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Authors: Jones, Selene, and Bloom, Paul

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Rush immunotherapy in two cats with atopic skin syndrome

Selene Jones* and Paul Bloom*

Abstract

Case series summary Two cats with feline atopic skin syndrome (FASS) were included in this case series. They were diagnosed with FASS by a combination of history, physical examination and exclusion of other pruritic diseases. They underwent rush immunotherapy (RIT) after determination of offending environmental allergens by either serum IgE or intradermal testing. Cats were premedicated with an antihistamine and hospitalized for the day to undergo the procedure and to ensure adequate observation. Allergen extracts were administered subcutaneously at increasing concentrations every 30 mins until the maintenance dose of 20,000 protein nitrogen units/ml was reached. Both cats successfully completed RIT without any adverse reactions and their clinical signs improved afterwards. RIT appears to be an alternative treatment option for cats with FASS. Larger studies are needed to more accurately assess the safety and long-term efficacy of RIT in the feline patient, as well as the incidence of adverse reactions and optimal premedication protocol. Further evaluation of the route of injections for RIT is also warranted.

Relevance and novel information RIT has been reported to be a safe treatment option in canine atopic dermatitis. Its use in FASS is limited to a pilot study of four cats. The purpose of this series was to describe two additional cats that underwent RIT using a different premedication protocol.

Keywords: Rush immunotherapy; atopic skin syndrome; allergen immunotherapy; allergies; non-flea, non-food hypersensitivity dermatitis; NFNFHD; FASS

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Introduction

Feline atopic skin syndrome (FASS) is a common skin disease in cats.[1–3] The diagnosis of this disorder is based upon clinical history, physical examination and the exclusion of ectoparasites and other pruritic diseases.[1–3] Clinical signs are varied and can include pruritus, miliary dermatitis and eosinophilic lesions.[1–3] The immunopathogenesis has not been completely elucidated. However, T cells appear to be involved as there is an increased proportion of $CD4^+$ T cells present in the skin of these cats.[1,3] There is no cure for this disorder and management involves maintaining patient comfort and limiting the number of flare-ups.[1,3]

Allergen-specific immunotherapy (ASIT) has been used successfully in the treatment of cats with FASS.[1–4] Conventional ASIT requires a prolonged induction period where there is an increasing number of allergens administered over several weeks until a maintenance dose is reached.[2,4–7] Rush immunotherapy (RIT), where gradually increasing amounts of allergen are administered over several hours instead, has been reported as an alternative protocol to conventional immunotherapy. Its use may increase owner compliance and decrease obstacles to beginning immunotherapy.[2,4–7] In dogs, the protocol for RIT includes administration of an antihistamine 1–2 h before allergen injection.[4] Although reported as safe and efficacious in people and dogs, the use of RIT has only been reported once before in FASS and once in an experimental model of allergic feline asthma.[2,5]

Allergy, Skin and Ear Clinic for Pets, Livonia, MI, USA

*Selene Jones and Paul Bloom contributed equally to this work

Corresponding author:
Selene Jones DVM, Allergy, Skin and Ear Clinic for Pets, 31205 Five Mile Road, Livonia, MI 48154, USA
Email: drselenejones@gmail.com

Table 1 Rush immunotherapy injection volume and concentration

	Injection number	Volume (ml)	Dose (PNU)
Vial #1 (200 PNU/ml)			
	1	0.1	2
	2	0.2	40
	3	0.4	80
	4	0.8	160
	5	1.0	200
Vial #2 (2000 PNU/ml)			
	6	0.2	400
	7	0.4	800
	8	0.8	1200
	9	1.0	2000
Vial #3 (20,000 PNU/ml)			
	10	0.2	4000
	11	0.4	8000
	12	0.8	16,000
	13	1.0	20,000

PNU = protein nitrogen units

The purpose of this case series was to describe two additional cats with FASS that successfully underwent a RIT protocol with improvement of their clinical signs afterwards.

