Original Research Paper

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Ophthalmology

CLINICAL & HISTOPATHOLOGICAL ANALYSIS OF PRESUMED OCULAR SURFACE SQUAMOUS NEOPLASIA(OSSN).

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ABSTRACT

BACKGROUND - Ocular surface squamous neoplasia (OSSN) is an encompassing term for precancerous and cancerous epithelial lesions of the conjunctiva and cornea. It includes the spectrum of dysplasia, Carcinoma In Situ (CIN), and invasive Squamous Cell Carcinoma (SCC). In recent times, the incidence of OSSN seems to be on the rise, especially in developing countries like India.

AIM-To analyze the clinical presentation and Histopathological features of presumed OSSN. DESIGN – Retrospective cross-sectional study. **METHODS** - We analyzed 27 patients with suspected OSSN from June 2017 - May 2018. Patients were examined to determine the type, location, corneal involvement. All patients underwent excision biopsy with 4mm free margin. RESULTS – 19(70.3%)cases out of 27 were histopathological proven OSSN.

Age range of patients was found to be 13 to 79 years, mean age being 55.20 years. Majority of patients were males accounting for 68%. Gelatinous type is the most common clinical variety. 2 patients had Xerdoderma pigmentosa(XP) and 5 were tested positive for HIV. **CONCLUSION** – OSSN is more commonly found in males and outdoor workers and also has positive association with XP and HIV. Leukoplakic type is commonest variety. Thorough knowledge of clinical presentation and clinical examination is necessary for an ophthalmologist and surgical excision with a clear margin should be done in all doubtful cases of OSSN.

KEYWORDS : OSSN, HIV, HPV, Xeroderma, CIN

INTRODUCTION

Ocular surface squamous neoplasia (OSSN) is an encompassing term for precancerous and cancerous epithelial lesions of the conjunctiva and cornea. It includes the spectrum of dysplasia, CIN, and invasive SCC.[1-3]Majority of cases are CIN, which accounts for 39% among all premalignant and malignant lesions of conjunctiva.[4]Incidence of invasive SCC is comparatively less, varying from 0.02 to 3.5/1,00,000 population.[5]Ocular surface squamous neoplasia is mostly unilateral and is seen in middle-aged and older patients. Rarely, it is bilateral in immunosuppressed patients. Risk factors for OSSN are prolonged exposure to UV light, Xeroderma Pigmentosa, HPV,HIV and old age.UV-B causes pyrimidine dimer formation and damage to nucleotide excision repair which is responsible for DNA repair. It has also been seen to cause p53 mutation which can be seen in OSSN.[6]XP is an autosomal recessive disorder with defective DNA repair mechanism which predisposes to OSSN with aggressive clinical presentation at a younger age. OSSN has been reported as early as 3 years of age in a patient of XP.[7] Human papilloma virus(HPV) - HPV 6, 11 has been associated with dysplasia and malignant lesions of conjunctiva and cornea. HPV 16, 18 has also been implicated in conjunctival intraepithelial neoplasias.

Human immunodeficiency virus*:* HIV infection is now established as a risk factor for the development of squamous cell neoplasia of the conjunctiva.[8,9] OSSN can also be clinical presentation of HIV in young patients.[10] OSSN occurring in HIV patients are more aggressive and invasive that may require enucleation or even exenteration. Other risk factors include chemical exposure (beryllium, arsenicals, petroleum products) cigarette smoking, vitamin A deficiency, and viruses like herpes simplex virus (HSV) type I. OSSN can be misdiagnosed as nondysplastic lesions such as pterygium, pingecula inflammatory process, or epithelial hyperplasia.[11,12]Although pathological diagnosis through an excision of a lesion is essential to identify OSSN, excisional biopsy carries a risk of inducing scarring and limbal deficiency in the cornea. Hence, it would be beneficial for patients as well as for clinicians if there are clinical findings that correlate with pathological diagnosis indicating dysplastic lesions such as SCC or CIN.

STUDY DESIGN AND ETHICAL CLEARANCE

A retrospective cross-section study was conducted on patients presenting to the out-patient Department of Ophthalmology at K S Hegde Charitable Hospital, Mangaluru over a period of 1year from June 2017 to May 2018. Ethical clearance was obtained from the Ethics Committee, the study adhered to the principles as laid down by the Declaration of Helsinki. Informed consent for surgery was obtained from all the eligible participants.

MATERIALS AND METHODS

We analyzed 27 subjects who were suspected clinically to have OSSN and included them in the study.

