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Histopathology

HISTOMORPHOLOGICAL SPECTRUM OF OCULAR SURFACE SQUAMOUS NEOPLASIA: A 5 YEAR STUDY.

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ABSTRACT Ocular surface squamous neoplasia encompasses the entire spectrum of epithelial dysplasias and neoplasia including squamous cell carcinoma. It may arise from ocular surface of conjunctiva, cornea and limbus. Purpose: The aim of this study is to demonstrate varying degrees of histomorphological spectrum in Squamous neoplasias of ocular surface. **Materials and Methods:** This is a Retrospective study conducted at Department of Pathology for a period of 5 years in Sarojini devi eye Hospital, Hyderabad, Telangana, India. The data collected was subjected to statistical tabulations and analysis was done. Results: The mean age of presentation was 46.39 years (6 to 82 years) with male preponderance (64.9%). The most common age group of presentation was 31-40 years (n=31, 22.62%) .The most common type of OSSN was invasive Squamous cell carcinoma seen in 37.22% (n=51) followed by Carcinoma in situ 20.43% (n=28). Out of 51 patients diagnosed with Squamous cell carcinoma, male patients were 34 (66.6%) and female patients were 17 (33.3%), among females diagnosed with SCC 13 cases(76.7%) were well differentiated type and remaining 4 cases(23.52) were moderately differentiated type. Only 1 male patient had Poorly differentiated type of Squamous cell carcinoma, 3 patients (5.8%) had infiltrating tumor into surrounding tissues. 7 Patients (5.10%) diagnosed with OSSN were HIV positive. **Conclusion:** OSSN occurred in a relatively young age group with male preponderance possibly due to outdoor exposure . Based on Histopathology, Squamous cell carcinoma is the most common form of OSSN in the Asian Indian population.

KEYWORDS : OSSN, Conjunctiva, Dysplasia, Carcinoma, HIV.

Introduction

The conjunctiva is composed of Stratified non-keratinising squamous epithelium and an underlying substantial propria. The terminology 'Ocular surface squamous neoplasia' (OSSN) was first coined by Lee & Grant in 1995 as an umbrella term that encompasses a spectrum of dysplastic, pre-invasive and invasive squamous epithelial lesions of the conjunctiva and cornea(2). In current usage, the term OSSN refers to various grades of conjunctival and corneal squamous intraepithelial lesions, as well as in-situ and invasive squamous cell carcinoma(3,4).

Risk factors that have been associated with OSSN includes ultraviolet (UV) radiation exposure, HIV and HPV infections and smoking(4,5). UV light induces the formation of pyrimidine dimers and is mutagenic for p53 gene(3,5,6). The inability to repair UV-induced DNA damage explains the high incidence of OSSN lesion in patients with xeroderma pigmentosum(5). Association with xeroderma pigmentosa may cause OSSN at a younger age compared to general population, and OSSN in this group is reported as early as at 3 years of age(8,9,10). Carreira et al.(11) documented an eight fold increase in OSSN risk in patients with HIV.

Conjunctival squamous intraepithelial neoplasia arises from conjunctival epithelial cells that originate from the ocular surface ectoderm(12). Clinically Conjunctival squamous cell carcinoma's are typically elevated and relatively well demarcated, most are unilateral. Advanced cases can infiltrate the cornea and sclera(16) and rarely the tumor may extend into the orbit. Differentiating intraepithelial neoplasia from SCC is clinically challenging and excisional biopsy is needed for definitive histopathological diagnosis.

Histopathology plays a crucial role in the accurate diagnosis of OSSN. Conjunctival squamous intraepithelial neoplasia is classified as mild, moderate and severe depending on the extent of the epithelial involvement and the degree of cellular atypia. Mild dysplasia is confined to the lower third of the conjunctival epithelial thickness . Moderate dysplasia extends to the middle third and Severe dysplasia spreads to the upper third but retains substantial surface differentiation(17,18). Carcinoma in-situ exhibits full thickness replacement of the surface epithelium with dysplastic epithelial cells(19), it is a precursor lesion of conjunctival SCC. Invasive squamous cell carcinoma breaches the epithelial basement membrane and extends into the subepithelial stroma. Grading of SCC is based on the degree of differentiation. Histologically Well differentiated tumors produce keratin, have abundant eosinophilic cytoplasm, readily identifiable intercellular bridges, low mitotic counts and minimal nuclear pleomorphism. Moderately differentiated SCC show variable keratinizaion, they are mitotically active and show more nuclear pleomorphism. Poorly differentiated SCC can have basaloid or spindled morphology.

The estimated incidence of Conjunctival squamous intraepithelial neoplasia is 17-20 cases per 1 million person- years(20). Worldwide a high incidence rate has been demonstrated among HIV positive individuals(21,22,23) and in other immunosuppressed populations(24,25).

Unawareness or ignorance of these lesions can result in debility, visual compromise and its attendant psychosocial impact. Histopathological diagnosis and grading of OSSN gives clinicians a better idea for further management and it aids in the prognostic implications. We have undertaken this study to determine the histomorphological spectrum of OSSN to contribute to the literature information regarding the severity of lesions of clinically diagnosed OSSN patient's biopsy specimens received in our tertiary care setup.

Methods

Type of study and Place of study: Retrospective data reviewed over the past 5- years of all the biopsies of clinically diagnosed OSSN received in the Department of Pathology , Sarojini Devi Eye Hospital, Hyderabad, India. A search was conducted in our medical records and ophthalmic pathology data base for the OSSN diagnosed cases during the period of 2018 to 2022 and were included in this analysis.

