

Malignant Transformation of Laryngeal Papillomatosis: Case Report

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ABSTRACT

Laryngeal papillomatosis is a benign tumor caused by the human papillomavirus (HPV). Very few cases of spontaneous malignant transformation of recurrent adult-onset laryngeal papillomatosis in non-irradiated patients have been reported in the literature. Low-risk HPV types 6 and 11 are most commonly associated with laryngeal papillomatosis; however, high-risk HPV types may also be present. We report a case of invasive laryngeal carcinoma arising in preexisting laryngeal papillomatosis in a 50-year-old adult who presented with inspiratory dyspnea. Nasofibroscope revealed an ulcerative tumor of the larynx obstructing the laryngeal airway. A diagnosis of squamous cell carcinoma was confirmed following a biopsy. The patient subsequently underwent total laryngectomy.

Keywords: Laryngeal papillomatosis; Human papillomavirus; Low-risk HPV; Nasofibroscope

Introduction

Papilloma is the most common benign tumor of the larynx, presenting either as a single occurrence or as recurrent lesions affecting one or more sites, as seen in laryngeal papillomatosis (LP)¹. LP can manifest in two forms: juvenile laryngeal papillomatosis (JLP), which begins before the age of 5 and adult laryngeal papillomatosis (ALP), which affects individuals between 20 and 40 years old. ALP is more prevalent in males² and is generally less aggressive than JLP. ALP is considered the primary clinical manifestation of human papillomavirus (HPV) infection in the larynx, primarily associated with the low-risk HPV types 6 and 11, which are less likely to cause malignancy. The disease can be progressive, characterized by a high recurrence rate that may require over 100 surgical interventions,

although spontaneous remission is also possible^{3,4}. Malignant transformation of LP is rare, with reports indicating an incidence of approximately 1-4%⁵. We present the case of a patient with recurrent laryngeal papillomatosis, whose biopsy revealed squamous cell carcinoma.

Case Report

It's about a 50-year-old man who has been followed since 2018 for laryngeal papillomatosis, having undergone instrumental peeling in 2018 and 2023. The evolution was marked by the onset of dyspnea, the patient was subsequently tracheostomized in the emergency department. The nasofibroscope showed an ulcer-like tumor of the left vocal cord extending to the right vocal

cord and to the anterior and posterior commissure, with fixation of the left vocal cord and arytenoid. The direct laryngoscopy, showed the presence of a budding ulcer tumor on the left vocal cord extending to the anterior commissure and involving the ventricular band and homolateral arytenoid with infiltration of the subglottic level. The biopsy showed a moderately a moderately differentiated invasive squamous cell carcinoma. The CT scan showed a tumor process centered on the left vocal cord extending to the anterior commissure, with lysis of the thyroid cartilage. The patient underwent total laryngectomy followed by radiotherapy and chemotherapy (**Figures 1 and 2**).

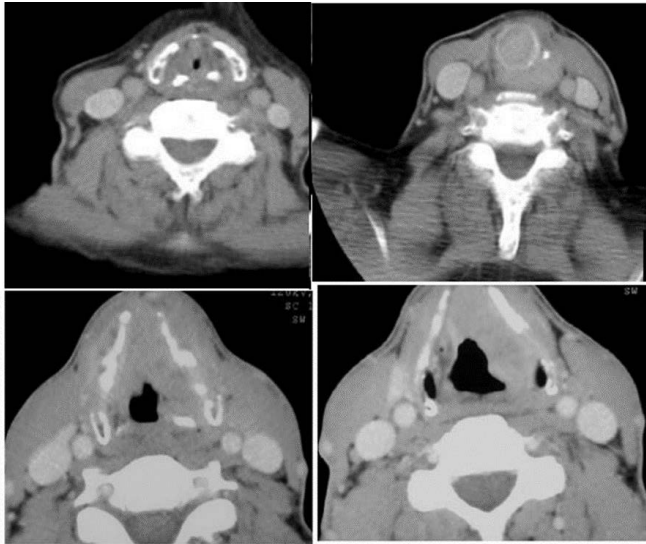


Figure 1: CT scan show a tumor process centered on the left vocal cord, extending to the anterior commissure, with lysis of the thyroid cartilage.

