

Fluoxetine in the management of chronic itch in a cat: a case report

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SUMMARY

Background – Chronic itch is a common finding in many inflammatory/allergic skin diseases and systemic disorders in cats. However, it could also have a neuropathic origin, that leads to dramatic self-trauma injuries, often refractory to any conventional symptomatic therapy.

Case report – An approximately two-year-old male neutered domestic short hair cat was brought in with severe ulcerative dermatosis localized in the neck region, that was associated to compulsory scratching. The diagnostic protocol failed to determine the underlying cause, although a hypersensitivity dermatitis was suspected. However, immunosuppressant therapy did not control itch. Suspecting a neuropathic itch syndrome, a treatment with gabapentin was attempted, although scarcely effective. Conversely, fluoxetine (0.4 mg/kg PO twice daily) brought about in a couple of weeks a marked reduction in self-trauma injuries, which were completely healed two months later. Fluoxetine was maintained at the same dosage for two years, as itching relapsed at any attempt to taper the drug; no side effects were noticed. Now, five years after the onset of the treatment, the cat is still receiving the full dose every other day and his behavior is normal.

Conclusions and clinical importance – Fluoxetine, a selective serotonin re-uptake inhibitor, was the only drug that was able to solve the severe chronic itch seen in this cat, likely related to a neuropathic origin. The prolonged therapy was safe, as no side effects were observed.

KEY WORDS

Cat, neuropathic itch, fluoxetine

INTRODUCTION

Itch is defined as an unpleasant cutaneous sensation leading to the desire to scratch, that can be evoked in the skin directly by mechanical and thermal stimuli or indirectly through chemical mediators (pruriceptive itch). It may also be generated in the central nervous system independently on peripheral stimulation (central itch).(4) Within the biological mechanisms that lead to the sensation of itch, peripheral and central sensitization processes may occur, similarly to that occurring during pain elicitation. These phenomena lead to allodynia and hyperknesis.(7)

In the cat, itch is a common finding in many infectious/parasitic skin diseases, as well as in systemic disorders, including hypersensitivity dermatitis (HD), which are usually caused by environmental, food and/or flea allergens. However, it can also appear without a clear cause, probably due to a dysfunction or disease of the itch-signaling neurons characterized by an uncoupling of the stimulus-response curve for itch sensation. The so-called neuropathic itch syndromes are therefore characterized by chronic itch, sometimes leading to compulsory scratching often directed towards specific regions of the body and resulting in dramatic skin lesions.(10) Several therapies are taken into account for the treatment of itch. Most of them are aimed at dealing with pruriceptive

itch (e.g. antihistamines, immunosuppressants), but often they are not effective in the treatment of central itch, for which molecules able to target the central origin of pruritus (e.g. anticonvulsants, antidepressants, opioid antagonists) should be considered.(9)

This paper discusses a case of chronic itch in which fluoxetine, a selective serotonin re-uptake inhibitor, proved effective in solving dramatic episodes of self-trauma.

CASE REPORT

In May 2012, a male domestic shorthair cat, approximately two years old, weighing 5 kg, was found abandoned outside the Veterinary University Teaching Hospital in a pet carrier, wearing an Elizabethan collar. When examined, a full-thickness ulcerative, necrotizing and crusting dermatitis was observed, extending all around the neck from interscapular area to the mandibular angle, approximately four centimeters wide (Fig. 1). When palpated, the ulcerative lesions were unpainful and did not elicit any scratching response. In the absence of an owner, the cat was hospitalized and entrusted to a member of the staff. Skin scraping, cytology and bacterial/fungal culture were negative for pathogens. Hematological and biochemical profiles revealed only a mild leukocytosis; feline leukemia virus and feline immunodeficiency virus



