NOTE *Internal Medicine*

Topical 0.03% Tacrolimus for Treatment of Pemphigus Erythematosus in a Korea Jindo Dog

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(Received 16 April 2007/Accepted 12 December 2007)

ABSTRACT. Topical 0.03% tacrolimus was used for treatment of a Korea Jindo dog diagnosed with pemphigus erythematosus. The dog was slowly improved following application of tacrolimus but did not achieve complete remission until end of this study. No adverse effects on clinical or laboratory parameters were noted during the topical tacrolimus therapy period.
KEY WORDS: canine, pemphigus erythematosus, topical 0.03% tacrolimus.

J. Vet. Med. Sci. 70(4): 415–417, 2008

Pemphigus erythematosus is thought to represent a more benign form of pemphigus foliaceous or possibly a cross-over syndrome between pemphigus and lupus erythematosus and is characterized by erythematous, pustular dermatitis of the face and ears and texture of the nasal planum that frequently progresses to erosion or ulceration. Typical skin lesions include oozing crusts, depigmentation, scales, alopecia and erosion. Lesions may be exacerbated by sun exposure and may have a waxing and waning course [5, 9]. Tacrolimus (formerly known as FK506) is a 23-member macrolide that exhibits potent immunosuppressive properties by its ability to block transcription of cytokine genes in activated T cells. In human medicine, tacrolimus has been studied, and the benefit of tacrolimus for treatment of several cutaneous diseases, including variants of pemphigus, has recently been reported [2, 10, 11]. Only one study has been reported in veterinary medicine concerning treatment of canine pemphigus erythematosus using topical 0.1% tacrolimus [3]. This short communication describes treatment of a Jindo dog with canine pemphigus erythematosus using topical 0.03% tacrolimus.

A 6-year-old female Jindo dog weighing 20 kg was presented to the Veterinary Teaching Hospital of Seoul National University due to formation of crust and erosion on the nasal bridge and planum and alopecia of the ear margin (Fig. 1A). CBC, serum chemistry and basic dermatologic examinations including skin scraping, bacterial cultures, and fugal cultures showed no abnormalities. Imprint smears of the inner surface of the crust revealed numerous neutrophils, mostly non-degenerate, with a few scattered rounded up epithelial cells. The latter were considered acantholytic cells, which suggested an immune mediated skin disease. The result of an ANA test was negative. Biopsy samples were obtained from skin lesions for diagnosis of pemphigus erythematosus by histopathology and immunochemical staining. Histopathology of the skin biopsy specimens revealed that the epidermal pustule contanined acantholytic cells and that the remaining epidermis was characterized by acanthosis, spongiosis and an overlying orthokeratotic hyperkeratosis (Fig. 2). The underlying superficial epidermis contained ballooning degeneration and neutrophilic exocytosis. Immunohistochemistry was performed on paraffin embedded tissue sections with anti-canine IgG (H+L) antibody, and immunolabelling was found in the intercellular space of the spinous layer. Based on these results, the dog was diagnosed with pemphigus erythematosus.

The dog was initially treated with oral prednisolone as an immunosuppressive dose (2 mg/kg, q12h) for four weeks and was prescribed cephalexin (30 mg/kg, PO, q12h) to prevent secondary infection, but the clinical manifestations did not improved. Despite increasing the dose of oral prednisolone, no improvements were seen in the skin lesions, and the dog began to show signs of polyuria, polydipsia and weight gain. Therefore, in place of prednisolone, topical 0.03% tacrolimus was applied twice daily to lesions, which consisted of erythema, erosion and hemorrhagic crust of the nasal planum and bridge of the nose. After 4 weeks, the erosion, hemorrhagic crust and area of the skin lesions gradually decreased; however, depigmentation and scarring of the dorsal aspect of nasal planum remained. After therapy with only topical 0.03% tacrolimus for 4 months, marked regrowth of hair was observed in half of alopecic areas and erosion, erythema and hemorrhagic crust were mild to non-existent; however, depimentation of the nasal planum was unchanged. At this time, skin biopsy of the erythematous,

