Case report

Asymptomatic chronic red eye: A surgical technique case report

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ABSTRACT

Introduction and importance: Ocular Surface Squamous-cell Neoplasia (OSSN) is an infrequent diagnosis whose clinical suspicion assumes great importance and should not be overlooked. The following case-report aims to describe the diagnosis and treatment of a patient with OSSN whose complaints were mild in comparison to the severity of the disease. The chosen surgical technique was paramount for a disease-free outcome while minimizing the scarring effects of surgical removal.

Case Presentation: Patient presented mild discomfort right eye and painless persistent hyperaemia. Slit-lamp observation showed a clear diagnosis and lesion's extent evaluated through multimodal imaging. After surgical excision the patient underwent topical ocular treatment with mitomycin-C for a higher margin of safety even before the pathology results were available.

Discussion: Ancillary exam technology improvement has allowed a higher margin of safety while determining the extent of OSSN lesions. In the absence of clear diagnostic criteria and guidelines, clinical reasoning and OSSN awareness are critical for timely diagnosis and treatment, as several treatment options are available, allowing an increasing number of patients to be treated non-invasively. In this case-report, we highlight the importance of early-recognition and the reasoning for choosing a combined treatment option with a higher margin of safety.

Conclusion: Early recognition and prompt treatment of OSSN lesions is of paramount importance to avoid ocular invasiveness and potentially preclude both ocular and systemic complication. The choice of a combined surgical and medical approach may provide a higher margin of safety for suitable cases. This patient is currently disease-free at 6-month follow-up.

1. Introduction

Ocular Surface Squamous Neoplasia (OSSN) is defined as a dysplastic squamous epithelial cell growth on the surface of the eye, which encompasses a wide and heterogeneous spectrum of disease.

The acquired lesions are further subdivided based on origin of the mass into surface epithelial, melanocytic, vascular, fibrous, neural, histiocytic, myxoid, myogenic, lipomatous, lymphoid, leukemic, metastatic and secondary tumors [1]. OSSN incidence has been reported to range from 0.13 to 1.9 per 100,000 individuals, and is known to vary according to geography and environmental or genetic factors, with ultraviolet radiation exposure being the strongest risk factor identified [2]. Xeroderma pigmentosum and human immunodeficiency virus (HIV) are also frequently reported risk factors for younger patients. Presentation is usually unilateral, and clinical suspicion is of critical importance for OSSN diagnosis, which may be confirmed with multimodal imaging, cytology, or histology [3].

The ‘no touch technique’, described by Shields et al. [1,4] in 1997, is the gold standard technique for surgical removal in the management of small OSSN lesions. The basic principle of this technique is to remove the tumour with macroscopically clear margins while minimizing the risk of microscopic seeding. There is no universal consensus on the optimal margin used during surgery [3].

The increasing diagnostic power of anterior-segment optical coherence tomography (AS-OCT), high-resolution optical coherence tomography (HR-OCT) and ultrasound biomicroscopy (UBM) has allowed an increasing number of patients to be treated conservatively, using topical monotherapy with chemotherapeutic drugs and immunomodulatory
agents [3,5,6], which may replace surgery as the standard of care in the future. Currently, there is no consensus regarding the best way to manage OSSN with no existing guidelines to date [7,8]. This patient was treated at a tertiary care university hospital and the following case-report was conducted in line with the SCARE criteria [9].

2. Presentation

A 78 years-old patient was referred to the Ophthalmology Department for chronic hyperaemia of the right eye with 3-month presentation. The patient denied any related ocular trauma or any accompanying symptoms besides chronic hyperaemia.

Patient's medical record was unremarkable apart from a non-complicated and medically controlled arterial hypertension and history of asthma during childhood. Patient’s wife reported she was the trigger for the appointment because she didn’t like to see the patient’s “red-eye”. Visual acuity was 10/20 in both eyes and the patient had no other complaints.

A full ophthalmic examination was performed, and the results are shown on Table 1.

