TACROLIMUS: A NOVEL APPROACH AGAINST WANDERING RASH - A PILOT STUDY

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ABSTRACT
Background: Wandering rash or geographic tongue is a common condition of tongue mucosa which frequently presents as small, irregular atrophic lesions over dorsal surface and lateral borders of tongue. It is also referred to as erythema migrans, wandering rash of the tongue, glossitis areata exfoliativa, glossitis areata migrans. Even though the disease has been known for decades, there is no definite treatment to stop its recurrence. Here, we report symptomatic recalcitrant cases of geographic tongue that were successfully treated with topical tacrolimus which is a macrolide antibiotic that acts by suppressing the release of pro inflammatory cytokines.

Materials & Methods: All the patients were screened for the presence of geographic tongue. The positive cases included both the new cases and the cases which were resistant to previous treatment therapies. Ten patients (five female and five male) were included in the study, these were subjected to topical application of 0.1% tacrolimus twice daily for about two weeks.

Result: Subjective symptoms like relief from burning sensation and objective symptoms like regression in size of lesion were noted & no exacerbation was found after the follow-up period of 2 months.

Conclusion: Though symptomatic recalcitrant cases of geographic tongue have been successfully treated with topical tacrolimus further clinical trials are needed to confirm the efficacy and the safety of tacrolimus in treating geographic tongue.

Keywords: erythema migrans, wandering rash of the tongue, glossitis areata exfoliativa, glossitis areata migrans, tacrolimus, macrolide.

INTRODUCTION

Geographic tongue (GT) is a benign condition primarily affecting the tongue. It is typically seen as reddish pink, atrophic patches on dorsum or lateral border of the tongue, that are surrounded by slightly elevated thin yellow white, circinate borders. The central smooth erythematous patch represents loss or atrophy of filiform papillae. The lesion persists for a period of time (several days or weeks) depending on the individual and disappears and migrates and reappears in other location on the tongue. This typical pattern has been linked to land masses and oceans on a map, from which synonym ‘geographic tongue was derived.1,2

The cause of geographic tongue is unknown. However, situations and conditions producing stress, including allergies, hormonal disturbances, nutritional deficiencies, psychological disturbances, Reiter’s Syndrome, and even spicy foods, are related to GT. There are also strong associations with certain other...
diseases such as psoriasis and juvenile diabetes. The association of GT with fissured tongue, which has a strong hereditary component, suggests a genetic predisposition for GT. The microscopic characteristics of GT are similar to those of psoriasis, and this leads some to consider Geographic tongue a form of psoriasis. Tacrolimus is effective against many dermatological conditions namely atopic dermatitis, vitiligo, oral lichen planus and psoriasis. There have been many reports regarding the association between geographic tongue and psoriasis. Considering the histopathological similarities between psoriasis and geographic tongue it can be tried in treatment of geographic tongue also. Here, we report our experiences of patients with tacrolimus and their responses to treatment within a period of two months.

METHOD

Tacrolimus ointment was made using tacrolimus powder with orabase. Five hundred milligrams of tacrolimus powder was mixed with three hundred grams of orabase on a clean glass slab using a stainless steel spatula under aseptic conditions to get a mixture of 0.1% tacrolimus. This preparation was then packed into plastic container so that each contained at least 20g of the medication. Ten patients for the study were selected among the subjects attending the outpatient department who were clinically diagnosed with geographic tongue which included both the new cases and the cases which were resistant to previous treatment therapies. These selected patients were then asked to use this preparation twice daily for about two weeks. [fig-1a,2a]

RESULT

At first recalled visit (after two weeks) subjective symptoms like relief from burning sensation and objective symptoms like regression in size of lesion were noted & no exacerbation was found after the follow-up period of 2 months.[fig-1b,2b]

DISCUSSION

Geographic tongue was first of all described by Reyer in 1831. Even though erythema migrans has been documented for many years, the etiopathogenesis is still unknown. Many risk factors have been proposed including hormonal disturbances and oral contraceptive use, psychological findings, diabetes mellitus, allergic conditions such as atopy, hay fever and rhinitis. HLA B-15 antigen is common in patients with geographic tongue. The typical clinical findings are well circumscribed red depapiliated areas of the dorsal aspect of the tongue delineated by an elevated whitish-yellow annulus. The microscopic appearance of psoriasis varies with lesion age and activity. The early lesion shows parakeratosis and acanthosis with budding at the tips of the rete ridges and thinning of the suprapapillary plate.