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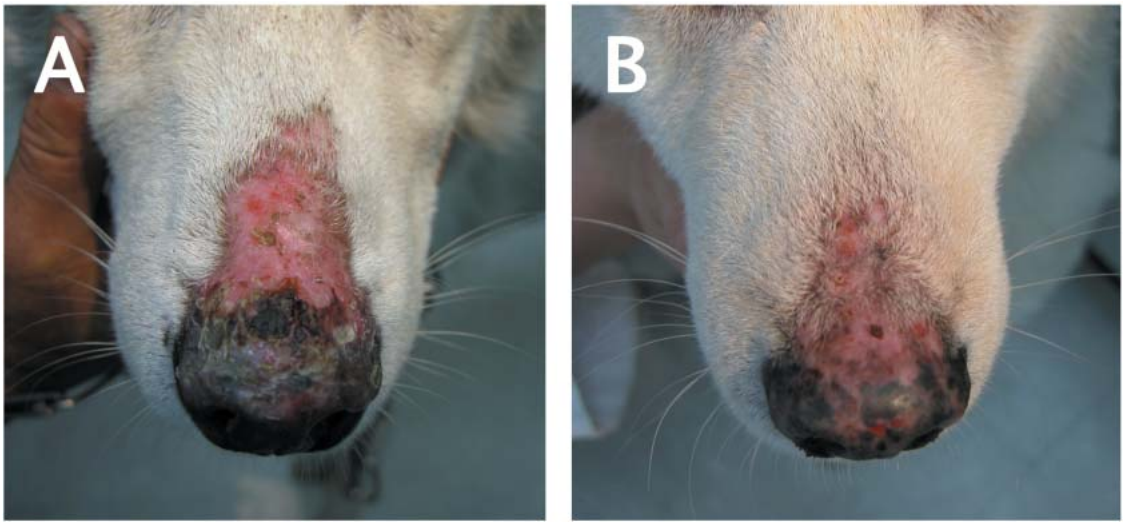

Fig. 1. Photograph of the nasal planum and bridge of the nose before treatment (A) and 8 months (B) following topical 0.03% tacrolimus therapy.

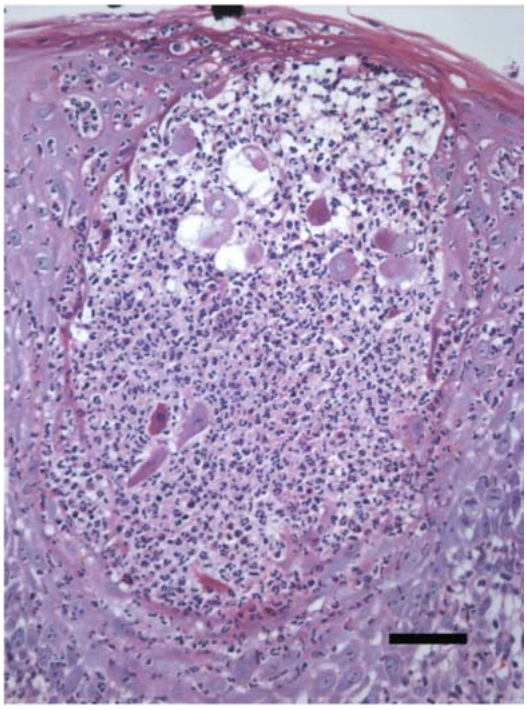

Fig. 2. High magnification of an epidermal pustule. Note the free floating and scattered acantholytic cells. Bar=50 um.

depigmented and alopecic areas of the nasal planum was performed to investigate the histopathologic changes after topical tacrolimus therapy. Microscopically, there were epidermal hyperplasia, parakeratotic hyperkeratosis and epidermal pustules. However, the superficial dermis contained fewer inflammatory cells with a focal distribution. The epidermal pustules also contained fewer degenerative neutrophils and few acantholytic cells. These histopathologic findings indicated that there was some macroscopic improvement compared with the original state of the lesions, although there still remained a degree of inflammation associated with pemphigus erythematosus. Following a second histopathologic examination, despite continuation of topical tacrolimus therapy for 3 months, the remaining skin lesions remained static and there was no complete remission [Fig. 1B]. During tacrolimus therapy, the results of CBC and serum chemistry were all within the normal ranges and clinical abnormalities, including increased redness, pruritus, and pain response following application, were not observed.

Pemphigus erythematosus may initially be treated topical glucocorticoid, tetracycline/nicinamide or systemic glucocorticoid [6, 7, 9]. If these drugs are not effective, vitamin E, azathioprine, cyclosporine, topical tacrolimus, chlorambucil or mycophenolate mofetil may be added to the regimen or administered as a sole therapy [3, 6–8]. The use of topical tacrolimus therapy in dogs has been previously reported for canine perianal fistulas, atopic dermatitis, discoid lupus erythematosus and pemphigus erythematosus [1, 3, 4]. In particular, treatment of two cases of pemphigus erythematosus using topical 0.1% tacrolimus in previous report produced an excellent response, and there were no adverse effects associated with the medication [1, 3, 4].

In the current case, complete remission was not achieved during the treatment period. However, most of the lesions, which consisted of erosion, hemorrhagic crust, scale, and alopecia were markedly decreased or absent, although depigmentation and scaring of some of the nasal planum remained. Therefore, topical 0.03% tarolimus may be a safe and effective treatment for pemphigus erythematosus.

ACKNOWLEDGEMENTS. This work was supported by the Brain Korea 21 Program for Veterinary Science. Further support was also provided by the Research Institute of Vet-

erinary Science, College of Veterinary Medicine, Seoul National University, and a Korean Research Foundation Grant (KRF-2006–005-J02902).

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