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Case report

Conjunctival squamous papilloma refractory to interferon α-2b in a patient on systemic immunosuppression (tacrolimus)

Preethi S. Ganapathy [a], Thomas Plesec [b], Arun D. Singh [a, *]

[a] Cole Eye Institute, Cleveland Clinic, Cleveland, OH, USA
[b] Pathology Institute, Cleveland Clinic, Cleveland, OH, USA

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ABSTRACT

Purpose: To describe a case of diffuse conjunctival papilloma in an immunocompromised individual on tacrolimus that was refractory to treatment with interferon α-2b, but responded to topical mitomycin-c.
Observations: A 79-year-old Caucasian female with a history of a liver transplant twenty years ago, who was immunosuppressed with tacrolimus (2 mg daily) presented with a diffuse conjunctival and corneal squamous papilloma. Following treatment with four weekly subconjunctival interferon-α2b injections (3 million units/0.5 mL) and 3 months of topical interferon-α2b therapy (1 million units/mL), four times daily, slow progression was documented. The patient was switched to topical mitomycin-c drops (0.04%) administered four times daily (one week on and one week off) with dramatic regression of the tumor.
Conclusions and importance: In cases of conjunctival squamous papilloma that do not respond readily to topical interferon, topical mitomycin-c is an alternate therapeutic option. We hypothesize that use of tacrolimus may have contributed to the lack of response to topical interferon-α2b.

1. Introduction

Conjunctival squamous papilloma is a benign tumorous growth of the conjunctival epithelium.[1] It is strongly associated with human papilloma virus infection.[1] Although squamous papilloma carries minimal risk of malignant transformation, treatment is recommended for larger papillomas, as they can cause irritation.[1] Traditional treatment involves the no-touch technique of surgical excision with cryotherapy to prevent viral dissemination,[2] and larger or recurrent papillomas are treated with supplementary topical interferon-α, mitomycin-c, or oral cimetidine.[1] Herein, we describe a case of diffuse conjunctival papilloma in an immunocompromised individual on tacrolimus that was refractory to treatment with interferon α-2b, but responded to topical mitomycin-c.

2. Case report

A 79-year-old Caucasian female presented to the oncology service for evaluation of a conjunctival lesion of the right eye. She complained of intermittent redness of the right eye for the last year, and intermittent blurring of vision in the affected eye for the last two months. Prior to the onset of these symptoms, her last eye exam was over seven years ago. Past medical history was significant

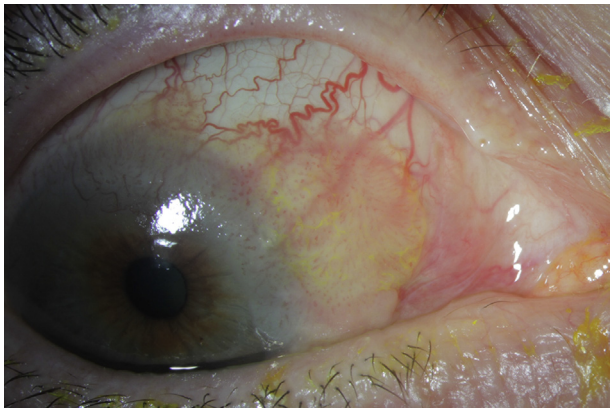

Fig. 1. Photograph of right eye, demonstrating size and characteristics of conjunctival papilloma on initial presentation. Lesion with limbal involvement from 11 to 4 o'clock, corneal involvement from 11 to 4 o'clock, and conjunctival involvement from 11 to 12 o'clock and 1–4 o'clock.

* Corresponding author. Cole Eye Institute, Cleveland Clinic, 9500 Euclid Ave., Cleveland, OH 44195, USA.
E-mail address: singha@ccf.org (A.D. Singh).

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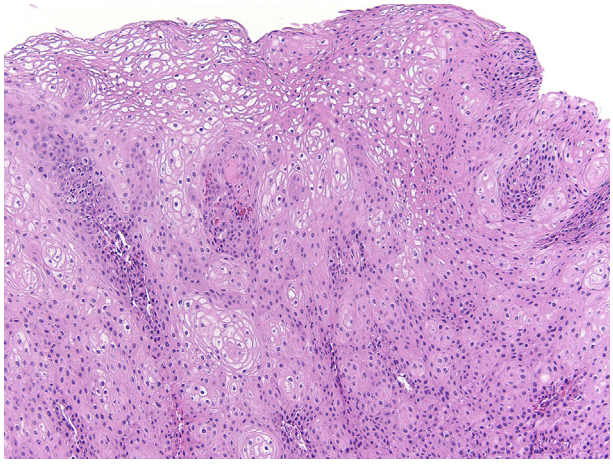

Fig. 2. Histopathology demonstrated a papillary squamoproliferative lesion characterized by acanthotic squamous epithelium and fibrovascular cores. No goblet cells were present within the lesion. Features of high-grade dysplasia such as full-thickness basaloid population lacking orderly maturation were not identified. (Hematoxylin and eosin, 100x).

