Clinical profile of ocular surface tumours at a tertiary care centre

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ABSTRACT

Background: Corneal and conjunctival squamous lesions are uncommon but important because of their potential for causing ocular and even systemic morbidity and mortality. The ocular surface tumors can be congenital or acquired and show a broad spectrum ranging from non-neoplastic benign tumours and others demonstrate premalignant or malignant tumours such as squamous cell carcinoma, malignant melanoma or Kaposi sarcoma. The types and frequency of conjunctival tumours differ with demographic features such as age and race, systemic immune status, and chronic exposures, along with specific location within the conjunctiva. Objectives of this study was to study ocular surface neoplasm in terms of demographics, histopathological and clinical presentation.

Methods: This histopathological, prospective biopsy specimen series comprised of 107 patients of either sex and all age groups presenting with conjunctival lesion either benign or malignant. The study was carried out from December, 2017 to December, 2019 in the Department of Ophthalmology, S. P. Medical College and Associated Group of Hospitals, Bikaner in collaboration with Pathology Department. All enrolled cases of conjunctival lesion were screened by consecutive sampling after obtaining written consent.

Results: 39.25% patients had nevus followed by ocular surface squamous neoplasia (OSSN) (20.56 %). Various ocular surface neoplasia with respect to mean age, age group, occupation was statistically highly significant (p<0.05) whereas gender was statistically non-significant. On histopathological examination most common benign ocular surface neoplasia was nevus and most common malignant tumor was ocular squamous surface neoplasia (OSSN).

Conclusions: A large variety of conjunctival lesions may appear in the eye with variable presentation, most common benign ocular surface neoplasia was nevus and most common malignant tumor was ocular squamous surface neoplasia.

Keywords: Nevus, Ocular surface tumor, OSSN

INTRODUCTION

Ocular surface tumours include neoplasms originating from squamous epithelium, melanocytes and the resident lymphocytic cells in the conjunctival stroma. Squamous lesions can involve the conjunctiva or the cornea, but more commonly start in the conjunctiva and extend across the limbus to the adjacent cornea. The conjunctival tumours can be congenital or acquired and show a broad spectrum ranging from non-neoplastic benign tumours such as nevus, dermoid and lipodermoid (choristomas), simple granuloma, papilloma, adenoma, fibroma and angiomas, to malignant lesions such as ocular surface squamous neoplasia (OSSN), primary acquired melanoma, malignant melanoma and lymphoid tumour which may cause visual loss.

The incidence of OSSN is about 0.02 to 3.4 cases per 1,00,000 population per year and shows ethnic and geographic variations. OSSN are important because they mimic many common indolent lesions like pterygium and have a potential for causing ocular and systemic morbidity and mortality. The precise etio-pathogenesis of these lesions is not very clear. Risk factors including fair skin,
male sex and advancing age, exposure to ultraviolet radiations, cigarette smoking, organ transplant, autoimmune conditions, infection with Human Papilloma virus (HPV) and Human Immunodeficiency Virus (HIV) also thought to have effect.\(^4\)\(^-\)\(^7\) Systemic associations of the development of OSSN include xeroderma pigmentosa and Papillon–Lefèvre syndrome.\(^8\) Regarding lymphoma, predisposing conditions include benign reactive lymphoid hyperplasia, immune deficiency (HIV), immune dysfunction and chronic inflammation/infection (Helicobacter pylori, Chlamydia psittaci). Conjunctival melanocytic tumors are common and this class of melanocytic tumors includes many types such as nevus, complexion-related melanosis, PAM, secondary acquired melanosis, melanoma and metastases. Of these lesions, conjunctival nevus represents 45% and primary conjunctival melanoma represents 23% of all melanocytic tumors.

The various diagnostic tests available for these neoplasms are Rose Bengal staining, Exfoliative and Impression Cytology, Histopathology, Anterior Segment Optical Coherence Tomography (AS-OCT), Ultrasonic biomicroscopy and Confocal Microscopy.

