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## Case Reports

### Recurrent Respiratory Papilloma in Pregnancy

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#### Abstract

**Recurrent respiratory papilloma (RRP) is the most common benign neoplasm of the larynx, both in children and in adults. The aetiology of recurrent respiratory papilloma is Human Papilloma Virus (HPV), which in 20% of the cases lies in normal epithelium, hence the high rate of recurrence.**

**We report a case of an adult onset large glottic papilloma seen in a two-day postpartum female. She was treated by a dual modality, using the laryngeal microdebrider followed by microflap surgery. The effect of pregnancy, role of viral typing and latest modalities of treatment in RRP such as cidofovir are discussed in this article with a review of literature.**

#### Introduction

Recurrent respiratory papilloma (RRP) is a disease of viral aetiology that is caused by recurrent proliferation of benign squamous papilloma within the respiratory tract. The aetiological agents of respiratory papillomas are human papilloma virus 6 and 11 (HPV 6 and 11). These viruses are tissue specific, targeting stratified squamous epithelium of oropharynx, larynx and anogenital region but not targeting epidermis. Two forms of laryngeal papilloma have been described, an adult onset (AORRP) and the more aggressive juvenile onset (JORRP). Almost 60% to 80% of cases are thought to be of childhood onset usually before the age of 3 years. Despite much speculation in the past that remission and even permanent regression of respiratory papillomatosis often correlates with puberty this does not in fact appear to be the case. On the other hand, pregnancy is associated with accelerated papilloma growth with reactivation of latent disease.

We present a case of AORRP, which was aggravated by pregnancy and was managed by debulking with a laryngeal microdebrider followed by microflap surgery.

#### Case Report

A 30 year old, postpartum day two lady, was referred to the ENT out patient department with the chief complaints of hoarseness and vocal fatigue. The patient gave history of hoarseness since 4 years for which she was operated 3 years ago but no details were available with her. The symptoms of hoarseness subsided following surgery but recurred during the second trimester of pregnancy. The patient was a known case of bronchial asthma, rheumatic heart disease and hypothyroidism on treatment. She also gave a history of abdominal kochs for which she had received 6 months of anti-kochs treatment.

On general examination, the patient appeared anaemic. A rigid 70 degree telescopic laryngoscopy revealed a large polypoidal mass with a mottled appearance moving in and out of the glottis with respiration, attached to the left vocal cord near the anterior commissure.

The clinical diagnosis of adult onset laryngeal papilloma was made and the patient underwent microlaryngoscopy under general anaesthesia. As the patient suffered from bronchial asthma and hypothyroidism a short general anaesthesia was advised by the anaesthesiologists.

The lesion was first debulked with a laryngeal microdebrider followed by precision excision using the microflap technique. A 4mm laryngeal microdebrider blade (Xomed 3000 XPS) was used at 1500rpm. Following this, examination under the highest magnification of the microscope revealed papillomas on the site of pedicle attachment on the superior surface of the left vocal cord anteriorly.

Infiltration of 1: 1,00,000 saline adrenaline in the subepithelial space in these areas followed by microflap excision of the residual papilloma was performed by microflap technique. In the microflap technique, an incision is made on the superior surface of the vocal cord just lateral to the lesion. Using a microflap elevator the epithelial flap is elevated preserving maximum underlying superficial lamina propria. In cases of epithelial pathology, such as RRP, this flap is excised and sent for histopathology. Care must be taken at all times not to have opposing raw surfaces at the anterior commissure.

Prior to excision a biopsy was taken for histopathological confirmation and viral typing. The viral typing of our patient was

indicative of HPV 16. Post operatively the patient was adviced ten days of complete voice rest. We have explained the importance of long-term follow up for both the patient and her child.

