Conjunctival papilloma: a case report and a brief review of literature

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Background: Conjunctival papilloma commonly develops in infants and children. It is believed that the etiologic agent, human papillomavirus (HPV), gets implanted from the infected maternal birth canal in the conjunctival sac of the new borne while parturition. It grows as solitary or multiple pedunculated benign masses adjacent to the caruncle. It is uncommon but if growing in adults it grows on the limbal conjunctiva and could be malignant.

Case Description: An Afro-American adult male developed two distinct conjunctival growths on his left lower lid. One growth was pedunculated and the second one sessile. The initial diagnosis of 'benign conjunctival papillomas' was made. Patient was recommended to wait and watch. After about two years the neoplasia had doubled their sizes. Surgical excisional biopsy was performed for diagnostic and therapeutic reasons. The tumor beds were treated with intra-operative cryotherapy using liquid nitrogen and applying double-freeze-thaw technique. Histopathology proved the masses to be benign and caused by HPV. Recurrence and seeding of virus during surgical excision leading to multiple new masses are dreaded complications during management of conjunctival papilloma. Though a short follow-up, yet after three months there were no signs of recurrence.

Conclusions: A brief review of literature is presented to highlight the fact that rarely such conjunctival papillomas may develop at unusual sites and in adults. We believe that the uncommon demographic and anatomic presentation of this case is worth sharing with ophthalmic community.

Keywords: Conjunctival neoplasia; case report; viral papilloma; pedunculated; sessile papilloma

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Introduction

Conjunctival growths such as Pinguecula and Pterygium (1,2) are quite common and are very slow growing. On the contrary, patients with growths such as papillomas seek medical attention because of their rapid growth (3-8) and rule out malignancy. Most of the conjunctival growths are benign but some are malignant. The patients who seek medical attention either complain of pain and redness associated with such growths or their rapid progression. Conjunctival papillomas (3-8) belong to the latter group; their rapid growth and fleshy appearance are interpreted by the patients as 'cancerous.' I present the following article in accordance with the CARE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-3506/rc).

Case presentation

A 56-year-old Afro-American, otherwise healthy male, initially presented with "something growing inside the left eye." He first noticed redness and a growth inside the left lower lid over a year ago. He did not recall any recent trauma, pain, redness, discharge, systemic tumor diagnosis, or exposure to any new sexual partner. Ophthalmic

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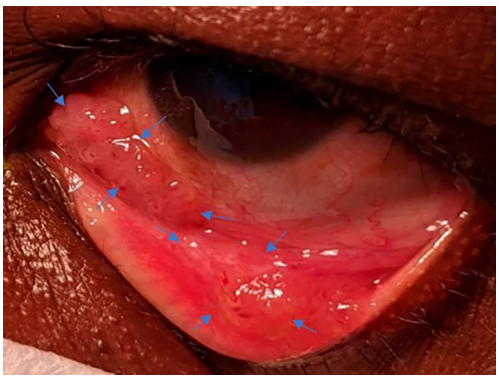

Figure 1 Two distinct papillomatous neoplasia/growths in left inferior fornix (within blue arrows) seen on initial encounter (June 2020).

Figure 2 Same two papillomatous neoplasia/growths (within blue arrows) look confluent after two years (April 2022).

examination of both eyes was within normal limits for the anterior and posterior segments, as well as for the adnexal structures of the right eye. Vision and intraocular pressure were within normal limits.

Left lower tarsal conjunctiva had two globular papillomatous growths, one in nasal inferior fornix and close to caruncle, the second growth on the tarsal conjunctiva close to lid margin (*Figure 1*). These measured about 1.5×0.5 and 1.0×1.0 cm respectively. Based on the initial clinical examination, patient was explained that the growths or masses were papillomas, most likely benign and of viral etiology. Most of these growths are known to undergo spontaneous regression (9). The patient had experienced the growths not regressing spontaneously, rather were gradually getting larger in size than a year before. Based on patient's history of gradual progression of both lesions surgical excisional biopsy was recommended. Potential risks of continued growth and implantation of seeds for more papillomatous growths were also explained. Patient wanted to think it over and discuss with the family before scheduling surgical procedure.