Demographic data including age, sex, occupation and detailed history were obtained. Thorough examination under slit-lamp was done and clinical features such as site, size, type, location, extent of the lesion, and corneal involvement was noted. Routine investigations like Hb%, CT, BT and HIV test were done after obtaining informed consent of the subjects. Patients who had Sessile, fleshy, papillomatous, elevated lesion. Frosted epithelium over peripheral corneal surface adjacent to limbal lesions. Pigmented lesions and Dilated feeder vessels were selected.

All surgeries were performed under local anesthesia. All tumors were resected intact, using the 'No touch technique' with at least 4mm clear margin. Cryotherapy was applied on edges of conjunctiva and bare sclera using double freeze-thaw technique for 30-45secs. Amniotic membrane graft was placed over the excised area and sutured with 10-0 ethilon. Superficial keratectomy was done in cases where cornea was involved.

All excised tissues were sent for histopathologic evaluation.

RESULTS

Out of 27 cases 19(70.3%) were histopathological proven OSSN cases and were analyzed further. Out of 19 cases 13(68%) were males and 6(32%) were females.

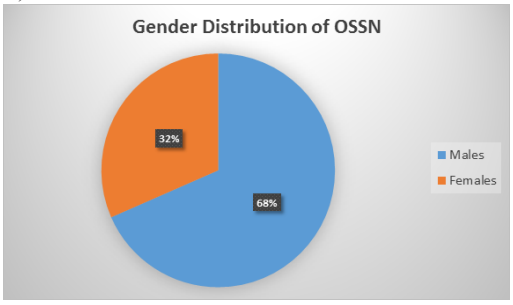

Fig 1 : Gender Distribution of OSSN

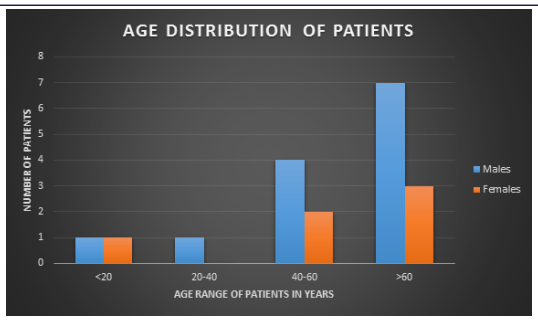

Fig 2 : Age distribution of patients.