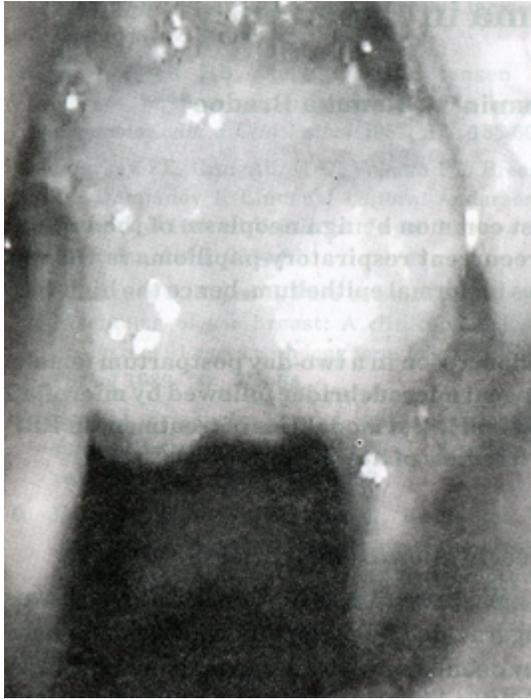


Fig. 1 : Preoperative rigid tele-laryngoscopy picture of the papillomas.



Fig. 2 : Immediate post-operative direct laryngoscopy picture of the vocal folds.

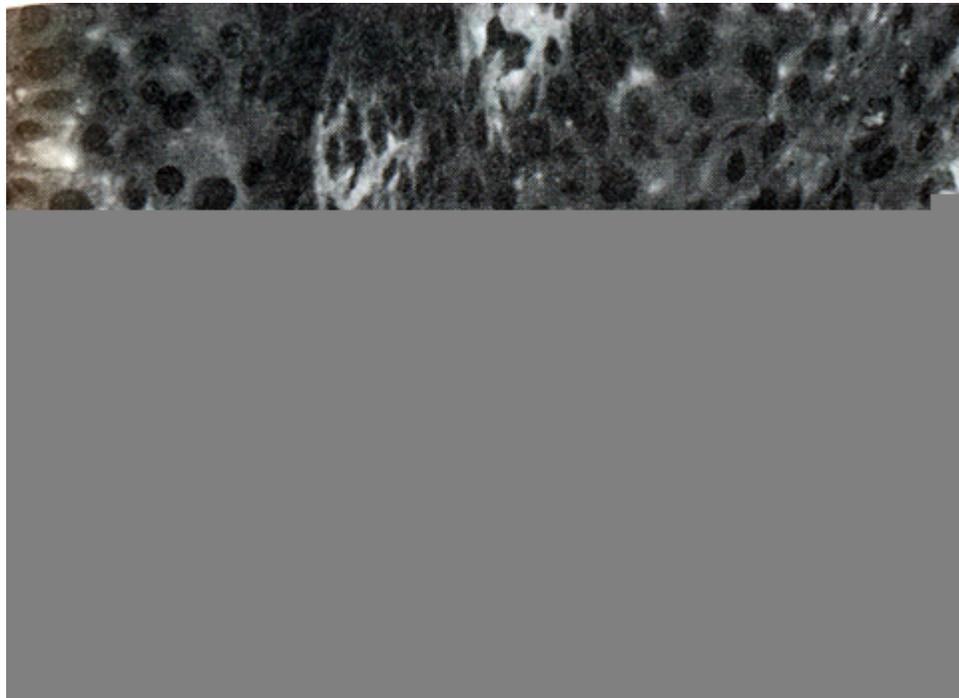


Fig. 3 : Histopathology slide of papilloma specimen (haematoxylin-eosin) 400X showing papillary fronds of multilayered benign squamous epithelium.

### Discussion

HPV types 6 and 11 cause benign papillomas in the airway and are responsible for genital warts.<sup>1</sup> HPV types 16 and 18 have

most often been associated with cancer in the genital area and upper aerodigestive tract in both children and adults.<sup>2</sup>

The HPV genome exists as a circular episomal DNA separate from the host cell nucleus in benign or low-risk HPV lesions, such as those typically associated with HPV types 6 and 11. The genomes of high-risk HPV types 16 and 18 are typically integrated into the host cell DNA in malignant lesions. Integration of the viral genome into the host cell genome is considered a hallmark of malignant transformation.<sup>3</sup>

Once transmitted to the airway, HPV establishes itself in the basal layer of the mucosa, where viral DNA enters the cell and produces ribonucleic acid (RNA) to produce viral proteins, similar to the replication mechanism of other viruses. This action incites the transformation of the mucosa to papilloma formation.

