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Abstract

Background: Various non-invasive modalities have been described in diagnosing conjunctival lesions, but histology remains the gold standard. Shortages in ophthalmology services and pathology laboratories in non-urban areas is one of the main reasons for delayed presentation and appropriate treatment in sub-Saharan Africa. The purpose of this study is to determine the spectrum of histopathologic findings in conjunctival lesions from patients at St John Eye Hospital (SJEH).

Materials and methods: Data of patients who underwent conjunctival surgical biopsies was retrieved from the main theatre register of SJEH for a 3-year period, from 01 November 2016 to 31 October 2019. This data was used to retrieve histology reports from National Health Laboratory Services (NHLS).

Results: A total of 679 patient records were retrieved from the theatre register, only 585 histology reports from 584 patients could be analysed. There were 305 benign lesions. Pterygia were most of the benign with a total of 249 (42.56%). 174 premalignant lesions were recorded, and severe ocular surface squamous neoplasia (OSSN) made up the bulk of premalignant lesions 147/174(84.48%). Squamous cell carcinoma (SCC) was the most common malignancy. There were 102 SCC of a total 106 malignancies.

The age ranged from 1 to 90 years with mean of 43.14 years. The patients were predominantly black, Caucasians constituted only 1%. The average age for SCC was 41.3 years, severe OSSN 43.6 and pterygia 46.3 years.

Benign and premalignant lesions had a slightly higher predilection for females at 55.4% and 58.6% respectively.

Malignancies were common in males.

Conclusion: Pterygia are the most common excised benign conjunctival lesions and severe OSSN is the most common premalignant lesion excised at SJEH. SCC made up the bulk of conjunctival malignancies excised at SJEH. Pterygia, OSSN and SCC occur in significantly younger patient group compared to reports from elsewhere.

Disclosures: None.

Introduction

Lesions of the conjunctiva submitted for histology include a broad spectrum of pathologic conditions ranging from benign lesions such as pterygia, pingueculae and squamous papilloma, premalignant lesions for instance, severe OSSN/carcinoma in situ (CIN) and Primary Acquired Melanosis (PAM) with atypia, to aggressive malignant tumours such as SCC, Kaposi Sarcoma (KS), malignant melanoma and lymphoma which can result in vision loss and sometimes fatality if diagnosed late.[1]

The term OSSN was first described by Lee and Hirst in 1995 to denote an entire spectrum of dysplastic, pre-invasive and malignant squamous lesions that originate from the epithelium of the cornea or conjunctiva.[2]

The distribution pattern of conjunctival lesions varies geographically. OSSN and pterygia are the most common conjunctival lesions submitted for histological diagnosis in sub-Saharan Africa. OSSN affects a younger age group in Africa unlike in Europe and the USA where it is still regarded as a disease of older white males. Differentiating early malignancies from benign lesions can be clinically challenging, hence it is important to send all excised lesions for histological assessment.[3]

Tissue examination remains the gold standard for definitive diagnosis of conjunctival lesions. The two surgical biopsy methods include, incisional

biopsy reserved for extensive suspicious tumours that are symptomatic,[5] or showing evidence of invasion of the globe on imaging. The other is excisional biopsy, more commonly performed and is appropriate for smaller tumours (≤4 clock hours limbal tumour or ≤15 mm basal diameter) that are symptomatic or suspected to be malignant.[4]

The aim of this study was to determine the spectrum of histopathologic findings in conjunctival lesions from patients at St John Eye Hospital (SJEH).

Materials and methods

This was a retrospective study of conjunctival surgical biopsies submitted for histologic assessment at SJEH theatres during a 3-year period from 01 November 2016 to 31 October 2019. All specimens were submitted to the National Health Laboratory Services (NHLS) histopathology department at the Chris Hani Baragwanath Academic Hospital (CHBAH) based in Soweto. The main register of SJEH which covers three theatres was used to retrieve records of all patients who underwent conjunctival surgical biopsies during the set study period. Patients' demographic information and histopathologic diagnoses were retrieved from original biopsy reports. Permission to collect data was given by the Head of Departments (HOD's) at SJEH and NHLS. Approval from the Human Research Ethics Committee (HREC) and the Post Graduate Committee of the University of Witwatersrand was obtained.

