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Clinicopathological study of ocular surface squamous neoplasia in non-HIV patients and effect of topical cyclosporine

Dadapeer K[1], Sahana R. Manipur[2,*], Kavitha CV[3], Pavana Acharya[4], Lakshmi BR[5]

[1]Former Associate Professor, [2,5]PG Student, [3]Professor & HOD, [4]Assistant Professor, Dept. of Ophthalmology, Hassan Institute of Medical Sciences, Hassan

***Corresponding Author:**
Email: sahanamanipur@gmail.com

Abstract

Introduction: Ocular Surface Squamous Neoplasia is a spectrum of conjunctival and corneal epithelial neoplasia manifesting as dysplasia, carcinoma-in-situ and squamous cell carcinoma. Study was aimed to know the clinicopathological manifestations of OSSN in non-HIV patients and efficacy of topical cyclosporine.

Methods: 4 patients with conjunctival growth on medial side of eye suspecting OSSN were studied and all 4 underwent wide surgical excision followed by histopathological investigation. Followed up with topical 0.05% cyclosporine drops twice a day for 8 weeks.

Results: Case 1 and 2 showed moderately differentiated Squamous cell carcinoma. Case 3 showed full thickness dysplasia and case 4 showed conjunctival tissues with no evidence of malignancy. Case1 showed recurrence after 2 months and case 2 and 3 did not show recurrence.

Conclusion: OSSN in Non-HIV patients can present in similar fashion to HIV patients but with better prognosis.

Keywords: Dysplasia, Non-HIV patients, Ocular surface squamous neoplasia, Squamous cell carcinoma, Topical Cyclosporine.

Introduction

Ocular Surface Squamous Neoplasia is a spectrum of conjunctival and corneal epithelial neoplasia manifesting as dysplasia, carcinoma-in-situ and squamous cell carcinoma (SCC). It is the third most common ocular tumour and most common malignancy of conjunctiva.[1,2] Risk factors associated are male sex, advanced age, ultraviolet-B exposure, HPV-16,18 or HIV infection, Xeroderma pigmentosum or any condition where limbal microenvironment is altered.[1] It can present as leukoplakic, papillomatous, or gelatinous lesion. Diagnosis is made by clinical picture and histopathological examination of the tissue. Treatment modalities include surgical excision, cryotherapy, post-operative topical chemotherapy, topical/intralesional immunotherapy, contact radiation therapy depending on the size of the lesion, its location, invasion, recurrence, age and general condition of patient.[3]

Aim

Studies have been done on patients with OSSN and effect of topical chemotherapy with Mitomycin-C or 5-FU. As few studies are there and clinically OSSN is difficult to diagnose, this study was aimed to know the clinicopathological manifestations of OSSN in non-HIV patients and efficacy of topical cyclosporine 0.05% on outcome in terms of recurrence and complications.

Materials and Methods

Prospective consecutive case series of 4 patients presenting with conjunctival growth on medial side of eye suspected OSSN were studied over a period of 6 months at Sri Chamarajendra Hospital, HIMS, Hassan. Ethical clearance was obtained from Institutional ethical committee.

After history taking, all cases were examined under slit lamp and site, size, laterality and extension of the lesion noted. After taking informed consent and necessary investigations all patients were posted for surgery that is wide excision of the lesion keeping a safe margin of 2 mm of normal appearing conjunctiva and tissue sent for histopathological investigation.

Histopathology report of first 3 cases confirmed it as OSSN. They were followed up post-operatively with antibiotic-steroid eye drops 6 times and tapered over a period of 4 weeks and topical 0.05% cyclosporine for 8 weeks and were examined at 1, 3 and 6 months after surgery and looked for recurrence and complications.

Results

Out of 4 cases of suspected OSSN, diagnosis was confirmed in 3 cases. Mean age was 51 (30-65) years and 2 were women. All 3 lesions were located in nasal quadrant and corneal invasion was seen in 2 cases.

Case 1 was an elderly male patient with gelatinous mass of about 2x1cms with leukoplakic plaque in right eye nasal quadrant extending 5 clock hours over cornea. (Fig. 1)

Fig. 1: Case 1

Case 2 was a young female patient with cystic lesion of conjunctiva of about 1x1 cm in left eye nasal quadrant and it was confined to conjunctiva. (Fig. 2)

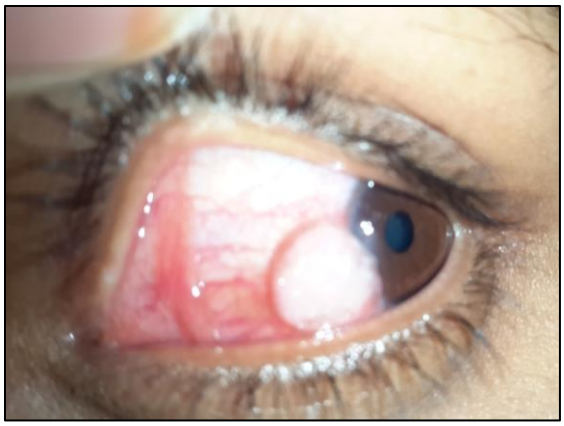

Fig. 2: Case 2

Case 3 was an elderly female patient with papillomatous growth of about 2x2.5 cms in left eye nasal quadrant extending 6 clock hours covering pupillary area. Feeder vessels were present. (Fig. 3)

