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Keratosis pilaris rubra successfully treated with topical sirolimus: Report of a case and review of the literature

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Abstract

Keratosis pilaris rubra (KPR) is a subtype of keratosis pilaris (KP) presenting with numerous "grainlike" follicular papules in a background of confluent erythema most often affecting the face and upper extremities with persistence beyond puberty. Treatment has remained challenging with inconsistent benefit from topical therapies such as emollients, keratolytics, corticosteroids, and retinoids, though case reports documenting success with pulsed dye laser therapy have been found. We present a case of KPR in a 15-year-old boy who was successfully treated with topical sirolimus 1% cream.

KEYWORDS
adolescent, face, keratosis pilaris, sirolimus, topical administration

1 | INTRODUCTION

Keratosis pilaris rubra (KPR) is a clinical variant of keratosis pilaris (KP) classically described as having numerous "grainlike" follicular papules within a background of confluent erythema. It is usually located on the face, trunk, and outer upper extremities. It is differentiated from erythromelanosis follicularis faciei et colli by its erythema and from keratosis pilaris atrophicans by its lack of atrophy. No gold standard of treatment was found, and topical therapies including emollients, keratolytics (urea, lactic acid, and salicylic acid), retinoids, corticosteroids, and vitamin-D analogs are often ineffective.[1] More recently, several case reports of improvement with pulsed dye laser are found.[2,3] Herein, we present a case of KPR in a 15-year-old boy successfully treated with topical sirolimus 1% cream.

2 | CASE REPORT

A healthy 15-year-old Caucasian boy with a history of atopic dermatitis presented for evaluation of persistent and worsening erythema and small bumps on the cheeks, neck, and upper extremities associated with a burning sensation. His condition was worse with exposure to wind and with flushing. He had previously been diagnosed with keratosis pilaris and trialed ammonium lactate 12% lotion and tretinoin 0.1% microsphere gel without any improvement. Physical examination showed small, monomorphic papules with surrounding prominent erythema and some telangiectases coalescing into large erythematous vascular patches on the bilateral cheeks extending down the lateral neck (Figure 1A,B). A similar appearing eruption was present on his bilateral arms and legs. Due to recent reports describing the use of topical sirolimus in the setting of superficial vascular anomalies, and reports of successful treatment of KPR with pulsed dye laser, it seemed reasonable to consider KPR as a mild superficial vascular anomaly, and so we decided on a novel approach to treatment with the use of topical sirolimus 1% cream.[2,4] This was prescribed with twice daily application to the affected areas on the face and neck. This medication was dispensed through a compounding pharmacy.

Eighteen months later, the patient returned for follow-up with near complete resolution of his facial and neck erythema as well as

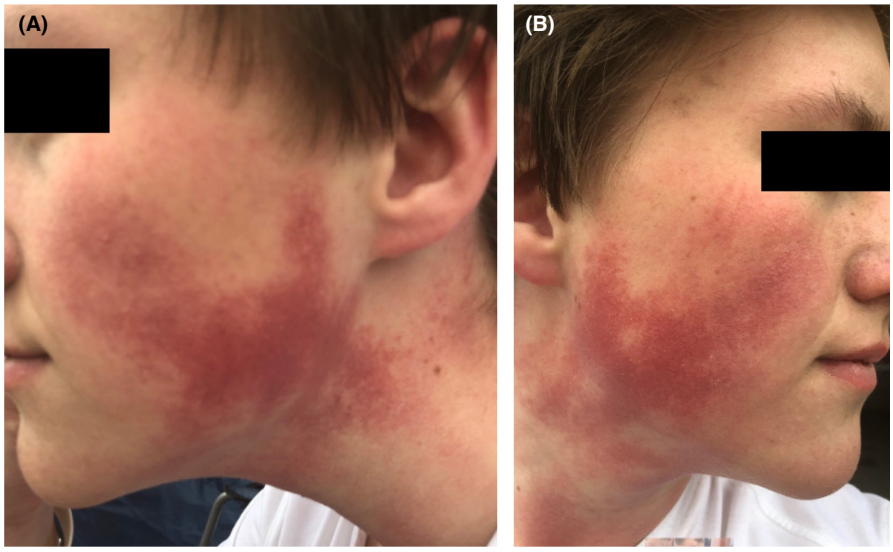

FIGURE 1 (A, B) The patient's cheeks and neck demonstrating small, monomorphic papules coalescing into large, red-purple vascular patches consistent with a diagnosis of keratosis pilaris rubra

