Scholars LITERATURE

La Prensa Medica Argentina

Review Article

DOI: https://doi.org/10.47275/0032-745X-404
Volume 109 Issue 6

Conjunctival Papilloma: A Literature Review

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Abstract

Objective: The aim of this literature review article is to analyze the characteristics of conjunctival papilloma such as prognosis, prevalence, relationship with HPV (Human papillomavirus), diagnosis, treatment, and importance of its presence.

Method: The following article was carried out by searching scientific articles in Spanish and English, which were obtained through databases such as Scopus, PubMed, and Google Academic. We used the virtual platform of the Catholic Library of Cuenca using advanced search commands (“ “), AND, OR. Finally, 15 articles were included in the bibliographic review.

Results: Conjunctival papilloma is a benign squamous cell tumor of the conjunctiva with a minimal tendency to malignancy. These tumors are related to HPV specifically types VI and XI. To obtain a diagnosis it is important to perform a thorough anamnesis and ophthalmologic examination, a biopsy after removal of the lesion, high-definition optical coherence tomography (HR-OCT), and ultrasonic biomicroscopy (UBM). The MSP has developed an initiative called “Expanded Program of Immunizations”, same that consists of the vaccination process of the female population of 9-, 10- and 11-years old belonging to public and private schools.

Conclusion: It is important that educational institutions promote more eye health because when there is an HPV infection there is a risk of having conjunctival papilloma and people are unaware of this means of transmission. In addition, vaccination should be promoted in children because any gender is prone to acquire HPV.

Keywords: Conjunctival papilloma; Human papillomavirus; Papillomas; Prevention; Prevalence

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Citation: Calle-Fernandez P, Vera-Mena D, Vidal-Carvalli D, Cervantes-Anaya L (2023) Conjunctival Papilloma: A Literature Review. Prensa Med Argent, Volume 109:6. 404. DOI: https://doi.org/10.47275/0032-745X-404

Received: September 19, 2022; **Accepted:** November 13, 2023; **Published:** November 17, 2023

Introduction

Conjunctival papilloma is a benign neoplastic lesion that has a tendency to become a malignant lesion. It can be present in various age groups; however, it has been shown to be more common during the fourth decade of life, making it one of the most common tumors. located in the eyelids and conjunctiva, it is a condition that presents as a peduncular conjunctival mass, it occurs more frequently in the male population [1,2].

Among the main causes of its development are exposure to UV rays, HPV infection, trauma and immunodeficiencies. Considering that currently the HPV is present in a large percentage of the population, the prevention measures taken are a problem, since it has been identified that the HPV vaccine is not free in all countries. countries and is normally indicated for women, leaving aside the male population [3].

The objective of this bibliographic review article is to analyze the characteristics of conjunctival papilloma such as prognosis, prevalence, relationship with HPV, diagnosis, treatment, and the importance of its presence. Bearing in mind that it has currently been considered a research problem, considering that within the health area the most relevant thing is prevention, it is of great importance to know how to act in certain situations, in this case the analysis and management of papilloma. conjunctival.

Methodology

This article was carried out using a systematic strategy, in which bibliographic sources were used in various scientific databases such as: Scopus, PubMed and Google Academic, and Google Books. It was used from the virtual platform of the Catholic Library of Cuenca using advanced search commands (“ “), AND, OR. The search used journals, clinical cases and scientific articles of bibliographic review and originals, in English and Spanish, excluding those documents that have been published in distant dates.

Theoretical Framework

Concept

The word papilloma refers histologically to various tumors with a respective morphology. Papillomas are most common on the conjunctiva and eyelids (Figure 1). Conjunctival papilloma is a benign squamous cell tumor of the conjunctiva with a minimal tendency toward malignancy. These types of tumors are associated with HPV infection, specifically types VI and XI [4-6].

