



Combined Trimodality Treatment for Juvenile Onset Recurrent Respiratory Papillomatosis: An Effective Way for Treatment

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Abstract

Juvenile onset recurrent respiratory papillomatosis is a chronic disease of the airway caused by infection with human papilloma virus type 6 or 11. It is a relatively rare disease and primarily affects the larynx in early age group. Children usually present with change in voice and variable degree of respiratory obstruction, to the extent that emergency tracheostomy may be required at first visit. Mainstay treatment modality is removal of papilloma's by laryngeal microsurgery, using microbrewer / laser or cryotherapy. Other treatment options include photodynamic therapy and chemotherapy using various agents. Although spontaneous remission is possible, but clinical course may include frequent recurrence of disease with significant morbidity. Frequent surgical procedures are required. We present a case of 5 year old child, who was referred to us with recurrence of the early laryngeal papillomatosis after primary surgery. We treated the child using combined tri-modality treatment using excision by microbrewer, topical application of mitomycin - C and oral Acyclovir. Tracheostomy was not required at any step. The child has been under follow up for more than one year and is free of disease.

Keywords: JORRP (Juvenile Onset Recurrent Respiratory Papillomatosis); HPV (Human Papilloma Virus); Microdebrider; Photodynamic Therapy; Mitomycine C

Abbreviations

JORRP: Juvenile Onset Recurrent Respiratory Papillomatosis; HPV: Human Papilloma Virus

Introduction

Recurrent respiratory papillomatosis (JORRP) is a chronic disease which affect the airway. As per the age distribution this disease has been recognized to affect in two patterns, i.e. juvenile onset and adult onset. Disease is more aggressive in children as compared to the adult type. Potentially morbid consequences are more with juvenile onset disease as it has frequent recurrences. In recurrent respiratory papillomatosis, papilloma is most frequently involves

the larynx [1]. Infection with human papilloma virus type 6 or 11 is responsible for producing these respiratory papillomas [2]. Human papilloma virus has also been implicated in etiology of other benign proliferations such as skin warts, anogenital condyloma. This virus may remain as latent in clinically normal appearing mucosa surrounding papillomas, and residual viral genome remains in it even after all gross evidence of papillomas has been removed [3]. Primary treatment modality is removal of papillomas by laryngeal microsurgery. Although there are various therapeutic options available such as alpha interferon, indol - 3 - carbinol, cidofovir intralesional injection, photodynamic therapy and pulsed dye laser,

nothing has shown consistent effectivity for treatment of JORRP [4-7]. The disease may also undergo spontaneous remission following repeated surgical excisions. Acyclovir is a DNA polymerase inhibitor and having effectivity against DNA encoded viruses. Results for laryngeal papilloma removal using microbrewer or CO₂ laser have been comparable, along with better cost effectivity in microbrewer arm at some institutions [8]. The use of Mitomycin - C has also been shown to be effective for achieving remission in respiratory papillomas both systemic as well as topical agent [9,10]. Acyclovir as systemic therapy in post-operative period has been found to prolong the time interval between the successive surgeries [11]. We present a case of a 5 year old female child, who was referred to us with recurrent laryngeal papillomatosis. The child was treated with combined trimodally treatment (removal of papillomas by laryngeal microbrewer with topical application of Mitomycin-C and post-operative systemic Acyclovir). The disease regressed with the treatment and has not recurred in past one year.

Case Report

A 5 year old female child was referred to ENT opd of our hospital with recurrence of laryngeal papillomatosis. She has undergone micro laryngeal surgery for papilloma removal 2 months prior to visiting us. The child started developing gradually progressive change in voice and respiratory obstruction. On laryngoscope assessment, multiple polypoidal masses were present on both true vocal folds, adjacent medial surface of right false vocal cord (Figure 1). The papillomas were removed under general anesthesia using laryngeal microdebrider, keeping the structural integrity of vocal folds (Figure 2). No visible gross papillomas were left behind. 1 cc of 0.5 mg/ml Mitomycin - C was applied to the raw surface of both true vocal folds and right false vocal fold. Patient was extubated without any difficulty. A small papilloma tissue taken separately during surgery was examined for histopathology, which confirmed it to be benign respiratory papilloma. The compliance for voice rest from child could not be assured completely. In post - operative period she was given oral acyclovir at a dose of 80 mg/kg/d in three divided doses for a continuous period of 3 weeks. The child was reassessed after 2 weeks under general anesthesia for residual/recurrent disease. Small papillomas were seen on anterior thirds of both true vocal folds and anterior commissure (Figure 3). These papillomas were again removed using laryngeal microdebrider and topical application of Mitomycin - C which was carried out on

to the raw surface in same doses. Third assessment was done two weeks later to this (Figure 4). In the similar manner, small papillomas limited to anterior commissure were removed along with topical application of Mitomycin - C. On forth assessment (Third post - operative), again 2 weeks later, there were no visible papillomas (Figure 5). Still topical application of Mitomycin - C was done. The voice quality of child improved gradually. She has been under follow up for more than 1year and still free from disease.