The patient returned for reevaluation of the growths after two years. The masses had grown significantly, were exposed, and extruded between the eyelids on lid closure (*Figure 2*). Lately, the patient observed whitish 'mucopurulent' discharge (*Figure 3*) on the surface of the nasal growth and sought medical advice.

The clinical examination showed the nasal and fornix-based mass had grown to 2.5 cm × 1.25 cm pedunculated and the tarsal conjunctival mass had grown to 2.0 cm × 1.0 cm sessile tumors (*Figures 2,3*). There was no new papilloma on conjunctiva of either eye. Patient signed informed written consent for 'excisional biopsy' of both the conjunctival papillomas while understanding the risks of recurrence and/or new mass or masses. Under local infiltration anesthesia, both masses were excised *in-toto*. Nasal pedunculated tumorous growth was excised with mild dissection, but the tarsal conjunctival growth required moderate dissection to excise the entire mass. Hemostasis was achieved with thermal cautery without complications.

Highlight box

Key findings:

- Conjunctival Papilloma, a benign neoplasia commonly diagnosed in infants and young children, may present in adults as well.

What is known and what is new?

- Human Papillomavirus gets implanted onto conjunctiva of a newborn during parturition from infected maternal birth canal.
- Our case report is a rare presentation of a middle-aged male who probably got infected from a carrier sexual partner.

What is the implication and what should change now?

- Though histologically confirmed as benign yet their unusual presentation at uncommon locations in the form of two distinct masses and located away from the caruncle or conjunctival fornix should raise concern about these being malignant.
- Patient deferred treatment for more than three years from the time a mass was first noticed despite recommendations of 'Excisional Biopsy to rule out malignancy'.
- Deferred treatment in turn shed more light on the natural course of these benign but rarely seen as sessile neoplasia.
- This unique information makes the case report worth sharing with ophthalmic community.
- Initially, though patient was reluctant for surgery yet such cases should be alarmed of the potential malignancy and encouraged for early management.

Figure 3 Large papillomatous neoplasia (growth) with mucopurulent discharge extruding between the closed left eyelids forced the patient, after about two years, to seek medical help.

Figure 4 Same left lower lid as seen immediately post-excisional biopsy of tumorous papillomas and local cryotherapy of the beds of both neoplasia.

Both tumor bases were treated with cryotherapy to prevent recurrences and to destroy any seedlings dropping from the primary tumors (*Figure 4*). Cryoablation was performed using liquid nitrogen in a canister. Cryoprobe was used to treat the beds of tumorous growths. Multiple applications were applied to cover the entire bed; each application was for one minute and both areas were treated twice applying double-freeze-thaw technique. Care was taken to cover full length and breadth of the tumorous beds and even extending 1.0 mm beyond the edges of the excised area. The eye was treated with combination of antibiotics steroid ointment (neo-poly-dex ointment) three times a day for two weeks and then twice a day for another week. Histopathologic examination confirmed the growths to be of viral etiology and benign in nature. At the last examination, three months post-excisional biopsy, the eyelid had healed well and without any signs of tumor recurrence or new masses.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Timeframe

This study was conducted between June 2020 and July 2022. The patient first reported to us in June 2020 with growths on the conjunctiva of his left lower lid. He did not return for examination till March 2022 when he had excisional biopsy of the conjunctival masses/growths. He was followed up for three months, till July 20, 2022, without any signs of recurrences. Subsequently, patient failed to return for examination and was lost to follow-up thereafter.

Discussion

Conjunctival papillomatous neoplasia is relatively common and more frequently seen in young children (3-8). Most of the time the culprit virus gets implanted onto conjunctiva of the newborn during its passage through the infected maternal birth canal (10). This could lead to uniocular or binocular conjunctival neoplasia as solitary or multifocal masses. The virus is transmitted by direct contact as happens during parturition (3-8,10). This patient was a middle-aged male adult, which suggested that the transmission of the virus might had happened during sexual contact with an infected partner. Though rare still papillomatous neoplasia of conjunctiva can be encountered in adults (3-8), as illustrated by this case report.

