Case Series

Ocular Surface Squamous Neoplasia (OSSN): Early Diagnosis and Case-based Approach to Management

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Abstract

Objective: To evaluate four cases of ocular surface squamous neoplasia (OSSN), with unilateral and bilateral presentation and follow a case based approach to management emphasizing the importance of interferon alpha-2b in the management.

Methods: The mean age of patients at presentation was 53 years. The mean size of the lesion was 8.0×8.7×4.0 mm (range: 4×5×1 mm to 16×14×10 mm). While one of the cases had no corneal involvement, three of the cases presented with different extents of limbal and corneal involvement. After making a clinical diagnosis of OSSN, two patients were given peri-lesional and two intra-lesional interferon Alpha 2B and topical interferon alpha 2b was started four times a day in the affected eye in all patients. One of the patients was shifted to 5-fluro-uracil due to ocular irritation with interferon alpha 2b. In another, surgical excision with amniotic membrane transplantation was required due to the large size of the lesion.

Results: Recurrence occurred in one of the cases but shifting the patient from mitomycin-C to interferon alpha 2b resulted in remission in the next 3 months. Two cases were followed up on interferon alpha 2b therapy alone. A six month follow up in all four cases showed remission and no evidence of recurrence of disease.

Conclusion: OSSN is the most common malignancy of the ocular surface. Early diagnosis and proper treatment are important for a favourable outcome. Interferon-alpha-2b plays an important role in the treatment showing excellent outcomes after initiation of therapy however, an individualised approach to treatment with various combinations is necessary in some cases.

Keywords: Ocular surface squamous neoplasia (OSSN), Interferon alpha-2b, Intra-lesional, Peri-lesional, Exophytic mass, Cornea, Limbus, Conjunctiva.

Introduction

Ocular surface squamous neoplasia (OSSN) encompasses a spectrum of dysplastic and neoplastic lesions of the conjunctival and corneal epithelium, ranging from conjunctival intra-epithelial neoplasia to invasive squamous cell carcinoma. It is the most common malignancy of the ocular surface and typically presents as non-pigmented lesion involving the conjunctiva and/or cornea.[1] The reported incidence varies geographically, with rates ranging from 0.02 to 3.5 cases per 100,000 population per year, and is particularly high in regions with intense ultraviolet radiation exposure and a high prevalence of human immunodeficiency virus infection.[2] Risk factors associated with OSSN include ultraviolet-B exposure, human papillomavirus infection, immunosuppression, chronic ocular surface inflammation, and advanced age.[2] Despite its generally favourable prognosis, OSSN demonstrates considerable variability in clinical presentation and biological behaviour, necessitating careful evaluation and individualized treatment planning.

Traditionally, surgical excision using the no-touch technique with adjunctive cryotherapy has been regarded as the standard treatment for OSSN.[3] However, advances in diagnostic imaging and medical management have led to increasing utilization of topical and injectable chemotherapeutic agents such as interferon alpha-2b, 5-fluorouracil, and mitomycin-C.[4] These treatment modalities

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have demonstrated excellent efficacy in selected cases while minimizing surgical morbidity and preserving ocular surface anatomy and function. Although topical chemotherapy has become an effective treatment for OSSN, ocular surface toxicity remains a concern. Mitomycin C is associated with the highest incidence of adverse effects, including limbal stem cell deficiency, punctal stenosis, and persistent epithelial defects, whereas 5-fluorouracil commonly causes transient ocular irritation and keratitis. Interferon α-2b has the most favourable safety profile, with predominantly mild and reversible ocular side effects like blurring of vision, dry eyes and conjunctivitis.[5]

Recent evidence suggests a paradigm shift from a uniform treatment approach toward personalized management based on tumour characteristics and patient-specific factors.[6] Parameters such as tumour size, limbal and corneal involvement, multi-focality, recurrence status, ocular surface health, visual potential, and patient compliance play an important role in determining the optimal therapeutic strategy. Consequently, contemporary management of OSSN increasingly relies on tailoring treatment modalities to individual clinical presentations in order to maximize tumour control while minimizing recurrence and treatment-related complications.

The present case series illustrates the diverse clinical spectrum of OSSN and highlights how management can be customized according to the characteristics of each case. Through these cases, we aim to demonstrate the rationale behind individualized treatment selection and the outcomes achieved with a tailored therapeutic approach.

Case Series

CASE 1

A 33-year-old male presented to the eye OPD with complaints of redness and ocular pain in the right eye (OD) for 6 months. There was no history of trauma or systemic illness. Examination of the left eye (OS) revealed a best corrected visual acuity (BCVA) of 0.0 in logMAR with normal intraocular pressure (IOP).

