Corneal intraepithelial neoplasia as a cause of visual acuity decrease: a low-cost approach

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Abstract

Introduction: Intraepithelial corneal neoplasia is a dysplastic disease within the spectrum of ocular surface squamous neoplasia. It is a rare disease that is often subdiagnosed, especially when it presents in its diffuse form. When suspected, the diagnosis and treatment can be simple, even when we are dealing with a disease that can be disastrous. **Case report:** We present the case of a 63 year-old male patient that presents complaining of poor vision on the right eye with 2 weeks of evolution. Visual acuity maintained at 20/40 while corrected and at examination showed a superior corneal geographical lesion with frosted appearance. After other diseases were discarded, an epithelial scraping was performed and a low grade intraepithelial corneal neoplasia reported. Treatment with two series of 2 weeks of mitomycin C at 0.02% with three applications per day was decided accompanied with fluorometholone 0.1% at same dosage. **Conclusions:** The authors recommend the use of mitomycin C in countries in developing countries.

Key words: Neoplasia. Cornea. Frosting. Epithelial. Mitomycin C. INF α -2B.

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Introduction

Conjunctival-corneal intraepithelial neoplasia (CCIN) is a non-invasive dysplastic pathology that occurs in the conjunctival-corneal epithelium, also regarded as carcinoma in situ. CCIN is part of ocular surface squamous cell neoplasia dysplastic spectrum. Squamous cell carcinoma lesions start with dysplastic changes (carcinoma in situ that can be mild, moderate or severe), to finally cross the lamina propria and turn into invasive squamous cell carcinomas (Table 1)^{1,2}.

Of all tumors occurring in the eye globe and its adnexa, those of the ocular surface are the most common, and of these, neoplasms comprising the epithelium account for one third to half of cases. When epithelial tumors are diagnosed, 65% have not yet crossed the lamina propria. An incidence of conjunctival-corneal tumors of 0.13-1.9/100,000 has been reported, depending on the geographic provenance^{3,4}. As in all tumors, changes in ocular surface squamous cell neoplasia are due to a loss of control of affected cells' life cycle and division. Most important known risk factors are chronic exposure to ultraviolet rays, infection with the human papillomavirus, *p53* gene defective expression, belonging to the male gender, age older than 60 years and HIV seropositive status².

CCIN clinical presentation can occur in two forms. The first case is the most common, and it shows growths or masses that may have changes in normal coloration, erosions, bleeding, reddening and foreign body sensation. In the diffuse case, the patient can be asymptomatic or, if there is diffuse corneal invasion, experience decreased visual acuity³.

Establishing the diagnosis in a case suspicious of CCIN has to be done by means of histopathology, either by first performing an epithelial scraping or after en bloc resection of the tumor⁵. Traditionally, CCIN had been treated with tumor excision, but up to 56% were shown to relapse, and the use of radiation, cryotherapy or topical chemotherapeutic agents was therefore added to the treatment. Recently the use of chemotherapeutic agents alone (5-fluorouracyl, mitomycin C [MMC] or interferon), has been found to be as effective as excision plus cryotherapy⁴.

Table 1. Ocular surface squamous cell neoplasia evolution

CCIN (carcinoma in situ)
– Mild
– Moderate
– Severe
Conjunctival-corneal squamous cell carcinoma

In this work, we describe one case of newly-onset corneal intraepithelial neoplasia with main complaint of decreased VA and that was topically treated with MMC.

Clinical case

A 63-year old male patient attended our private office with main complaint of VA decrease over the two previous weeks. The patient had no relevant previous medical or personal history, and used bifocal glasses for hypermetropia and presbyopia. He also had no relevant family or hereditary history. His occupation was electrician, and at that time he was working installing telecommunication equipment in a private company. The patient referred right eye VA acuity decrease even when wearing glasses since 2 weeks prior and that it had been progressive; he denied any other symptoms. On physical examination, right eye best corrected VA of 20/40 (logMar 0.3) with +4.50 -2.25 x 97° was found, and left eye VA of 20/20 (logMar 0), with +3.25 -0.50 x 93°, with best corrected VA in both eyes of 20/20 (logMar 0). Ocular movements and pupillary reflexes showed no alterations. Intraocular pressure on both eyes was 14 mmHg. On slit-lamp examination, a geographical lesion at the upper half of the cornea, which included the pupillary area, with frosty appearance and dotted within, was observed in the right eye. Left eye slit-lamp examination showed no anomalies. Since there was doubt on whether it was a corneal lesion caused by chemicals or a thermoelectric lesion that the patient would have not noticed, treatment was started with ciprofloxacin/dexamethasone eye drops of 3/1 mg/mL topically applied on the right eye thrice daily for two weeks, with indication for reassessment in a visit two weeks later.