Human papillomavirus (HPV) is one of the members of Papovavirus family of viruses (3-8,11-16). Conjunctival papillomas are commonly caused by HPV 11. Some variants such as HPV 6, 6a and 45 have also been associated with this neoplasia (3-8,11-16). HPV is tumorigenic and leads to benign cauliflower shaped or multipronged finger like fleshy growths that rarely may turn into malignant tumors. Most of the growths involve the caruncle or grow in its proximity (*Table 1*). The tumorous growths in adults are more commonly sessile limbal masses than pedunculated (3-8). This adult male patient presented with both pedunculated and sessile growths. The pedunculated cauliflower shaped mass grew in the inferior fornix adjacent to the caruncle. The sessile mass grew at an unusual site on the tarsal

Table 1 Literature search

Topic of literature search	Details of literature search
Date of search	This search was conducted between March 01, 2022 and September 15, 2022
Databases and other sources searched	For review of literature, search was performed on PubMed, NIH Library, Google Search engines
Search terms used	Used search keywords: Conjunctival Papilloma, Conjunctival Neoplasia, Viral Papillomas, Squamous cell carcinoma of conjunctiva, Human Papillomavirus, Conjunctival Papilloma in Adults, free text
Inclusion and exclusion criteria used	There was no specific inclusion or exclusion criteria used; just search for conjunctival papilloma and its management. The time frame for the search was 1960s to present
Selection process	Only one ophthalmologist, GS, conducted the study independently, without any financial or other interest, and consensus was not required

conjunctiva adjacent to the lid margin (*Figures 1-3*). Most of the times, conjunctival papillomas are slow growing masses. Usually, it is more of a cosmetic problem when these become noticeable than being malignant.

The presented case is a typical example of the slow growing nature of conjunctival papillomas. On the initial visit, patient had a significantly large sized mass that brought him to seek medical help (*Figure 1*). It had been growing for over a year as patient could recall. The second small lesion on the tarsal conjunctiva almost in the middle of lower lid was an additional finding during ophthalmic examination. At the second visit both the tumor masses had grown to be almost twice their sizes in 2 years (*Figure 2*). These slow growing papillomatous masses, often being asymptomatic, are frequently ignored by the patients till they become large. This patient had a similar history and was getting concerned when mucopurulent discharge (*Figure 3*) developed in the nasal canthal area and on the growth in the affected eye.

Patients are initially reassured and recommended to wait and watch because most of the times these are 'benign neoplasia' and frequently regress spontaneously over time (3-9). Surgery is postponed because of associated potential risks of recurrences (3-8,17,18), along with seeding and more lesions developing while excising the papilloma (3-8,17,18). This patient was accordingly recommended to watch the natural course of the initial lesions. At that stage surgical excision and histopathology were indicated. Excisional biopsy was performed under local infiltrative anesthesia. The masses were excised in toto and meticulously not to leave behind the edges of the masses. After achieving hemostasis with thermal cautery, the tumor bed was treated with cryotherapy (3-8,19) to prevent recurrence or seeding problem. At the last visit, three months post-operatively, to patient's satisfaction, there were no signs of recurrence or secondary papillomas from seeding. Longer follow-up is indicated and was discussed with the patient.

Numerous modalities have been used as adjunct therapies to surgical excision of conjunctival papillomas, but mostly to treat recurrences or recalcitrant squamous papillomas (20-29). These include dinitrochlorobenzene immunotherapy (20), intra-muscular Interferon injections (21-24), topical adjunct application of mitomycin-C after excision (25), oral Tagamet (Cimetidine) (26,27), Carbon-dioxide (CO_2) laser (28,29), cryotherapy (19), thermal and electrodessication and intralesional bleomycin (4) etc. We applied cryotherapy as an adjunct treatment to surgical excision of the papillomas because it is considered the most effective and safe adjunct treatment. It is an easy procedure to perform with minimal damage to the adjoining tissue and with minimal scarring. It is the preferred adjunct treatment to excisional biopsy of conjunctival papillomas, especially in recurrent and recalcitrant tumors.

Conclusions

Two distinct masses, histologically diagnosed Conjunctival Papillomas, growing away from caruncle and conjunctival fornix as sessile neoplasia in a middle-aged male makes it an unusual case report, worth sharing with ophthalmic community. Excisional biopsy was followed by adjunct cryo-treatment to the tumor beds to prevent recurrences and/or accidental seeding of the HPV.

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Footnote

Reporting Checklist: The author has completed CARE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-3506/rc

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Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-3506/coif). GS serves as an unpaid editorial board member of *Annals of Translational Medicine* from April 2022 to March 2024. The author has no other conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s)and with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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