Benign tumors and choristomas are excised only if there are a cosmetic or functional concern. The standard modality for treatment of OSSN has been wide surgical excision with “no-touch” technique and adjunctive cryotherapy. However, due to high recurrence rates ranging from 5% to 66% after surgical excision, nonsurgical management with topical chemotherapeutic agents (5-fluorouracil) and mitomycin C (MMC) has become the preferred choice for management of OSSN.\(^9\)\(^-\)\(^11\) Recently Interferon-a 2b (IFNα2b) as well as pegylated IFNs are regularly being used in a select subsets of OSSN for treatment.\(^3\) As study had very few reported cases of confirmed Ocular surface neoplasm in our area, present study was an effort to assess prevalence, histopathology and clinical profile of various types of ocular surface neoplasm.

**METHODS**

After obtaining permission from institutional review board and written consent 107 consecutive patients who present with conjunctival tumour either benign or malignant at the OPD of Department of Ophthalmology, S.P. Medical College, Bikaner from December, 2017 to December, 2019 were included in the study. A thorough clinical examination of the lesion regarding its location, shape, size, border, margin, ulceration, induration and mobility over underlying surface was done both under torch light and slit lamp. Patients presenting with degenerative lesions of the conjunctiva and not willing to give consent for ophthalmic examination were excluded in this study.

Diagnosis was made by clinically and histopathological examination. Benign tumours were kept under observation and tumours appearing malignant clinically were surgically excised with minimal touch technique. Benign lesion was excised for cosmetic purpose, foreign body sensation and increasing size or pigmentation. Histopathological examination of specimen was done at the Department of Pathology, S. P. Medical College, Bikaner for excised/ biopsied tumour. Data thus collected were entered into Microsoft Excel sheet. Statistical analyses were performed using the Epi Info software. Results were analyzed as tables, proportions in case of qualitative data, mean and standard deviation in case of quantitative data. A \(p\) value of less than 0.05 was considered to be statistically significant.

**RESULTS**

In our study conjunctival lesions were observed most frequently in 11-20 years age group (31.78%). Male female ratio was 1.8/0.82. Majority 75.70% population were from rural area. When association of Ocular surface neoplasia was studied with various risk factors, the clinical diagnosis was found to be significantly associated with age group and occupation type (\(p<0.005\)) whereas sex was observed to be statistically insignificant (\(p>0.05\)).

Table 1: Distribution of cases according to clinical diagnosis with respective age.

| Clinical diagnosis | 0-20 | 21-40 | 41-60 | 61-80 | >80 | Mean age |
|-------------------|------|-------|-------|-------|-----|---------|
| Ossn (22)         | 0    | 2     | 12    | 8     | 0   | 54.10±13.17 |
| Nevus (42)        | 23   | 12    | 6     | 1     | 0   | 23.00±14.31 |
| Pam (14)          | 4    | 7     | 3     | 0     | 0   | 26.00±12.96 |
| Dermoid (6)       | 6    | 0     | 0     | 0     | 0   | 13.00±5.72  |
| Inflammatory cyst (6) | 1    | 5     | 0     | 0     | 0   | 24.33±3.66  |
| Dermolipoma (5)   | 2    | 3     | 0     | 0     | 0   | 19.60±7.12  |
| Inclusion cyst (6) | 2    | 1     | 1     | 1     | 1   | 40.33±30.23 |
| Haemangioma (3)   | 2    | 0     | 1     | 0     | 0   | 22.33±20.50 |
| Lipoma (1)        | 0    | 0     | 0     | 0     | 1   | 80.00±0.00  |
| Lymphangioma (2)  | 0    | 1     | 1     | 0     | 0   | 40.00±14.14 |
| **Total (107)**   | 40   | 31    | 24    | 10    | 2   | 30.94±19.71 (\(p<0.05\)) |

\(p<0.0001^*\).
Table 2: Histopathological examination.

| Histopathological examination | N  | %   |
|-------------------------------|----|-----|
| Sq. cell ca                   | 15 | 29.42 |
| Dysplasia                     | 5  | 9.80 |
| Ca in situ                    | 2  | 3.92 |
| Nevus                         | 12 | 23.51 |
| Melanosis                     | 4  | 7.85 |
| Dermoid cyst                  | 3  | 5.90 |
| Inclusion cyst                | 5  | 9.80 |
| Infected haemangioma          | 1  | 1.96 |
| Benign lymphoid hyperplasia   | 1  | 1.96 |
| Lymphangioma                  | 1  | 1.96 |
| Angiolymphoid hyperplasia     | 1  | 1.96 |
| Retention cyst                | 1  | 1.96 |
| Total                         | 51 | 100.00 |