Case series description

Two atopic cats presented to the Allergy, Skin and Ear Clinic for Pets, Livonia, MI, USA, for RIT. The diagnosis of FASS was made previously based on compatible history, physical examination and the ruling out of potential differential diagnoses, such as ectoparasites and food allergy. This was carried out by placing the cats on an appropriate ectoparasite control, performing skin scrapes if indicated and conducting an elimination diet trial, as previously described.[1,3] The owners had previously been given the option of pursuing conventional immunotherapy or RIT. They had been made aware of potential risks and complications, including anaphylaxis and death, and signed a consent form. One owner elected to pursue RIT owing to difficulty in catching the cat to medicate it, while the other elected to pursue it for scheduling purposes. Pruritus was recorded using the Pruritus Visual Analogue Scale (PVAS) with descriptors adapted from dogs.[8]

Allergen extracts

Individual allergens selected for immunotherapy were chosen based upon clinical history and a positive test result by intradermal testing (IDT) or by identifying allergen-specific IgE antibodies in the patient's serum (Veterinary Allergy Reference Laboratories; VARL) that correlated with their clinical history. All immunotherapy extracts were prepared in-house using allergen extracts from Greer Laboratories. The first five injections administered used antigen concentrations at a range of 200 protein nitrogen units (PNU)/ml. The next four injections utilized 2000 PNU/ml and the last four injections utilized the maintenance concentration of 20,000 PNU/ml (Table 1).

RIT protocol

Each patient underwent a physical examination before beginning the RIT protocol to establish baseline vital signs and to ensure they were in good health. They were then premedicated with 2.2 mg/kg diphenhydramine intramuscularly 30 mins before beginning RIT based on recommendations for RIT in dogs.[4] The protocol used was adapted from a prior study.[6] A 22 G intravenous catheter was placed in a cephalic vein and bandaged in place before the first injection and patency was maintained until discharge from the hospital. Individual injections of increasing concentration of allergens (see Table 1) were administered subcutaneously on a rotating basis in each distal limb. An injection was given every 30 mins until the maintenance dose was reached. Vital signs (pulse, temperature, respiratory rate, capillary refill time and mucous membrane color) and pruritus scores were assessed before each injection together with any changes identified on physical examination.

If the pulse and/or respiratory rate increased by >30%, if the temperature rose above 102.5ºF (39.2ºC), the capillary refill time became longer than 2 secs or any abnormalities were noted on the physical examination, the next injection was not administered and the cat was re-evaluated 30 mins later. If parameters normalized, the

Table 2 Positive allergens for each cat

	Case 1	Case 2
Indoor		*Dermatophagoides farinae* *Dermatophagoides pteronyssinus*
Trees	Alder Elm Maple Oak mix	Alder Black willow Box elder Eastern cottonwood Eastern sycamore Hazelnut Maple Mulberry Oak mix Walnut
Grasses	Timothy	Timothy Brome grass Kentucky bluegrass
Weeds	Annual sage dock/sorrel Spiny pigweed Thistle	Annual sage Kochia Marsh-elder/burweed Plantain Ragweed mix Russian thistle
Molds	*Aspergillus* species *Mucor* species	*Alternaria* species *Aspergillus* species *Cladosporium* species

next injection would be administered. If not, no further injections would be administered.

Cats were monitored closely at all times during the first day of treatment until at least 2 hours after the last injection was administered. Cats that completed the protocol were discharged on an initial maintenance dose (1 ml of 20,000 PNU/ml) subcutaneously every week.

Case 1

A 7-year-old spayed female domestic shorthair presented for RIT with a history of year-round pruritus that was exacerbated in the summer and fall. A serum test (VARL) was used to determine antigens for immunotherapy, owing to owner preference (Table 2). It was positive for several trees, grasses, weeds and molds that were consistent with the cat's seasonal fluctuations in clinical signs. On physical examination prior to RIT, there was evidence of self-traumatic alopecia on the ventral abdomen/chest and pruritus was rated by the owner as PVAS +5/10. Medications to treat pruritus were declined by the owner.

Ten days post-RIT, the PVAS had decreased to +1–2/10. Forty days post-RIT, the self-traumatic alopecia had significantly improved. The owner rated the pruritus as PVAS +1–2/10. The cat continued to do well until 10 months after RIT was performed. The cat's pruritus at that time increased to a PVAS +3/10 and it developed focal crusted papules on the ventral abdomen and inguinal region. Cytology of the lesions showed 0–5 cocci and 0–3 neutrophils/high-power field. One drop of thiabendazole, dexamethasone, neomycin sulfate solution (Tresaderm; Merial) was applied topically to each of the lesions once daily. The lesions resolved within a week of treatment.