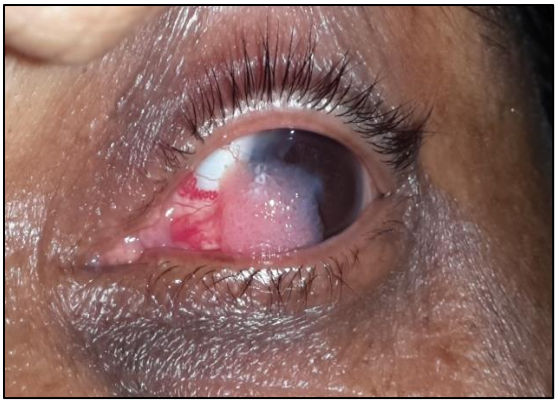

Fig. 3: Case 3

Case 4 was an elderly female patient with gelatinous mass of about 0.5x0.25 cms in left eye nasal quadrant extending 3 clock hours over cornea. (Fig. 4)

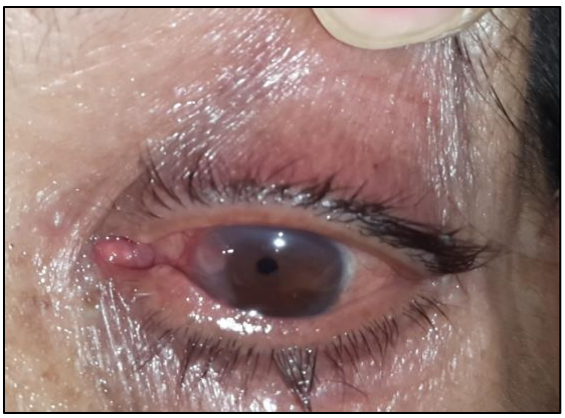

Fig. 4: Case 4

All 4 cases were non-reactive to HIV test.

Histopathological report of Case 1 showed moderately differentiated Squamous cell carcinoma with positive tumour margin.

Case 2 showed moderately differentiated Squamous cell carcinoma.

Case 3 showed full thickness epithelial dysplasia.

Case 4 showed conjunctival tissue lined by stratified squamous epithelium with no evidence of malignancy.

Demographic and clinico-pathological profile of OSSN patients are given in Table 1.

Table 1: Demographic and clinico-pathological profile of patients with OSSN

Case	Age (in years)	Sex	Type	Laterality	Histology	Associated Diseases	Recurrence
1	65	Male	Gelatinous with leukoplakic plaque	Nasal	Squamous cell carcinoma with positive tumour margin	_	Yes
2	30	Female	Cystic	Nasal	Squamous cell carcinoma	_	No
3	58	Female	Papillomatous	Nasal	Epithelial	_	No

					dysplasia		

With topical therapy with cyclosporine 0.05% for 8 weeks, case 1 showed recurrence within 2 months of follow-up (Fig. 5). Patient underwent resurgery and started on topical Mytomycin C (0.04%) on and off cycles. Patient did not show recurrence further.

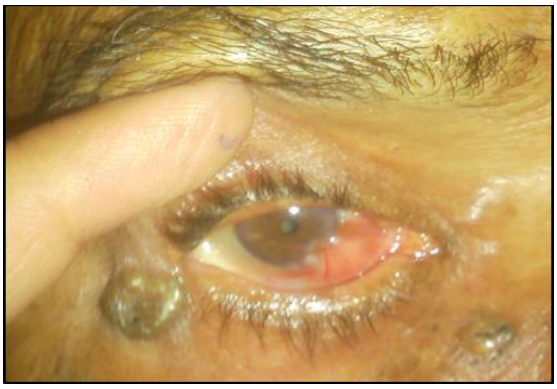

Fig. 5: Recurrence in Case 1

Case 2 and 3 did not show any recurrence or complications by the end of 6 months follow-up.

Discussion

Tiong T et al. found that more women were enrolled in their study on cases with suspected OSSN and more males were associated with squamous cell carcinoma compared to female gender.[2]

Chowdhury R K et al. found equal involvement of OSSN in males and females, unlike other studies where there was male preponderance.[1]

In our study also female enrolment was more and Squamous cell carcinoma was seen in one male and one female patient.

In a study conducted by Kim BH et al, majority of SCC were located at nasal side of conjunctiva and cornea.[4]

All 3 cases in our study showed OSSN in nasal quadrant of conjunctiva.

Tiong T et al. also found association between lesion size and squamous cell carcinoma that is; larger the tumour size more invasive is the lesion.

Case 3 in our study, with larger tumour size showed epithelial dysplasia without invasion.

Othman suggested use of reduced concentration of topical Mitomycin C (0.01%) when it is combined with cyclosporine 0.05% in invasive SCC and also mentioned side effects of topical Mitomycin like transient keratitis, redness and irritation.[5]

Flynn T H et al. could not implicate topical cyclosporine as the causative agent for occurrence of OSSN in their case report, since no patient with topical cyclosporine use during 3 years period had developed OSSN.[6]

Chowdhury R K et al. found recurrence of lesion following surgery is common in invasive squamous cell carcinoma and concluded that if at all recurrence occurs after wide excision, can be treated with re-surgery and topical Mytomycin C.[1]

We have tried monotherapy with topical cyclosporine 0.05% in all 3 OSSN patients in our study, so that side effects of Mitomycin were eliminated. Recurrence was seen in one patient with SCC with positive tumour margin and other two did not show recurrence or any complications. Recurrence was treated with re-surgery and topical Mytomycin C on and off cycles (0.04%).

Limitations of study were small sample size and short term follow-up.

Conclusion

Clinical picture of OSSN in non-HIV patients showed gelatinous, cystic and papillomatous lesions in 3 cases respectively and histo-pathological picture showed moderately differentiated squamous cell carcinoma in 2 cases and dysplasia in one case which is similar to manifestations in HIV patients in related studies. Early diagnosis and appropriate treatment with wide excision and topical cyclosporine (0.05%) results in better outcome by preventing recurrences and complications.

Conflict of interests: None

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