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Resolution of giant ocular surface squamous neoplasia with topical 5-fuorouracil 1%

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Abstract

An 82-year-old man presented with a left eye elevated single ocular surface squamous neoplasia. The tumor involved 360° of limbus, three quadrants of cornea and conjunctiva; this was compatible with the diagnosis of giant ocular surface squamous neoplasia. Topical 5-fluorouracil 1% was planned four times daily for 1 week followed by 3 weeks off-treatment. Patient inadvertently continued 5-fluorouracil, four times daily for 4 weeks, presenting with clinical resolution of the ocular surface squamous neoplasia and subtotal corneal epithelial defect associated with 5-fluorouracil toxicity. One month later, we observed a transparent cornea and no signs of toxicity. Total tumor resolution was observed for at least 6 months of follow-up.

Keywords

Ocular surface squamous neoplasia, OSSN, 5-fluorouracil

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Introduction

The ocular surface squamous neoplasia (OSSN) is the most common type of ocular tumor. However, it is rare with an incidence of 8.4 per million people per year.[1] We report a case of a giant OSSN treated with topical 5-fluorouracil (5-FU) 1%. The treatment is a matter of debate, with a tendency toward the use of topical chemotherapeutic agents in recent years. Very few data exist in relation of treatment and efficacy in giant OSSN.[2–6] We share our experience in the treatment of giant OSSN with topical 5-FU as monotherapy.

Case history

An 82-year-old man presented with a 24-month history of a slowly growing corneal and conjunctival mass in his left eye. It was accompanied with red eye, pain, photosensitivity, and foreign body sensation. He was otherwise healthy with no other relevant medical record. Examination revealed best-corrected visual acuity of 20/60 and 20/125 in his right and left eye, respectively. On slit-lamp examination, we found bilateral cataracts and left eye showed diffuse moderate hyperemia, tortuous vessels, and an elevated flesh-like, keratinized mass of salmon color, involving 360° of limbus, three quarters of the cornea, and three quadrants of conjunctiva (Figure 1(a) and (b)). We made the clinical diagnosis of giant OSSN. On high-resolution optical coherence tomography (HR-OCT), we observed the typical characteristics of OSSN, with thickened hyper-reflective epithelial layer, abrupt transition from normal epithelium, and marked separation between the lesion and the underlying tissue (Figure 1(c) and (d)).

Topical chemotherapy with 5-FU 1% was started four times daily for 1 week followed by 3 weeks off-treatment. Instead, the patient inadvertently continued 5-FU 1% four times daily for 4 weeks. He arrived with significant clinical resolution of the OSSN, but with ocular surface toxicity due to 4 weeks of topical

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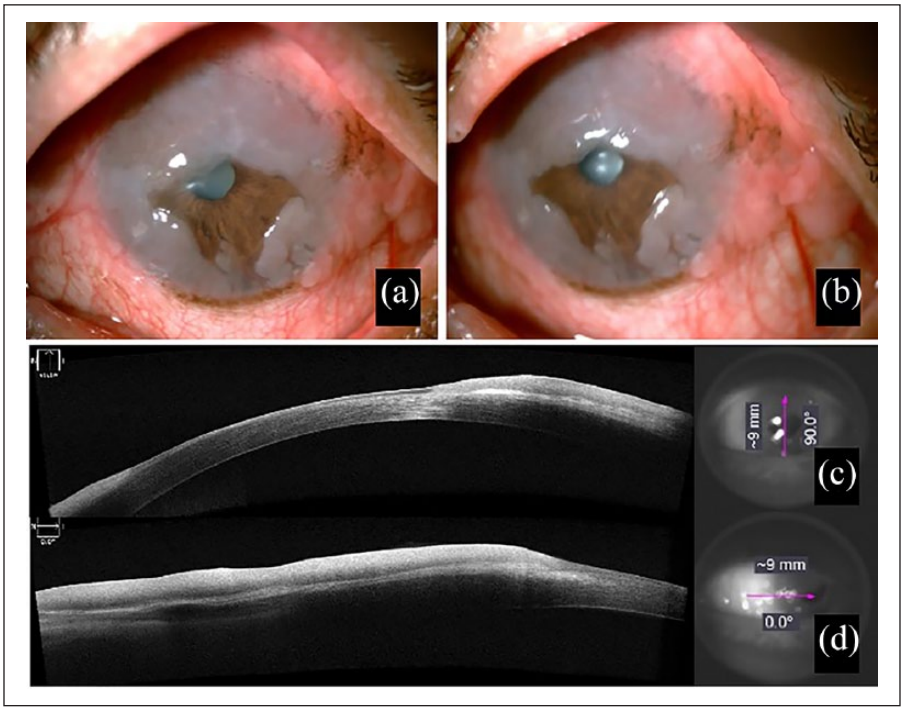