Case 2

An 8-year-old castrated male domestic longhair cat presented for RIT with a history of non-seasonal pruritus without seasonal fluctuations. IDT was used to determine allergens to be used for immunotherapy, selecting those antigens with a 2+ reaction or higher. Positive reactions to dust mites, several molds, trees, grasses and weeds were identified (Table 2).

On presentation for RIT, the cat had generalized self-traumatic alopecia. Pruritus was rated by the owners as PVAS +8/10. Medications for pruritus were declined by the owner owing to difficulties in medicating the cat. A long-acting steroid injection was also declined due to the potential risk of diabetes associated with steroids. A onesie was recommended but not tolerated by the cat. Owing to the COVID-19 pandemic, the cat was unable to be examined in person after the RIT visit. However, on a telephone call with the owner 30 days post-RIT, the owners felt that the cat was significantly less pruritic, although the owners found it

difficult to give an exact PVAS score. Six weeks later, COVID-19 restrictions were still in place. The owners reported that the cat was doing well, and that the pruritus was minimal. The owner found it difficult to give a PVAS score. However, they had no concerns. They were then lost to follow-up.

Discussion

Both cats successfully underwent the RIT protocol. The protocol was tolerated well and neither cat had any immediate nor delayed adverse reactions. There have been previous reports of reactions associated with RIT use in cats.[2,5] In these studies, most of the adverse events in cats with FASS were mild.[2] Two of the four cats had increased grooming behavior after one of the injections but did not react to subsequent injections.[2] Two cats developed firm, dermal nodules on their necks a week after treatment.[2] These were suspected to be delayed injection site reactions and they resolved with the application of topical tacrolimus.[2] There was a larger incidence of adverse events reported in the asthmatic cats. All seven of those cats experienced localized swelling of the injection site and one cat experienced systemic anaphylaxis.[5] Two cats showed agitation during the procedure, three cats experienced vomiting and several had increases in their vital signs (respiratory rate, heart rate or temperature).[5] Although more adverse events were seen in the study of asthmatic cats, the reason behind this is unclear. It may be related to the differences in the diseased organ (respiratory vs cutaneous) and the underlying pathophysiology of the diseases. This is demonstrated by the fact that ASIT is often considered part of the therapy in humans with allergic rhinitis or asthma, while its use in those with atopic dermatitis is considered controversial.[9–13]

In humans, a variety of premedication protocols are used for RIT, though most include glucocorticoids.[14] A recent practice parameter update recommended the use of antihistamines and/or glucocorticoids for rush aeroallergen immunotherapy in humans.[15] The premedication protocol chosen for this report was based on recommendations for dogs undergoing RIT.[4]

To our knowledge, the efficacy of immunotherapy based upon this method of induction has not previously been evaluated in atopic cats. In dogs, RIT has been used successfully and may lead to more rapid improvements in clinical signs than conventional immunotherapy.[4,7] Both cats in the present report had marked decreases in pruritus within 1–2 months after starting RIT. Seasonal changes were not thought to contribute to the improvement in clinical signs as case 1 began RIT in the middle of the cat's worst allergy season and case 2 did not have seasonal fluctuations in pruritus. Although these cats seemed to improve within a short time frame, many patients require 6–12 months of ASIT to see a clinical improvement.[3–7] The limitations of this case series include the small number of participants and that the second cat was unable to be examined in person to verify improvement.

Conclusions

The RIT protocol used was tolerated well and led to clinical improvement in both treated cats. However, larger studies are needed to more accurately assess the safety and long-term efficacy of RIT in the feline patient, as well as the incidence of adverse reactions and optimal premedication protocol. Further evaluation of the route of injections (subcutaneous vs intranodal) for RIT is also warranted.

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Ethical approval This work involved the use of non-experimental animals only (including owned or unowned animals and data from prospective or retrospective studies). Established internationally recognized high standards ('best practice') of individual veterinary clinical patient care were followed. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*.

Informed consent Informed consent (either verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (either experimental or non-experimental animals) for the procedure(s) undertaken (either prospective or retrospective studies). No animals or humans are identifiable within this publication, and therefore additional informed consent for publication was not required.

ORCID iD Selene Jones https://orcid.org/0000-0003-2861-8614

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