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Original Article

Ophthalmology Section

Comparative Analysis of Clinical Factors Associated with Ocular Surface Squamous Neoplasia in HIV Infected and Non HIV Patients

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ABSTRACT

Introduction: Ocular surface squamous neoplasia (OSSN) refers to a spectrum of conjunctival and corneal epithelial disease ranging from dysplasia to invasive carcinoma. HIV infection is an important risk factor postulated for the development of disease.

Aim: To compare and to find out any statistically significant difference in patient demographics, clinical features and pathological findings in HIV infected and non-HIV infected histologically proven cases of ocular surface squamous neoplasia (OSSN).

Materials and Methods: In the present retrospective case study, data from indoor case records and ocular pathology records of histologically proven cases of OSSN was obtained. The data was then tabulated under various clinicopathological headings in HIV affected and non HIV affected groups.

A chi-square test was applied to compare data of two groups and look for any significant difference between two groups. A p-value less than 0.05 was considered significant.

Results: Amongst the total of 48 patients, 11 were HIV positive and 37 were HIV negative. Age of the patients ranged from 14-66 years in HIV and 22-66 years in non HIV group with a preponderance of younger age patients in HIV positive group. 54.5% patients with lesion having base more than 5mm were observed at the time of presentation in HIV positive population as compared to 21.6% in non HIV cases. Feeder vessels were seen in all HIV patients and a significantly greater degree of fornicial involvement was noted in comparison with non-HIV group. Histopathological analysis showed 63.63% of cases to be of invasive carcinoma amongst the HIV positive group and 54.05% of invasive carcinoma in non HIV group.

Conclusion: Younger age and aggressive looking tumour at presentation should caution ophthalmologist to look for an un-diagnosed HIV infection in OSSN patients.

Keywords: Conjunctival squamous neoplasia, HIV and ocular neoplasia

INTRODUCTION

Ocular surface squamous neoplasia (OSSN) refers to a spectrum of conjunctival and corneal epithelial disease including mild to severe dysplasia, intraepithelial carcinoma, and invasive carcinoma [1].

The precise aetiopathogenesis of these lesions is not very clear but various postulated risk factors include exposure to ultraviolet radiations, cigarette smoking, male sex, advancing age, links with Human Papilloma virus (HPV) infection and human immunosupression virus (HIV) infection [2,3].

The most common treatment for OSSN is generally excision with a 4mm safe margin along with cryo to edges of resected conjunctiva and base of the lesion [4]. Topical chemotherapy mitomycin or flurouracil is used as adjuvant therapy in treating noninvasive surface dysplasia and neoplasia [5-7]. Local brachytherapy and topical interferons also have been used in treating OSSN as an adjuvant therapy [4,6,8]. In a study extensive disease topical chemotherapy alone has been tried in the treating the lesions [9].

OSSN has gained interest in the past few years due to its association with the HIV pandemic and it has been observed that increase in incidence of OSSN is collinear with the increase in HIV [10]. With the upsurge of HIV infection, a changing trend in the age of presentation, clinical features and prognosis of patients of OSSN is observed. In this study we aimed to compare patient demographics, clinical features and pathological findings in HIV infected and non-HIV population with histologically provenocular surface neoplasia. In particular, our aim of this comparison was to find out any statistically significant difference between clinicopathological features of OSSN in HIV and non-HIV groups.

MATERIALS AND METHODS

This was a retrospective study conducted at a tertiary referral center. All the patients, enrolled between April 2009 and March 2014 at M&J Western Regional Institute of Ophthalmology, BJ Medical College, Civil Hospital, Ahmedabad of histologically proven OSSN were included in the study. Data from indoor case records, clinical slit lamp photographs and ocular pathology records of histologically proven cases of OSSN were obtained. All such cases with complete records were included in the study. Patients with OSSN but incomplete records were excluded from the study. A total of 48 cases fully filled our requirement and were finally included in the study. The data was then tabulated under various clinic-pathological headings in HIV affected and non HIV affected groups.

Patient details regarding registration number, age of patient, sex, duration of symptoms, vision, fundus details, slit-lamp examination were noted. The details of tumour size, appearance, multifocality, pigmentation, presence of feeder vessel, palpable lymph nodes were noted in every case. The biomicroscopic/morphological appearance of tumour was noted as leukoplakia, papillary, nodular, diffuse or gelatinous. From the ocular pathological laboratory all data regarding detailed histopathological analysis was obtained. All the ocular tumour in the records was graded in mild, moderate and severe dysplasia and well, moderate and poorly differentiated squamous cell carcinoma with severe variants as mucoepidermoid

or spindle cell carcinoma. We broadly divided the OSSN cases into two groups carcinoma in situ or the non-invasive tumour and squamous cell carcinoma or the invasive carcinoma on the basis of histopathological data hence obtained for analysis regarding invasiveness of tumour.

As all the patients undergoing any surgery at our institute are subjected to HIV Rapid test (COMB.AID HIV1/2) which if found positive is followed by ELISA, hence, status with regards to infection with HIV as positive/negative was easily retrieved and noted. The patient's awareness of his own HIV status was also recorded either from case records or on telephonic conversation with the patients.

