

# TREATMENT OF OCULAR SURFACE SQUAMOUS NEOPLASIA (OSSN) WITH SURGICAL EXCISION & ADJUNCTIVE TOPICAL MITOMYCIN C THERAPY

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## Ophthalmology

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### Abstract:

**Background:** To report the outcome of treatment of ocular surface squamous neoplasia with surgical excision and adjunctive Mitomycin C Therapy over a period of 5 years.

**Methods:** 7 eyes of 7 patients were included in the study between July 2010 & July 2015. Protocol for the management comprised of surgical excision with cryotherapy followed by histological evaluation of the lesion with a 2 mm of healthy rim followed by topical Mitomycin C 0.02% four times a day to all postoperative patients in 3-4 cycles of alternate on and off weekly courses. At each visit, patients were looked for recurrence of tumor and corneal alterations like keratitis or erosions. Successful treatment was defined as no clinical recurrence of OSSN in 1 year of follow up.

**Result:** Average age in this study was 45.28 years with 4(57%) patients above 40 years with 57% male preponderance. With a follow up period of 1 year, 100% success rate was found despite of late stage presentation in our study.

**Conclusions:** Mitomycin C treatment following surgical excision decreases the recurrence rate of primary ocular surface neoplasia and should be considered as an adjunctive therapy in primary treatment.

**Keywords:** Mitomycin C, ocular surface squamous neoplasia, recurrence of ocular surface squamous Neoplasia.

### Introduction

The term ocular surface squamous neoplasia (OSSN) was first described in 1995 by Lee and Hirst to denote a spectrum of neoplasm originate from squamous epithelium ranging from simple dysplasia to invasive squamous cell carcinoma (SCC), involving the conjunctiva, the limbus, and the cornea.<sup>1</sup> This tumor is considered as a low grade malignancy but invasive lesion can spread to the globe or orbit. OSSN is considered an uncommon

disease with geographic incidences which vary from 0.2 to 3.5 per 100,000; with greater frequency near the equator. OSSN accounts for only 5% of all ocular malignancies.<sup>1</sup> Prior to HIV pandemic, OSSN was noted to occur predominantly in the elderly for whom it was the third most common oculo-orbital tumor after malignant melanoma and lymphoma.<sup>1</sup>

Squamous cell neoplasia may occur as a localized lesion confined to the surface epithelium (conjunctival intraepithelial

neoplasia) or as a more invasive squamous cell carcinoma that has broken through the basement membrane and invaded the underlying stroma.<sup>2</sup> Currently, the accepted term for the localized variety is conjunctival intraepithelial neoplasia (CIN). Those cases where the cornea is invaded by the process are usually called conjunctiva-cornea intraepithelial neoplasia (CCIN).

Primary treatment is usually surgical excision, however tumor recurrence is common; we assessed the effect of adjunctive 0.02% topical Mitomycin C in reducing recurrence rate.

## Methods

7 eyes of 7 patients with primary OSSN who presented between July 2010 and July 2015 were included in this study. A detailed history on demographic details, symptoms and its durations, exposure to risk factors were taken and written consent taken from all patients.

Clinical examination included visual acuity, refraction, anterior segment, evaluation for shape, size, extent, mobility of the lesion, anterior chamber reaction, involvement of cornea, sclera, fluorescein, and 1% rose bengal staining under slit-lamp biomicroscopy, lymphadenopathy to make a clinical diagnosis. Routine laboratory work up including human immunodeficiency virus (HIV) serology tests was done. Inclusion criteria were clinically diagnosed cases of OSSN by slitlamp bio microscope and OSSN which were confirmed on HPR.

Protocol for the management comprised of surgical excision of the lesion with a 2 mm of healthy rim, using no irrigation and single touch technique, instruments were changed once the tumor was removed, followed by reverse cryotherapy (to avoid unnecessary cryoablation of underlying sclera and uvea) to the cut end of conjunctiva for 30 seconds and the cornea and limbus for 10 seconds using double freeze thaw technique.

The ocular surface was left to heal or amniotic membrane grafting was done if the ocular surface defect was bigger than 4\*4 mm. Specimen was sent for histopathological examination. After corneal epithelial healing, topical Mitomycin C 0.02% four times a day to all postoperative patients in 3-4 cycles of alternate on and off weekly courses was advised. The drug is available in a vial (2 mg/ml); it is

further reconstituted with 10 ml of normal saline to make it 0.2 mg/ml. The drug should be stored under refrigerator after reconstitution to preserve its potency and under these conditions, it is potent for 14 days. Patients were followed up weekly after the start of treatment protocol and monthly after treatment ended. At each visit, slit-lamp examination with sodium fluorescein was performed along with routine examination for recurrence of tumor and corneal alterations like keratitis or erosions. Efficacy of Mitomycin C as an adjuvant therapy was measured in terms of clinical cure and recurrence of the tumor.

## Results

Mean age of patients was 45.28 years (range: 15-75years). A total of 3 of 7(43%) patients were below 40years and with male preponderance (57%). [Table 1] Symptoms at presentation mainly were foreign body sensation followed by mass per eye, redness, injury, burning sensation etc. [Table 2] Duration of symptoms showed that 2 patients (28%) presented beyond 6 months [Table 3]. Sunlight exposure was present in 6 (85%) patients, 3 (43%) were smokers and 2 were having a history of Xeroderma Pigmentosa. [Table 4]

Smallest mass was measured 2.5\*3.2 mm; while the largest was 13.2\*12.7 mm. Corneal infiltration was evident in 4(57%) cases. Visual acuity remained stationary or improved in cases where lesion covered the visual axis postsurgery; no deterioration of VA was observed. Clinically, OSSN was leukoplakic lesion to large cauliflower-surfaced gelatinous lesion. Histopathologically, 5(71%) cases had SCC either with well or moderate differentiation [Table 5], with 2(28%) having carcinoma in situ. Only 2(28%) cases showed marginal clearance, while 4(57%) had at least one margin showing dysplasia and 1(14%) cases had at least two margins showing dysplasia. [Table 6] Mean follow-up of 1 year revealed no recurrence with success rate being 100%.

