Invasive laryngeal carcinoma in a 15 year-old with neglected papillomatosis

J Zuckerman, B Shehata, C Hill, S Sobol

Citation

J Zuckerman, B Shehata, C Hill, S Sobol. *Invasive laryngeal carcinoma in a 15 year-old with neglected papillomatosis*. The Internet Journal of Otorhinolaryngology. 2008 Volume 8 Number 2.

Abstract

Squamous cell carcinoma of the larynx is an extremely rare complication of recurrent respiratory papillomatosis (RRP) in children. Previous reported cases in the literature are isolated documentations providing little evidence for a systematic treatment approach. We review the case of a 15 year-old male who presented with a two-year history of progressive dysphonia. Microlaryngoscopy demonstrated laryngeal papillomas and a fixed right vocal cord. Biopsies were positive for dysplastic squamous papilloma with invasive squamous cell carcinoma. Viral subtyping was positive for HPV 11. The patient required a tracheotomy for respiratory distress and subsequently underwent treatment consisting of radiation and concurrent chemotherapy. This report highlights a case of neglected RRP undergoing malignant transformation into an aggressive carcinoma, and underscores the need for prompt evaluation of patients with progressive dysphonia.

Presented at the Society for Ear, Nose and Throat Advances in Children, San Francisco, CA, December, 2006

INTRODUCTION

LARYNGEAL CARCINOMA IN CHILDREN

The first documented case of laryngeal cancer in a child was reported by Rehn in 1868 in a 3 year-old child. For more than a century thereafter, only 54 cases of laryngeal carcinoma have been reported in children 15 years of age or younger. In a recent review by Ferlito, et al, 47 cases of laryngeal cancer were identified in children and adolescents with the most common malignancy being rhabdomyosarcoma (42%). In this study, 27.6% of patients were diagnosed with squamous cell carcinoma, with rare reported cases of other tumors including synovial sarcoma, malignant fibrous histiocytoma, non-Hodgkin's lymphoma, chondrosarcoma, Ewing sarcoma, fibrosarcoma, malignant schwannoma, ‘mixed sarcoma', and mucoepidermoid carcinoma [1].

What separates laryngeal cancer in children from that of adults is the timing of presentation. Younger patients tend to have a long history of progressive airway obstruction, dysphasia, or dysphonia, but lesions are not recognized until an otolaryngologist is consulted for a fiberoptic airway examination. A delay in diagnosis can be attributed to the erroneous attribution of voice changes to puberty, recurrent respiratory tract infection, and/or asthma. Adolescent carcinomas also appear to be linked to immunologic and genetic factors rather than more common risk factors such as tobacco use, previous radiation, and chemical carcinogens found in adult patients. Moreover, there is an even distribution of laryngeal carcinoma amongst males and females in the adolescent and pediatric patient population [2,3].

Due to the rarity squamous cell carcinoma in adolescents and children, it is difficult to find a consensus for treatment. All authors agree that a primary work up should consist of detailed radiologic imaging, endoscopy with biopsy, and possible tracheostomy for airway protection. Definitive management of squamous cell carcinoma in pediatric patients has varied based on the individual circumstance of the patient. [4,5]

MALIGNANT DEGENERATION OF JUVENILE RECURRENT RESPIRATORY PAPILLOMATOSIS

Human papilloma virus (HPV) is a small, oncogenic DNA virus that infects epithelial cells. It has been linked to the development of RRP, anogenital condylomas, skin warts, skin cancer in epidermodysplasia, and cervical cancer. The relationship of HPV to laryngeal carcinoma is unclear although some studies have attributed laryngeal irradiation as a predisposing factor in the development of carcinoma. Until the 1970s, malignant degeneration of RRP was seen in association with patients that underwent radiation therapy