The right eye (OD) also demonstrated a BCVA of 0.0 in logMAR with normal IOP. Slit-lamp examination of OD showed an elevated nasal conjunctival mass measuring 4 x 7 x 1-mm, with a gelatinous surface and a prominent feeder vessel supplying the lesion. An unusual finding of pigmentation was observed over the plica semilunaris.

The lesion stained positive with rose Bengal, indicating keratinisation. A provisional diagnosis of ocular surface squamous neoplasia (OSSN) in OD was made. The patient was started on topical interferon alpha 2B eye drops four times daily, following a perilesional injection of interferon alpha 2B administered on the same day of presentation.

At 4 weeks follow-up, the lesion had completely resolved, and there was no evidence of recurrence at 6 months.

CASE 2

A 56-year-old female presented to the Ophthalmology Outpatient Department with complaints of redness and foreign body sensation in her right eye for the past three months. There was no history of ocular trauma or systemic illness.

On examination, the left eye had a best corrected visual acuity (BCVA) of 0.0 in logMAR with normal intraocular pressure (IOP). The right eye also demonstrated a BCVA of 0.0 in logMAR with normal IOP. Slit-lamp examination of the right eye revealed an elevated, gelatinous mass measuring approximately 4 x 5 x 1 mm, extending over the nasal limbus (covering 2 clock hours) and spreading onto both the adjacent cornea and nasal conjunctiva. The lesion stained positively with rose Bengal dye. Based on these findings, a provisional diagnosis of ocular surface squamous neoplasia (OSSN) was made (Figure 1).

The patient was administered a peri-lesional injection of interferon alpha-2B (INF α-2B) on the day of presentation and was prescribed topical INF α-2B eye drops, four times daily for four weeks. At the two-week follow-up, she reported ocular irritation associated with drop instillation. Slit-lamp examination revealed conjunctival congestion. In view of these adverse effects, the treatment was modified to topical 5-fluorouracil (5-FU) eye drops, four times daily for three weeks.

At the three-week review, marked regression of the lesion was noted. The patient was followed up regularly, and no recurrence was observed over a six-month period.

CASE 3

A 65 year old male came to eye OPD with complaints of a mass growing in the left eye since one year. On examination, both eyes were pseudophakic and gave BCVA of 0.2 in logMAR.

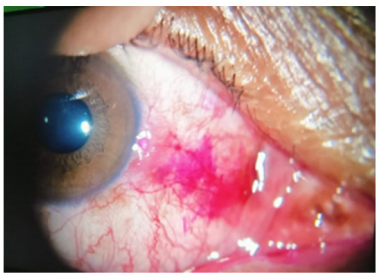


Figure (A)

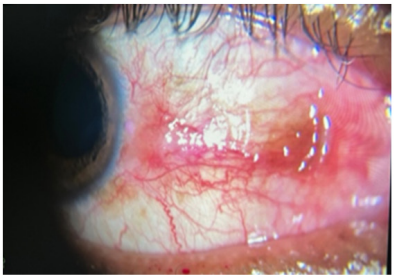


Figure (B)

Figure 1: (A) Staining of lesion with rose Bengal dye. (B) Regression of lesion after treatment



Figure (A)

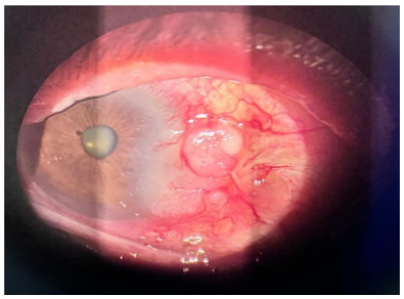


Figure (B)

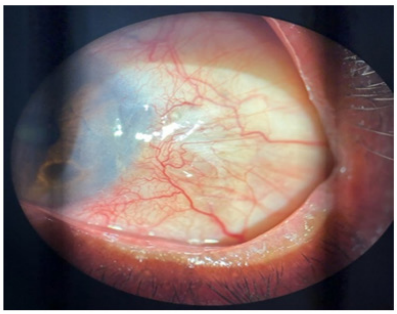


Figure (C)

Figure 2: (A) Image showing exophytic lesion in left temporal conjunctiva at the time of presentation. (B) Recurrence of lesion after surgical excision and topical mitomycin-c. (C) Regression of lesion after shifting to topical Interferon alpha-2B.