Table 1 showed distribution of cases according to clinical diagnosis with respective age (Mean±SD) and distribution of cases according to different age groups. 39.25% had nevus followed by OSSN (20.56%). Conjunctival lipoma was least common followed by lymphangioma. Among younger ages, dermoid and dermolipoma were common whereas lipoma and OSSN were more prevalent among older age groups. Mean age of all ocular surface neoplasms was found to be statistically highly significant with type of neoplasms (p<0.05). 86.92% had chief complaint of growth of mass in eye whereas 13.08% had chief complaint of brownish discoloration of eye. Mean duration of lesion was 23.35±27.65 months.

In our study maximum neoplasia 42.99% were circular in shape whereas nodular elevation was found in majority of OSSN patients. In majority 79.43% neoplasia was benign in nature. Nevus was the most common benign tumour while all cases of malignant tumours was present in the form of OSSN. One case of malignant melanoma coexisted with OSSN.

On histopathological examination, squamous cell carcinoma and nevus were most frequently reported histopathological variants (29.42% and 23.51% respectively) (Table 2). 3 Patients of nevus had associated with vernal kerato conjunctivitis. One patient of dermoid had associated Goldenhar syndrome with lobulated tragus of left ear. One OSSN patient had xeroderma pigmentosa while another one was on anti-retroviral treatment.
patients had benign lesions. Whereas male: female ratio 5.7:1 was observed by Ceylan et al and 2:1 by Mondal et al.13,16

In present study majority of patients were students and the most common lesion observed in them was nevus, as students have extra cosmetic demands, have regular early health check-up and awareness may also be a factor for this. 3/4th of our study population was resident of rural area. Frequency of these lesion in rural areas, can be attributed to outdoor occupations. Both benign and malignant lesions were observed with greater frequency in rural population.

86.92% of the study population had chief complaint of growth of mass in the eye, which was the most common feature of conjunctival tumour whereas 13.08% of them had brownish discoloration of the eye, which was feature of PAM. The mean duration of chief complaints in study population was 23.35±27.65 months. 32.71% had multiple complaints like foreign body sensation, watering, itching. These multiple complaints were frequently associated with inflammatory cyst, OSSN and giant nevus at caruncle. Foreign body sensation was common in almost all conjunctival lesions. Watering and itching were associated with inflammatory cyst and giant nevus at caruncle. 3 patients of Nevus had association with Vernal Keratoconjunctivitis which is an unusual finding observed in this study and not reported in any literature. Out of 42 patients, 10 patients had nevus located at the caruncle and it was associated with multiple complaints, so they wished to go for surgery for symptomatic relief and cosmesis. One patient with dermoid cyst was found to have association with Goldenhar syndrome (also known as oculo-auriculo-vertebral (OAV) syndrome) which is a rare congenital defect characterized by incomplete development of the ear, nose, soft palate, lip and mandible. It is associated with anomalous development of the first branchial arch and second branchial arch. Common clinical manifestations include limbal dermoids, preauricular skin tags and strabismus. Dermoid and dermolipoma were kept under observation, surgical excision was deferred unless for cosmetic considerations or in symptomatic patients with exuberant hair growth over the lesion. Visible portion of the dermolipoma may be debulked, and the ocular surface can be reconstructed with amniotic membrane graft and keratoplasty. One OSSN patient had xeroderma pigmentosa while another one was on anti-retroviral treatment, both of which are considered as risk factor of OSSN.

In our study diagnosis of nevus was made in 39.25% in benign category and OSSN (20.56%) was the most frequent malignant tumour which is universal in all related studies. Primary acquired melanosis (PAM) appeared as flat lesions in contrast to benign nevi which were scarcely pigmented, slightly elevated lesions.

Benign lesions were common in younger age whereas malignant lesion was more prevalent among older age

**DISCUSSION**

Conjunctiva unlike the other mucous membranes in the body is partially exposed to sunlight, which may be a factor in the development of some tumors.12 The caruncle, with its unique composition of both mucous membrane and cutaneous structures, can develop tumours found in both mucosa and skin.