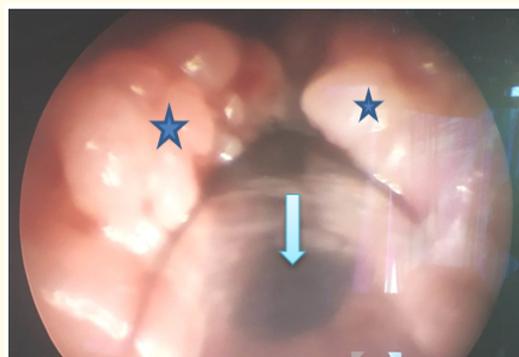


Figure 1: Intraoperative laryngeal assessment picture Showing multiple papillomas on both true vocal folds (star marked) and endotracheal tube (arrow).

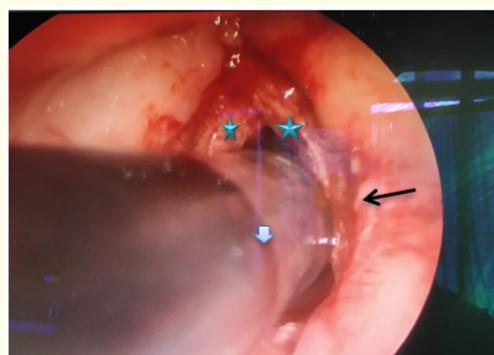


Figure 2: Intraoperative picture after removal of laryngeal Papillomas showing the raw surface bilaterally (star marked), Right false vocal fold (black arrow) and endotracheal tube (small arrow).



Figure 3: 1st post-operative assessment showing small Recurrent/ residual papillomas on both true vocal folds (shown by stars).



Figure 4: 2nd post-operative assessment showing minimal Residual/recurrent papillomas on bilateral true vocal folds.



Figure 5: 3rd post-operative picture showing both True vocal folds free of disease (shown by arrows).

Discussion

This case demonstrated a very potent response of severe Juvenile onset recurrent respiratory papillomatosis to our combined trimodally treatment, which includes removal of papillomas by laryngeal microdebrider, topical application of Mitomycin - C and post - operative systemic Acyclovir therapy. However this is a response from a single individual and not of a large population. The disease is also known to have spontaneous remission, possibility of which also cannot be excluded in this case. Although we still advocate this aggressive way of treating recurrent respiratory papillomas in children due to various reasons. Since the pediatric airway is at more risk of developing strider as compared to adults due to smaller cross sectional area of airway. The possibility of emergency tracheostomy increases with less aggressive modality. The tracheostomy site is also prone to develop the papillomas which aid further difficulty in achieving remission and decannulation. Tracheobronchial spread may also occur in a patient with prolonged tracheostomy [12]. Another point of concern is risk of malignant transformation, which is also there in respiratory papillomas of long duration [13].

We preferred microdebrider over removal of papillomas by micro laryngeal surgical instruments as well as CO₂ laser due to its safety profile along with less time consumption [14]. The apparent risk of disease spread in lower tracheobronchial tree is also less with microdebrider when compared with laser.

Mitomycin - C is a naturally occurring antibiotic derived from *Streptomyces chashitsu*'s. It exerts antitumor activity due to ability to act as an alkylating agent inhibiting the synthesis of DNA. Mitomycin - C when used topically has shown to reduce scar formation in a variety of clinical conditions [15]. Topical uses was given preference over systemic use to avoid side effects associated with it.

The infective organism in respiratory papillomas is human papilloma virus which has a double - stranded DNA. Acyclovir is a DNA polymerase inhibitor and hence effective against DNA encoded viruses. The side effects of this drug are even less with prolong use, so to use it for a shorter duration was very safe.

While systemic use of mitomycin C is feared with dreaded adverse effects like myelosuppression and pulmonary fibrosis, the side effect profile of topical application of mitomycin C, is limited to

minimal scarring and mild atrophy of vocal folds. These side effects are also reversible to some extent. Limited number of studies has proved safety profile of mitomycin C for topical end laryngeal application for up to 2 months (using consecutive weekly application regime) without causing significant side effects. Future prospective studies can add more in to this.

Since all three modalities can act synergistically without causing any significant side effects, we recommend use of these three modalities together for aggressive management of juvenile onset recurrent respiratory papillomatosis.

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