Sample collection and sampling method: A total of 137 conjunctival biopsies of clinically diagnosed OSSN were obtained from patients attending the Department of Ophthalmology of our institute.

Inclusion criteria: All the biopsies submitted of clinically diagnosed OSSN cases were studied as per epidemiological and histomorphological data.

The demographics (age, sex), indications for biopsies, clinical diagnosis and the histopathological diagnosis were noted. The original slides were retrieved and reviewed, fresh sections were cut from tissue paraffin blocks wherever necessary and stained by routine hematoxylin and eosin stains.

Exclusion Criteria: None

Statistical Methods: The data collected was subjected to descriptive statistical tabulation.

Results

A total of 137 biopsies of clinically diagnosed OSSN cases were reviewed during the 5 year retrospective study period. The patients were in the age group 6- 82 yrs. Mean age of presentation of OSSN was 46.39yrs. The most common age group of presentation was 31-40yrs (n=31, 22.62%). The distribution of OSSN lesions (males=89, females=48) with a ratio of 1.85:1 with male sex preponderance. The incidence of OSSN was found to be slightly higher in the right eye than the left (right=73, left=64). The most common type of OSSN was invasive squamous cell carcinoma seen in 37.22% (n=51), followed by carcinoma in-situ 20.43% (n=28). Out of the 51 patients diagnosed with squamous cell carcinoma, males were 34 (66.6%) and female patients were 17 (33.3%). Among females diagnosed with squamous cell carcinoma 13 cases (76.7%) were well differentiated type and remaining 4 cases (23.52%) were moderately differentiated type. Only 1 male patient had poorly differentiated type of squamous cell carcinoma, 3 patients (5.8%) had infiltrating tumor into surrounding tissues. 7 patients (5.10%) diagnosed with OSSN were HIV positive. The earliest age of presentation was of a 6yr old child with Squamous cell Carcinoma.

Table-1: Age wise distribution of OSSN

Age (in years)	Number of cases (total=137)	In percentage
0-10	1	0.72%
11-20	4	2.91%
21-30	19	13.86%
31-40	31	22.62%
41-50	29	21.16%
51-60	25	18.24%
61-70	21	15.32%
71-80	6	4.37%
81-90	1	0.72%

Chart – 1: Pattern of distribution of OSSN

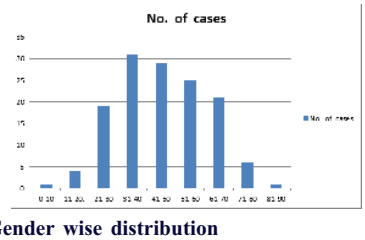

Table – 2: Gender wise distribution

Gender	No. of cases (total=137)	In Percentage %
Male	89	64.96
Female	48	35.03

Table – 3: Laterality of lesions

Laterality	No. of cases (total=137)	In Percentage %
Right	73	53.28
Left	64	46.71

Table – 4: Location of lesions in different sex

Laterality	Male	Female
Right	50(36.49%)	23(16.78%)
Left	39(28.46%)	25(18.24%)

Table -5: Clinical characteristics of OSSN cases

Pattern	No. of cases	Percentage%
Mild dysplasia	21	15.32
Moderate dysplasia	16	11.67
Severe dysplasia	21	15.32
Carcinoma in-situ	28	20.43
Squamous cell Carcinoma	51	37.22

Table -6: Comparision of incidence of Squamous cell carcinoma in both sex

Pattern of OSSN	Males	Females
Squamous cell carcinoma (total no. of diagnosed cases=51)	34 (66.6%)	17 (33.3%)

Discussion:

Our study is one of the largest local case series describing the histo-morphological spectrum of OSSN in clinically diagnosed patients. In our study there is male preponderance which was comparable with Dilip kumar mishra et al (26) study from Hyderabad, India , Ruhella R Hossain et al (27) study from New Zealand and is in disagreement with early observations across sub-Saharan Africa where an equal sex prevalence was generally reported (4,28,29).

In this study, Squamous cell carcinoma was the most common type of presentation accounting for (37.22%) which is in concordance with many studies. In a study of 101 cases of OSSN by Yousef et al.(30) OSSN distribution was CIN in 39%, invasive squamous cell carcinoma in 36%. The difference in presentation in different studies could be due to delayed presentation to the clinic in different countries.

In this study, association of OSSN with HIV is 7 cases(5.10%) out of total 137 cases ,there is high degree of association of OSSN in many studies. The highest rate of incidence of OSSN is in the first two years of acquired immunodeficiency syndrome (AIDS) (31). HIV infection has been associated with younger age at presentation of OSSN (32,33), more severe course (34,35) , bilaterality (36) worse prognosis (37).

In this study females diagnosed with OSSN were 48 cases out of total 137 cases. Among the 48 cases of OSSN, Squamous cell carcinoma was diagnosed in 17 cases (33.3%)..

Conclusions:

Most common type of OSSN was Squamous cell Carcinoma in the Asian-Indian population. Among the females Squamous cell Carcinoma, well differentiated type was the most common to be diagnosed histopathologically. HIV is a risk factor of OSSN and is associated with younger age at presentation of OSSN. In conclusion histopathology serves as a tool for definitive diagnosis and grading of OSSN and also can give an idea about disease prognosis.

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