The frequency of the different types of conjunctival lesions was reported. Kruskal Wallis Test was used to determine correlation between age and type of lesion.

Results

A total of 679 conjunctival biopsies from 678 patients were found in the SJEH theatre main register from 01 November 2016 to 31 October 2019. Of these, 585 histology reports from 584 patients were retrieved from NHLS. Ninety-five cases were excluded because of errors in theatre data capturing.

There were 375 females and 297 males. The gender was not specified in six patients. 675 were black and four were white, no other races were recorded.

The age range was 1 to 90 years. The mean age was 43.1 years.

585 histology reports were retrieved from 584 patients *(Table I)* with one patient undergoing biopsies in each eye, histology reported SCC on the right eye and severe CIN on the left.

Benign lesions accounted for 305 cases with pterygium being the most common. Premalignant 174 cases and malignant 106 cases *(Table I)*.

Table I: Types of lesions

	Frequency	Percent
Benign lesion	305	52.1
Premalignant lesion	174	29.7
Malignant lesion	106	18.1
Total	585	100.0

Premalignant lesions comprised mostly of severe OSSN whilst SCC made up most of the malignancies.

Pterygia were diagnosed in older individuals, followed by severe OSSN and SCC which were found in slightly younger individuals. The age difference amongst pterygia, severe OSSN and SCC was statistically significant (p-Value = 0.016).

In our study, benign and premalignant lesions had a slightly higher predilection for females and malignant lesions higher in males *(Table II)*. This observation is clinically significant but was found to be statistically not significant *(p-value = 0.069) (Table III)*

Table II: Type of lesion and sex

			M	F	Unspecified	Total
Type of Lesion	Benign lesion	Count	131	169	5	305
		% within type of lesion	43.0%	55.4%	1.6%	100.0%
	Premalignant lesion	Count	71	102	1	174
		% within type of lesion	40.8%	58.6%	0.6%	100.0%
	Malignant lesion	Count	58	48	0	106
		% within type of lesion	54.7%	45.3%	0.0%	100.0%
Total		Count	260	319	6	585
% within type of lesion			44.4%	55.6%	1.0%	100.0%

Table III: Chi-Square tests

	Value	df	Asymptotic significance (2-sided)
Pearson Chi-Square	5.355[a]	2	.069
Likelihood ratio	5.334	2	.069
Linear-by-linear association	2.358	1	.125
N of valid cases	579		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 47.60.

We identified one case of carcino-sarcoma from a 38-year-old female patient who had had two previous surgical biopsies in the same eye. The first was reported as margin positive CIN in 2014. The second was margin positive high grade OSSN in 2016.

A case of conjunctival malignant melanoma was reported from a 54-year-old HIV negative African female patient. The histology reported deep stromal invasion with involvement of the margin, PAM with atypia was present in the background.

A case of B-cell lymphoma was reported in a 46-year-old black male patient.

There was one case of Kaposi Sarcoma (KS) in a 34 year old HIV positive black female patient. The tumour was involving the caruncle and bulbar conjunctiva.

A diagnosis of tuberculosis (TB) was reported in a patient with a granuloma of the bulbar conjunctiva.

Discussion

In this report, 99.4% of the specimens were from black patients which is to be expected since SJEH is in Soweto, a predominantly black township.

Pterygium was the most common conjunctival surgical biopsy finding accounting for 42, 56% of all surgical biopsies performed at SJEH theatres during the 3-year study period, with a M:F of (1:1.5).

The average age was 46.3 years which was similar to studies from India and Iran.[5]

Due to theatre constraints, only type 3 pterygia or those which cause significant astigmatism were eligible for excision at SJEH.