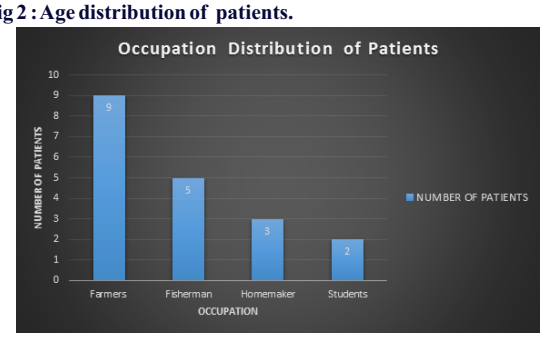

Fig 3 : Occupation Distribution of patients

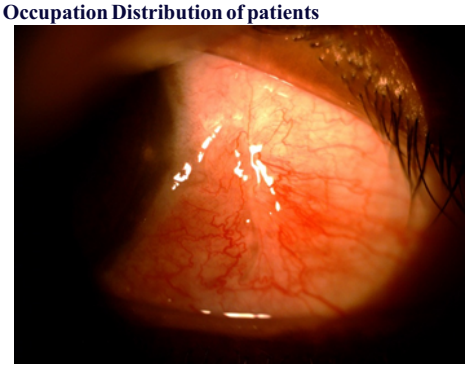

Fig 4 : Gelatinous type of OSSN

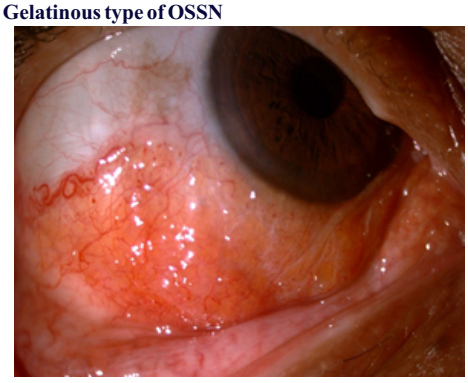

Fig 5 : Diffuse variety OSSN

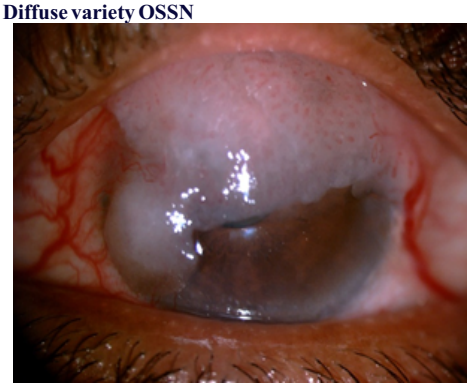

Fig 6 : Leukoplakic variety OSSN

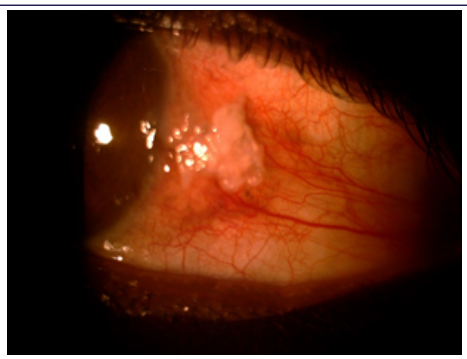

Fig 7 : Nodular variety OSSN

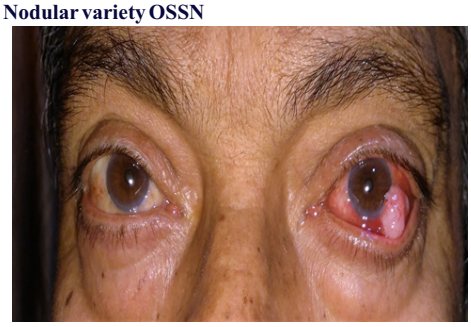

Fig 8 : Papillomatous variety of OSSN in left eye

Fig 8a : Papillomatous variety of OSSN showing intrinsic vascularization.

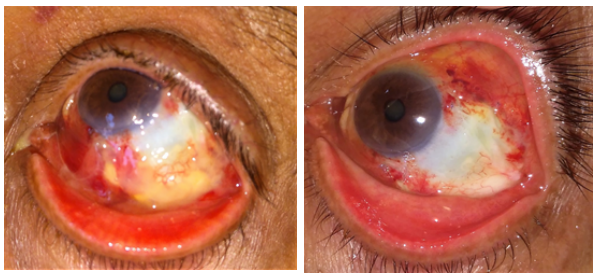

Fig 8b & 8c : Post-op Day 1 showing excised area of OSSN with amniotic membrane covering bare sclera (left image). Day 7 Post-op (right image)

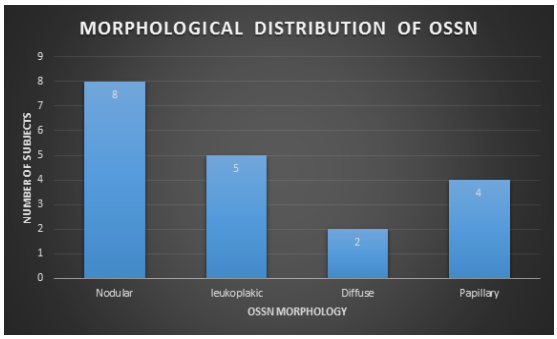

Fig 9 : Morphological distribution of OSSN.
The most common clinical variety was gelatinous (leukoplakic + papillary) followed by Nodular variety.

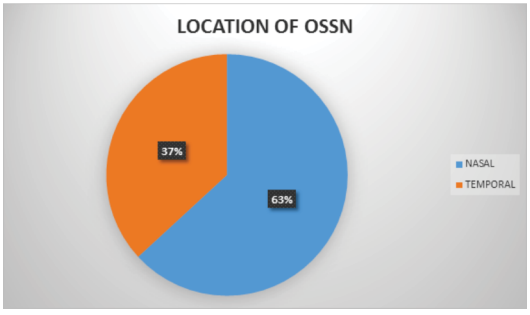

Fig 10 : Distribution of location of OSSN
63% had OSSN on nasal side as compared to 37% on temporal side.

