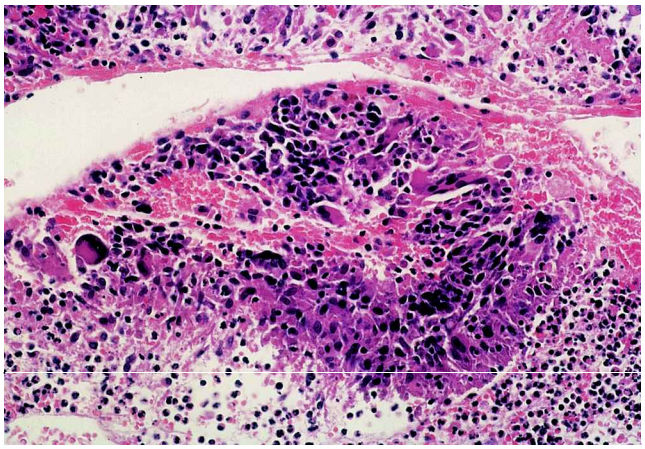

Fig. 2. Biopsy specimen showing epithelioid cell granulomas with multinucleated giant cells and neutrophilic infiltration in the dermis.

features of the present case are consistent with bilateral external chalazia. Pyogenic granuloma can be excluded because of the lack of capillary proliferation and the clinical features. Many dermatologists are not aware that chalazia, a very common ophthalmologic disease, can rupture anteriorly to produce cutaneous nodules of the eyelids. In the present case, when first confronted with the clinicopathological findings, we considered only dermatological diseases such as sporotrichosis. Since the histology of the lesion showed epithelioid cell granuloma, and active pulmonary tuberculosis was revealed, we tentatively diagnosed the present case as scrofuloderma. Retrospectively, a dimple on the palpebral conjunctiva was an indication that the lesion had adhered to the palpebral conjunctiva.

The reasons for anti-tuberculous combination chemotherapy being effective against the chalazion in the present case are probably because, first, the antibacterial activity of anti-tuberculous agents (probably rifampicin) (3) was effective as an adjunctive therapy for decreasing the local bacterial flora. Secondly, the chalazion was healed by spontaneous drainage, and anti-tuberculous agents were coincidentally introduced at the time of cure.

It is known that patients with rosacea exhibit a high incidence of chalazion formation (1). In our case, the patient suffered from alcoholic liver cirrhosis and diffuse telangiectasia was observed on the face, suggesting that the patient had rosacea.

REFERENCES

1. Bajart AM. Chalazion. In: Albert DM, Jakobiec FA, eds. Principles and practice of ophthalmology. Vol. 1, Philadelphia: W. B. Saunders, 1993: 101–103.
2. Williams HC, Aclimandos SA. Salisbury J. Bilateral external chalazia presenting as granulomas of the lower eyelids. Clin Exp Dermatol 1992; 17: 441–442.
3. Chambers HF. Antimycobacterial drugs. In: Katzung BG, ed. Basic and clinical pharmacology. 8th ed. New York: Lange Medical Books/McGraw Hill, 2001: 803–810.

Topical Tacrolimus (FK506): Treatment Failure in Four Cases of Alopecia Universalis

Sung-Wook Park, Jung-Wook Kim and Han-Young Wang
Department of Dermatology, Busan Paik Foundation Hospital, Inje University Medical College, 633-165, Kaekum-Dong, Busanjin-Ku, Busan 614-735, Korea. E-mail: alopark@hanmir.com
Accepted May 15, 2002.

Sir,

Alopecia areata is believed to be a T-cell-mediated autoimmune disease in which a mononuclear cell infiltrate develops in and around anagen hair follicles and causes circumscribed hair loss (1). Alopecia universialis and alopecia totalis are severe forms of alopecia areata. A wide range of treatments has been tried in alopecia universalis, but none is consistent in its efficacy.

Tacrolimus is the prototype of a class of topical immuno-suppressive agents with a great potential in the treatment of inflammatory skin diseases, primarily atopic dermatitis (2). Tacrolimus acts by inhibiting calcineurin, resulting in suppression of T-cell activation and inhibition of inflammatory cytokine release (2).

Recently, a number of reports have been published on the excellent effects of topical tacrolimus in experimental bald animal models, such as mice, rats, and hamsters. On the basis of those results, we tried topical tacrolimus on 4 patients with alopecia universalis.

PATIENTS AND METHODS

Four patients (2 females and 2 males, aged 17 to 27 years) diagnosed with alopecia universalis agreed to participate in a therapeutic trial of topical tacrolimus. The average duration of disease was 4.5 years (range 1–8 years) and the average period of treatment given prior to this study was 15.8 months (range 6–21 months). Previously, all 4 patients had received diphencyprone sensitizer, systemic and topical corticosteroids, and methylprednisolone pulse therapy, but all of the treatments were found to be ineffective. All treatments were stopped 3 months before this study.

