To Report a Case of OSSN with an Excellent Surgical Outcome

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Abstract: Ocular surface squamous neoplasia (OSSN) represents a rare spectrum of disease ranging from mild dysplasia to carcinoma in situ to invasive squamous cell carcinoma of the ocular surface. OSSN is more common in elderly males, in countries closer to equator and countries where exposure to excessive sunlight is more common. Diagnosis of OSSN is mainly based on clinical suspicion. Definitive diagnosis needs histopathological evaluation. In this article, we report a case of OSSN in a 60 year old male patient.

Keywords: Cornea, Ocular Surface Squamous Neoplasia, OSSN, Conjunctival Auto graft, interferon

1. Introduction

Ocular surface squamous neoplasia (OSSN) represents a rare spectrum of disease ranging from mild dysplasia to carcinoma in situ to invasive squamous cell carcinoma of the ocular surface involving the conjunctiva and the cornea, occurring usually in the interpalpebral area, mostly at the limbus.1

The aetiology of OSSN appears to be a multifactorial, and likely involves a variety of environmental factors in a susceptible host. Smoking and exposure to petroleum products have been implicated in the pathogenesis of OSSN.2 Other causes include:

**Ultraviolet light:** It is well recognized that the prevalence of OSSN is increased in populations that live within 30-degrees latitude from the equator.1,4 In addition, OSSN is more common in Caucasians with light complexions and patients with xeroderma pigmentosum, a genetic condition that increases susceptibility to DNA alterations secondary to UV light. Furthermore, ocular lesions are most commonly located within the sun-exposed interpalpebral fissure, specifically in the nasal or temporal zones.2

**Immunosuppression/ HIV:** In Africa, studies have shown an HIV infection rate as high as 79% in patients with OSSN compared to 14% in the general population.6 In the United States, a study done at Bascom Palmer Eye Institute found that OSSN may be a possible marker for undiagnosed HIV.3 The study found that half of patients diagnosed with OSSN under the age of 50 were seropositive for the virus.3

**Human papillomavirus (HPV):** The association of HPV with OSSN remains unclear. Although some studies have shown a clear association of OSSN with HPV, other studies have not.7,8 Whereas HPV 6, 8, and 11 have been linked with benign conjunctival epithelial lesions, HPV 16 and 18 have been associated with malignant neoplastic lesions.2 However, HPV status does not appear to correlate to treatment response.

**Mutation or deletions of tumour suppressor gene p53:** Mutations of p53, a tumour suppressor gene, are thought to be the most common genetic anomalies in human malignancies.6 Some have hypothesized that HPV or UV-B may alter p53, resulting in the development of OSSN in susceptible individuals.9 Clinically, the diagnosis is suspected by the appearance of epithelial changes of the ocular surface. Slit-lamp examination shows gelatinous, leukoplakic, papilliform or nodular lesions. Histopathological evaluation is essential for the definitive diagnosis and also to differentiate the three lesions in the spectrum of OSSN i.e., epithelial dysplasia, carcinoma in situ and invasive squamous cell carcinoma. We report a case of OSSN in a 60-year-old male

2. Case Report

A 60-year-old male patient presented with the chief complaint of mass in his left eye since 3 months, which was progressively growing in size, and associated with redness. The patient had no history of trauma or surgery to that eye in the past. He had not taken any treatment for his left eye condition
General examination and systemic examination were normal. He is a chronic smoker since 40 years. Best corrected visual acuity in his left eye was 6/9. On local examination of the left eye, a greyish white nodular lesion of size 5.5 mm × 5 mm was present at the limbus between 7°-8° clock position with presence of feeder vessels. The surface of the lesion was irregular. Blood investigations were normal. Serology test for HIV was negative. Left eye ultrasonography was normal.

AS-OCT shows no involvement of the sclera and ciliary body.

Surgical excision is the predominant modality of management for OSSN.\textsuperscript{10} The possibility of the lesion being malignant, further steps of treatment based on the pathology report and chances of recurrence of the lesion were discussed with the patient and informed written consent was taken.