STATISTICAL ANALYSIS

An excel sheet was made and all data was entered and analyzed. All the patients were divided into either HIV positive or non-HIV groups. The obtained data was tabulated under various clinicopathological headings. For statistical analysis a chi-square test was applied to compare the two groups and p-value less than 0.05 was considered significant.

RESULTS

Eleven patients were HIV positive and 37 patients tested negative and thereby formed the non-HIV group [Table/Fig-1].

Parameters	HIV	Non-HIV	Chi-Square	*p-Value
Age				
≥ 50	1	19	6.23	0.012
< 50	10	18		
Gender				
Male	10	32	0.152	0.697
Female	1	5		
Duration				
≤ 6 months	10	33	0.0267	0.87
> 6 months	1	4		
Feeder Vessels				
Present	11	36	0.152	0.697
Absent	0	1		
Base of lesion				
≤ 5mm	5	29	4.449	0.035
> 5mm	6	8		
Fornix Involvement				
Present	3	5	1.156	0.282
Absent	8	32		
Pathology				
Carcinoma in situ	4	17	0.316	0.574
SCC	7	20		

[Table/Fig-1]: Patient details and study results.
*If p-value is less than alpha (0.05) then we reject the null hypothesis

Age of the patients ranged from 14-66 years with a mean of 33.90 and median of 32 in the HIV group. Age range in the non HIV group was 22-66 years. The mean age was 48.4 and median age was 50 in non-HIV group. We observed that 90.9% of people were below 50 years in HIV group whereas 48.6% of people were below 50 in the non-HIV group. This difference was statistically significant between both groups.

Males were affected in 90.9% in HIV group whereas 86.4% affected were males in non HIV group. 54.5% patients of HIV were unaware of their HIV status till their first presentation in our outpatient department.

At the time of presentation a tumour base more than 5mm diameter on examination was noted in 54.5% of cases in HIV group whereas in non HIV group such cases with the tumour base more than 5mm were 21.6% at the time of presentation. Among the HIV infected group fornicial involvement was seen in 27.2% of cases and feeder vessel in 100% of cases. The non-HIV group also had feeder vessels in 97.2% of cases but the fornicial involvement was seen in only 13.5% of cases. A statistically significant difference in the tumour size on presentation and fornicial involvement was observed in both the groups.

Morphologically the most common variant in both HIV positive and non HIV group was leukoplakia which constituted 36.36% and 42.23% of total cases respectively in each group. Analysis of the histopathological data showed 63.63% of cases to be of invasive carcinoma amongst the HIV positive group. Among the non HIV group 54.05% of all cases documented were of invasive carcinoma. The statistical test did not point to any significant difference between the two groups in histopathological analysis.

DISCUSSION

In the present study, both the HIV and Non HIV groups were statistically analyzed to look for any significant difference in patient demographics, morphology and histopathological analysis.

Amongst all patients of OSSN who were HIV positive, 42.3% of patients exceeded the non-HIV group in less than 50 years age group. This difference was statistically significant and clearly shows that OSSN and HIV is a disease of young. HIV positive patients present with OSSN at younger age as compared to non HIV population. Also, we observed that in 54.5% patients of HIV, OSSN was the first presenting clinical feature ophthalmologically and systemically and patients were till then unaware of their HIV status. ART Centre reference was hence advised for them for a complete systemic examination, counselling and management. In other studies a similar trend was observed. OSSN have become more prevalent and aggressive over recent decades in Sub-Saharan Africa, with higher rates of young people being affected [11]. These changes are largely attributed to human immunodeficiency virus (HIV) infection [12-15].

In the present study, we observed that males predominated both the groups. In various other studies on OSSN from this subcontinent, similar finding was noted [16]. Published studies from the western world showed similar data [5,17]. Interestingly in a study in sub-Saharan population by Makupa et al., females formed the larger proportion [18].

We found a greater number of cases with lesion having a base more than 5mm and with fornicial extension at the time of presentation in HIV positive population. We observed a significant p-value in these two groups though the underlying pathology was not very clear. Feeder vessels were seen in all HIV infected cases. Comparison of the histopathological data showed that though a higher percentage of population in HIV group showed more invasiveness there was no significant difference in both the population groups regarding invasiveness of the tumours. Hence, no clear concluding comment can be made regarding the difference in aggressiveness of tumour between the two groups in our study. In a similar study by Makupa et al an association between feeder vessel and HIV was also noted. A higher grade of malignancy was also noted in HIV infected OSSN population [18-21].

Two important parameters regarding CD4 counts and recurrence rates of OSSN tumours in HIV and non HIV population were not compared in this study due to the lack of proper data. On literature search we found a very limited number of studies comparing such data from South Asian subcontinent hence with the increasing HIV upsurge in our population, collection, detailed analysis of data from both HIV and non HIV affected OSSN patients would be extremely useful in determining role of Anti Retroviral therapy in the affected population. An interesting fact we noticed in this study was that a significant number of HIV positive OSSN patients were apparently normal systemically and were unaware of their HIV status.

CONCLUSION

Younger age and aggressive looking ocular surface neoplasia with feeder vessels at presentation should caution ophthalmologist to look for an undiagnosed HIV infection in OSSN patients.

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