Polymorphonuclear leukocytes migrate through the epithelium with the formation of intraepithelial microabcesses. Although the formation of microabcesses (Munro abscesses) is characteristic of psoriasis, it is not specific to the disease nor are the microabcesses always present. Within the connective tissue papilla, engorgement of the capillaries occurs and a mixed inflammatory cell infiltrate is commonly seen. In the oralcavity, this microscopic presentation, known as psoriasiformmucositis, is shared by psoriasis, Reiter’ssyndrome (a disease of unknown origin characterized by the triad of urethritis, arthritis and conjunctivitis), benign migratory glossitis (also known as geographic tongue) and erythema migrans (lesions that are clinically and histologically similar to geographic tongue but involve oral mucosa other than the dorsum of the tongue).
Oral lesions of psoriasis are rare clinical observations. Early reports of intraoral psoriasis lacked microscopic confirmation of the clinical findings. As a result, the number of cases reported and the incidence of intraoral psoriasis cannot be accurately determined from the literature. Reports of oral psoriasis that are well documented show no consistent lesion pattern. Patterns range from raised, white, scaling lesions predominantly on the palate or buccal mucosa to well-demarcated, flattened, erythematous lesions with a slightly raised, white, annular or serpiginous border. These latter lesions closely resemble geographic tongue. Oral lesions may disappear quickly or they may undergo exacerbations or remissions concomitantly with skin lesions. There have been many other reports regarding the association between geographic tongue and psoriasis. Histopathological findings are parakeratosis and psoriasiform hyperplasia with neutrophilic infiltration into the epithelium. Extrapolating this histopathological similarity between geographic tongue and psoriasis, topical tacrolimus ointment may be tried to treat geographic tongue. Many other treatment modalities including use of Zinc supplements (200-220mg/day), vitamin B, steroid ointment may be applied topically for symptomatic benefits. Burning may also be reduced by taking antihistamines. But all these treatment modalities have only resulted in temporary relief and the conditions revert back. Since geographic tongue is usually asymptomatic and only rarely does significant pain develop and persist, patients do not require any treatment. Symptomatic treatment have not been evaluated rigorously. Our patients complained that the lesional pain was strong. We tried various therapies including topical steroids for their painful conditions but those treatments were not effective. Considering histological similarities between two entities i.e geographic tongue and psoriasis, we introduced topical tacrolimus ointment. Within two weeks, their troublesome condition was improved without any side effects and no exacerbation was found after the follow-up period of 2 months.

Tacrolimus is a 23-member macrolide produced by soil fungus Streptomyces tsukubaensis. The name tacrolimus is derived by taking the "t" for Mount Tsukuba (where the organism was discovered), "acrol" for macrolide and "imus" for immunosuppressant. Tacrolimus is an immunosuppressive macrolide and its anti-inflammatory action is similar to that of cyclosporine. Which involves the inhibition of interleukin 2 (IL-2) production by T-cells. Because of its high molecular weight (822.03), tacrolimus hardly penetrates through the stratum corneum when it is applied to normal skin. Since the permeability of the barrier becomes greater in the mucosa and/or in the lesional skin of inflammatory skin disorders, tacrolimus easily penetrates the barrier and exerts immunosuppressive actions after topical use. Sometimes, topical tacrolimus causes stinging at the application site, but our patients did not complain about stinging after its topical use.

**CONCLUSION**

The results of therapies on two patients are difficult to interpret because of the possibility that the observed response may merely reflect the natural course of the disease rather than the effect of the medication. However, in our cases, we believe that a real therapeutic effect took place because the persistent lesions have not recurred with topical tacrolimus. Further clinical trials are warranted to confirm the efficacy and the safety of the tacrolimus for geographic tongue.
REFERENCES

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Figure 1: Clinical photograph of 34 year old female patient showing:

a: Irregular erythematous patches and whitish elevated borders on the dorsum surface of the tongue (Before therapy)
b: Healed erythematous patches on the dorsum surface of the tongue (After therapy)
Figure-2: Clinical photograph of 46 year old male patient showing:
a: Irregular erythematous patches and whitish elevated borders on the dorsum surface of the tongue (Before therapy)
b: Healed erythematous patches on the dorsum surface of tongue (After therapy)