Biomicroscopic observation (Fig. 1) showed an elevated ocular surface lesion on the right eye, extending from the inferior and nasal conjunctiva towards the corneal surface, with a translucent, mucoepidermoid, gelatinous mass with irregular borders and fimbriated configuration. Conjunctival feeding vessels were apparent alongside the adjacent neoplastic conjunctival pannus.

Anterior segment optic coherence tomography (AS-OCT) showed the invasive lesion was hyperreflective, with a thickened epithelium and presented an abrupt transition from normal to abnormal tissue (Fig. 2). No stromal involvement was apparent, and this information was confirmed through UBM. This image modality has shown a superficial layer of likely epithelial origin, without apparent stromal extension or any other signs of depth invasion (Fig. 3).

The patient underwent a surgical procedure for OSSN removal with a “no-touch technique” in which the feeding vessels and the conjunctival blood supply was severed first, with extensive cauterization of the feeding vessels to ensure ischemia of the neoplastic lesion, therefore decreasing the cellular adhesions between neoplastic tissue and the underlying, apparently uninvoluted tissue. After careful dissection of the lesion with 2 mm margins of safety and bare sclera cauterization of the feeding vessels, the OSSN lesion was peeled off from the ocular surface with minimal trauma with consequent formation of an epithelial defect corresponding the peeled off location as seen on post-operative day 1 (Fig. 4).

A bandage contact lens was applied for comfort during epithelial healing and the patient was medicated with fluorometholone bid, levofloxacin every 4 h, and lubricant drops.

At 1-week follow-up the scleral surface underlying the previous site of lesion removal did not appear to present any signs of neoplastic recurrence and the epithelial defect had healed completely and the patient was prescribed an outpatient mitomycin-C (MMC) 0.04 % topical therapy cycles and presented without any signs of local disease recurrence, the corneal epithelium layer was intact, without any staining defects. The conjunctival margins and the sclera previously overlapped by the OSSN lesion did not show any abnormal growth lesions and there was no surrounding hyperaemia or signs of recurrence of the “feeding vessels”. AS-OCT showed no signs of relapsing lesion or any residual hyperreflective epithelial foci (Fig. 6).

Pathology report confirmed the diagnosis of pre-invasive OSSN with conjunctival and corneal intraepithelial neoplasm, but showed no invasion of the surgical margins, a sign of good long-term prognosis.

Visual acuity and refraction did not change during treatment and keratic specular microscopy showed a physiologic rate of endothelial cell loss.

3. Discussion and conclusion

The improvement in the technology of ancillary exams has allowed a higher margin of safety while determining the extent of OSSN lesions.

HR-OCT of the anterior segment findings include thickened, hyper-reflective epithelium and an abrupt transition from healthy to diseased epithelium, similar to morphological findings seen on histopathology and possibly assisting in the differential diagnosis [10].

AS-OCT and UBM may be of critical importance while determining tumour thickness, shape and tumour extension into the sclera, cornea and intraocular structures [5,10–12] therefore contributing to distinguish between intraepithelial versus invasive OSSN. A hyporeflective clear plane of separation is seen beneath the thickened hyperreflective epithelium in 90 % cases of intraepithelial versus invasive OSSN, while there is no plane of separation in cases of invasive OSSN indicating scleral extension of tumour [12].

In the absence of clear diagnostic criteria and guidelines, clinical reasoning and OSSN disease awareness are critical for a timely diagnosis and treatment plan, as several treatment options are available in the treatment of OSSN lesions despite the usefulness of most recent imaging AS-OCT, HR-OCT and UBM in diagnostic and follow-up differentials, allowing an increasing number of patients to be treated non-invasively.

Surgical excision with wide margins using the “no-touch” method was originally the most popular treatment for OSSN. However, in the past two decades, the use of topical medications for OSSN treatment has increased for being an effective alternative to surgical excision. When selecting a topical agent, interferon alpha-2b (IFNα-2b) and 5-fluorouracil (5-FU) are often considered first line therapies for OSSN due to their high-resolution rates and mild side effect profiles [13].