External ocular examination of left eye revealed a large, exophytic, fleshy mass of size, 16 x 14 x 10 mm arising from the ocular surface, predominantly involving the temporal bulbar conjunctiva and prolapsing through the palpebral fissure. The lesion appears pink with a lobulated and keratinized surface with prominent vascularity. The mass was broad based, non-pigmented occupying the inter palpable area and obscuring the underlying sclera and 3 mm of cornea (Figure 2).

Right eye for comparison showed relatively normal ocular surface with age related changes. No similar lesion was noted in the right eye.

The ocular surface lesion was evaluated with vital staining using rose Bengal, which demonstrated positive uptake over the surface of the mass, highlighting devitalised epithelium. Cross-sectional imaging with computed tomography (CT) scan of the orbit revealed a well defined soft tissue mass, localised to the ocular surface without evidence of scleral invasion, involvement of extra-ocular muscles or orbital structures, indicating the lesion was confined to superficial tissues, helping in planning management and surgical approach.

The patient was initially treated with two sequential perilesional injections of Interferon alpha 2b along with topical Interferon alpha 2b eye drops however, no significant regression of the lesion was observed. Subsequently, surgical excision with amniotic membrane transplantation was performed. The excised tissue was sent for histopathological examination, which revealed moderately differentiated squamous cell carcinoma.

Postoperatively, the patient was started on adjuvant therapy with mitomycin C 0.04% eye drops. At 3-month follow-up, the patient developed punctate keratopathy along with regrowth of the lesion. The patient was then shifted to topical interferon alpha-2b eye drops (QID), which resulted in complete resolution of the lesion within 6 weeks.
No recurrence was noted at the 6-month follow-up.

CASE 4

A 59 year old male presented to eye OPD with complaints of redness and a mass growing in the right eye since one month, patient had no systemic illness.

Both eyes visual acuity was 0.2 in logMAR. Slit lamp evaluation of right eye reveals a corneal and conjunctival based mass extending from 4 o'clock to 12 o'clock in limbal region. The lesion is elevated, irregular and gelatinous, showing areas of leucoplakia along with patchy pigmentation over the conjunctival area of the mass (Figure 3A).

The lesion demonstrates positive staining with rose Bengal dye highlighting areas of the devitalised epithelium. There is associated prominent vascularity with dilated tortuous vessels, approaching the lesion along with surrounding conjunctival congestion and hyperaemia (Figure 3B).

Overall, the features are suggestive of lesion within the OSSN spectrum and was managed as follows. The patient was started on immunotherapy using interferon alpha-2b. Intra-

Table 1: Demonstrates the comparison between the findings in each case.

	Case 1	*Case 2*	*Case 3*	*Case 4*
Age/Sex	33/Male	56/Female	65/Male	59/Male
Presenting complaints	Redness and pain in OD for 6 months	Redness and foreign body sensation in OD for 3 months	Growing mass in OS for 1 year	Redness and mass in OD for 1 month
Eye involved	Right eye	Right eye	Left eye	Right eye
BCVA (logMAR)	0.0	0.0	0.2	0.2
Lesion size (LxWxH) (mm)	4x7x1	4x5x1	16x14x10	Diffuse lesion from 4 o clock to 12 o clock at limbus
Lesion morphology	Elevated gelatinous nasal conjunctival mass	Elevated gelatinous limbal conjunctival mass	Large exophytic, lobulated , keratinized mass	Elevated gelatinous corneo-conjunctival lesion with leukoplakia
Corneal involvement	No	Yes	No	Yes
Limbal involvement	No	Yes	Yes	Yes
Pigmentation	Pigmentation over plica semilunaris	Absent	Absent	Patchy pigmentation present
Rose Bengal staining	Positive	Positive	Positive	Positive
Feeder vessel	Present	Present	Present	Present with tortuosity
Imaging	Not performed	Not performed	CT orbit showed no scleral/orbital invasion	Not performed
Initial treatment	Peri-lesional IFN alpha 2B + topical IFN alpha 2B	Peri-lesional IFN alpha 2B + topical IFN alpha 2B	2 IFN alpha 2B injections + topical IFN alpha 2B	3 IFN alpha 2B injections + topical IFN alpha 2B
Response to initial treatment	Complete resolution within 4 weeks	Ocular irritation and congestion	Poor response	Progressive regression
Additional treatment	None	Switched to topical 5-Fluoro uracil QID X 3 weeks	Surgical excision + AMT + topical Mitomycin-C 0.004%	None
Histopathology	Not done	Not done	Moderately differentiated SCC	Not done
Time to complete resolution	4 weeks	5 weeks	6 weeks after restarting IFN alpha 2B	3 months
Complications	None	Ocular irritation with IFN alpha 2B	Punctate keratopathy and recurrence after mitomycin-C	Residual nebulo-macular corneal opacity
Recurrence	None at 6 months	None at 6 months	Recurrence after Mitomycin-C, resolved with IFN alpha 2B	None at 6 months
Final outcome	Complete resolution	Complete resolution	Complete resolution	Complete resolution with residual corneal opacity