Etiology

There are several risk factors for the development of a conjunctival papilloma, including: UV radiation, papillomavirus infection and trauma; On the other hand, there are theories that are related to this,

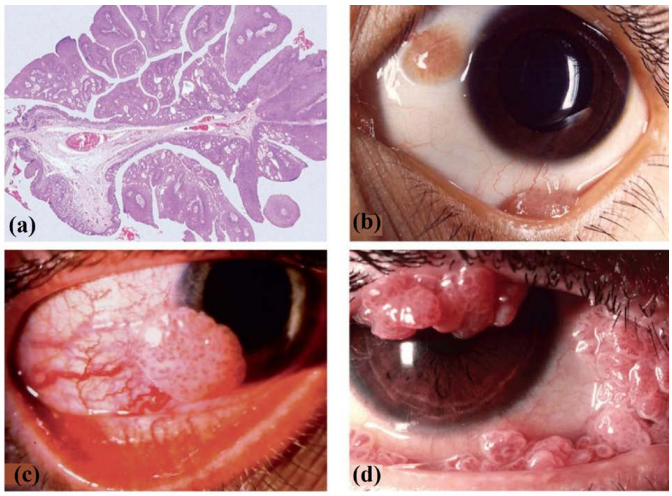

Figure 1: Conjunctival papilloma. **(a)** Histology, **(b)** Sessile papilloma, **(c)** Sessile papilloma with nutrient vessels, and **(d)** Pedunculated papillomas [16].

among them is: rubbing the eyes with the hands, especially in the lower eyelid and interpalpebral region, which are related to tear drainage of the superotemporal fornix with autoinoculation of papillomavirus. Humans, it should also be considered that they are directly related to surgical interventions and the manipulation of tumor tissue, shedding viral particles to the surrounding tissue [1,7,8].

Pathophysiology

HPV is part of the Papovavirus family. Papillomaviruses have their own site and cell type specificity, for example, in the case of HPV 6 and 11: they are benign skin warts or condylomas of the female genital tract and conjunctival papilloma. Likewise, HPV 6a and 45 subtypes, being new, are related to conjunctival papilloma. As is known, HPV has a tendency to produce tumors. The form of transmission is through direct contact with people. Transmission is through direct human contact. HPV type 11 has been the most frequent in conjunctival papilloma thanks to the analysis performed by "PCR", the polymerase chain reaction [9,10].

Risk factors

HPV types 6 and 11 are most frequently detected in conjunctival papilloma's, however, types 5b, 13, 16, 20, 23, 33 and 45 have also been found. Low-risk types 6 and 11 are found mainly in children and adults with conjunctival papilloma, while high-risk types 16 and 18 are mainly found in adults with OSSN [11].

This seems consistent with the fact that most genital warts are associated with low-risk HPV types, while high-risk types are mainly associated with cancer and cervical intraepithelial neoplasia [12]. The route of ocular transmission of HPV is believed to vary from vertical transmission from mother to child during childbirth to inoculation when the eyes come into contact with contaminated surfaces or hands. There is a history of the presence or coexistence of genital warts, skin tags and conjunctivitis, that is, HPV infection can occur in several sites simultaneously [12].

In this sense, other risk factors are trauma, in addition to UV radiation. Therefore, the bulbar conjunctiva and limbus are the anatomical sites that have been most affected in this type of injury, as well as the interpalpebral area of the conjunctiva, where most of the injuries are located due to its exposure. and for this reason, it is the one that receives the effects of ultraviolet solar rays. Atopy has also been reported as a risk factor in the development of OSSN [1].

Clinical manifestations

The conjunctiva consists of a layer of epithelial lining of the eye and, therefore, lesions can manifest from any of its histological components, whether benign (papilloma), premalignant or even malignant [12,13]. Patients can present with a wide range of symptoms, depending on the size and location of the tumor. Thus, small lesions are generally asymptomatic, while large lesions can produce a sensation of a foreign body and dryness due to inadequate closure of the eyelids, chronic discharge of mucus and consequently visual impairment due to secretion. Likewise, this may be associated with conjunctival hemorrhages, visual impairment, and amblyopia. Likewise, less frequent symptoms are associated with complete obstruction of the canalicular duct, invasion of the nasolacrimal sac, tears, and epistaxis [12,13].