Although these are safe options in most cases of non-invasive OSSN, this patient also presented a high likelihood of needing subsequent intraocular intervention for cataract surgery in the near future, which is known to be one of the key triggers for intraocular tumour extension [12].

Therefore, a combined approach with surgical excision followed by topical Mitomycin C (MMC) was chosen, even while considering its higher toxic profile. This method also provides a definitive pathology diagnosis, which may be useful for research and characterization of different types of OSSN including the development of future guidelines. A careful dissection of OSSN blood supply prior to corneal excision may be helpful due to the ischemic effect on cellular and molecular adhesions between the lesion and the underlying stroma, potentially decreasing stromal damage.

Multimodal imaging techniques are continuously improving and may provide a higher margin of safety in the usage of newer and less studied agents, such as immune checkpoint inhibitors, retinoic acid, cidofovir and anti-vascular endothelial growth factor for the treatment of OSSN, and may prove helpful throughout the patient's follow-up, including post-operative evaluations to detect the completeness of surgical removal and ensure early detection of potential relapses.

Table 1

<table>
<thead>
<tr>
<th>Evaluation</th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oculomotricity</td>
<td>Full motricity, no diplopia reported in cardinal gaze positions</td>
<td></td>
</tr>
<tr>
<td>Auto-refractometry</td>
<td>+1.00-2.75 × 80°</td>
<td>-3.00-0.50 × 115°</td>
</tr>
<tr>
<td>Visual acuity</td>
<td>10/20</td>
<td>10/20</td>
</tr>
<tr>
<td>Intraocular pressure</td>
<td>9 mmHg</td>
<td>12 mmHg</td>
</tr>
<tr>
<td>Keratic specular microscopy</td>
<td>2399 cells/mm²</td>
<td>2498 cells/mm²</td>
</tr>
</tbody>
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Fig. 1. Pre-Operative anterior segment photography of Ocular Surface Squamous Neoplasia.

Fig. 2. Pre-operative anterior segment optic coherence tomography.
Employment statement

None of the authors is currently employed by any institution who will benefit from this research, nor do any of the authors intend to begin such relationship with any such institution.

Non-financial

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.
Submission statement

This submission has not been published elsewhere previously and it is not being considered for any other publication simultaneously.

Informed consent

A written-format informed consent was obtained from the patient before image collection and further case-report file compilation. Written informed consent was obtained from the patient for

Fig. 5. Week-4 post-operative result of surgical removal of OSSN.

Fig. 6. Week-8 post-operative AS-OCT and corneal anterior axial curvature.
publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request. The following case-report was conducted in compliance of the Declaration of Helsinki.

**Patient consent**

The patient signed an informed consent regarding collection, treatment, and presentation of images as well as data related to his condition, diagnosis, treatment or others. The patient also waives any proprietary rights or copyrights he might have over any of such data, images or related materials and presentations.

**Ethical approval**

Additional ethical committee approval for this study was not necessary due to its anonymous case-report nature, as stated by the Centro Académico de Medicina de Lisboa and Centro Hospitalar Universitário Lisboa Norte, both at Avenida Professor Egas Moniz MB, 1649-035 Lisboa.

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**Author contribution**

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Data Analysis or Interpretation: Diogo Bernardo Matos; Paulo Guerra; Ana Quintas; Carlos Marques Neves

Revision work and Structural Refinement: Paulo Guerra; Carlos Marques Neves

**Guarantor**

Diogo Bernardo Matos is the guarantor of the study.

Diogo Bernardo Matos is fully responsible for the presented data, has access to all data, conducted the study and controlled the decision to publish.

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3. Hyperlink to your specific registration (must be publicly accessible and will be checked): N/A

**Conflict of interest statement**

None of the authors have any proprietary interests or conflicts of interest related to this submission.

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**References**


