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The Effect of Topical Interferon Alpha-2b in Refractory Limbal Vernal Keratoconjunctivitis: A Case Report

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ABSTRACT

Purpose: Reporting our results on the management of a steroid-resistant limbal vernal keratoconjunctivitis (VKC) by topical interferon alpha-2b (IFN-∝2b) eye drops.

Methods: Case report.

Results:A 20-year-old man was admitted 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-∝2beye drops, thata rapid therapeutic response was observed.Afterthree months ofusing the topical IFN-∝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 symptoms and signs of VKC.

Conclusion: In a refractory VKC, topical IFN-∝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 ocular disorder, which is mostly observed in low-aged cases and in areas with mild temperature and dry weather.Pruritus, photophobia, tearing, and mucoid depletion may be seen in cases with VKC. Also, clinical presentations such as superior tarsal and limbal papillae, conjunctival hyperemia, and corneal involvement in the form of punctate epithelial keratitis, macroerosions, shield ulcers, plaque formation, and corneal neovascularization are reported in these patients. [1].

The major medication for the treatment of anterior segment inflammation is the use of corticosteroids and the topical use of these drugs is still one of the main therapy methods for inflammation, but undesirable ocular complications including glaucoma and cataract usually inhibit the chronic use of them.Cyclosporine A and tacrolimus, which have calcineurin inhibiting effect, are now widely used as "steroid-sparing" topical drugs for the prevention and treatment of diseases with T-cell-mediated pathophysiology and most cornea and ocular surface disorders [2-6]. To avoid steroid-related complications, and in resistance cases,immunomodulator drugs including 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 many applications in the ocular surface and corneal chronic inflammations. [3, 7-10].

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 [11]. In one comparative study 2immunomodulatory agents, tacrolimus and IFN-∝2b compared in the treatment of VKC that had an equal effect in that's therapeutic effects.[12]In the present case report, a case of recalcitrant limbal VKC that properly managed with topical IFN-∝2b eye drops was studied.

Case Report

The patient was a 20 years-old man with a complaint of reduced vision, ocular burning, and photophobia in both eyes since10 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

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and nodular lesions were seen. (Figure 1).

The differential diagnosis of limbal nodules may have many categories of allergic, inflammatory, infectious, and neoplastic diseases [13]. 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.Results were recorded using digital corneal photography (Imagenet; Topcon SL-8Z, Tokyo, Japan) during follow-up period. 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-∝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 preparationswere 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

Clinical forms ofvernal keratoconjunctivitis include palpebral, limbal and mixed. The palpebral form is specified by polygonal, flat-topped, giant cobblestone papillae of the superior tarsal conjunctiva. The limbal form is less usual and specified by a broad, thickened, opacification of the superior limbus.The tissue is formed of lymphocytes, plasma cells, macrophages, basophils, and a great number of eosinophils. The specific Horner-Trantas dots are white dots of eosinophils and epithelial debris. Corneal disorders can be seen in 50% of patients that range from punctuate epithelial keratitis to superficial pannus to corneal shield ulcers.Ten percent of cases show signs of corneal ulcers. The clinical diagnosis of VKC is performed considering the records of the patient and ocular examination. Conjunctival scrapings and exhibiting eosinophils can help acknowledge, however, they are not necessarily required for diagnosis.The enlarged size of papillae and the long time bulbar form of inflammation demonstrate a less favorable prognosis and induce further complications such as limbal stem cell deficiency (LSCD).[14, 15]

Contrary to its name, VKC disease can be regularly observed in all seasons. Although this disease was reported to be not singly IgE-mediated, 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 andLSCD [1, 15, 16]like our patient who had some goblet cells in the impressioncytology that represented as partially LSCD.

For the therapy of VKC, various drugs have been prescribed such as antihistamines, mast-cell stabilizers, and non-steroidal anti-inflammatory medications.The major therapeutic method is the use of topical steroids for moderate to severe cases of VKC; but some patients can still be seen with symptoms, in spite of therapy with topical steroids. Chronic consumption of steroids can be related to several side effects including glaucoma, cataract, and secondary infections. In order to elude these side effects in refractory cases, immunomodulator drugs such as topical cyclosporine A,tacrolimus and IFN alpha- 2b have formerly been consumed. [11, 17].

Topical tacrolimus 0.05% can be helpfulin decreasing the use of corticosteroids and is anefficient alternative for the treatment of resistant VKC, with lower complications.[14]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 shrinkagesthe limbalpapillary hypertrophy.

IFN alpha-2b is a type of IFN considered to be an immunomodulatory cytokine. The efficacy of topical IFN drops in the therapy of ocular disorders such as pterygium has been evaluated.[17, 18].

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Recently, Turan-Vural et alshowed good efficiency and safety of short-term therapy 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 favorable effects achieved were during the 2-month therapy with IFN alpha-2b, they were sustained after thecessation of therapy until 6 months. They concluded that the use of IFN alpha-2b could be considered as a promising treatment for short-term therapy[11].In another comparative study 2 immunomodulatory agents, tacrolimus and IFN-∝2b compared in the treatment of VKC that had an equal effect in that's therapeutic effects [12].

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-∝2btreatment. Ultimately the cornea was clear without any conjunctivalization. We observed that the topicalIFN-∝2bis so effective in the steroid-resistant VKC and efficient in alleviating signs and symptoms of severe VKC that was refractory to topical steroid treatment.This indicated that IFN-∝2b is more available and cheaper than topical tacrolimus in the treatment of recalcitrant VKC.

In conclusion, in a refractory VKC, topical IFN-∝2bcan be used to enhance remission in such complex cases and canresolvepatient's complains rapidly.

Consent

Written informed consent was obtained from the patient before the preparation of this case report.

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

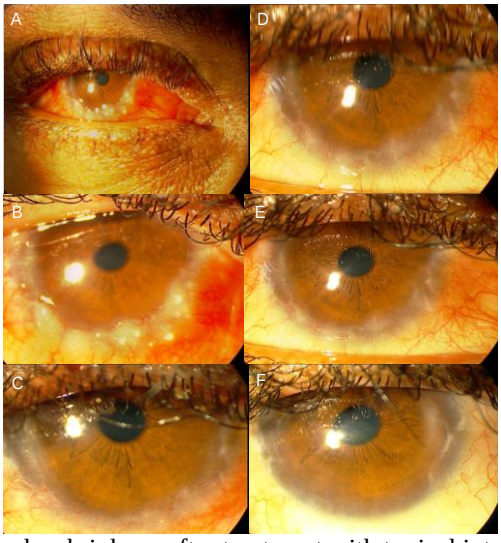

Figure 2. Limbal papillary hypertrophy shrinkage after treatment with topical interferon alpha-2b eye drops, (A) at a baseline, (B) 7 days, (C) 14 days, (D) 28 days, (E) 2 months, and (F) 3 months after treatment

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