

Successful Management of Conjunctival Intraepithelial Neoplasia by Interferon α -2b

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Background: Interferon α -2b (IFN α 2b) was recently shown to be effective as an alternative therapy for conjunctival intraepithelial neoplasia (CIN). Herein, we report our successful management of CIN by the use of IFN α 2b.

Case: A 73-year-old woman presented with a complaint of irritation due to a tumorous lesion in her left eye. Slit-lamp microscope examination revealed a tumorous lesion involving the bulbar and palpebral conjunctiva as well as the limbus, from the 3-o'clock position to the 8-o'clock position. She had already undergone cryotherapy in the same eye in another hospital, twice for a lesion on the lower tarsal conjunctiva and once for a lesion on the upper tarsal conjunctiva. The histological diagnosis had been CIN.

Observations: In treating this patient, IFN α 2b was injected subconjunctivally twice and also applied as eye drops for 12 weeks. Two weeks after the initial treatment, the tumorous lesion disappeared. During a 1-year follow-up period, no recurrence was noted.

Conclusion: Topical and subconjunctival IFN α 2b is a valuable treatment option for CIN.
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Key Words: Conjunctival intraepithelial neoplasia, interferon α -2b.

Introduction

Conjunctival intraepithelial neoplasia (CIN) is often treated by a combination of extended surgical resection and application of cryotherapy to the surgical bed. Alternative therapies for CIN include topical chemotherapy using mitomycin C¹ or 5-FU², radiation, and recently, Interferon alpha-2b (IFN α 2b).³ The interferons, discovered more than 40 years ago, are natural body defenses against viral infections and also play an important role in combating tumors and regulating immunity.⁴ The interferons consist of three families of protein molecules (α , β , and γ), and IFN α 2b has been shown to be effective for treating

CIN.³ Herein, we report our successful management of a case of CIN by subconjunctival injection and topical applications of IFN α 2b.

Case Report

A 73-year-old woman presented with a complaint of irritation due to a tumorous lesion in her left eye. Slit-lamp microscope examination revealed a tumorous lesion involving the conjunctiva as well as the limbus, from the 3-o'clock position to the 8-o'clock position (Figure 1A). Fluorescein staining of the lesion was positive (Figure 1B). Palisade of Vogt was visible except in the area of the tumorous lesion. No other abnormalities were observed in her left eye. In another hospital, she had already been diagnosed histologically as having CIN by biopsy of the lesion (Figure 2). Subsequently, she had undergone cryotherapy twice on a lesion on the lower tarsal conjunctiva and once on a lesion on the upper tarsal

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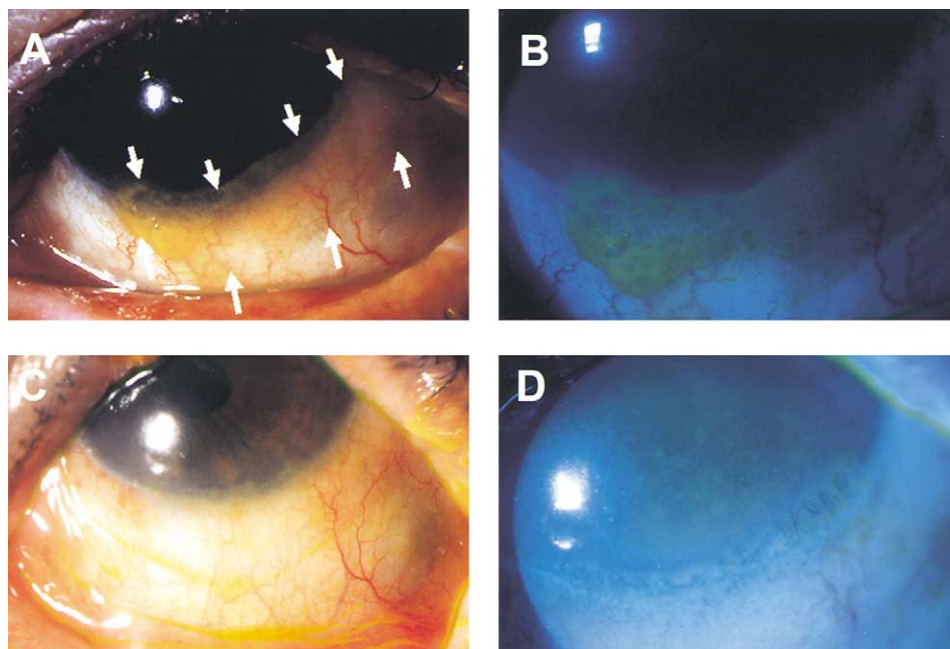


Figure 1. (A) Anterior segment photograph before treatment with interferon (IFN) α 2b. A tumorous lesion involves the conjunctiva and the limbus from the 3-o'clock to the 8-o'clock position (arrows). (B) The lesion was stained by fluorescein. (C) 2 weeks after the initial treatment with IFN α 2b. Note that the tumor has disappeared. (D) Mild focal superficial punctate keratopathy was observed by fluorescein staining.

