Short communication

Conjunctival intraepithelial neoplasia. Interferon as a rescue therapy after failure of mitomycin C

R.I. de la Cruz Aguiló*, A. Duch-Samper, D. Hernández Pérez, J. Marí Cotino
Servicio de Oftalmología, Hospital Clínico Universitario de Valencia, Valencia, Spain

Article history:
Received 26 May 2013
Accepted 18 November 2013
Available online 26 November 2014

Keywords:
Conjunctival intraepithelial neoplasia
Mitomycin-C
5-fluorouracil
Interferon alfa 2B
Immunotherapy

Clinical case: The case of a 60-year-old male with a conjunctival lesion diagnosed as conjunctival intraepithelial neoplasia (CIN), who was treated with mitomycin-C for 3 weeks with minimal improvement. The therapy was change to interferon 2B. Six month later, and after a complete remission of the lesion, the treatment was suspended, with no signs of relapse.

Discussion: The treatment of these lesions is currently made with chemotherapy and immunotherapy agents, such as mitomycin-C, 5-fluorouracil, and interferon alfa 2B. The latter, even although is the least used, gives excellent results with fewer secondary effects than mitomycin-C, resulting in an optimal therapy for the non-invasive treatment of CIN lesions.

© 2013 Sociedad Española de Oftalmología. Published by Elsevier España, S.L.U. All rights reserved.

Neoplasia intraepitelial conjuntival. Interferón como terapia de rescate tras fracaso de la mitomicina C

Caso clínico: Varón de 60 años con lesión conjuntival diagnosticada de neoplasia intraepitelial conjuntival (NICC), iniciándose tratamiento con mitomicina C. Tras 3 semanas y mínima mejoría, se reemplaza por interferón alfa 2B. Seis meses después, con completa remisión, se suspende el tratamiento sin signos de recidiva.

Discusión: Actualmente, el tratamiento de estas lesiones se realiza con agentes quimioterapéuticos o inmunomoduladores como la mitomicina C, el 5-fluorouracilo y el interferón alfa 2B. Este último, a pesar de ser menos utilizado, presenta excelentes resultados con efectos secundarios menores que la mitomicina C, resultando una alternativa óptima para el tratamiento no invasivo de las NICC.

© 2013 Sociedad Española de Oftalmología. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

* Please cite this article as: de la Cruz Aguiló RI, Duch-Samper A, Hernández Pérez D, Marí Cotino J. Neoplasia intraepitelial conjuntival. Interferón como terapia de rescate tras fracaso de la mitomicina C. Arch Soc Esp Oftalmol. 2014;89:463–465.

* Corresponding author.
E-mail address: delacruzaguilo@gmail.com (R.I. de la Cruz Aguiló).

2173-5794/$ – see front matter © 2013 Sociedad Española de Oftalmología. Published by Elsevier España, S.L.U. All rights reserved.
Introduction

Conjunctival corneal intraepithelial neoplasms (CCINs) are mobile limbal lesions of papilliform, gelatinous or leukoplasmatic appearance, with a characteristic vascular tuft, which grow slowly. The corneal epithelium is usually involved, showing a grey, opaque and thickened appearance. Even though these lesions may progress to squamous cell carcinomas, they have a minimum risk of malignancy.

There are many risk factors for developing a CCIN, including: phototype, exposure to petroleum, male sex, older age, ultraviolet radiation exposure, HIV and HPV. The diagnosis is clinical and may be confirmed by biopsy or touch cytology. The diagnostic and follow-up techniques we have available right now are the following: slit lamp

![Fig. 1 - CCIN. (A) Raised lesion of papillomatous appearance invading the cornea. (B) Appearance of the lesion after three weeks of treatment with mitomycin-C; note the little improvement. (C and D) The same lesion after one month of treatment with interferon; a significant reduction of the lesion is observed. (E) Appearance one month after discontinuing interferon, where no signs of recurrence are seen.](http://www.elsevier.es)
The high are admitted. Historically, clinical exam, touch cytology and histopathological analysis. The use of ultra-high-resolution optical coherence tomography has recently been proposed for the diagnosis and follow-up of CCIN.

The traditional treatment includes surgical excision combined with cryotherapy of borders. High recurrence rates, the presence of non-recteable lesions and the risk of damage to limbal cells make the surgical resection a non-ideal option; so now topical treatments with chemotherapeutic or immunomodulating agents, such as mitomycin-C, 5-fluorouracil (5-FU) and interferon, are being widely used, showing excellent outcomes in the cure of these lesions and facilitating a non-invasive method for their treatment.

**Clinical case**

We present the case of a 60-year-old male patient who was admitted due to a 7-day course episode of reddened left eye associated with a fast-growing lesion in the nasal area. No relevant personal history and one unit of visual acuity in both eyes.

The slit lamp exam revealed a conjunctival lesion invading the cornea, raised, with a papillomatous appearance and vessels on its surface (Fig. 1A). A clinical diagnosis of CCIN was made and treatment with 0.02% mitomycin-C four times a day was initiated.

In the second week of treatment, the patient reported mild discomfort and presented with punctate keratopathy and moderate conjunctival hyperaemia, so artificial tears were added and treatment was continued. However, after three weeks, the patient showed a slight improvement of the lesion and persistent discomfort (Fig. 1B); therefore, the treatment was modified and interferon alfa 2B was started at one million IU, four times a day.

After one month with this new therapy, the patient experienced a major regression of his lesion (Fig. 1C and D). After six months of interferon treatment, the lesion showed complete remission and a minimum corneal leukemia remained. There are no current signs of recurrence (Fig. 1E).

**Discussion**

Historically, the treatment of squamous neoplasms on the ocular surface has consisted in wide local excision with or without cryotherapy on the borders. Despite intraoperative precautions, such as cryotherapy or the use of intraoperative alcohol, recurrence rates range from 15 to 52%.

For approximately the last 18 years, there has been a change in the treatment of these lesions and the growing trend is to use topical agents as adjuvant therapies or primary treatments.

These therapies offer a non-invasive method to treat the entire conjunctiva, regardless of the tumour limits, showing a high concentration at ocular level with minimum systemic side effects, which may be continued or suspended based on the clinical response.

Mitomycin-C has been successfully used for the treatment of CCIN, with a recurrence rate of 24%. However, most patients experience side effects such as epitheliopathy, lacrimal punctum stenosis and allergic reactions. Besides, the use of mitomycin-C has been associated with limbal stem cell deficiency.

On the other hand, interferon has fewer side effects, although longer treatment periods are necessary.

Little has been published about the use of 5-FU in the treatment of these lesions, although it has proven to be effective with minimum associated adverse effects.

In summary, while less used, interferon alfa 2B provides excellent results with a side effect profile inferior to that of mitomycin-C, proving to be an optimal alternative for the non-invasive treatment of CCINs.

With an adequate safety profile and good efficacy, chemotherapeutic and immunomodulating agents have changed the way we treat CCINs, although they may be potentially toxic for the eye surface and the long-term consequences of their prolonged use are unknown, particularly for interferon and 5-FU.

It should be noted that the ideal treatment schedule (dose, drug strength and treatment duration) has not been standardized and continues to be studied.

**Conflicts of interest**

The authors declare that they do not have any conflicts of interest.

**References**

The authors declare that they do not have any conflicts of interest.