Successful Treatment of Two Dogs with Allergic Dermatitis by Anti-Allergic Peptides (MS-antigen™)

Song-Jung PARK¹, Naoko YOSHIDA¹, Koji NISHIFUJI¹, Maiko SEKIGUCHI¹, Yasuyuki MOMOI¹, Tsuneo FUKADA¹ and Toshiro IWASAKI¹*¹

¹Gifu University, Veterinary Medical Teaching Hospital, Gifu 501-1193, Japan

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ABSTRACT. The effects of non-specific immunotherapy with anti-allergic peptides extracted from the urine of human allergic patients (MS-antigen™), in two dogs with allergic dermatitis (AD) have been described. Clinically, severe pruritus accompanied by secondary bacterial pyoderma did not respond to conventional therapy with systemic antibiotics. The first clinical change appeared as a significant reduction in pruritus within 3 months, around the time of the 15th injection in both cases. The clinical condition was stabilized after 5 months, allowing the gradual withdrawal of concurrent therapies and an increase of injection intervals. The correlation between the results of intradermal skin tests before and after treatment and the improvement of clinical signs was not obvious.

KEY WORDS: canine allergic dermatitis, MS-antigen, non-specific immunotherapy.

The 80% of dogs with atopic dermatitis (AD) develop non-seasonal clinical signs which usually require long-term therapy [7]. Therapeutic options for canine AD include avoidance of sensitized antigen, management of secondary complicating factors such as bacterial or yeast infections, topical therapies, hyposensitization (immunotherapy) and systemic antipruritic drugs [7]. Immunotherapy has been described as a safe, efficacious and cost-effective AD therapy of dogs, in which avoidance of antigen is impossible, clinical signs are present throughout the year, and antipruritic drugs are unsatisfactory [7].

Currently performed antigen-specific hyposensitization requires determination of sensitized antigens based on the results of intradermal skin testing (IDST) or in vitro IgE testing. However, IDST is available in relatively few specialty clinics and university hospitals, and has also some difficulties when skin condition is not appropriate or the owner does not agree to clip hair [10].

In vitro serologic IgE testing have been available as an alternative diagnostic option for determining sensitized antigens. However, most veterinary dermatologists still consider results of IDST as the most reliable and preferred method for formulating the immunotherapeutic program [4].

Another concern of antigen-specific immunotherapy is breed predilection in efficacy to hyposensitization. Based on the previous study in our laboratory, West Highland White Terrier (WHWT) was shown to have poor response to hyposensitization as 25% efficacy despite total efficacy of 64% [3]. Another study reported that certain breeds such as WHWT and Boxer had poorer responses to this therapy as well [12].

There may be another disadvantage to antigen-specific immunotherapy. The number of allergens selected for hyposensitization may affect the efficacy, since no more than 10 allergens are used at once by convention [7, 8].

For these inappropriate cases for antigen-specific immunotherapy, it would seem valuable to provide non-specific immunotherapy as an alternative. Several anti-allergic drugs for non-specific immunotherapy have been launched in Japan such as Histaglobin (Nihon Zohki), Neurotropin (Nihon Zohki), and MS-antigen (MS-A, Hitachi Chemical). These drugs have been used for the treatment of type I allergic diseases in humans, as an ancillary therapy in combination with the first-line symptomatic therapies and as an option in cases in which other therapies are ineffective.

MS-A is extracted peptides from the urine of human allergic patients as average molecular weights of 1600 [5]. Previous clinical reports in humans have demonstrated 62.5% efficacy for chronic urticaria [6]. Though several anti-allergic mechanisms that may account for the clinical effect have been proposed, the mode of action remains unclear. In this report, we describe the effects of non-specific immunotherapy with MS-antigen on the clinical symptoms of two cases of canine AD.

Case 1: A 5-year-old, male WHWT presented with a 3-year history of AD with facial, pedal and truncal non-seasonal intense pruritus. Age of onset was 1 year, involved only the pedal regions, and then the lesions extended to the abdominal trunk. The dog had been previously treated, but the symptoms were refractory to the conventional therapy including corticosteroids, and the case was referred to the Gifu University Veterinary Teaching Hospital for further clinical and diagnostic evaluation. Marked erythema, lichenification and alopecia were observed in the abdomen, four limbs, axillary and inguinal regions with secondary superficial bacterial pyoderma (Fig. 1). Periocular and interdigital redness and swelling, and bilateral otitis externa were also present.

Skin scrapings were negative for ectoparasites. Impres-
sion smears for secondary bacterial pyoderma and Malassezia dermatitis were performed, and numerous bacteria organisms were detected. IDST showed positive reactions to mite mix, flea and mugwort common. Initially, the dog had been treated with ofloxacin, clemastine fumarate and homochlocyclizine combined with twice-weekly shampoos using an anti-seborrheic and moisturizing agent on a rotational basis. This initial therapy failed to improve the pruritus and the condition of the dog worsened.

As the case 1 dog had shown relatively poorer responses to hyposensitization based on our clinical study, the owner intended therapy beyond the therapeutic trial of non-specific immunotherapy with MS-A. MS-A was injected every 3–4 days from 0.2 (4 mg) up to 1.0 (20 mg) ml with a gradually increased dose, thereafter reducing the frequency from once weekly to monthly, depending on the response as a maintenance basis. The protocol used for the immunotherapy is shown in Table 1.

