

Squamous papillomas of the conjunctiva: A retrospective clinicopathological study

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Abstract

Background: There is very limited literature on squamous papillomas of the conjunctiva from Nigeria and sub-Saharan Africa. In an attempt to contribute to the literature on the subject, we studied the clinicopathological characteristics of patients histologically diagnosed with squamous papilloma of the conjunctiva in Ibadan, Nigeria.

Materials and Methods: Clinical and pathological records of patients with histological diagnosis of squamous papilloma of the conjunctiva made in the Department of Pathology, University College Hospital, Ibadan, between January 1985 and December 2004, were reviewed.

Results: There were totally 26 cases. Patients' ages ranged from 2 to 58 years with a mean age of 32 years. Male to female ratio was 1.4:1. Size of tumors ranged from 2 to 10 mm. Duration of presenting complaints was from 2 months to 10 years. The lesions in 10 cases were located in the medial canthus, at or close to the limbus in another 10 cases, and in the tarsal conjunctiva in a single case. Five cases had no documentation of location. Sixteen cases (61.5%) had multiple papillomas. Four cases had a history of chemical injury (alkaline based – hair relaxer in a single case, acid based – wet cell car battery fluid in two cases, and unknown chemical in a single case) preceding the lesion by at least 6 weeks. Fourteen cases had *koilocytosis* on histology suggestive of Human Papilloma Virus (HPV) etiology. HIV screening test was negative in the three patients who had the screening done. Preoperative clinical diagnosis was squamous papilloma in 16 cases, pterygium in 6 cases and squamous cell carcinoma in 2 cases.

Conclusion: In the environment where we practice, conjunctival squamous papilloma occurs most commonly in the fourth decade of life. Only very few cases are submitted for histological diagnosis. HPV infection and chemical injury are the main etiology. We strongly advocate that all excisions of the conjunctiva, irrespective of the clinical impression, should be submitted routinely for histological assessment.

Key words: Squamous, papillomas, conjunctiva

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Introduction

Conjunctival papillomas are benign neoplasms of the squamous epithelium, characterized by finger-like projections that have a fibrovascular core and are covered by acanthotic squamous epithelium.^[1] A review of the available medical literature did not reveal any definite information on its precise incidence or prevalence.

Conjunctival papillomas are categorized into infectious (viral), squamous cell, limbal and inverted, based on histological appearance, location and propensity to recur

after excision.^[2] They can also be classified based on gross clinical appearance, as either pedunculated or sessile.^{1,2}

Squamous papillomas can arise anywhere in the conjunctiva, but are more commonly located close to, at or just inferior to the medial canthus, and they may be unilateral or bilateral in presentation.^[1,3-6]

The Human Papilloma Virus (HPV) types 6, 11 and 16

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have been associated with benign conjunctival papillomas, especially when they are bilateral and multiple.^[1,3,7-9] Other etiological factors include ultraviolet light exposure, which is commonly associated with limbal papillomas, chemicals such as trifluridine, arsenicals and beryllium, ocular injury and vitamin A deficiency.^[2,10]

In view of the limited literature about the lesion from this part of the world, we decided to carry out a retrospective study to determine the morphology, clinical characteristics and possible etiology of conjunctival papillomas and treatment modalities used in the tropical environment where we practice.

Materials and Methods

The study period spanned 20 years, from January 1985 to December 2004. All the notes of consecutive cases histologically diagnosed as squamous papilloma during the study period from the records of the Department of Pathology, University College Hospital (UCH), Ibadan, were retrieved. The clinical and pathological records of all the patients were reviewed. Each patient's record and data were analyzed for age, sex, presenting symptoms and its duration, possible associated etiological factors, history of trauma, HIV status, tumor size and location on the conjunctiva, treatment modalities, preoperative clinical diagnosis and clinical recurrence. The histopathology slides were reviewed by GOO and EEA for accuracy of the diagnosis, presence of koilocytosis, actinic and dysplastic changes.