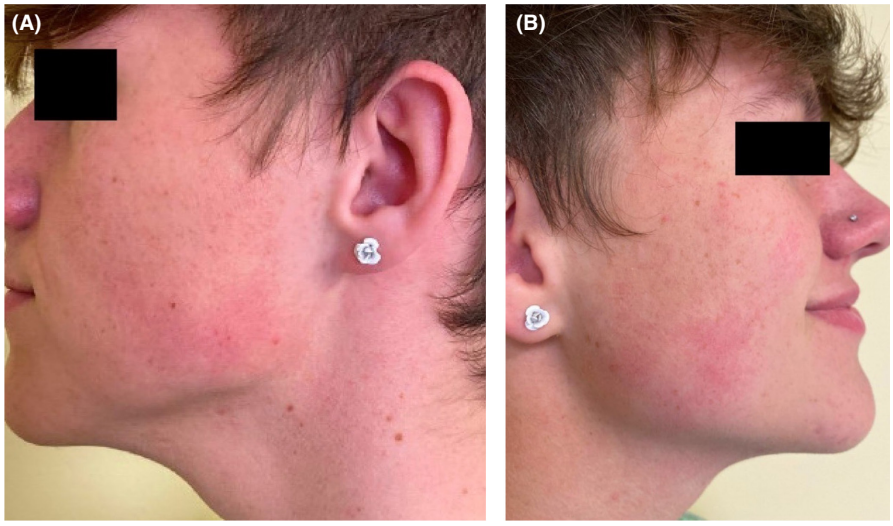

FIGURE 2 (A, B) The patient's cheeks after 2 months of twice daily topical sirolimus therapy followed by 14 months of daily application. The patient reported that the painful burning sensation resolved in addition to his facial redness

the associated burning symptoms (Figure 2A,B). He reported noticeable improvement after 2 months of twice daily application and had been able to sustain these results with once daily application to the face for the past several months. He reported no adverse effects. At this visit, serum sirolimus level was obtained and revealed systemic absorption of <3 ng/ml, which is considered clinically insignificant. Patient was advised to trial discontinuation of topical sirolimus cream to the face and begin treatment of the arms with plan for close follow-up.

3 | DISCUSSION

Keratosis pilaris rubra is an underrecognized variant of KP with more pronounced erythema and tendency for persistence beyond puberty. The pathophysiology is incompletely understood but felt to be due to abnormal keratinization of the follicular epithelium with resultant inflammation. It is often bothersome for patients both cosmetically and due to burning and stinging sensations. Unfortunately, treatment is challenging with inconsistent improvement from topical therapies including emollients, keratolytics, corticosteroids, vitamin-D analogs, and retinoids. To date, the most effective treatment based on case reports is pulsed dye laser (PDL). The effectiveness of PDL treatment is possibly due to apoptosis of vascular endothelial cells along with a subsequent decrease in vascular endothelial growth factor levels.[2,3]

Sirolimus is a macrolide compound derived from *Streptomyces hygroscopicus* with significant antitumor/antiproliferative and immunosuppressive properties. It is commonly used for the prevention of allograft rejection in organ transplant patients. Sirolimus interacts with intracellular binding protein FK to form a sirolimus:FKBP complex. These complexes lead to the suppression of mTOR expression, thereby halting the progression of the cell cycle from the G1 to the S phase in numerous cell types.[5] We postulate that similar to systemic sirolimus, topical administration leads to local inhibition of vascular

smooth muscle and endothelial cell proliferation as well as reduced focal inflammation.[6]

Systemic sirolimus has been used for many indications, including as an off-label treatment to slow the progression of plexiform neurofibromas in neurofibromatosis type 1. It has also been reported as a potential off-label treatment for scleromyxedema, dermatomyositis, graft-vs.-host disease, and Kaposi's sarcoma. Pediatric dermatologists may use systemic sirolimus in the management of vascular tumors and malformations.[7] Recently, topical sirolimus 0.2%–1% has been reported as a safe and effective treatment for facial angiofibromas in tuberous sclerosis, and it is emerging as a topical therapy for a variety of vascular anomalies.[4]

A previous systemic review assessing the efficacy and safety of sirolimus in the treatment of vascular anomalies found that of those patients treated with either topical or oral sirolimus, only those who received oral sirolimus experienced adverse side effects.[8] These side effects included oral mucositis, dyslipidemia, leukopenia, and subsequent infectious complications. This review also found that of the 56 patients receiving topical sirolimus, only two were reported to have detectable blood levels. Both of these patients were noted to have capillary malformations, and no reported change in management as a result of these findings was found.[8] It is unclear whether regular lab monitoring is warranted in patients using topical sirolimus. We advise deferring to clinician judgment for monitoring serum concentrations when prescribing topical sirolimus for KPR. Elements including, but not limited to, severity of erythema, body surface area involved, application frequency, and patient characteristics should be considered.

The potential uses for topical sirolimus cream appear to be increasing over time. In our case, topical sirolimus was very effective in reducing the erythema and symptoms related to KPR for over 1 year without any side effects. Further research is needed with regard to establishing efficacy and treatment protocols. However, this case provides initial support for the use of topical sirolimus as a novel, well-tolerated treatment for KPR.

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None.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

CONSENT STATEMENT

Informed consent for submission was obtained from the patient and his parent.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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