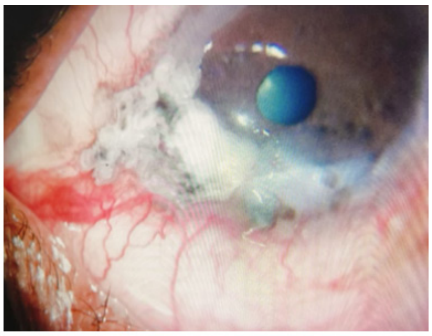


Figure (A)

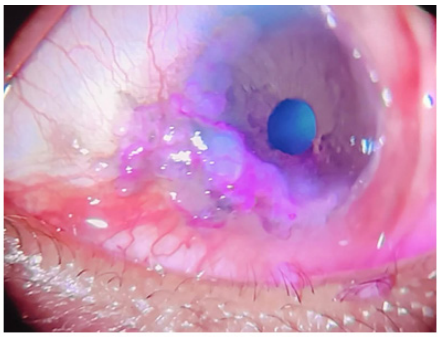


Figure (B)

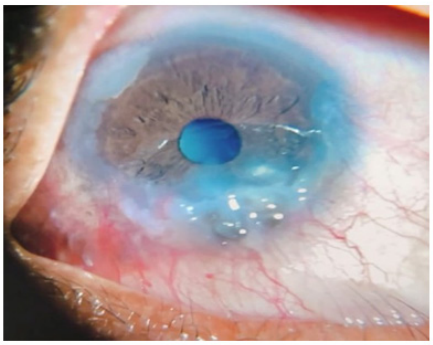


Figure (C)

Figure 3: (A) Lesion showing prominent feeder vessel with patchy pigmentation in right eye. (B) Rose Bengal dye staining of the lesion. (C) Regression of lesion after treatment

lesional interferon alpha-2b injections were administered in three doses at 3-week intervals, along with topical interferon alpha-2b eye drops (1 million IU/mL) instilled four times daily.

The lesion showed progressive regression with complete clinical resolution over a period of 3 months (Figure 3C). At final follow-up, there was no evidence of residual or recurrent mass, with healing noted in the involved area. However, a macular grade corneal opacity persisted in the previously affected region, corresponding to the site of prior lesion involvement.

Discussion

Ocular surface squamous neoplasia (OSSN) represents a spectrum of dysplastic and neoplastic epithelial lesions ranging from conjunctival intraepithelial neoplasia to invasive squamous cell carcinoma. Although traditionally considered a disease of elderly individuals, recent literature has demonstrated considerable heterogeneity in age at presentation, tumour morphology, and treatment response. Contemporary management has shifted from a predominantly surgical approach to individualized treatment strategies incorporating topical and injectable chemotherapeutic agents, particularly interferon alpha-2b (IFN α-2b).[2,4,6,8]

In the present series, patients ranged from 33 to 65 years of age. While OSSN is most commonly reported in the sixth and seventh decades of life, younger patients may also be affected, especially in regions with significant ultraviolet exposure.[2,4] The 33-year-old patient in our series (Case 1) highlights this variability and emphasizes that OSSN should remain a differential diagnosis even in relatively young individuals presenting with chronic conjunctival masses.

Clinically, all lesions demonstrated characteristic features described in the literature, including gelatinous appearance, feeder vessels, leukoplakia, corneal extension, and positive rose Bengal staining. Höllhumer *et al*. reported that gelatinous and leukoplakic lesions with prominent intrinsic vascularity remain among the most common clinical presentations of OSSN.[2] Similarly, Tsatsos *et al*. emphasized that feeder vessels and epithelial staining patterns continue to be important clinical clues despite advances in imaging modalities.[7] In our series, rose Bengal positivity was observed in all cases and proved useful in delineating devitalized epithelium and guiding diagnosis.