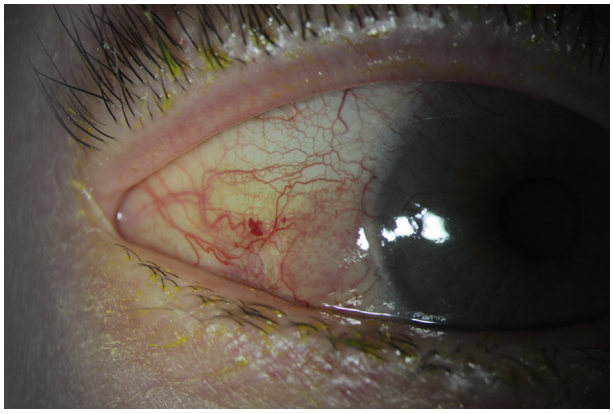

Fig. 3. Progression of conjunctival papilloma despite extended treatment with interferon-α2b, with extension nasally.

for a liver transplant twenty years ago following liver failure due to primary biliary cirrhosis; she was immunosuppressed with tacrolimus (2 mg daily).

On presentation, visual acuity was 20/70 in the right eye, and intraocular pressure was normal. Anterior segment examination revealed a flesh-colored lesion involving the limbus from eleven to four o'clock, with associated corneal involvement from eleven to four o'clock, and bulbar conjunctival involvement from eleven to twelve o'clock and from one to four o'clock (Fig. 1). Clinical diagnosis of diffuse squamous papilloma of the conjunctiva and cornea was confirmed by incisional biopsy (Fig. 2).

Treatment with four weekly subconjunctival interferon-α2b injections (3 million units/0.5 mL administered immediately beneath the lesion, compounded at institutional pharmacy) was initiated followed by 3 months of topical interferon-α2b therapy (1 million units/mL), four times daily in the affected eye. At the three-month visit, a new, previously undetected, area of conjunctival and limbal involvement was noted temporally (Fig. 3). Given progression on interferon-α therapy, the patient was switched to topical mitomycin-c drops (0.04%) administered four times daily (one week on and one week off as per our standardized protocol) with punctual plug placement. The patient was seen following completion of cycle #1 and marked improvement in the temporal lesion was observed. The decision was made to continue the patient on three additional cycles of mitomycin-c. Six months following initial diagnosis, the patient demonstrated complete resolution of squamous papilloma without evidence of ocular surface toxicity (Fig. 4). Topical drops of interferon- α2b and mitomycin-c were used off-label for the treatment of squamous papilloma and were in accordance with our ethics committee. Appropriate informed consent was obtained prior to giving the medications.

3. Discussion

In cases of diffuse conjunctival squamous papilloma that are not amenable to resection alone, topical therapy with interferon-α2b or mitomycin c, has been shown to be effective.[3–6] The primary mechanism of action of interferon-α2b involves activation of T cells and sensitization of the host immune system against the aberrant

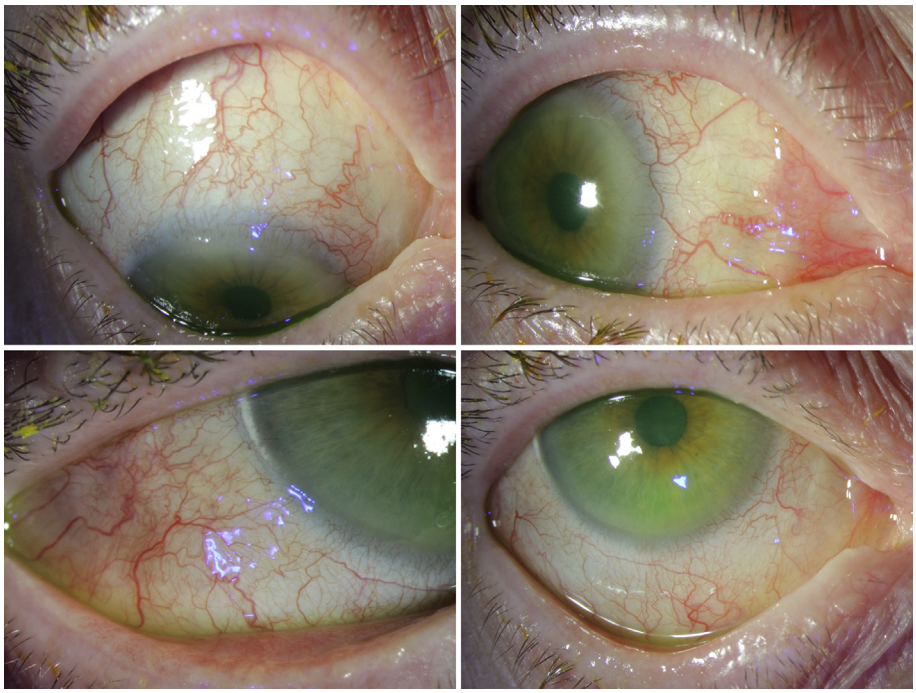

Fig. 4. Complete regression of conjunctival papilloma 6 months following four cycles of topical mitomycin c therapy.

cells.[7] In several reported cases complete regression of the papilloma using intralesional and topical interferon-α2b has been documented.[8,9] Mitomycin c, on the other hand, functions as a DNA alkylating agent, and directly disrupts rapid cell proliferation.[10] Two reports describe its use as adjunctive therapy for recurrent papilloma.[5,6] Despite its potency, mitomycin c is not often selected as a first-line therapy due to its larger side effect profile including surface irritation, limbal stem cell deficiency, and canalicular stenosis.[1] Our immunocompromised patient was on oral tacrolimus, an agent that functions via suppression of T cell proliferation and activation.[11] One report asserts that tacrolimus directly inhibits the interferon-signaling pathway in human hepatocyte cells.[12]

4. Conclusions

In our case of conjunctival squamous papilloma that did not respond readily to topical interferon-α2b, we hypothesize that concomitant use of tacrolimus may have contributed to the lack of response.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Conflict of interest

The following authors have no financial disclosures: (PG, TP, AS).

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