Results

There were 26 cases identified over the study period. Not all the parameters were available in all patients. There were 15 males and 11 females, with a ratio of 1.4:1. The age range was from 2 to 58 years, with a mean age of 32 years. The modal age group was 30–39 years [Figure 1]. Duration of presenting complaints ranged from 2 months to 15 years, with an average of 3.2 years.

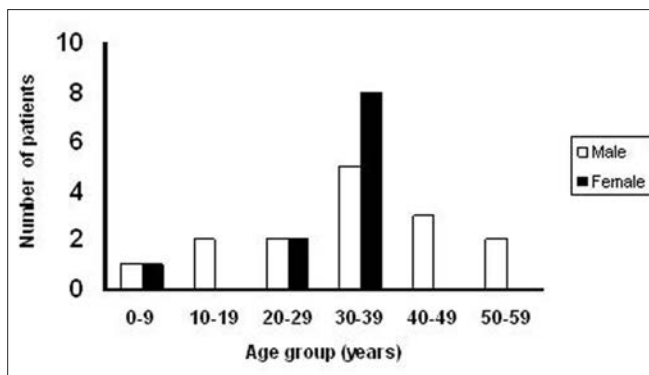


Figure 1: Age and sex distribution of the patients

The lesions in 10 cases were located in the medial canthus and at or close to the limbus in another 10 cases. The only case in the tarsal conjunctiva was located both inferiorly and superiorly. This was the only patient who had multiple recurrences in the same eye over 15 years. Five cases had no documentation of location in their notes. Sixteen patients had multiple papillomas (two or more).

Figure 2 shows a photomicrograph of a typical squamous papilloma of the conjunctiva in our series.

Four of the patients had prior chemical injury (wet cell battery fluid with its main content being acidic in two cases and hair relaxer lotion which is mainly alkaline in a single case and an unknown chemical in the fourth patient). These four patients developed a growth in the affected eye within 6 weeks (hair relaxing lotion) and 8 weeks (wet cell battery fluid) of exposure of the conjunctiva to these agents. HIV screening test was negative in the three patients who had the screening done. Tumor size ranged from 2 to 10 mm, with an average of 8 mm. Typical clinical description of the lesions includes mulberry bush, pterygium-like and multiple papillomas. The preoperative diagnoses based on clinical examination were squamous papilloma in 16 cases (correct diagnosis in 62% of cases), pterygium in 6 (23%) cases and squamous cell carcinoma in 2 cases. Two patients did not have a preoperative clinical diagnosis. Simple excision was the main treatment modality in all patients. In addition, the patient with multiple recurrences had cryotherapy with β irradiation, while three patients with preoperative clinical diagnosis of pterygium had topical 5-Fluorouracil (5-FU). The histology showed that 16 patients (62%) had koilocytic cytopathic effect in the squamous epithelial cells. This effect is strongly associated with HPV etiology. None of the 26 cases showed dysplastic epithelial changes or actinic changes.

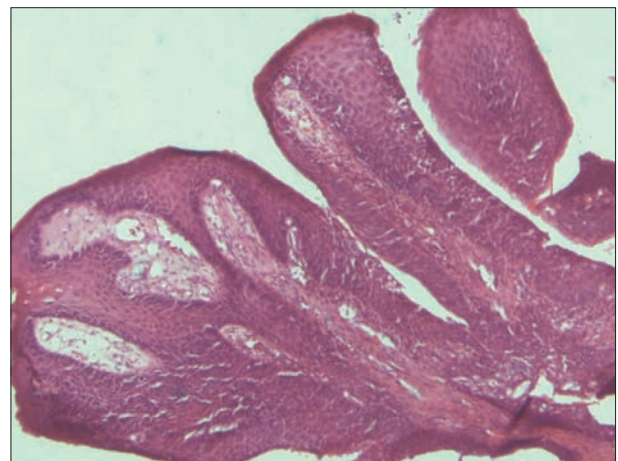


Figure 2: HandE ($\times 100$): Photomicrograph of a typical conjunctival squamous papilloma in one of the patients in this series