Intraoperatively: The mass was lying near the limbus and no involvement of the bowmen’s membrane was seen.

Mass was excised along with 2 mm of conjunctiva and a conjunctival auto graft (3.5 x 5.5 mm) was taken from supero temporal side and placed on the bare sclera. And the specimen was sent for histopathological evaluation. Postoperatively patient was given topical antibiotic with steroid drops in a tapering dose. AS-OCT was repeated and reported to have no reoccurrence.

To prevent reoccurrence he was started on interferon α2b eye drops one drop 4t/d for 3 months.

3. Histopathology report showed

Hyperplastic stratified squamous epithelium with severe degree of dysplasia composed of atypical cells having irregular hyperchromatic nucleus with dense eosinophilic cytoplasm an occasional atypical mitosis. And reported as: OCULAR SURFACE SQUAMOUS NEOPLASIA (CIN III)

Post-operative:
4. Discussion

Treatment of these tumours includes medical (IFN-a2b, mitomycin C [MMC], 5-fluorouracil [5-FU]), surgical or a combination of medical and surgical treatment.

The following table gives details of the chemotherapeutic agents:

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<th>Agent</th>
<th>Mechanism of action</th>
<th>Details of agent</th>
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<tr>
<td>Topical mitomycin C (MMC) is an antimetabolite</td>
<td>alkylates DNA and disrupts the production of RNA.¹¹</td>
<td>MMC comes in either 0.02% or 0.04%. The lower concentration is usually prescribed continuously for a month; whereas, the higher concentration may be used for a week followed by 2 to 3 weeks off treatment. It must be refrigerated at +4 degree C. The disadvantages of MMC includes ocular pain, possible limbal stem cell loss, and other ocular surface toxicity. Punctal plug occlusion is advised to decrease the risk of punctal stenosis.</td>
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<td>Interferon-α2b (IFNα2b) is a cytokine produced by immune cells to combat microbes and viruses.</td>
<td>It’s mechanism of action is thought to be related to its antiproliferative, cytotoxic, and antigenic properties.¹¹</td>
<td>May be injected sub conjunctivally or used topically as an eye drop. The concentration for the topical eye drop is 1 million IU/mL. The efficacy rate after topical IFNα2b ranges from 80% to 100%.¹² unfortunately, although well tolerated, IFNα2b is only available through specialized compounding pharmacies &amp; requires refrigeration.</td>
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<td>5-fluorouracil (5-FU) blocks DNA synthesis by acting as a pyrimidine analog after incorporation into RNA.¹¹</td>
<td>Its efficacy rate has been reported to be 100% after one to five cycles (1 month on and 3 months off), with a recurrence rate of up to 20%.¹³ Others prescribe it for 4 to 5 days every month; however, this dosing is associated with a higher recurrence rate.¹⁴ The disadvantages of 5-FU include mild ocular irritation and occasional conjunctivitis.</td>
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Surgical Excision

Surgical excision with "wide margin, no touch" technique is currently the best established form of treatment. Nevertheless, recurrences of these lesions are common after surgical excision, depending on the involvement of the surgical margins. Recurrence rates following excision of OSSN alone range from 15 to 52%, with an average of 30%. Recurrence rate is 5% when the surgical margins are free and 53% when the surgical margins are involved.¹⁵ Conjunctival defect can be closed primarily. Larger defects require either transpositional conjunctival flaps, free conjunctival flaps from the other eye, or amniotic membrane grafts. Adjunctive therapy to reduce recurrence includes intra operative cryotherapy and brachytherapy, postoperative topical chemotherapy using mitomycin C, 5-FU and interferon alfa-2b.

Differential Diagnosis of OSSN

- Corneal pannus
- Pterygium
- Pingueculum
- Melanoma
- Conjunctival nevus
- Dyskeratosis
- Pyogenic granuloma
- Keratoacanthoma
- Conjunctival lymphoma (salmon patch)

Prognosis

OSSN is a low grade malignancy with overall good prognosis and low incidence of lymph node or distant metastasis. Most significant prognostic factor for recurrence is presence of neoplastic cell in margins after tumour excision.
References