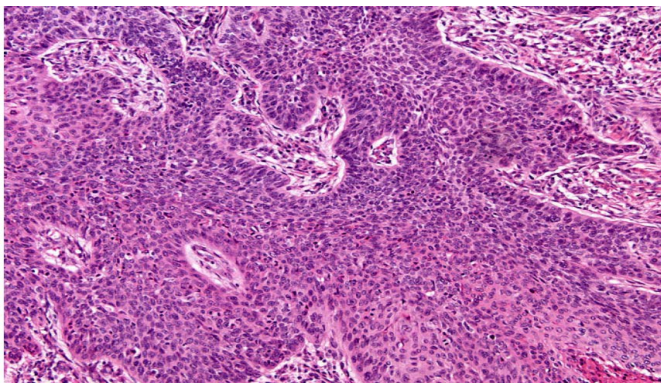


Figure 2: Histological features of laryngeal squamous cell carcinoma at 10x Magnification.

Discussion

Juvenile laryngeal papillomatosis typically manifests as recurrent and multiple papillomas that emerge in infancy or childhood and may spontaneously regress during adolescence⁶. A similar form of papillomatosis can also develop in adults, though it tends to be solitary, less likely to recur after surgical removal and is associated with a reduced risk of malignant transformation⁷. In adults, the condition is usually characterized by isolated lesions, yet the potential for malignancy remains a concern, especially in more aggressive cases⁸.

Malignant transformation of juvenile laryngeal papillomatosis has been reported in only a few cases without prior radiation therapy⁹. The reported incidence of malignant transformation is about 2 to 3% of cases, especially in the presence of known

risk factors such as smoking and irradiation¹⁰⁻¹². However, a search of the English literature reveals only a few documented cases. The diagnosis of synchronous invasive carcinoma in the setting of papillomatosis is difficult to make both clinically and pathologically⁴. Findings consistent with carcinoma in situ do not carry the same severity in patients with juvenile laryngeal papillomatosis unless there is a history of irradiation. Although the juvenile form is often associated with florid papillomatosis, malignant transformation remains rare unless the lesion has been irradiated^{5,13}. However, in patients whose disease follows a more aggressive course, particularly those in whom the condition persists into adulthood, the following signs are observed:

- Persistence of the disease into adulthood.
- Airway obstruction requiring tracheotomy.
- Spread to the subglottic region.

In adults, malignant transformation is a rare but critical event, as demonstrated in the present case, where an adult patient developed malignant transformation in the absence of known risk factors. The treatment of laryngeal papillomatosis remains symptomatic and as existing lesions are surgically removed, new lesions often arise de novo in adjacent sites or other areas of the larynx¹⁴. Various chemical treatments have been tried in conjunction with or independently of surgery to better control the disease. In addition to conventional treatments such as CO₂ laser vaporization and microsurgical excision, other modalities like microdebriders and antiviral therapies, including acyclovir, have been explored. Microdebriders offer a less invasive method for excising lesions, which can result in less tissue trauma and quicker recovery times compared to traditional surgery^{2,3,9,15}. Acyclovir, an antiviral agent, has been tested for HPV-associated lesions with some success in reducing recurrences, though its effectiveness is still being evaluated.

This case highlights the potential link between HPV infection as an initiating event in the papilloma-to-carcinoma sequence, even in adult cases. Laryngeal papilloma patients in Taiwan show a relatively high conversion rate to malignancy¹. Patients who initially clear their HPV infection are at higher risk for developing laryngeal carcinoma when subsequently infected with HPV, compared to patients with persistent HPV-associated laryngeal papilloma's.

Malignant transformation of recurrent respiratory papillomatosis is a rare occurrence, with about 40 cases reported in the literature. Among those for which HPV genotyping was performed, 100% demonstrated evidence of HPV-11 infection³. Furthermore, Reidy and colleagues have shown that HPV-11 genes can integrate into the host genome, a known mechanism underlying the malignant conversion of "high-risk" papillomavirus types, including HPV-16 and HPV-18. These authors suggest that patients with juvenile laryngeal papillomatosis and HPV-11, currently considered a "low-risk" virus, should be closely followed due to its more aggressive clinical course and emerging potential for malignant transformation^{16,17}.

Conclusion

This case serves as an important reminder of the potential for malignant transformation in juvenile laryngeal papillomatosis, particularly in adult patients. It emphasizes the importance of periodic biopsies, histopathological reviews and vigilant

monitoring, as malignant transformation can occur even in the absence of known risk factors such as smoking and irradiation. Advances in treatment modalities, such as CO₂ laser vaporization, microdebridors and antiviral therapies like acyclovir, have improved disease management. Additionally, vaccination with Avastin (bevacizumab), which inhibits the growth of blood vessels supplying the tumor, may offer a new approach in treating more aggressive forms and cases of malignant transformation. Although its effectiveness is still under evaluation, further research into this innovative treatment is crucial. Regular follow-ups are essential for patients with juvenile laryngeal papillomatosis to ensure early detection and prompt intervention in case of malignant development.

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