conjunctiva without any surgical resection of the lesions. As a result of the cryotherapy, the lesion on the tarsal conjunctiva disappeared macroscopically. Surgical resection and/or cryotherapy was recommended to treat the remaining lesion on the bulbar conjunctiva, but she declined such therapy for fear of experiencing intolerable pain from the cryotherapy. After informed consent was obtained, the patient agreed to the use of IFN α 2b for the lesion on the bulbar conjunctiva. Examination showed a visual acuity of 20/25 in her left eye. It is significant that she had had a long history of severe bronchial asthma. One milliliter of IFN α 2b (Schering Plough, Kenilworth, NJ, USA; 3 million units in 1 mL of distilled water) was injected subconjunctivally on March 1, and again on March 8, 2000. The same drug was subsequently prepared as 1 million units in 1 mL as eye drops, and administered four times a day for 12 weeks. Topical administration of 0.3% ofloxacin 4 times daily was also prescribed. Two weeks later, the tumorous lesion had disappeared clinically (Figure 1C), and faint diffuse superficial punctate keratopathy was visible (Figure 1D). It disappeared immediately after discontinuance of the IFN α 2b eye drops. The Palisade of Vogt of the upper limbus was preserved after the treatment with IFN α 2b. On the first day of this treatment, the patient had a fever (38°C),

which was relieved by a Diclofenac sodium suppository. Hematological tests were performed weekly, but no abnormalities of hepatic or renal function were noted. During a 1-year follow-up period, no recurrence was noted.

Discussion

In this report, we described successful treatment of a case of CIN by subconjunctival injections of 3 million units of IFN α 2b once a week for 2 weeks, and IFN α 2b eyedrops prepared as 1 million units in 1 mL administered four times daily for 12 weeks. The tumor disappeared and no recurrence was noted after follow-up for 1 year.

In the management of CIN, Tunc et al reported that the recurrence rate was as low as 5.4% for 56 months with a combination of tumor resection and cryotherapy.⁵ However, they noted that this combined therapy is not appropriate for cases where the tumor cannot be removed completely or for cases where the corneal limbus has been extensively affected. In the case presented here, the limbus was only mildly affected. Therefore, other treatment might have been effective. However, the patient had felt intolerable pain during cryotherapy on her eyelids and was afraid of having an asthma attack during

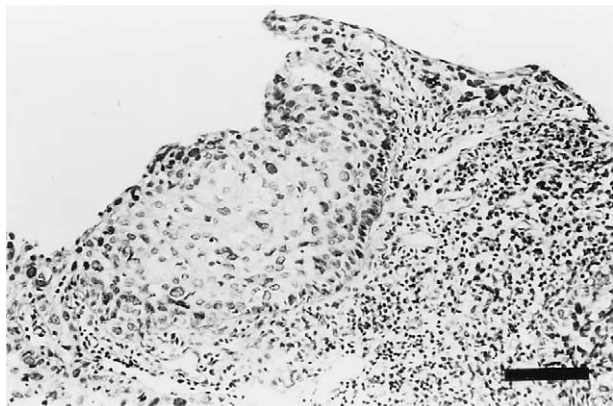


Figure 2. Intraepithelial proliferation of atypical squamous cells are seen. Hematoxylin-eosin stain. Bar = 50 μ m.

surgery. She preferred the use of topical medication and peri-lesional injection of IFN α 2b to the lesion on the bulbar conjunctiva. Radiation is sometimes used with or without surgical resection, but may result in adverse reactions such as cataract and retinopathy. Treatment with mitomycin C (MMC) and 5-FU, which has been reported to yield favorable results for CIN,^{1,2} may cause pain, ocular surface inflammation, epitheliopathy, and dry eye symptoms. Also, topical MMC might cause vision-threatening side effects such as scleral melt, as is seen after pterygium surgery.

IFN α 2b has been used to treat condylomata acuminatum, chronic hepatitis B and C, malignant melanoma, and hairy cell leukemia.⁴ Although systemic side effects caused by IFN α 2b, such as flu-like syndrome, hypotension, tachycardia, somnolence, and anorexia, have been reported,⁴ only overnight fever and muscle pain have been reported as side effects of the topical and subconjunctival use of IFN α 2b.³ In the present case report, the superficial punctate keratopathy and a transient fever that occurred following treatment might have been side effects of the IFN α 2b. The former subsided immediately after the

IFN α 2b eyedrops were discontinued, while the latter remitted within 1 day after the use of Diclofenac sodium suppository. The mechanism of action of IFN α 2b for treating CIN may comprise a direct antiproliferative effect on targeted tumor cells, achieved by promoting the immune response and by activating host cytotoxic effector cells to lyse target tumor cells more efficiently.⁴

The patient presented in this paper had severe asthma as an underlying systemic disease. Although no case of CIN with a background of severe asthma has yet been reported, a co-author of this paper (S.C.G.T.) has seen several cases of CIN accompanied by severe asthma or atopy, suggesting that there may be a causal relationship between allergic predisposition and the occurrence of CIN.

In conclusion, topical and subconjunctival IFN α 2b is a valuable and safe treatment option for CIN, especially in a patient who does not want surgical treatment. Additionally, it seems to have fewer side effects compared to topical MMC or 5-FU. Also, the use of topical and subconjunctival IFN α 2b is not invasive, compared to surgical resection, and is less likely to induce devastating complications, such as limbal stem cell deficiency.

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