In this context, they usually show a type of pattern that consists of an exophytic growth, either sessile or pedunculated, with a geometrically ordered set of red dots, it is important to emphasize that these findings can commonly be found in slit lamp examination. Thus, the location can be in eyelid, cul-de-sac, caruncle, bulbar conjunctiva, or limbus, of which the latter two are the most affected [14,15].

Diagnosis

After an adequate anamnesis and an exhaustive ophthalmological examination to be certain of the diagnosis of conjunctival papilloma, it is extremely important to perform a biopsy after the removal of the lesion, considering that the histopathological diagnosis is essential for this section, allowing the doctor to carry out follow-up. appropriate to the patient; On the other hand, there are new diagnostic techniques that can be considered as a choice for the identification of lesions, such as: HR-OCT, a non-invasive imaging technique that obtains sections of the retina; and UBM, ultrasound that allows visualization of Schelemm's canal, useful for the study of the anterior segment of the eye, in which the cornea, sclera, and ciliary sulcus can be observed. Considering that since it is HPV, the diagnosis can be made through histological appearance through microscopic confirmation, real-time PCR should also be considered, being one of the methods of choice to confirm the diagnosis and be able to classify said infection [16-18].

Thanks to a study on the detection of HPV in normal conjunctiva, which included 165 biopsies of conjunctival papillomas and also 20 control biopsies for normal conjunctiva, the presence of this virus was demonstrated in 81% of papillomas. So, a total of all samples from a normal conjunctiva were negative for HPV. Indicating that there is a great association/relationship with conjunctival papilloma and HPV [19].

Treatment

Likewise, there are several treatment options, among them are adjuvant medications such as interferon alpha 2b, considering that interferons are glycoproteins with certain antiviral and antiproliferative properties, this being a recombinant form; mitomycin C, 5-fluorouracil, and cimetidine, which are also used intraoperatively. It should be emphasized that intraoperative mitomycin and 5-fluorouracil are effective even in very large lesions. Likewise, surgical excision with cryotherapy and intraoperative medications usually eradicates the papilloma of the bulbar conjunctiva and prevents its post-surgical recurrence. Thus, several researchers recommend a modified double-

freeze thaw technique, which includes two applications of cryotherapy throughout the base of the removed tumor, followed by a second application to all conjunctival margins [20,21].

Interferon is a cytokine with antiviral and antineoplastic activity, due to the combination of antiproliferative, antiangiogenic, and cytotoxic effects. It can be used topically, intra-lesionally or systemically based on the location and type of lesion. The benefit of using oral cimetidine and/or topical interferon for three months has been reported with the aim of reducing the risk of recurrence, especially in patients with immunosuppression or multiple tumors [22].

Excision of the lesion can present frequent recurrences and possible seeding, giving rise to multiple new papillomas. It is worth mentioning that this recurrence is more common in children and adolescents than in adults. Regarding non-malignant lesions, but with a tendency to recurrence, pharmacotherapy seems to be a better alternative associated with the effective use of topical H_2 receptor antagonists, dinitrochlorobenzene, mitomycin C and interferon alfa-2b, the latter associated with a reduction in the recurrence rate [23].

Likewise, it is worth mentioning the cytotoxicity of topical mitomycin C, which can cause serious side effects, such as the following: dry eyes, melting of the cornea and punctual stenosis [24].

In this way, with the advent of topical chemotherapy, the options have expanded, providing not only the possibility of a non-invasive primary treatment, but also an adjuvant treatment [12]. On the other hand, topical immunotherapies have been described, which can be considered within the treatment when the patient has not presented a positive response to other methods; however, the results found on this type of therapy are controversial.

