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Letter

Rosacea-like eruption due to topical pimecrolimus

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Abstract

Topical calcineurin inhibitors have been used outside their approved indications for a number of conditions, including topical steroid-induced rosacea. However, tacrolimus ointment itself has been reported to trigger rosacea in a small number of cases. We report a case of a rosacea-like eruption in a 39-year-old woman occurring after the use of pimecrolimus cream for 12 months for atopic dermatitis. Withdrawal of pimecrolimus combined with treatment with oral lymecycline, topical metronidazole, and an emollient resulted in resolution of the eruption. There have been 5 previously reported cases of a topical pimecrolimus-induced rosacea-like eruption suggesting that this rare side-effect may be a class effect of all topical calcineurin inhibitors. Dermatologists prescribing these drugs should be aware of this uncommon complication and may wish to warn patients of its occurrence as a potential side-effect when using topical calcineurin inhibitors in facial skin in adults.

Introduction

The calcineurin inhibitors tacrolimus and pimecrolimus are effective topical treatments for moderate to severe atopic eczema and are indicated for this condition from the age of two years. These agents have been important in decreasing the risk of topical steroid-induced cutaneous atrophy in forms of chronic dermatitis. They inhibit T-cell activation by blocking the transcription of early cytokines. Pimecrolimus inhibits interleukin (IL)-2, interferon gamma, IL-4, and IL-10 synthesis in human T-cells and the release of inflammatory cytokines and mediators from mast cells.

In recent years, calcineurin inhibitors have been used outside their approved indications for a number of conditions, including topical steroid-induced rosacea [1]. However, topical tacrolimus itself has been reported to trigger rosacea in a small number of cases and there are rare reports of topical pimecrolimus having a similar effect. We report a patient with rosacea-like eruption occurring after the use of pimecrolimus, and review the literature concerning this rare side-effect, which appears to be a class effect of all topical calcineurin inhibitors.

Case synopsis

A 39-year-old woman had been successfully treated for long-standing atopic eczema of the face and neck with 1% pimecrolimus cream once daily over a 12-month period. No topical steroid was being used and there was no previous history of rosacea. She reported increasing redness of the face after sun exposure. An erythematous papular eruption of the forehead, cheeks, chin, and jaw had gradually developed, sparing the perioral region (Figure 1). Pimecrolimus-induced rosacea was suspected and the eruption cleared with discontinuation of pimecrolimus and initiation of oral lymecycline 408mgs daily for 8 weeks, 0.75% metronidazole cream twice daily, and an emollient. Following an infected atopic dermatitis flare requiring topical and oral antibiotics, her atopic eczema was subsequently well-controlled with emollients alone. Rechallenge with pimecrolimus was considered clinically inappropriate.

Figure 1. An erythematous papular eruption of the forehead, cheeks, chin and jaw had gradually developed, sparing the perioral region

Discussion

Calcineurin inhibitors are increasingly used for the treatment of atopic eczema at thin skin sites in adults and children when there is a requirement for prolonged use of topical corticosteroids or when there is steroid phobia. Clinical studies have demonstrated the long-term efficacy of topical calcineurin inhibitors, with minimal systemic absorption and a paucity of side effects. Both pimecrolimus and tacrolimus are recommended by the manufacturers only for intermittent use when used long-term. Our patient had used pimecrolimus daily because she had found that her eczema flared if application was less frequent than this.

Adverse effects of topical calcineurin inhibitors have been well-documented, but to date, their safety profile has been favorable. Transient localized irritation is much less frequent with topical pimecrolimus than topical tacrolimus. Cutaneous viral or bacterial infection, although a contraindication to concurrent use, is uncommon with either treatment. There is a theoretical risk of increased incidence of cutaneous malignancy with long-term use of calcineurin inhibitors. However, long-term safety data have not shown any increase in incidence.

Topical tacrolimus has been reported to induce rosacea-like eruptions, with 26 reported cases in the literature since the initial report in 2003 by Bernard et al [2] .Overgrowth of Demodex folliculorum associated with localized immunosuppression, occlusive properties of the tacrolimus ointment, and vasoactive effects are thought to be the likeliest mechanisms to explain the development of tacrolimus-induced rosaceiform dermatoses [3]. Pimecrolimus, on the other hand, lacks vasoactive effects and produces less occlusion [4]. Pimecrolimus cream has been suggested as an effective treatment for spontaneous rosacea [5], for steroid-induced rosacea, and for the papulopustular eruption associated with epidermal growth factor receptor inhibitors [6]. Rosacea is mentioned as a potential rare side-effect in the summary of product characteristics (SPC) for tacrolimus ointment, but not in that for pimecrolimus cream.

There have been 5 previous reported cases of a topical pimecrolimus-induced rosacea-like eruption (Table 1) [4, 7-10]. Unlike our patient, in all five cases, the onset of the eruption was within 2 months of beginning treatment with pimecrolimus, and in 4 out of 5 it was within a week. In most cases, withdrawal of pimecrolimus and treatment with oral tetracycline and/or topical metronidazole resulted in resolution. Our patient had no previous history of rosacea and was not using any topical steroid; the eruption cleared rapidly following the discontinuation of pimecrolimus, supporting the clinical suspicion that it was the cause.

Table 1. Reported cases of rosacea-like eruption associated with topical pimecrolimus

Sex/age	Previous disease	Duration of use of pimecrolimus	Treatment	Reference
F, 43	AD	3 days	Doxycycline	Lubbe J et al [7]
M, 36	SD	4 days	Minocycline	Gorman and White[8]
F, 23	Discoid lupus erythematosus	2 months	Clindamycin, doxycycline and metronidazole	El Sayed et al [9]
M, 43	SD	7 days	Minocycline	Yoon TY et al[4]
F, 48	SD	7 days	Minocycline	Pasmatzi E et al[10]
F, 39	AD	12 months	Lymecycline and metronidazole	El-Heis S and Buckley DA

AD: atopic dermatitis; SD: seborrhoeic dermatitis

Conclusion

We would like to highlight rosacea-like eruptions as a potential complication of topical calcineurin inhibitors, including pimecrolimus. Dermatologists prescribing these drugs should be aware of this uncommon complication. When prescribing calcineurin antagonists to use on the face, prescribers may wish to advise patients of the possibility of a papular rosacea-like eruption and should remind patients to avoid continuous use.

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