The precise mode of HPV transmission is unclear. Most studies indicate that childhood-onset RRP (CORRP) occurs during exposure of a child's upper aerodigestive tract to the cervix and vagina of a mother with genital HPV infection during normal abdominal delivery. Why CORRP develops in only a few per cent of children who are born abdominally to mothers with active genital condyloma is not well understood. The risk of a child contracting RRP following vaginal delivery from a mother with active genital lesions has been estimated to range from 0.25 to 3%. Cryotherapy is advisable to debulk visible condylomas before abdominal delivery. Caesarean section should be strongly considered in young, primiparous women with recently acquired HPV.<sup>4</sup>

For adult-onset RRP (AORRP), oroanal or orogenital contact is considered a possible mode of virus transmission versus a latent virus becoming active.<sup>4</sup>

Children with CORRP usually present when aged 2-3 years with hoarseness, stridor, or airway obstruction.

Histologic appearance of laryngeal papillomas is characterized by papillary fronds of multilayered benign squamous epithelium that contain fibrovascular cores. No surface keratinization is observed. Koilocytes (vacuolated cells with clear cytoplasmic inclusions that signal presence of viral infection) are observed.<sup>4</sup>

The carbon dioxide laser is well absorbed by most tissues of the body because of the high water content of the tissues. As the superficial lamina propria has a high water content it absorbs laser and the chances of damage are more than cold instruments.<sup>4</sup>

The surgical microdebrider has recently been employed for laryngeal and tracheal papillomas. First used in orthopaedic surgery, the surgical microdebrider (colloquially referred to as a "hammer") is used widely by otolaryngologists for removal of tissue in the sinuses, especially for polyps. The microdebrider uses suction and cutting mechanisms for tissue removal, allowing the surgeon to quickly remove tissue, while providing good visualization of the area because of the suctioning of secretions during cutting. A long laryngeal blade is now available for use in the larynx and trachea. When papillomas are simultaneously present in the larynx and trachea, use of the surgical microdebrider is the best method to remove them without having to reposition the patient.

Goals of intraoperative removal include reducing the papilloma burden, creating a safe airway, improving voice quality, and increasing the time interval between surgical procedures.

As complete removal is difficult and need for future surgeries unquestionable, one should leave only small amounts of papilloma in locations where significant complications could occur.

In a patient undergoing multiple surgeries a year, a lesion may only need to be removed because it is symptomatic and not necessarily every lesion needs to be removed in every surgical procedure.

Up to 30% of patients who have had surgical excision of papilloma in the anterior commissure of the larynx have developed anterior glottic scarring and web formation. Unless the surgeon can be assured that iatrogenic injury will not result from their technique, papillomas should be left in the anterior commissure in children requiring several surgeries a year.

Tracheostomy should be avoided at almost all costs. Frequent surgical excision is preferable to tracheotomy for children or adults who have recurrent aggressive disease. Tracheostomy is believed to induce spread of the papilloma down the trachea and into the bronchi and lung.<sup>5</sup>

Several medical therapies have been tried as adjuvant therapy for laryngeal RRP. The effectiveness of any reported medical therapy for RRP is difficult to determine because the underlying aggressiveness of the disease is poorly understood. Medical therapy for papillomas seems to have the best chance of leading to a breakthrough in RRP treatment.

Cidofovir is the newest antiviral being investigated through prospective interinstitutional trials. It has a broad-spectrum antiviral activity against herpes, pox, and papilloma viruses. Cidofovir in the dose of 2.5 mg/ml to 5 mg/ml is injected intralesionally at the base of the RRP every fortnight.<sup>6</sup>

## Conclusion

The main aim of management of RRP is to maintain the airway without a tracheostomy and to give the patient a reasonably good voice. The microflap technique maximally preserves superficial lamina propria, which is an important factor to keep in

mind, as cases of RRP often require multiple surgeries.

Biopsy taken during surgery should be sent for histopathology to detect early dysplastic changes and for viral typing as 16, 18 are known to induce dysplasia.

Pregnancy aggravates RRP due to immune suppression and local treatment of genital warts such as cryotherapy is advisable prior to vaginal delivery.

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