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# Topical interferon Alpha-2b in refractory limbal vernal keratoconjunctivitis: A case report

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**Abstract**---Purpose: To report our experience of managing a steroid resistant limbal vernal keratoconjunctivitis (VKC) by topical interferon alpha-2b (IFN- $\alpha$ 2b) eye drops. Methods: Case report Results: A 20-year-old man was referred to our cornea clinic with the chief complaints of itching and photophobia in eyes and foreign body sensation, redness, and ptosis in a both eyes. He had a 10-year history of gradually enlarging limbal gelatinous masses on both eyes, which according to the other signs and impression cytology (IC) was diagnosed as a VKC. As the disease in his left eye was more severe and persistent with maximum topical steroid usage, we started the topical IFN- $\alpha$ 2b eye drops, that a rapid therapeutic response was observed. After three months of using the topical IFN- $\alpha$ 2b all ocular surface inflammation and other symptoms rapidly disappeared and we continued this drug till another 3 months, at 12-months follow-up, there was no recurrence of the limbal papillary hypertrophic lesions and other signs and symptoms of VKC. Conclusion: In a refractory VKC, topical IFN- $\alpha$ 2b can be used and enhance remission in such complex cases and can resolve patient's complains rapidly.

**Keywords**--- *Vernal keratoconjunctivitis, Interferon alpha-2b, Steroid resistant vernal keratoconjunctivitis.*

**Introduction**

Vernal keratoconjunctivitis (VKC) is a seasonal bilateral chronic allergic inflammatory disease of the ocular surfaces, mainly occurring in children and adolescents living in dry and temperate regions. Itching, photophobia, tearing, and mucoid discharge may occur in patients with VKC. Superior tarsal and limbal papillae, conjunctival hyperemia, and corneal involvement in the form of punctate epithelial keratitis, epithelial macroerosions, shield ulcers, plaque formation, and corneal neovascularization are also observed (1).

Corticosteroids still remain the mainstay of therapy for anterior segment inflammation and are the most widely used topical anti-inflammatory drugs. However, unwanted ocular side effects such as glaucoma and cataract often preclude their use on a chronic basis. Calcineurin inhibitors such as cyclosporine A and tacrolimus are now commonly used as “steroid-sparing” topical agents to prevent and treat diseases with T-cell-mediated pathophysiology treatment of most cornea and ocular surface diseases (2-4). To avoid steroid-related complications, and in resistance cases, immunomodulatory agents such as topical cyclosporine A and tacrolimus have recently been used for the treatment of VKC, tacrolimus is a drug that suppresses the immune system and has a many application in the ocular surface and corneal chronic inflammations. (3,5-6)

In a recalcitrant case of VKC, use of other immunosuppressant may be the optimal method. Interferons are a group of natural proteins that act as immunomodulatory agents. Tacrolimus in multiple studies and interferon alpha-2b (IFN alpha-2b) in a few studies have been successfully used for treatment of such cases (7). In one comparative study 2 immunomodulatory agents, tacrolimus and IFN- $\alpha$ 2b compared in the treatment of VKC that had an equal effect in that's therapeutic effects. (8) In this case report, we study a case of recalcitrant limbal VKC that properly managed with topical IFN- $\alpha$ 2b eye drops.

### **Case Report**

The patient was a 20 years-old man with a complaint of decreased vision, ocular burning, and photophobia in both eyes since 10 years ago that referred to our cornea clinic. His complains was aggravated since last 2 years. The past medical history was unremarkable. He was under medical treatment by topical steroids for a long time, but his complains aggravated despite these medications. On slit-lamp biomicroscopy, bilateral limbal papillary hypertrophic and nodular lesions were seen. (Figure 1)

The differential diagnosis of limbal nodules may have many categories of allergic, inflammatory, infectious, and neoplastic diseases (9). Our approach for confirming the diagnosis was obtaining impression cytology (IC). Impression cytology specimens were taken from both cornea and tarsal conjunctiva. Some goblet cells and many eosinophils could be seen on IC. According to this finding of IC, the diagnosis was the vernal keratoconjunctivitis with a hypertrophic limbal papillary reaction. The presence of some goblet cells in IC represented to some degree of stem cell damage in this case. Findings were documented using digital corneal photography (Imagenet; Topcon SL-8Z, Tokyo, Japan) at all follow-up visits. All risks and benefits were clearly explained, and informed consent was obtained from the patient.

The patient had a history of long-time treatment with topical antihistamines, mast cell stabilizers, and steroids that had not a marked improvement. This allergic inflammatory reaction was resistant to steroid therapy that previously prescribed and we used for another 2 weeks without any improvement in his conditions. We used the IFN- $\alpha$ 2b eye drops every 6 hours that continued for 6 months. After 3 months treatment, all signs and symptoms were reduced and the

limbal papillary hypertrophy were regressed and maintained until 12 months follow-up time.

