these three Sphinx cats was consistent and differs from the haematological findings in children with UP. Cytokines released from cutaneous mast cells may play a role in inducing peripheral eosinophilia and basophilia. This is the first report in cats of a highly characteristic, clinically distinct, clinicopathological entity which most closely resembles UP in children. The diagnosis of UP was based primarily upon the young age of onset (5–7 months) in closely related cats, the occurrence of bizarre linear skin lesions and brown patches, and the presence of a primarily mastocytic infiltrate seen with skin histopathology. It is possible that these cats may have had an underlying allergic skin disease; however, this seemed unlikely based upon the clinicopathological findings. Morphologically, the mast cells in all three cats appeared benign. In cat 3, visceral involvement was not found. These findings, in conjunction with the lack of clinical signs of systemic disease, suggest a biologically benign behaviour in all three related cats. Because all three Sphinx cats had the same grandsire, this report also suggests that the disease described here resembling urticaria pigmentosa may have a hereditary component. This syndrome, feline urticaria pigmentosa has not, to the authors’ knowledge, been described previously in cats.

REFERENCES

Feline urticaria in three related Sphinx cats