Discussion

Only 26 cases were documented over a study period of 20 years in contrast to 245 cases over a period of 15 years reported by Sjö *et al.* in Copenhagen, Denmark.^[5] The large number from that study may be due to the specialized nature of the center where this Danish study was carried out. The reason for the very low number of cases in our study is likely to be multifactorial. We speculate that the contributing factors for the low numbers may include the fact that papillomas can be present in the conjunctiva for years without any complication and this may not pressurize the patient to present to an ophthalmologist. Another likely strong factor is the nonsubmission of specimens from conjunctival excisions for histological assessment. Additionally, in our environment, patients usually present very late to physicians and in a few cases spontaneous regression of the papillomas may occur.^[6] The late presentation is typified by the average duration of presenting complaint in this study, which is 3.2 years. The male to female ratio, modal age group affected and mean age in our study are similar to the findings by Sjö *et al.* and McDonnell *et al.*^[5,9] They had more males affected with peak incidence in the 20–29 and 30–39 age brackets and mean age of 31 and 39.6 years, respectively. These findings show that conjunctival papillomas often affect younger people and they are not common in children. We found two cases in children of age 2 and 3 years. Furthermore, Elsas and Green documented that only 7% of epibulbar tumors in children younger than 15 years of age were conjunctival papillomas.^[11] It has been reported that conjunctival papillomas can also occur in infants born to mothers with HPV infection of the vulva following vaginal delivery.^[12] It is well known that HPV may be present in tissues for many years without clinical signs of infection.^[13]

Clinical recurrence of the tumor several months or years after spontaneous regression or excision of a previous papilloma is common.^[6] The recurrence might be induced by the same viral infection that caused the previous papilloma to develop.^[5] The only case of clinical recurrence documented in this series had three episodes spanning a period of 15 years with intervals of 7 and 8 years preceding the second and third presentations. Other studies have shown recurrence frequency ranging from 6 to 27%.^[5,9,14]

Koilocytosis, a cytopathic effect induced by HPV, is characterized by the presence of cytoplasmic vacuoles which are mainly perinuclear in superficial squamous cells. This effect was observed in 16 (62%) cases in this study. This demonstrates that HPV is a strongly associated factor in the development of conjunctival papilloma in our study. This has also been alluded to in studies where genotyping identified HPV particles in the cytoplasm of cells of conjunctival papillomas.^[7-9] HPV typically infects tissues in a multicentric pattern.^[13] It is therefore not surprising that 16 (62%) of

our cases had multiple papillomas on clinical examination.

Generally, papillomas tend to be located medially and inferiorly in the conjunctiva, as documented in this study and as observed by Sjö *et al.*, Elsas and Green, and Ash.^[5,11,14] This distribution pattern reinforces the fact that HPV infection is an important etiologic factor in the development of conjunctival papilloma. The distribution correlates with an affinity of HPV to infect the inferior and medial aspects of conjunctiva based on the explanation offered by Sjö *et al.*^[5] They elucidated that factors that influence this pattern of distribution may include the tear flow and rubbing of the eyes. It is postulated that as tear flows from the superolateral fornix to the lacrimal lake, HPV particles are moved by the flow to the medial and inferior conjunctiva. Rubbing of eyes primarily involves the nasal part of the eyes and this might lead to autoinoculation of HPV particle.

Four of the patients in our series had chemical injury that predated the development of the papillomas. The lesions developed within 6 and 8 weeks from time of injury with alkaline and acidic contents as primary constituents of the chemicals, respectively. This may be related to exuberant growth as a result of attempt at repair of the resultant ulcerated conjunctiva in these patients.

It is pertinent to note that 6 (23%) cases in our series had a preoperative diagnosis of pterygium. This highlights the difficulties of making a firm diagnosis preoperatively and the need for histological diagnosis of all biopsies from the conjunctiva.

In conclusion, we found out that there are few cases of conjunctival papilloma histologically diagnosed in the environment where we practice. This is likely due to nonpresentation, arising from the asymptomatic nature of the lesion. Conjunctiva papillomas in our environment most frequently present in the fourth decade of life and are mainly located at the medial canthus and at or close to the limbus. HPV infection and chemical injury are the main associated etiological factors. We strongly advocate that all excisions of the conjunctiva, irrespective of the clinical impression, should be submitted routinely for histological diagnosis.

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