In this study, 1,000,000 IU/mL IFN alpha-2b ophthalmic preparations were used for topical treatment. It was prepared with a dilution of 3,000,000 IU/mL IFN alpha- 2b solution (3 MIU/cc PDferon-B; Pooyesh Daru Co, Iran) in artificial tears (Tear lose; Sinu Daru Co, Iran). It should be stored in 2–8°C.

## **Discussion**

Clinically, there are three forms of vernal keratoconjunctivitis: palpebral, limbal and mixed. The palpebral form is characterized by polygonal, flat-topped, giant cobblestone papillae of the superior tarsal conjunctiva. The limbal form is less common and marked by a broad, thickened, opacification of the superior limbus. The tissue is composed of lymphocytes, plasma cells, macrophages, basophils and a high level of eosinophils. The characteristic Horner-Trantas dots are white dots of eosinophils and epithelial debris. There is corneal involvement in half of the cases that range from punctuate epithelial keratitis to superficial pannus to corneal shield ulcers. Corneal ulcers are observed in 10% of patients. The diagnosis of VKC is made clinically, based on history and ocular examination. Conjunctival scrapings, exhibiting eosinophils can help confirm, but is not necessary, for diagnosis. (1,2) Increased size of papillae and the long time bulbar form of inflammation exhibit poorer prognosis and result in a higher complication rate such as limbal stem cells deficiency (LSCD). (10,11)

In VKC despite its name, the disease can be frequently present all year round. VKC was shown to be not solely IgE-mediated, but its pathogenesis is multifactorial, mediated by Th2 lymphocytes, eosinophils, IgE, mast cells, and a complex network of interleukins and cell mediators. In most cases, the clinical course of VKC is self-limiting and may disappear following puberty. Some long standing limbal VKC patients will face sight-threatening complications, which are mainly due to corneal involvement and LSCD (1,11) like our patient who had some goblet cells in the impression cytology that represented as partially LSCD.

For the treatment of VKC, a variety of medications have been used which include antihistamines, mast-cell stabilizers, and non-steroidal anti-inflammatory drugs. Topical steroids are the mainstay of treatment for moderate to severe forms of VKC. Some cases, however, remain still symptomatic despite treatment with topical steroids. Prolonged use of topical steroids may be associated with various complications, such as glaucoma, cataract, and secondary infections. In refractory cases and to avoid steroid-related complications, immunomodulatory agents such as topical cyclosporine A, tacrolimus and IFN alpha- 2b have recently been used for the treatment of VKC. (7,12)

Topical tacrolimus 0.05% can help in reducing corticosteroid usage and is a safe and effective alternative for the treatment of resistant VKC. (10) In our case that was resistant to topical steroids, we used the topical IFN alpha- 2b ophthalmic eye drops that well tolerated and rapidly subsided the inflammation and shrinkages the limbal papillary hypertrophy. (14-16)

IFN alpha-2b is a type of IFN considered to be an immunomodulatory cytokine. The efficacy of topical IFN drops in the treatment of ocular diseases such as pterygium has been evaluated. (12,13)

Recently, Turan-Vural et al showed good efficacy and safety of short-term treatment with IFN alpha-2b in treatment of resistant VKC. The result of this study is compatible to our result. In this study although most of the beneficial effects achieved were during the 2-month treatment with IFN alpha-2b, they were maintained after discontinuation of the treatment until 6 months. They concluded that the use of IFN alpha-2b could be considered as a promising treatment for short-term therapy (7). In another comparative study 2 immunomodulatory agents, tacrolimus and IFN- $\alpha$ 2b compared in the treatment of VKC that had an equal effect in that's therapeutic effects (8).

In our patient, the limbal lesion was due to an allergic inflammatory process that was diagnosed according to clinical presentations and IC. The limbal inflammation in limbal VKC should be controlled as soon as possible especially in steroid resistant cases that IFN alpha-2b is the one of proper toll in these situations. In our case, papillary hypertrophic lesions completely healed after 3-months of topical IFN- $\alpha$ 2b treatment. Ultimately the cornea was clear without any conjunctivalization. We observed that the topical IFN- $\alpha$ 2b is so effective in the steroid-resistant VKC and effective in alleviating signs and symptoms of severe VKC that was refractory to topical steroid treatment. This indicated that IFN- $\alpha$ 2b is more available and cheaper than topical tacrolimus in the treatment of recalcitrant VKC.