HPV prevalence

In Ecuador, figures from 2015 corresponding to Azuay were recorded, in which there was a prevalence of HPV of 25.6%, of which they were divided into low risk (4.8%) and high risk (20.8%) in women of between 17 and 50 years old; On the other hand, throughout Ecuador there was an alarming figure since women between 18 and 77 years old, 86% of the cohort corresponding to 164 had HPV. In Ecuador, 4 million women are at risk of developing cervical cancer due to contact with HPV. It was shown that in Quito the incidence of cervical cancer per 100,000 inhabitants is 19%, compared to Loja where the figures were even worse, since for every 100,000 inhabitants it is 32% [25].

Reality of Ecuador

Currently, in Ecuador, as part of the measures of a national health strategy for the prevention of uterine cancer, the Ministry of Public Health has developed an initiative called "Expanded Immunization Program", which consists of the process of vaccination of the female population from 9 to 11 years of age belonging to both public and private schools. In this way, the vaccine complies with a two-dose schedule and is within the basic vaccination schedule. Therefore, this strategy aims to reduce both the incidence and mortality from cervical cancer in Ecuadorian women, thus preventing possible infection by the main agents [26,27].

As a general data, it is mentioned that conjunctival papillomas in men have a percentage of 60.3% of cases, being more frequent. But the highest incidence is found between the ages of 20 to 29 years of conjunctival papillomas. This information is related to the study by Dunne et al., who indicated that there is a high prevalence of cervical-vaginal infection due to HPV in women between 20 and 24 years of age [28].

Prevention

The key to curing any disease is to start with prevention so that in this way it is possible to prevent a disease from progressing in a person's body. The best way to prevent HPV is through vaccination and education about how one can avoid contracting the HPV. In this case, the contagion of conjunctival papilloma is from person to person with skin contact and warts may appear in the eyes. The important thing is to avoid physical contact with someone who suffers from this virus and more [29].

Recommendations

It is known that HPV vaccination is given to girls when they turn 9 years old, but however, boys are not included in this process. It is known that women are the main victims of acquiring HPV, but it does not rule out that men can also be part of this risk and infect other people. This is why it is important and recommended that children also receive vaccination so that in this way there is a lower percentage of contagion and to promote the risks that this disease has in the education of children and adolescents and thus promote prevention by preventing it from spreading. HPV to more people.

Discussion

Conjunctival papilloma is a lesion that has become a problem of discussion, especially considering the relationship it presents with the HPV, since prevention must be present within the health system through the disposition of the population. in the face of certain methods such as vaccines, which are not easily accessible.

On the other hand, a point to consider is its administration for both men and women, since currently it is not taken into account in the case of men, who could be carriers of the virus and affect the health of their partner, exposing them. to develop conditions such as conjunctival papilloma.

Regarding the treatment of conjunctival papilloma, Rojas-I. and her collaborators indicate in the Cuban Journal of Ophthalmology that mitomycin C is considered an adjuvant medication used intraoperatively. On the other hand, according to the article published by The Canadian Journal of Ophthalmology, it is stated that there is cytotoxicity caused by topical mitomycin C, which in turn can cause serious side effects, among which stands out; dry eyes, corneal melting, and punctual stenosis [24].

Conclusion

Most inoculations could be avoided, however, due to the great lack of knowledge about conjunctival papilloma, this issue continues to remain unknown. For this reason, HPV prevention through vaccination is essential, leaving aside sex segregation. Surgical excision, cryotherapy, and interferon alfa-2b are associated with both the eradication of bulbar conjunctival papilloma as well as the prevention of its recurrence. Thus, the choice of therapy for each patient becomes individual, taking into account that it depends on various factors that include age, location, comorbidities and the degree of aggressiveness of the papilloma, as well as the patient's ability to comply with treatment, your indication to undergo surgery, and any financial limitations that may exist.

Acknowledgements

None.

Conflict of Interest

The authors declare that they have no conflicts of interest.

Ethics Statement

The work has been approved by the ethics committee responsible in the workplace.

Funding

Authors do not declare means of financing of the work carried out.

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