Fig. 1: lesion at presentation

tests were also negative. The initial treatment included the surgical curettage of the lesion and the application of a primary wound care (One Vet®, Phytoceuticals Ltd, Zurich, Switzerland); cephalexin was also administered (Rilixine®, Virbac Srl, Milan, Italy, 30 mg/kg PO once daily). In the following days, it became clear that the cat suffered episodic itching: any time the collar was removed the cat obsessively scratched the neck, the left supraorbital area and the scapulae, particularly on the left side of the body. A modified Elizabethan collar protecting the shoulders as well was therefore applied (Fig. 2). A biopsy of the pathological tissue of the neck was performed by removing also a small border of the healthy skin: the histopathological evaluation showed an extensive focal full thickness ulceration of the epidermis with necrosis of the superficial dermis. Underneath the ulceration, there was a severe, perivascular to diffuse infiltration mainly characterized by neutrophils, a lower number of macrophages and lymphocytes and fewer eosinophils. Cells were embedded in a highly edematous, loosely arranged reactive connective tissue with small caliber blood vessels lined by reactive endothelial cells that



Fig. 2: modified Elizabethan collar

were frequently arranged perpendicular to the surrounding fibrous connective tissue (granulation tissue). The PAS staining was negative for fungi. Due to the presence of a severe inflammatory reaction in the dermis and the lack of a subepidermal band of fibrosis, the lesions were not typical of feline idiopathic ulcerative dermatitis; however, considering the history and the eosinophilic infiltration, a hypersensitivity disorder was suspected and the cat received prednisone (Deltacortene®, Bruno Farmaceutici Spa, Rome, Italy, 2 mg/kg PO once daily) together with a restriction diet (z/d Hill's Pet Nutrition, Inc., Rome, Italy). After six weeks, the ulcerative lesions were almost completely healed (Fig. 3), but every time the collar was removed, compulsory scratching was observed. At the end of July, the cat was able to remove the protective dressing during the night, and produced a large and deep wound all around the neck (Fig. 4). A more aggressive immunosuppressive therapy was thus advised, and cyclosporine (Atoplus®, Novartis Animal Health Spa, Origgio (Varese), Italy, 7 mg/kg PO once daily) was started. Each time the collar was removed for medication, the cat showed compulsive licking around the wound (See



Fig. 3: evolution of the lesions after the immunosuppressive therapy with cortisonics. At this stage, it was impossible to remove the protective dressing, as compulsory itching was yet present



Fig. 4: dramatic relapse of self-injuries after the initial resolution of the lesions induced by the immunosuppressive therapy

May 2012	<ul style="list-style-type: none"> • severe self-trauma injury all around the neck associated to compulsory itching • treatment: surgical curettage, application of a primary wound care, antibiotic therapy (cephalexin) • no control of itching
June 2012	<ul style="list-style-type: none"> • application of a modified protective dress and started prednisone and a restriction diet • after 6 weeks, the ulcerative lesions were completely healed but it was impossible to remove the protective dress (compulsory itching)
July 2012	<ul style="list-style-type: none"> • the cat removed the protective dressing and self-produced a large and deep wound all around the neck • surgical curettage and started cyclosporine
September 2012	<ul style="list-style-type: none"> • no improvement in the scratching and licking behavior, even if the wound was healing • started gabapentin (10 mg/kg PO SID for two weeks, then 10 mg/kg PO BID for two weeks, finally 10 mg/kg PO SID for two weeks) • slightly reduction of the scratching behavior
December 2012	<ul style="list-style-type: none"> • the wound was completely healed and the cat was adopted • impossible to remove protective dress as, if so, the cat wounded itself • therapy with gabapentin continued • after a few weeks in the new house, the owner reported that the scratching episodes seemed mainly manifested when a member of the family suddenly showed to the cat
January 2013	<ul style="list-style-type: none"> • impossible to remove the protective dress • tapered gabapentin (in four weeks)
February 2013	<ul style="list-style-type: none"> • started fluoxetine (0.4 mg/kg PO SID) • the owner noticed a substantial reduction in the scratching behavior in a couple of weeks
March 2013	<ul style="list-style-type: none"> • it was possible to substitute the protective dressing with a flexible bandage around the neck
April 2013	<ul style="list-style-type: none"> • the bandage was substituted by a bandana
April 2014	<ul style="list-style-type: none"> • therapy with fluoxetine continued (0,4 mg/kg PO SID) • no episodes of self-mutilation • attempt to reduce the daily dose resulted in increasing scratching
April 2015 - present (Nov. 2018)	<ul style="list-style-type: none"> • full dose of fluoxetine every other day • no deterioration in the following month • the cat is still receiving fluoxetine