Topical tacrolimus was used as a 0.1% solution or a 0.1% ointment (commercially available formulation Protopic® was unavailable in Korea at the time of the study). FK 506 (Prograf, Fujisawa Pharmaceutical Company, Osaka, Japan) in powder form was made into a 0.1% solution by dissolving 0.1 g in 56 ml ethanol

to which 24 ml distilled water and 20 ml propylene glycol were added (3). To formulate 0.1% ointment, 0.1 g FK506 powder was mixed with 100 g hydrophilic petrolatum, which is composed of white petrolatum containing 8% bleached beeswax, 3% stearyl alcohol and 3% cholesterol (4).

The two female patients were given the 0.1% solution and the 2 male patients received the 0.1% ointment. The patients were instructed to apply 0.5 ml of solution and 0.5 g of ointment twice daily to approximately 10 × 10 cm of hairless patch on the right hemisphere of their scalp for 12 weeks. A follow-up examination was carried out 6 months after treatment.

RESULTS AND DISCUSSION

No evidence of hair growth from all 4 patients treated with topical tacrolimus was observed during the 3-month application period and 6-month follow-up. Adverse effects of itching, scaling or hyperpigmentation were observed but were not severe enough to stop treatment. Laboratory routine examinations before and after treatment were normal.

Recently, reports have been published on the excellent effects of topical tacrolimus in experimental bald animal models. Freyschmidt-Paul et al. (5) have reported that FK506-treated C3H/HeJ mice with alopecia areata showed complete hair regrowth. McElwee et al. (3) have reported that topical tacrolimus is effective in hair growth and in reducing hair follicle inflammation in the Dundee experimental bald rat. Maurer et al. (6) and Jiang et al. (7) have separately reported that tacrolimus is effective in anagen induction, and catagen inhibition in experiments using C57BJ/6J mice. In their study using CD-1 mice, Syrian golden hamsters, and SCID mice, Yamamoto et al. (8) report that oral tacrolimus is ineffective in restoring hair, but that topical use of the drug led to hair growth at the site of application in all the animals. This suggested that topical tacrolimus may be effective also in alopecia areata in humans (9).

So far, there has been only one case report where 0.3% topical tacrolimus was used for 6 months to treat alopecia areata, but no evidence of hair regrowth was found (10). Similarly, we were unable to observe any induction of hair regrowth in alopecia universalis using topical tacrolimus. Possible reasons for the ineffectiveness of the drug in our study were insufficient skin penetration compared with that in experimental animals, an inadequate treatment period, and the severity of the disease in the studied patients.

REFERENCES

1. Perret C, Wiesner Menzel L, Happle R. Immunohistochemical analysis of T-cell subsets in the peribulbar and intrabulbar infiltrates of alopecia areata. Acta Derm Venereol 1984; 64: 26–30.
2. Ruzicka T, Assmann T, Homey B. Tacrolimus: the drug for the turn of the millennium? Arch Dermatol 1999; 135: 574–580.
3. McElwee KJ, Rushton DH, Trachy R, Oliver RF. Topical FK 506: a potent immunotherapy for alopecia areata? Studies using the Dundee experimental bald rat model. Br J Dermatol 1997; 137: 491–497.
4. Henderson CA, Ilchyshyn A. Successful treatment of resistant facial lesions of atopic dermatitis with 0.1% FK506 ointment. Br J Dermatol 1995; 133: 492–500.
5. Freyschmidt-Paul P, Ziegler A, McElwee KJ, Happle R, Kissling S, Sundberg JP, et al. Treatment of alopecia areata in C3H/HeJ mice with the topical immunosuppressant FK506 (Tacrolimus). Eur J Dermatol 2001; 11: 405–409.
6. Maurer M, Handjiski B, Paus R. Hair growth modulation by topical immunophilin ligands. Am J Pathol 1997; 150: 1433–1441.
7. Jiang H, Yamamoto S, Kato R. Induction of anagen in telogen mouse skin by topical application of FK506, a potent immunosuppressant. J Invest Dermatol 1995; 104: 523–525.
8. Yamamoto S, Jiang H, Kato R. Stimulation of hair growth by topical application of FK506, a potent immunosuppressive agent. J Invest Dermatol 1994; 102: 160–164.
9. McElwee KJ, Spiers EM, Oliver RF. In vivo depletion of CD8 + T cells restores hair growth in the DEBR model for alopecia areata. Br J Dermatol 1996; 135: 211–217.
10. Thiers BH. Topical tacrolimus: treatment failure in a patient with alopecia areata. Arch Dermatol 2000; 136: 124–125.