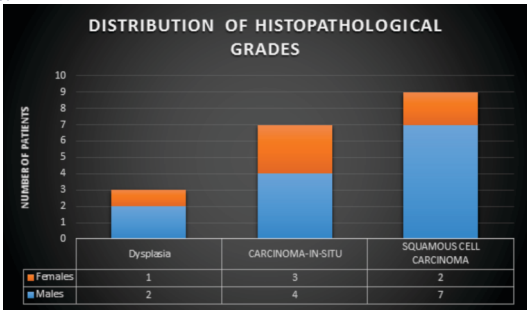

Fig 11 : Distribution of Histopathological grades

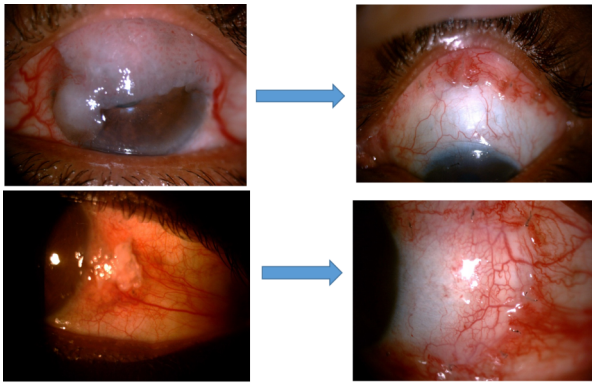

Fig 12 : Pre-op and post-op pictures of fig6&7

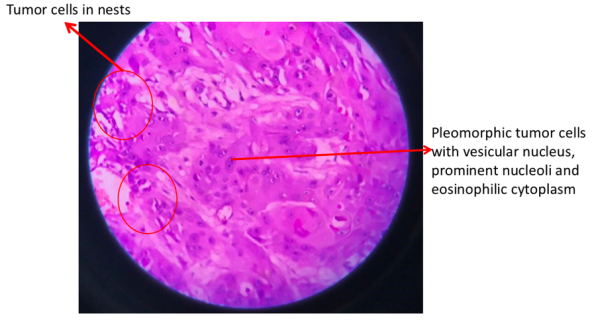

Fig 13 : Histopathology well differentiated SCC.

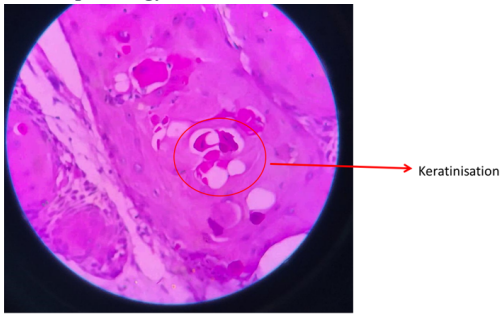

Fig 13a : Histopathology of SCC showing keratin pearls

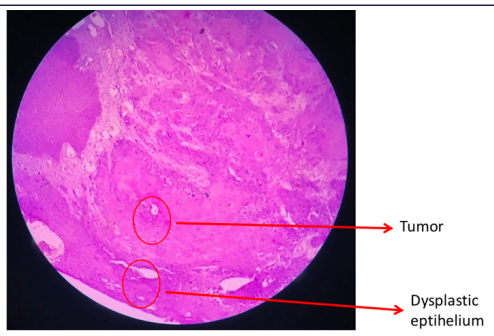

Fig 14 : Histopathology of CIN showing dysplastic epithelium and tumor cells.

DISCUSSION

In our study 19 cases(70.3%) were histopathological proven OSSN and remaining 5 were pterygium and 3 were conjunctival cysts.

The age range of the patients in this study is 13 to 79 years and the mean age was 55.20 years.

In our study 68% of those affected were males. It is mostly related to profession involving outdoor activity thereby increased UV-B exposure.

Padma Prabha Dandala *et al* also found that OSSN has male preponderance and is more common in outdoor workers.[13] This observation is also mentioned in other studies as well where males outnumbered females.

73.68% were outdoor workers. 2 patients had XP and 5 were tested HIV positive. Many studies have found that OSSN is more common in HIV and XP patients.[14,15]

The most common clinical variety was gelatinous i.e leukoplakic (Fig6) & papillary(Fig8) followed by Nodular variety(Fig 7). According to study done by Rohit Bang *et al* and Padma Prabha Dandala *et al* Nodular variety was found to be 53% and 57% respectively.[13,16]

63% patients had lesions on the nasal side of the eye which is mostly related to reflected sunlight for nasal bridge. According to a study done at Bascom Palmer Eye Institute 54% presented with nasal lesions.

In our study 9 and 7 cases were found to be SCC(fig8&13) and CIN (Fig15) respectively. Maudgil A, et al, Andrew A. Kao et al in their study found that CIN is more common than SCC. however there are studies showing that SCC was more commoner than CIN.[12,17]

0.04% topical Mitomycin-C (MMC) for 4 times a day (qid), 4 days in a week for 4 cycles in cases where it was histologically proven to have SCC and CIN.

CONCLUSION

Increased incidence of OSSN was observed in males and outdoor workers. Leukoplakic variety was found to be more common. Majority of cases were SCC followed by CIN.19(70.3%) of presumed cases were histopath confirmed. Hence surgical excision with a clear margin should be done in all doubtful cases of OSSN.

LIMITATIONS OF THE STUDY

Anterior segment OCT was not done due to unavailability. It would have been very useful to find out deeper extensions of OSSN.
Topical interferon therapy is an alternative modality and newer method of treating large limbal and recurrent OSSN,[18] which we want to try in future.

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