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

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Background: Interferon α-2b (IFNα2b) 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 IFNα2b.

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, IFNα2b 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 IFNα2b is a valuable treatment option for CIN.


Key Words: Conjunctival intraepithelial neoplasia, interferon α-2b.
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 IFNα2b 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 IFNα2b (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 IFNα2b eye drops. The Palisade of Vogt of the upper limbus was preserved after the treatment with IFNα2b. 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 IFNα2b once a week for 2 weeks, and IFNα2b 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. 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

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*Figure 1.* (A) Anterior segment photograph before treatment with interferon (IFN)α2b. 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 IFNα2b. Note that the tumor has disappeared. (D) Mild focal superficial punctate keratopathy was observed by fluorescein staining.
surgery. She preferred the use of topical medication and peri-lesional injection of IFNa2b 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, 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.

IFNa2b has been used to treat condylomata acuminatum, chronic hepatitis B and C, malignant melanoma, and hairy cell leukemia. Although systemic side effects caused by IFNa2b, such as flu-like syndrome, hypotension, tachycardia, somnolence, and anorexia, have been reported, only overnight fever and muscle pain have been reported as side effects of the topical and subconjunctival use of IFNa2b. In the present case report, the superficial punctate keratopathy and a transient fever that occurred following treatment might have been side effects of the IFNa2b. The former subsided immediately after the IFNa2b eyedrops were discontinued, while the latter remitted within 1 day after the use of Diclofenac sodium suppository. The mechanism of action of IFNa2b 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.

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 IFNa2b 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 IFNa2b is not invasive, compared to surgical resection, and is less likely to induce devastating complications, such as limbal stem cell deficiency.

References