Recent studies have increasingly supported medical therapy as a primary treatment modality for selected OSSN lesions. Interferon alpha-2b has gained popularity because of its favourable safety profile and ability to preserve limbal stem cells while achieving tumour control rates comparable to surgery.[4,6] Greenfield *et al*. described a major shift in the standard of care over the last two decades, with increased

utilization of topical immunotherapy either as primary treatment or adjunctive therapy.[8]

Cases 1 and 4 in our series demonstrated excellent responses to interferon-based therapy. Case 1 achieved complete resolution within four weeks following a combination of peri-lesional interferon injection and topical therapy. This rapid response is consistent with reports showing high success rates of IFN α-2b for localized OSSN lesions, particularly those of limited size and thickness.[4,6] Case 4, despite exhibiting extensive limbal involvement from 4 to 12 o'clock with associated leukoplakia and pigmentation, responded completely after three intralesional injections and topical interferon over three months. Similar outcomes have been reported by Monroy *et al*., who noted that larger lesions may require prolonged treatment duration but still demonstrate excellent tumour control with interferon therapy.[6]

Case 2 illustrates the importance of individualized treatment selection. Although the patient was initially started on interferon therapy, ocular irritation and conjunctival congestion necessitated a switch to topical 5-fluorouracil (5-FU). Following the change in treatment, marked regression was observed without recurrence during follow-up. Medical treatment reviews have shown that both IFN α-2b and 5-FU achieve comparable efficacy, with choice often influenced by cost, availability, adverse effects, and patient tolerance.[4,6] This case highlights the flexibility of modern OSSN management and supports the concept that treatment can be tailored according to patient-specific factors rather than adhering to a single therapeutic approach.

The most challenging case in our series was Case 3, which presented as a large exophytic lesion measuring 16 × 14 × 10 mm. Such extensive tumours are relatively uncommon and often raise concerns regarding scleral or orbital invasion. Agarwal *et al*. reported similar large corneal-conjunctival OSSN lesions and emphasized the importance of imaging in defining the extent of disease before intervention.[9] In our patient, CT imaging confirmed confinement of the lesion to superficial tissues, facilitating surgical planning. Unlike the smaller lesions in this series, the tumour demonstrated poor response to initial interferon therapy and ultimately required surgical excision with amniotic membrane transplantation. Histopathology confirmed moderately differentiated squamous cell carcinoma, representing the invasive end of the OSSN spectrum.

Current evidence suggests that surgery remains important for large, thick, invasive, or diagnostically uncertain lesions despite increasing use of topical therapies.[2,7,8] The management of Case 3 aligns with these recommendations. Interestingly, recurrence occurred despite adjuvant mitomycin-C therapy, manifesting as lesion regrowth accompanied by punctate keratopathy. Mitomycin-C is known to be highly effective but may be associated with ocular surface toxicity, including keratopathy, limbal stem cell deficiency, and conjunctival irritation.[4,6] Following conversion to topical interferon therapy, complete regression was achieved within six weeks, demonstrating the utility of interferon even in recurrent disease.

Another notable observation in our series was the presence of pigmentation in cases 1 and 4. Pigmented OSSN is relatively uncommon and may clinically mimic conjunctival melanocytic lesions, potentially leading to diagnostic confusion. Previous studies have documented pigmentation in a subset of OSSN cases, particularly in darker-skinned populations.[2,7] Recognition of this atypical presentation is important to avoid delayed diagnosis and inappropriate management.

No recurrence was observed in any patient during the six-month follow-up period. Although longer surveillance is required because recurrence may occur years after treatment, short-term outcomes in our series compare favourably with published reports demonstrating high tumour control rates following interferon-based therapy.[2,4,8] The absence of recurrence despite varied clinical presentations further supports the effectiveness of individualized treatment approaches.

Overall, our findings reinforce the current paradigm shift in OSSN management toward personalized therapy. Small and moderate-sized lesions responded well to interferon-based treatment, while extensive invasive disease required a multimodal approach involving surgery, histopathological confirmation, and adjunctive medical therapy. The clinical outcomes observed in this series are consistent with recent literature advocating treatment selection based on lesion characteristics, extent of involvement, patient tolerance, and risk of recurrence.[4,6-8]

Conclusion

Ocular surface squamous neoplasia demonstrates considerable variability in clinical presentation, tumour size, and response to treatment, highlighting the importance of an individualized management strategy. In our series, interferon alpha-2b proved to be an effective and well-tolerated first-line treatment for most lesions, while larger or invasive tumours required multimodal management with surgical excision and adjunctive therapy. Careful clinical evaluation, appropriate treatment selection based on lesion characteristics, and regular follow-up resulted in favourable outcomes with complete tumour resolution and no recurrence during the six-month follow-up period. These cases emphasize that a tailored approach can optimize tumour control while preserving ocular surface integrity and visual function.

Conflicts of Interest

There are no conflicts of interest.

Ethical Clearance

Ethical clearance was not required as this is an observational analysis that maintains strict patient anonymity.

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