When the patient returned two weeks later for reassessment, the lesion was observed to have spread to the right cornea lower pole and VA had not improved. Performing an epithelial scraping was decided for histopathological assessment. Two weeks later, the pathology report indicated a low-grade corneal intraepithelial neoplasia (fig. 1). Management was started with 0.02% MMC (0.02 mg/mL) eye drops thrice daily for two weeks, followed by two weeks' rest and, finally, other two weeks with three applications per day (two complete cycles), accompanied by 0.1% fluorometholone at the same dosage. Eight weeks after having initiated the MMC treatment, no lesion was found in the cornea, and VA had improved to 20/20 (logMar 0) in both eyes. One year after having completed the treatment, the patient had not experienced new problems. Currently, he is on follow-up for relapse early diagnosis (Fig. 2).

Figure 1. Corneal epithelium scraping sample. The arrow points at the basal third of the corneal epithelium, which shows dysplasia in its cells, normal architecture disorganization, pleomorphism and alteration of the nucleus-cytoplasm ratio. Neoplastic cells do not invade the stroma. It was reported as low grade CCIN.

Discussion

CCIN is a rare disease, and the diffuse presentation is even less common. Data consistent with decreased VA with an unclear explanation would probably lead the clinician to study other causes prior to directly considering a neoplasia. It is important highlighting that, although screening for most common diseases is imperative and unavoidable, this type of diseases should always be taken into account when performing differential diagnoses.

Recently, it was demonstrated that topical treatment of CCIN can be as effective as surgery, and that it can even have better long-term results if surgery is not combined with adjuvant treatment. In 2014, Nanji et al. failed to find statistically significant differences in terms of recurrence and complications between therapy with surgery or with interferon α -2B (IFN- α -2B) for the management of corneal squamous cell carcinoma in a case-control study. In this study, recurrence in patients with surgery was 5%, whereas in

Figure 2. Corneal intraepithelial neoplasia evolution in a patient presenting with right eye decreased VA. **A:** right corneal lesion at first visit; a frosted, dotted lesion is observed. **B:** right corneal lesion at first visit, stained with fluorescein. **C:** fluorescein-stained lesion two weeks after the first visit; there is advance of the lesion towards the corneal lower pole. **D:** right corneal lesion after MMC-treatment first cycle. **E:** right cornea after the conclusion of second cycle; the lesion is not visible anymore. **F:** right eye cornea one year after MMC-treatment; no lesions are shown at all.

the treated group it was 3%. Since there are no important differences, non-invasive intervention may be preferable.

This is a big step towards the possibility to avoid invasive treatments in patients and to expose them to less risk, while, at the same time, the advance is prevented of a disease that, without control, might get to cause blindness or even death, in a simple and tolerable form to the patient. It could be considered that the next step is to find the most effective topical treatment and with the best risk/benefit ratio. Currently, MMC and IFN- α -2B have been suggested to probably be the most effective medications to treat CCIN, although it has also been mentioned that the advantage IFN- α -2B has, is that it produces less adverse effects in comparison with MMC. The risks we expose our patients to when using MMC include pain, irritation, erosion, symblepharon and limbal stem cell deficiency, with these risks depending on the dose employed⁶.

In a prospective study conducted by Ballalai et al., with 23 patients being observed for 24 months after the use of MMC for the treatment of CCIN, all cases were resolved, only one patient experienced recurrence and 17.4% had corneal abrasion, which resolved easily with treatment⁷. In developing countries, obtaining IFN- α -2B is a costly option that is not accessible to the majority of the general population; however, our case bears witness that, with adequate evaluation and the necessary care, MMC remains an efficacious and safe treatment that is comfortable for the patient.

Conclusions

CCIN is a form of carcinoma in situ that belongs to the eye surface squamous cell neoplasia spectrum. Although it is a rare pathology, and the diffuse presentation is even more uncommon, it should be always taken into account in the differential diagnosis of our patients with acute VA decrease. Currently, diagnosis and treatment can be minimally invasive. For diagnosis, epithelial scraping and histopathological evaluation is sufficient, and treatment consists in topical chemotherapeutic agents, with resection being necessary in very large tumors. The authors recommend the use of 0.02% MMC in developing countries.

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Conflict of interest

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