In conclusion, in a refractory VKC, topical IFN- $\alpha$ 2b can be used to enhance remission in such complex cases and can resolve patient's complains rapidly.

**Consent:** The patient signed informed written consent before the preparation of the current case report.

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**Conflict of interest:** None

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**Ethics statement:** The ethics committee of Guilan University of Medical Science approved this study.

## References

- Sangwan VS, Jain V, Vemuganti GK, Murthy SI. Vernal keratoconjunctivitis with limbal stem cell deficiency. Cornea. 2011 May; 30 (5):491-6.*  
*Kheirkhah A, Zavareh M, Farzbod F, Mahbod M, Behrouz MJ. Topical 0.005% tacrolimus eye drop for refractory vernal keratoconjunctivitis. Eye (Lond) 2011;25:872-880.*

- Baradaran-Rafii A, Akbari M, Shirzadeh E, Shams M. Single block conjunctival limbal autograft for unilateral total limbal stem cell deficiency. *J Ophthalmic Vis Res* 2015;10:90-2.
- Mackensen F, Max R, Becker MD. Interferon therapy for ocular disease. *Curr Opin Ophthalmol*. 2006;17:567–573.
- Esquenazi S. Treatment of early pterygium recurrence with topical administration of interferon alpha-2b. *Can J Ophthalmol*. 2005;40:185–187.
- Iosseliani DG, Boshia NS, Sandodze TS, Azarov AV, Semitko SP. The effect of revascularization of the internal Carotid artery on the Microcirculation of the eye. *J. Adv. Pharm. Educ. & Res | Apr-Jun*. 2020;10(2):209-214
- Alattas OA, Hamdi AA, Mudarba FM, Alshehri AM, Al-Yahya MS, Almotairi SA, Saeed RA, Buamer MM, Alsuwailem MS, Alamri IA. Red Eye Diagnosis and Management in Primary Health Care. *Arch. Pharm. Pract*. 2019 Jul 1;10(3).1-5
- Dhyani A, Kumar G. A New Vision To Eye: Novel Ocular Drug Delivery System. *Pharmacophore*. 2019 Apr 1;10(1):13-20.
- Suryasa, I. W., Rodriguez-Gámez, M., & Koldoris, T. (2021). The COVID-19 pandemic. *International Journal of Health Sciences*, 5(2), vi-ix. <https://doi.org/10.53730/ijhs.v5n2.2937>
- Ghasemi H, Djalilian A. Topical Calcineurin Inhibitors. *J Ophthalmic Vis Res* 2019;14:398–399.
- Akbari M, Moghadam RS, Elmi R, Nosrati A, Taghiabadi E, Aghdami N. Adjunctive Tacrolimus for Herpetic Stromal Keratitis. *J Ophthalmic Vis Res* 2019; 14: 400–411.
- Shoughy SS. Topical tacrolimus in anterior segment inflammatory disorders. *Eye Vis (Lond)*. 2017;4:7.
- Akpek EK, Dart JK, Watson S, Christen W, Dursun D, Yoo S, et al. A randomized trial of topical cyclosporine 0.05% in topical steroid-resistant atopic keratoconjunctivitis. *Ophthalmology* 2004;111:476–482.
- Chatterjee A, Bandyopadhyay S, Bandyopadhyay SK. Efficacy, Safety and Steroid-sparing Effect of Topical Cyclosporine A 0.05% for Vernal Keratoconjunctivitis in Indian Children. *J Ophthalmic Vis Res* 2019;15–21.
- Turan-Vural E, Acar BT, Acar S. The efficacy of topical interferon alpha 2b treatment in refractory vernal keratoconjunctivitis. *Ocul Immunol Inflamm*. 2012;20:125–129.
- Zanjani H, Aminifard MN, Ghafourian A, Pourazizi M, Maleki A, Arish M, et al. Comparative Evaluation of Tacrolimus Versus Interferon Alpha-2b Eye Drops in the Treatment of Vernal Keratoconjunctivitis: A Randomized, Double-Masked Study. *Cornea* 2017;36:675–678.
- Akbari M, Elmi R. Herpes Simplex Virus and Human Papillomavirus Coinfections in Hyperimmunoglobulin E Syndrome Presenting as a Conjunctival Mass Lesion. *Case Reports in Medicine* 2017: Article ID 1650841.

Figure 1. Severe limbal papillary hypertrophy before treatment with interferon alpha-2b eye drops



Figure 2. Limbal papillary hypertrophy shrinkage after treatment with topical interferon alpha-2b eye drops, (A) at a baseline, (B) 7 days, (C) 14 days, (D) 28 days, (E) 2 months, and (F) 3 months after treatment