In this study, diagnoses of dysplasia occurring in the background of pterygia

were recorded as OSSN. A few studies are reporting on the incidence of pterygia associated with dysplasia and considering it as an entity on its own.[6] In some studies, pterygia are further subdivided into pure pterygia, pterygia associated with epithelial lesions (dysplasia/SCC) and pterygia associated with a cyst. This illustrates the importance of submitting all excised clinically diagnosed pterygia for histologic assessment as the management and follow up of dysplasia is completely different from that of pure pterygia.

Patients with a pingueculum are treated conservatively at SJEH, hence none were reported in this study.

Histology reports for premalignant lesions were reported as either mild, moderate or severe dysplasia and 'carcinoma in situ' (CIN). The descriptive term of OSSN was used for this publication. It is important to be familiar with various nomenclature used to describe lesions of the conjunctiva. Carcinoma in situ and severe OSSN essentially define similar pathologies. Severe OSSN was the most common conjunctival neoplasm in our study. This is contrary to most studies in Africa and the USA which reported SCC to be the common conjunctival neoplasm.[4,7] In this study, SCC made up the bulk of malignant tumours, with a higher predilection for males at 54.7% vs. 45.3% in females. SCC of the conjunctiva is regarded as a disease affecting older white males in Europe and the USA, but our study shows a preponderance towards younger black males, in keeping with most of the reports from other African studies.[8] OSSN and SCC affects the younger age group in sub-Saharan countries as is the case in our study. This is probably due to the high prevalence of HIV infection in the younger population group, which is associated with OSSN and SCC. The prevalence of benign and premalignant lesions was higher in females and malignant lesion higher in males.We postulate that the reason for this could be that female patients consult earlier than their male counterpart.

One case of malignant melanoma was recorded in a 54-year-old Black female patient. Malignant melanoma of the conjunctiva is a rare tumour occurring mostly in older White patients and up to 75% originate from PAM with atypia.[9]

A case of B cell lymphoma conjunctival lymphoma was reported in a 46-year-old male patient. The common conjunctival lymphoma is the low-grade extra nodal B-cell lymphoma which is usually seen in patients over the age of 60 years. It is important to note that the benign and malignant lesions may have similar clinical appearances and histologic assessment is the gold standard for a definitive diagnosis and appropriate management. It is reported that a third of patients with conjunctival lymphomas have co-existing systemic lymphoma and an ocular diagnosis should prompt for urgent appropriate referral for systemic work-up.[10]

Kaposi Sarcoma (KS) was reported in one HIV positive patient. KS of the conjunctiva can mimic a subconjunctival haemorrhage, a high level of suspicion in patients presenting with non resolving spontaneous 'subconjunctival haemorrhage' is paramount.[9,10,11]

TB of the conjunctiva was diagnosed in one patient. This could be an index presentation in a patient without a previous diagnosis of TB.

This study illustrates a high incidence of severe OSSN and SCC in our population. SCC constitutes the majority of malignant lesions affecting younger African patients in our setting. Male gender is mentioned as one of the risk factors for SCC but some studies report equal sexual distribution.[12]

Positive appraisal

This study is from a large Ophthalmology referral centre and a lot of data was collected within the study period.

The study demonstrates a predilection for SCC in males and OSSN in females in our setting.

It highlights the importance of submitting all surgical biopsies.

Limitations

This is a retrospective study.

Patient's clinical assessments were unavailable to match with histology findings.

In our study, the histology was reported by different pathologists, this may account for the differences in nomenclature.

Different pathologists reporting on the cases may also lead to Inter-observer variability.

Conclusion

Lesions of the conjunctiva vary tremendously. In most instances, excision biopsy is not only diagnostic but also therapeutic. On a few occasions, life threatening systemic disease can be firstly seen in the eye and diagnosed from conjunctival surgical biopsies e.g. Lymphoma, TB and Sarcoid, reiterating the importance of submitting all surgical biopsies.

Despite SJEH serving a predominantly city-based population with access to health facilities, and patients presenting with suspicious conjunctival lesions given priority for theatre, we still have a handful of patients presenting with advanced malignant disease (SCC) requiring exenteration. Aggressive health awareness campaign is needed to prevent unnecessary morbidity and mortality.

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