Table 1: timeline

supplement file - video). After eight weeks no improvement in the scratching and licking behavior was achieved, even though the wound was healing. Due to a lack of a definitive diagnosis and the failure of the immunosuppressive therapy, neuropathic itch was suspected: cyclosporine was suspended and gabapentin (Gabapentin generic) was started at 10 mg/kg PO once daily for two weeks, then 10 mg/kg twice daily for another two weeks, and finally 10 mg/kg three times daily. This dose was maintained for the following month, during which time the cat slightly reduced its scratching behavior. When out of the cage and released from the collar, the cat showed explorative activity and paid no attention to any parts of the body. However, when back in the cage he tried immediately to scratch and the protection needed to be immediately put back on. At the beginning of December, the wound was completely healed and the cat was adopted. The new owner accepted to continue the therapy with gabapentin and to monitor any change in the cat's behavior. After a few weeks, he reported that the scratching episodes seemed mainly manifested when a member of the family woke up in the morning or was back home from outside and was seen by the cat. In January 2013, attempts were made to reduce the protection, but the cat continued to scratch and injure himself. It was thus decided to taper gabapentin (over four weeks) and then start fluoxetine (galenic formulation, 0.4 mg/kg PO once daily). After a couple of weeks, the owner noticed a marked reduction in the scratching behavior: after one month, it was possible to substitute the protective dressing with a flexible bandage around the neck, and finally, one

month later, with a bandana. This therapy was maintained for one year, during which the cat behaved normally, with no relapse of self-trauma. Any attempt to reduce the daily dose resulted in increasing scratching. After a second year of fluoxetine and with the cat behaving normally, the dose of the drug was again reduced, this time administering the full dose every other day. No deterioration was noticed in the following months, and the cat is still receiving fluoxetine every two days. The prolonged therapy results to be safe as, after 4 years of continuative treatment, no side effects have been observed.

Table 1 resumes the time course of the pathology and the sequence of the treatments.

DISCUSSION

In our opinion, the clinical records support the hypothesis that the chronic pruritus observed in this cat was partly related to a neuropathic itch syndrome. From a clinical perspective, it should be noted that the cat showed scratching into deeper tissues: painless scratching and consequent self-trauma injuries are considered virtually pathognomonic of neuropathic itch, (2, 6) because of a co-localizing severe sensory loss, that permits itch to continue to the same point.(5) Furthermore, the lesions were localized in the forepart of the body, like in human beings affected by neuropathic hitch, where self-injuries are more common on the face.(5) However, the lesion's location is not considered a diagnostic criterion, as different skin disorders may share a similar distribution.(1) We were not able to perform any intradermal allergen testing or serum allergen specific IgE

testing in order to proceed with a diagnosis of a hypersensitivity disease: nevertheless, the type of lesion and the histopathological findings were consistent with an allergic dermatitis, and this supposition motivated the first therapeutic choice. However, immunosuppressant drugs normally used for these diseases failed to succeed, while drugs used in the human setting in order to treat neuropathic itch were successful. More specifically, of the two drugs used in sequence, fluoxetine showed to be particularly successful in solving the problem. Fluoxetine is a selective serotonin re-uptake inhibitor (SSRI) used for the control of behavioral disorders in cats, such as urine spraying,(3) at the dosage of 0.5-1 mg/kg PO daily. In humans, SSRIs are approved for the treatment of depression: however, they are also proposed as an antipruritic in chronic itching of any origin. (8) Although the mechanisms leading to the suppression

of itch are not fully understood, a cerebral suppression of pruritus can be assumed: in the central nervous system, SSRIs actually target Na⁺/Cl⁻-dependent transporters on synaptic membranes, which results in increased serotonin concentration acting on postsynaptic receptors.(11) We cannot exclude that fluoxetine was also effective due to its antidepressant effect, because of the behavioral signs noted by the owner. The chronic discomfort may have actually contributed to altering the behavior in a vicious circle. In summary, this case suggests fluoxetine as an effective treatment procedure for itch syndrome in cats, due to its antipruritic efficacy, low side-effect profile and low costs of prolonged treatment when compared to other antipruritic therapies. These properties should certainly be confirmed in future double-blind studies.

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SUPPORTING INFORMATION

Video: compulsive licking around the wound.