In the present study, it was found that bulbar conjunctiva was most commonly affected followed by limbus, caruncle and palpebral conjunctiva respectively. In the fornix, no conjunctival lesion was observed in the present study which correlated with studies done by Shields et al and Elshazly et al.13,14

In the study patients of all age and gender were included. Half of these patients were in the age group of 11-30 years whereas 1.87% belonged to >80 years age group. Benign tumours were more common in younger age groups and were more in number in study. In our study 80% of the lesions were benign in nature and were seen in younger age group. As younger age groups being more dedicated for regular health check-up. Malignant tumours were more prevalent in older age groups. The older age groups usually have many co-morbid illness and also tend to ignore minor conjunctival lesions, hence malignant lesions were more frequent in the elderly. The mean age among various types of diagnosis was found to be statistically significant. Age distribution observed by Sundeep et al in their study showed that maximum number of cases present between the age of 51 and 60 years (24%) followed by 31-40 years group (22%). Least number of cases was present between 81 and 90 years (0.5%).15

There was nearly 1:1 (1.18:0.82) ratio of males and females in our study. Benign tumours were almost equally affecting both genders whereas malignant tumours were more prevalent in males because males are usually engaged in outdoor activities resulting in increased exposure to risk factor like UV rays and other outdoor occupational hazards. In our study, maximum number of

![Figure 5: OSSN (squamous cell carcinoma) elevated nasal limbal mass involving the cornea with abundant keratin and feeder vessels.](image-url)
groups. Similar results were also observed by Navahi et al in their study.\textsuperscript{17} In our study most common benign tumor was nevus and malignant was OSSN which is according to their prevalence. Similar results were also observed by Ceylan et al.\textsuperscript{16} Mondal et al, Navahi et al and Shields et al in their studies.\textsuperscript{13,17,18}

In our study OSSN was reported maximum in 41-60 years age group followed by 61-80 year. Sundeen et al also observed similar results.\textsuperscript{15} Farmers had the highest prevalence of OSSN as they are more prone to exposure of risk factors (sun light UV rays and HIV). The occurrence of ocular surface neoplasia according to occupation was observed to be statistically significant (p<0.05).

In our study maximum conjunctival lesion 42.99% were circular in shape whereas nodular elevation was found in majority of OSSN patients which is a finding similar to study done by Meel et al found nodular elevation in the majority of cases.\textsuperscript{19}

Regarding morphological feature it was found that 80.37% neoplasia had smooth surface with 72.9% had regular margins in which 57.94% were mobile. 50% had right eye involvement with 25.23% corneal involvement and 47.66% required excision. 45.45% OSSN had smooth surface with irregular margin and right eye involvement in 59% (no relevant significance), all were immobile and almost all had corneal involvement and showed positive rose bengal staining. These are typical finding of OSSN.

In this study benign vs malignant ratio was 4:1 in clinical diagosed cases while on histopathological examination 56.87% were benign and 43.13% were malignant as we did surgery preferably for malignant tumours. Benign conjunctival lesions were the most common type of lesions across all age groups with decrease with growing age whereas malignant cases were observed in their prevalence with older age, in which aging was stated as an important risk factor for malignant conjunctival lesions. Similar result were found in Navahi et al study.\textsuperscript{17}

In our study most common benign tumor was nevus and malignant was OSSN which is according to their prevalence. Similar results were also observed by Ceylan et al, Mondal et al, Navahi et al and Shields et al in their studies.\textsuperscript{13,16-18}

CONCLUSION

To conclude, a large variety of conjunctival lesions may appear in the eye with variable presentation. Premalignant and malignant tumors such as carcinoma, lymphoma, or melanoma are aggressive, which jeopardize the vision and may endanger the patient's life. Therefore, early diagnosis is important and their existence must be confirmed by biopsy with histologic evaluation.

In our study, age as well as occupation type have been a proven to have a statistical significant association with occurrence as well as type of OSSN. This association can further help us to understand natural history of disease as well as to prevent occurrence along with timely appropriate management of OSSN.

Limitation

A long duration study will give more precise results.

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