Short communication

Conjunctival squamous cell carcinoma: paradoxical response to interferon eyedrops

E. Mata, E. Conesa, M. Castro, L. Martínez, C. de Pablo, M.L. González

Servicio de Oftalmología, Hospital Central Cruz Roja San José y Santa Adela, Madrid, Spain
Servicio de Anatomía Patológica, Hospital Central Cruz Roja San José y Santa Adela, Madrid, Spain

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ABSTRACT

Case report: A 67-year-old male was seen for a longstanding corneal-conjunctival tumor. Treatment included topical interferon α2b (IFN-α2b) 10 U/ml. A significant increase in lesion size was observed after 8 weeks. A surgical excision with cryotherapy was then performed. Pathological examination confirmed the diagnosis of squamous cell carcinoma. At this time the patient was found to have a positive HIV serology.

Discussion: Conjunctival intraepithelial neoplasia (CIN) is a pre-cancerous lesion of the ocular surface. Medical treatment of CIN is essentially with IFN-α2b due to its antiviral/antitumor properties. In patients with HIV, treatment response could be paradoxical. We recommend serology for HIV before treatment with topical IFN-α2b.

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Carcinoma epidermoide conjuntival: respuesta paradójica al colirio interferón

RESUMEN

Caso clínico: Varón de 67 años consulta por tumoración corneoconjuntival de larga evolución. Se inicia tratamiento con interferón α2b (IFN-α2b) tópico 10 U/ml. Tras 8 semanas existe importante aumento de tamaño de la lesión. Se realiza tratamiento quirúrgico/crioterapia. El estudio anatomopatológico confirma el diagnóstico de carcinoma epidermoide. La serología es positiva para VIH.

Discusión: La neoplasia conjuntival intraepitelial (CIN) es una lesión precancerosa de la superficie ocular. El tratamiento médico de elección del CIN es la terapia inmunomoduladora con IFN-α2b. En pacientes con VIH la respuesta puede ser paradójica. Recomendamos realizar estudio serológico para VIH antes del tratamiento con IFN-α2b tópico.

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Corresponding author.
E-mail address: eduardo_conesa@hotmail.com (E. Conesa).

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Introduction

Ocular surface squamous neoplasia (OSSN) is a condition with partial thickness neoplastic changes of the conjunctival epithelium or conjunctival intraepithelial neoplasia (CIN). If it affects the entire epithelium thickness, it is classified as carcinoma in situ (CIS). If it crosses the basal membrane and invades the stroma, it is called conjunctival squamous cell carcinoma (CSCC).

It predominantly affects men over 60 years of age. Its most common site is the interpalpebral conjunctiva and limbus. Its growth is slow and progressive. These are unilateral lesions, protuberant or flat, with a sentinel vessel in 65% of cases. Clinical differentiation between CIN and CSCC is difficult, and a biopsy is performed if the diagnosis is unclear. Genetic factors, ultraviolet B, human papillomavirus (HPV 16 and 18) and HIV are involved in its etiology. Lesion excision is the traditional treatment method; however, recurrences of it are from 24% to 39%. Immunomodulatory therapy is an alternative, and interferon α2b (IFN), 5-fluorouracil and mitomycin-C are equally effective. IFN α2b has few side effects and is used at 10⁶ IU/ml doses four times/day until complete lesion resolution (14–20 weeks).

Clinical case

A 67-year-old male was seen for a longstanding corneal-conjunctival tumor. His history included excision of cutaneous skin tags due to papillomavirus. The patient had a nodular, gelatinous, leukoplakic lesion in the interpalpebral nasal area invading the cornea (Fig. 1). The rest of the eye examination was normal. OSSN clinical diagnosis was performed. The patient refused surgery; therefore, treatment with topical IFN-α2b 10⁶ U/ml four times/day was suggested. At 4 weeks increased size was observed, a phenomenon already described by other authors; therefore, it was continued for an additional 4 weeks, after which the lesion grew to twice its initial size (Fig. 2). Ocular ultrasonography showed no signs of intraocular involvement. Due to the morphological changes, surgery was decided with the Shields “no touch” technique associated with conjunctival margin cryotherapy. The defect was covered with a conjunctival autograft with fibrin sealant (Fig. 3). After 3 years of follow-up, no signs of recurrence have been observed (Fig. 4). Pathological examination confirmed the CSCC diagnosis (Figs. 5 and 6).
Discussion

An increased risk of epithelial tumors on any site in patients with AIDS, including CSCC\(^5\) has been reported. Additionally, these tumors recur and have orbital extension more frequently (23%). HIV and HPV coinfection represents an increased risk of SCC. HPVs inactivate the FS3 tumor suppressor gene, which appears to be related to resistance to IFN-\(\alpha\). Surgery is the first-line treatment for OSSN, although recent studies support topical therapies, with success rates in 80–96% of cases\(^6,7\); IFN-\(\alpha_2\), 5-fluorouracil and mitomycin-C are equally effective (80–88%). Therefore, given the patient’s refusal of surgery, we opted for IFN-\(\alpha_2\) treatment, whose action mechanism appears to promote tumor cell apoptosis. Response is evaluated regularly by measuring lesion height, width and vascularization, looking for signs of regression. Initial response may be slow in the first month; some patients experienced increased size at the start of the treatment and later responded well to IFN.\(^3\) There are reports of resistance to IFN among 6–13% of CSCC cases regarding HPV infection.\(^3\)

In the case we presented clinical response to immunomodulatory therapy has been atypical because, after inception, the lesion has shown an increase in size with changes in its morphological characteristics. This behavior prompted us to conduct HIV serology. In HIV-infected patients, response to treatment may be paradoxical due to resistance to al IFN-\(\alpha_2\).\(^8\) Furthermore, OSSN boosts aggressiveness and tendency to invasion. HPV and HIV coinfection may have motivated resistance to IFN and increased lesion aggressiveness due to the patient’s immunosuppression.\(^8,9\) This synergy of both infections could justify the increased size paradoxical response. This response’s uniqueness led us to the surgical option for histopathological analysis, and given the good performance and lack of recurrence, we did not find it necessary to conduct other adjuvant therapies.

We recommend serology testing for HIV and looking for HPV superinfection in all patients with clinical suspicion of OSSN before initiating treatment with topical IFN-\(\alpha_2\). In case of co-infection, we advise surgery as a first-line therapy along with adjuvant antimetabolite therapy, given its more aggressive behavior.

Conflict of interest

The authors declare that they have no conflicts of interest.
REFERENCES