**Table 1: Demographic Profile**

Age in Years	No. of patients (%)
0- 20	1(14)
20-40	2(28)
41-60	2(28)
61-80	2(28)
<b>Gender</b>	
Male	4(57)
Female	3(43)

**Table 2: Symptoms of OSSN**

Symptoms	No. of patients (%)
Foreign body sensation	1(14)
Foreign body sensation + mass in eye	3(43)
Mass in eye	1(14)
Redness	2(28)
Burning Sensation	2(28)
Diminution of Vision	1(14)

**Table 3: Duration of presentation in OSSN**

Duration of symptoms	No. of patients (%)
<2 weeks	1(14)
2 weeks- <2 months	2(28)
2 months - <4 months	1(14)
4months- <6 months	1(14)
>6 months	2(28)

**Table 4: Risk factors in OSSN**

Risk factors	No. of patients (%)
Sunlight	4(57)
Sunlight+Smoking	2(28)
Smoking	1(14)
HIV	0
Xeroderma Pigmentosa	2(28)

**Table 5: Histological findings in OSSN**

Histological types	No. of patients (%)
Carcinoma in situ	2 (28)
Well differentiated Squamous cell carcinoma(SCC)	2 (28)
Moderately differentiated SCC	3 (43)

**Table 6: Marginal clearance after surgical excision**

Margin showing dysplasia	No. of patients (%)
Free margin	2 (28)
At least one margin	4 (57)
With two margin	1 (14)

**Figure 1(a):  
Pre op pic of patient having OSSN with a positive history of XP**



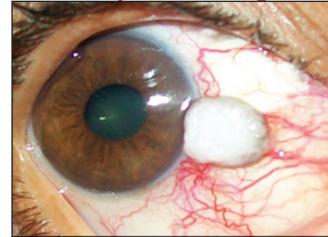
**Figure 1(b):**

**Follow up pic of the same patient undergone mass excision, cryoablation, Amniotic Membrane Grafting followed by topical MMC administration at 2 month follow up visit**



**Figure 2(a):**

**Pre op pic of patient having OSSN with a positive history of smoking**



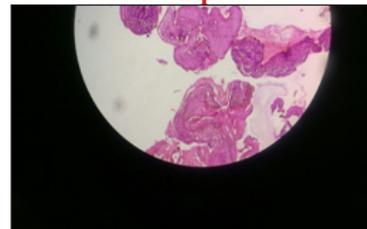
**Figure 2(b):**

**Post op pic of the same patient undergone mass excision, cryoablation and amniotic membrane grafting**



**Figure 2(c):**

**Histological study confirming SCC in excision biopsy sample**



**Figure 3(a):  
Pre op pic of a patient having OSSN with a positive  
history of sunlight exposure**



**Figure 3(b):  
Follow up pic of the same patient undergone mass ex-  
cision, cryoablation followed by topical MMC adminis-  
tration at 2 month follow up visit**



## Discussion

We had 7 patients with primary OSSN between July 2010 and July 2015. Mean age at presentation was 45.28 years; 64 years (range: 47-87),<sup>2</sup> 69 years (range: 32-94).<sup>4</sup> Most common risk factors were exposure to sunlight and smoking similar to other studies.<sup>5</sup> A total of 57% of eyes had FB sensation as the presenting symptom and 28% presented beyond 6 months, similar to that reported by Prabhasawat et al (57.1%).<sup>6</sup> A total of 71% had SCC slightly more than that of results to Babar et al study;<sup>7</sup> these presentations in our study suggested that our patients presented at an advanced stage.

Primary excision has been the mainstay of treatment for OSSN, as it is impossible to exclude invasive disease on clinical grounds or with impression cytology. Excision allows an immediate histopathological diagnosis, surgical debulking, and excludes life-threatening invasive carcinoma.<sup>8</sup> As per Kaines et al study<sup>9</sup>, the disadvantage of primary excision alone is the high recurrence rate which ranges from 15% to 52%. Therefore, numerous adjunctive treatments have been described in an attempt to decrease the rate of recurrence and the efficacy of various adjunctive therapies has been debated.

Despite the effort to excise the tumor with a wide healthy rim, only 2 cases (28%) had marginal clearance and the rest had residual dysplastic edges, suggestive of multifocal origin of OSSN or macroscopically invisible tumor edges. In such a situation, a repeat surgery to clear residual edges with safety margins would leave not only a large defect in ocular surface but also would lead to limbal stem cell deficiency.<sup>8</sup> Hence, Mitomycin C, an alkylating agent which acts by inhibiting DNA synthesis and produces cell death by apoptosis and necrosis was used.<sup>10</sup> As the drug has a preferential action for rapidly dividing cells, acts as a significant antitumor agent and since 1994, several groups have reported the use of MMC in the treatment of both primary and recurrent OSSN.

On histopathological study margins were free in only 2 patients after surgical excision; it clearly shows a need of adjunctive MMC as antitumor agent postoperatively.

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