Figure 1. Giant OSSN before treatment. (a, b) Slit-lamp picture of giant OSSN shows elevated flesh-like, keratinized mass of salmon color, involving 360° of limbus, three quarters of the cornea, and three quadrants of conjunctiva. (c, d) HR-OCT of giant OSSN shows thickened hyper-reflective epithelium, abrupt transition from normal epithelium, and marked separation between the lesion and the underlying tissue.

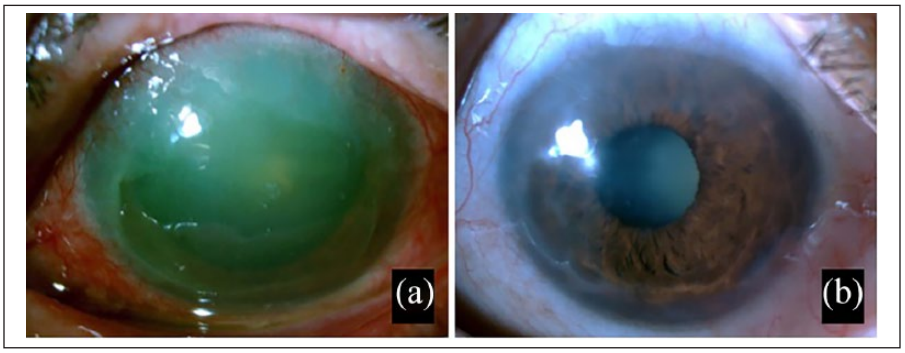

Figure 2. Ocular surface toxicity after 4 weeks of topical 5-FU. (a) Slit-lamp picture shows ocular surface toxicity to 5-FU with generalized hyperemia, chemosis, central corneal thinning, and fluorescein-staining subtotal corneal epithelial defect. (b) Slit-lamp picture after total resolution of surface toxicity with healed corneal epithelium, a stable corneal thinning, and further reduction in the size of the OSSN.

5-FU 1% usage. The observed local signs of toxicity were subtotal corneal epithelial defect, generalized hyperemia, chemosis and central corneal thinning of about 50% measured subjectively with slit-lamp by the evaluator (Figure 2(a)). In addition, he also presented systemic signs of toxicity, with asthenia and headache. We decided to immediately stop 5-FU and start conservative treatment with lubricant, steroid drops, and eye patch. Moreover, we referred him to the oncology department to rule out disseminated disease, which was discarded.

After 4 weeks of treating the ocular surface toxicity for 5-FU, we observed total resolution of the corneal epithelial defect, a stable corneal thinning of 50%, further reduction of the OSSN, and improvement of systemic symptoms (Figure 2(b)). After 2 months of follow-up, we observed a transparent cornea with mild peripheral haze, symmetrical residual corneal thinning, total resolution of the OSSN, and no systemic symptoms. The remission of the OSSN continued at least to the last documented follow-up visit at 6 months after topical 5-FU. Confirmation of clinical resolution was observed on HR-OCT images that showed a normal thickness epithelium and a normal transition between corneal and conjunctival epithelium at 6 months after the beginning of 5-FU (Figure 3(a) and (b)).

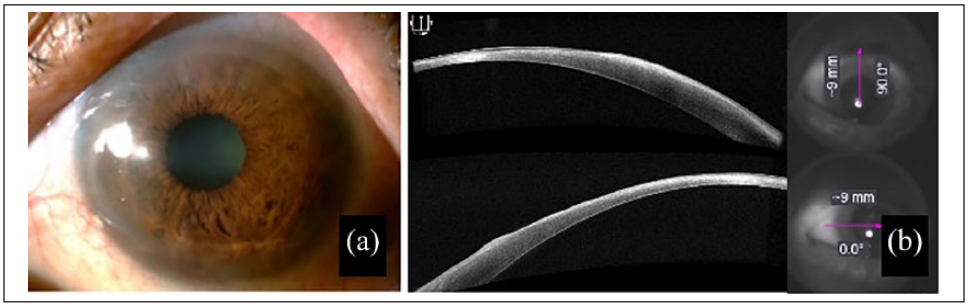

Figure 3. Six-month follow-up after topical 5-FU treatment of giant OSSN. (a) Clear central cornea with mild peripheral haze, symmetrical residual corneal thinning, and total resolution of the OSSN. (b) HR-OCT confirms the absence of OSSN and shows normal thickness epithelium and normal cornea–conjunctiva epithelial transition.