After 3 months from initiation of the MS-A therapy, at the 12th injection, the pruritus decreased. After 5 months, at the 20th injection, a marked improvement was noted as a resolution of the interdigital edema, redness and pruritus. Injections were tapered from once weekly to once every two weeks, and the symptoms were still controllable with shampoos. After 7 months, at the 24th injection, slight pruritus was confined to interdigital regions, and the alopecia and lichenification in foreleg region disappeared (Fig. 2). The owner was satisfied with the improvement of axillary hair regrowth.

After 11 months, the second IDST was performed with positive reactions to the same antigens that were shown at the first time. The injections were continued less frequently once every two months, and the atopic symptoms were well controlled with a weekly shampoo. There have been no systemic or local adverse reactions including hematological and serum biochemical findings during the entire course of immunotherapy.

**Case 2:** A 6-year-old, male black Labrador retriever presented with Veterinary Medical Teaching Hospital at Gifu University and a 4-year history of severe AD as pruritic papular dermatitis. Age of onset was 1 year old and the owner reported that the dog had severe non-seasonal and generalized pruritus. The lesions responded poorly to conventional antibiotics and steroids therapy. Cutaneous abnormalities included erythematous papules, epidermal collarettes on abdomen, axilla and interdigital regions suggesting secondary bacterial pyoderma. Multiple skin scrapings were negative, and tape preparations revealed numerous bacteria, but negative for Malassezia. IDST was performed, with strong positive reactions to mite mix, grass mix, flea, Japanese cedar, plantain and ragweed. Biopsy specimens revealed hyperkeratosis, acanthosis, and partial exocytosis predominating lymphocytes in the epidermis. The dog was otherwise healthy on physical examination. The therapy with cefalexin, clemastine fumarate, homochlocyclizine, combined with twice-weekly successive use of an anti-seborrheic and moisturizing shampoos resulted in temporary and partial improvement. According to the importance in limited number of selected antigens for hyposensitization, antigen-specific immunotherapy in this case seemed to have limited benefits, and the owner intended for the trial use of

![Fig. 1. Clinical findings of case 1 dog before treatment of MS-antigen injection. Caudal aspect of both forelegs and inguinal region show redness, pigmentation, hair loss and lichenification.](image1)

![Fig. 2. Clinical findings of case 1 dog 5 months after initiating treatment. There is no lesion in caudal aspect of a left foreleg.](image2)

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<th>Table 1. Protocol for MS-antigen injection</th>
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From day 21: 1.0 ml/once 10 days.
MS-A.

MS-A therapy was performed by the same protocol as that of the first case (Table 1), with systemic antibiotics and shampoos. Within 3 months of initiation of the therapy, the pruritus and severe scaling were decreased around the 15th injection. After 4 months, at the 20th injection, generalized pruritus was mostly improved and the redness and alopecia seemed recessive. However, when injections or other concurrent therapies were tapered, the condition relapsed and remained consistent. After 7 months, the second IDST was performed, with positive reactions to all the same antigens as the first time. At this point, skin lesions and hair loss remarkably resolved, and they were finally controllable with monthly injections and a weekly shampoo. The dog finally remained quite asymptomatic with once every two months injections with only a monthly shampoo. The owner was impressed by the significant change in degree in pruritus. Adverse reactions including clinical, hematological and serum biochemical findings from MS-A administration were not reported during therapy.

In both cases, the most striking effect of non-specific immunotherapy with MS-A was the marked reduction in pruritus. In humans, the standard protocol of MS-A injection states 1 ml (20 mg) for the first time, thereafter 2 ml (40 mg) of once-twice weekly of at least 15 injections [6]. The effects to these injections appeared around 5 to 80 injections with a wide range in allergic patients [1, 6]. Both dogs described in this report appeared to respond within 3 months after the initiation of the therapy, around the 15th injection. The condition seemed to be stabilized after 5 months, around the 25th injection with gradual reduction in concurrent therapy of antibiotics and shampoos, and an increase in injection intervals. Cutaneous lesions of case 2 remained recurrent until 4 months of the therapy, with difficulty to achieve the resolution in relapsing bacterial pyoderma. Finally the resolution in relapsing bacterial pyoderma was remarkable by 7 months. Immunotherapy is performed to allergic patients in an attempt to decrease the clinical response to exposure of natural allergens. The mechanism of action of hyposensitization is unclear as well as the complex pathogenesis involved in AD. The possible mechanism of antigen-specific hyposensitization include: (1) humoral desensitization (2) cellular desensitization (3) immunization (4) tolerization, and (5) some combination of thereof [11]. In general, there has been a poor correlation of the immunologic observations with clinical response to hyposensitization. No changes in IDST reactivity were observed in either of the dogs treated in this report.

In conclusion, it is suggested that non-specific immunotherapy with MS-antigen may be effective also for AD in dogs as well as in humans. Antigen-specific immunotherapy in veterinary medicine is an established procedure especially when other therapies are ineffective, or side effects are unacceptable to the owner or the patient. In inappropriate cases for hyposensitization with specific antigens, non-specific immunotherapy with MS-antigen may serve as an alternative method for the management of AD in dogs. Additional studies would be needed for further definition of these clinical findings to decide if this form of treatment has a place in the management of AD in dogs.

REFERENCES