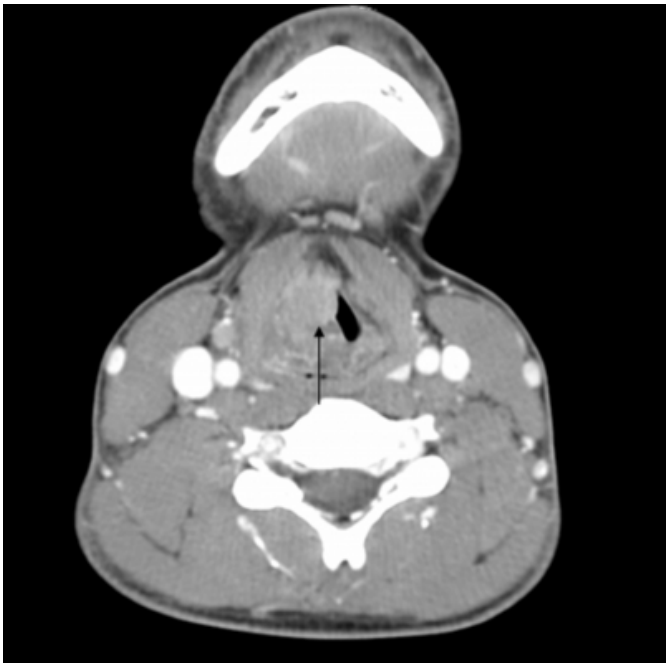
for their disease. Spontaneous malignant degeneration of RRP has been reported in the laryngotracheal and bronchioalveolar regions with an incidence rate of 2-3% [6]. The exact mechanism of this transformation is still to be determined. Previous studies have shown that malignant transformation can occur in both high risk and low risk subtypes of papilloma [7]. HPV types 16 and 18 have been well documented in cervical carcinoma in situ and invasive neoplasm of the cervix. HPV type 16 has also been linked to verrucous cancer of the larynx. HPV 11 has been linked with transformation of juvenile-onset recurrent respiratory papillomatosis. Gene studies have shown that respiratory papilloma may have high risk subtypes that can promote carcinogenesis [8]. HPV subtype11 has been demonstrated in association with squamous cell carcinoma of the lung in the setting of juvenile-onset RRP [9]. Recent studies at our own institution have identified the significance of specific oncogenes (E6 and E7) within the DNA sequence of HPV that can determine the aggressiveness of the clinical presentation [10].

CASE REPORT

A 15 year old male presented with a two year history of progressive hoarseness. One month prior to referral to our institution he had an episode of shortness of breath and respiratory distress. The patient denied a history of tobacco and alcohol use but had a family history of laryngeal carcinoma in his grandfather who was a smoker. He was evaluated by an otolaryngologist who performed flexible laryngoscopy and a computed tomography (CT) scan of the neck, demonstrating a laryngeal mass.

Figure 1

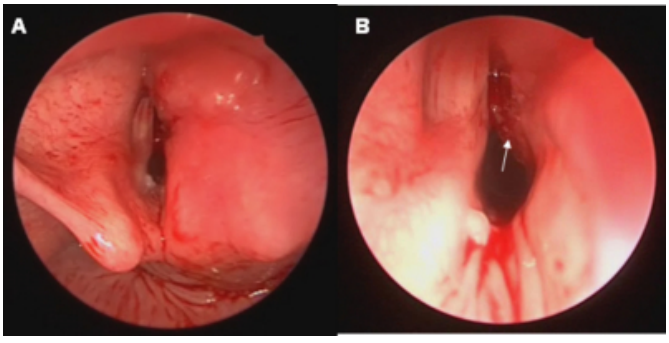
Figure 1: Axial CT Scan of the neck demonstrating a right transglottic mass extending to the thyroid cartilage (arrow).



The patient was referred to our institution where microlaryngoscopy demonstrated a fixed right vocal cord with an exophytic lesion on the right vocal fold and subglottis with infiltration of the adjacent arytenoid and aryepiglottic fold.

Figure 2

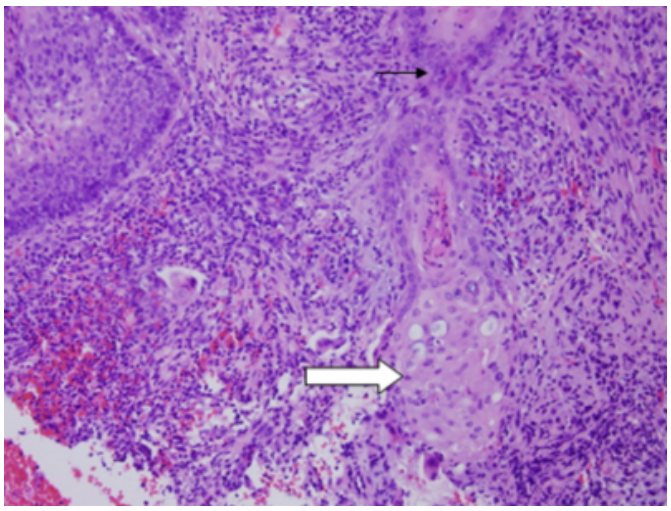
Figure 2: Laryngoscopy demonstrating (A) a submucosal lesion in the right aryepiglottic fold and false vocal cord and (B) papillomatosis lesion on the right vocal cord extending into the subglottis (arrow).



Biopsy specimens were positive for squamous papilloma with severe dysplasia and focal microinvasion.