Discussion

An OSSN may involve conjunctiva, limbus, and cornea and includes lesions ranging from simple dysplasia and carcinoma in situ to invasive squamous cell carcinoma.[7] Giant OSSN is generally defined as single tumor that measures ⩾15 mm in its basal diameter and/or involves ⩾180° of limbus.[2,8] The exact incidence of giant OSSN is not known.

The clinical diagnosis of OSSN is the most important. Histopathology is the gold standard because enables direct study of the tissue and assesses invasion.[7,9] However, it requires surgery and expertise taking biopsy, tissue processing, and histopathology analysis. As the treatment of OSSN trends toward topical chemotherapy, reliable noninvasive forms of diagnosis and follow-up are needed.[10] With the advent of HR-OCT, high-resolution images of OSSN lesions correlated well with its histologic appearance.[11] HR-OCT has become an excellent noninvasive real-time in-office diagnostic and follow-up tool and it could avoid biopsy.[12]

Two treatment options are available, surgical and topical chemotherapy. The traditional treatment of choice was surgical excision with no-touch technique and base cryotherapy. Although its efficacy has been proved, one of the main disadvantages is the risk of developing iatrogenic limbal stem cell deficiency (LSCD).[13] In our case, the limbus was affected 360° and therefore, the risk of LSCD was high. Another problem is a higher probability of recurrence.[14] Giant OSSN is generally widespread in cornea and conjunctiva and therefore the risk of recurrence is higher. That is because surgical removal of the neoplasia is often difficult or impossible because the margins of the neoplasia are not clearly demarcated.[15] Extensive surgical removal of tissue induces significant scarring with damage to the ocular surface and LSCD.

Topical chemotherapy is the second option and it is gaining popularity. One advantage is the reduced risk of recurrence because it is distributed all over the ocular surface killing neoplastic cells that are not visible. Another advantages are reduced risk of LSCD, lower costs, and less morbidity.[15] Available topical chemotherapy options 5-FU,[16–20] interferon alpha-2b (IFN-2b),[2,21–24] or mitomycin C (MMC).[5,19,20,24,25] These can be used as monotherapy or as adjuvant to surgery. There are isolated case reports of topical IFN-2b2, 5-FU, or MMC as monotherapy for giant OSSN.[2–6] Topical chemotherapy in such cases has the advantage that treatment is being applied all over the ocular surface reaching visible and nonvisible tumor, reducing the risk of recurrence and increasing its effectivity.[15] Topical 5-FU is not as toxic to the ocular surface as MMC. The duration of treatment is shorter with 5-FU than with IFN-2b. Ocular surface toxicity is greater with 5-FU than with IFN.[5] Another great advantage of 5-FU is that it does not require special storage after preparation as compared to IFN, which requires refrigeration and light protection. Finally, 5-FU is easily available and is not as expensive as IFN or surgery.[26] Frequent side effects are hyperemia, pain, irritation, tearing, and photosensitivity.[15] Exceeding the recommended doses and treatment durations may induce surface toxicity. The common dosing schemes of topical 5-FU range from a long course of four times daily for 1 month followed by 3-month holiday to a short course of four times daily for 4–7 days, followed by 3-week holiday until resolution.[16,27] Our patient did not follow the more conservative scheme of four times daily for 7 days; however, the scheme that he used was within the common dosing schemes. Ocular surface toxicity with epithelial defect was successfully managed topically with lubricants, topical steroids, and eye patching. Management of ocular surface toxicity and corneal melting includes stopping the toxic agent, use of non-preservative lubricants, eye patching, systemic doxycycline, and topical steroids, although its use might be controversial.[28]

Conclusion

We showed a case of giant OSSN successfully treated with topical 5-FU 1%. HR-OCT is an excellent noninvasive, real-time, and in-office diagnostic and follow-up tool. Advantages of topical 5-FU in giant OSSN are efficacy, low risk of recurrence and LSCD, low morbidity, lower costs, and not requiring special storage after preparation.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval to report this case was obtained from the ethics committee for research of our University Hospital "Dr. Jose Eleuterio Gonzalez" of the Autonomous University of Nuevo Leon (Project ID: OF13-001).

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Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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