Figure 3

Figure 3: Evidence of squamous cell invasion beneath basement membrane. Dark arrow shows basement membrane, white arrow demonstrates invasive cluster of squamous cells. Courtesy of Emory's Department of Pathology (Hematoxylin and eosin stain: original magnification x 100).



Additional cytokeratin staining demonstrated individual squamous cells beneath the basement membrane. Viral subtyping was performed using PCR with probe hybridization assessing for the presence of HPV 6 or 11. RT-PCR was utilized to determine the expression of the E6 and E7 oncogenes previously linked with a more aggressive expression of HPV 6 as previously described [$_{10}$]. Our patient's DNA was of the HPV 11 subtype but did not have significant expression of E6 or E7.

The patient was staged as a T3N0M0 laryngeal squamous cell carcinoma and discussed at our multidisciplinary tumor board where a consensus for laryngeal preservation therapy was obtained. He underwent six rounds of Taxol and Carboplatin treatments in conjunction with 6 weeks of radiation therapy consisting of 72 Gray to the larynx and 50 Gray to each neck. He did require a temporary tracheotomy after his first week of therapy due to airway edema. The patient is currently 9 months post treatment, is decannulated and has had no evidence of recurrent disease on endoscopic evaluation.

CONCLUSION

Recurrent respiratory papillomatosis is a very concerning problem in the pediatric population. Presentation of a child with hoarseness and stridor can be early indications of a laryngeal lesion. The above case report demonstrates the importance of prompt and thorough work up of the pediatric patient with progressive hoarseness. In our patient, early diagnosis and management of his RRP may have prevented the subsequent degeneration to carcinoma.

CORRESPONDENCE TO

Steven E. Sobol, MD, MSc Director of Pediatric Otolaryngology Emory Children's Center 2015 Uppergate Drive, NE Atlanta, GA 30322 404-727-1368 (Tel) 404-727-7996 (fax) ssobol@emory.edu

References

1. A. Ferlito, A. Rinaldo, G. Marioni. Laryngeal malignant neoplasms in children and adolescents. International Journal of Pediatric Otorhinolaryngology 1999;49:1-14.
2. W.F. McGuirt Jr., J.P. Little. Laryngeal cancer in children and adolescents, Otolaryngology Clinics of North America. 1997;30:207-214.
3. T.D. Gindhart, W. H. Johnston, S.E. Chism, H.H. Dedo, Carcinoma of the larynx of childhood, Cancer 1980;46:1683-1687.
4. R.H Ossoff, G.F Tucker, C.M. Norris, Carcinoma of the larynx in a 11 year old boy with late cervical metasis: report of a case with ten year follow-up, Otolaryngology Head and Neck Surgery 1980;88:142-145.
5. Brasilino de Carvalho et al. Head and Neck Squamous Cell Carcinoma in Childhood. Medical and Pediatric Oncology 1998;31:96-99.
6. Gaylis, B, Hayden RE. Recurrent respiratory papillomatosis: progression to invasion and malignancy. American Journal of Otolaryngology 1991;12:104-112.
7. Doyle DJ, Hendeson LA, Le June FEJ, Miller RH. Changes in human papilloma virus typing of recurrent respiratory papillomatosis progressing to malignant neoplasm. Archives of Otolaryngology 1994;120:1273-1276.
8. CE Moore, BJ Wiatrak, KD McClathey, CF Koopman, GR Thomas, CR Bradford, TE Carey. High-risk human papillomavirus types and squamous cell carcinoma in patients with respiratory papillomas. Otolaryngology Head and Neck Surgery 1999;120(5):698-705
9. Cook JR, Hill A, Humphry PA, Pfeifer JD, El-Mofty, SK. Squamous Cell Carcinoma Arising in Recurrent Respiratory Papillomatosis with Pulmonary Involvement: Emerging Common Pattern of Clinical Features and Human Papillomavirus Serotype Association. Modern Pathology 2000;13: 914-918.
10. Bahig M. Shehata1,2*, Kristine J. Otto3, Steven E. Sobol3, Christina A. Stockwell4,Cora Foulks2, Charles E. Hill2 E6 and E7 oncogene expression by human papilloma virus (HPV) and the aggressive behavior of recurrent laryngeal papillomatosis (RLP). In submission

Author Information

Jodi D. Zuckerman, MD
1) Department of Otolaryngology-Head and Neck Surgery, Emory University School of Medicine

Bahig M. Shehata, MD
Department of Pathology, Emory University School of Medicine

Charles H. Hill, MD
Department of Pathology, Emory University School of Medicine

Steven E. Sobol, MD, MSc
1) Department of Otolaryngology-Head and Neck Surgery, Emory University School of Medicine