Malignant Transformation of Respiratory Papillomatosis in a Solid-Organ Transplant Patient: Case Study

Roya Azadarmaki MD and Miriam N. Lango MD
Department of Surgery, Head and Neck Section
Fox Chase Cancer Center, Temple University Health System

INTRODUCTION

Respiratory Papillomatosis is a benign laryngeal lesion that has the rare potential to convert into malignancy in 3-7% of cases. The transformation into squamous cell carcinoma of the larynx, tracheobronchial tree, or lung has been reported as soon as several weeks to months in rare instances and, more commonly, as long as 20-30 years after the initial diagnosis of this benign lesion. Smoking, radiation, and some chemotherapeutic agents have been associated with a higher risk of malignant transformation.

In this poster we present a case of malignant transformation of respiratory papillomatosis in a solid-organ transplant patient.

CASE REPORT

A 77 year old non-smoker and non-drinker heart transplant patient underwent an emergent tracheotomy after presenting to an outside hospital in respiratory distress. Patient was found to have significant narrowing of the subglottic airway at the time of presentation. He was on immunosuppressive therapy since his heart transplant in 2001. He had multiple head and neck cancerous skin lesions excised since his transplant. He did not receive radiation for these lesions. Seven years after his transplant he was diagnosed with respiratory papillomatosis through an intraoperative airway evaluation after presenting with symptoms of progressive hoarseness. One and a half years later, a biopsy of a laryngeal papilloma revealed papillomatosis with evidence of severe dysplasia. He was followed locally with periodic laryngoscopies in the office. However, he subsequently developed worsening airway obstruction and stridor and underwent an emergent tracheotomy following a visit to the emergency room. Intraoperative evaluation at our institution revealed mild papillomatous changes involving the left true vocal cord associated with an obstructing malignant subglottic mass. Malignant transformation of his respiratory papillomatosis to moderately differentiated squamous cell carcinoma occurred primarily at the level of the subglottis. In addition, the papillomatous changes extended down the anterior tracheal wall half the distance between the subglottis and carina. Severe dysplastic changes were noted to extend along the anterior tracheal wall. The carina was free of dysplasia. A p16 stain was ordered and was negative.

CONCLUSIONS

Solid organ transplant patients may be prone to an increased risk of malignant transformation of respiratory papillomatosis due to their immunodeficient state. Close observation of organ transplant patients with respiratory papillomatosis is recommended for early detection of malignant transformation.

DISCUSSION

Over 20% of cancer incidence can be related to an infectious etiology. More than 15% of these cases are associated with viruses. Acquired infection by an oncogenic virus during an immunosuppressed state may lead to increased viral-induced genome modifications and mutations that predispose to malignant transformation.

The incidence of virally-mediated malignancies is disproportionately higher in the immunosuppressed population. Kaposi sarcoma, Merkel cell carcinoma, and cutaneous squamous cell carcinoma have been associated with HIV, Merkel cell polyomavirus, and HPV respectively. The incidence of cutaneous squamous cell carcinoma is increased by 65-fold in organ transplant patients compared with the general population. In HIV positive patients the standardized incidence ratio of Kaposi sarcoma and Merkel cell carcinoma is 1300 and 11 respectively. Melanoma, which is a non-viral associated cancer, however only has a standardized incidence ratio of 1.3, suggesting that not all cancers occur more frequently in the setting of immunosuppression.

Human Papilloma Virus has been demonstrated as a strong predisposing factor for many squamous cell carcinomas, including the cervix, anogenital region, and the oropharynx. The association with laryngeal cancer is not demonstrated. E6 and E7 proteins can lead to degradation of cellular tumor suppressor proteins retinoblastoma, p53, and others, inhibiting apoptosis, or programmed cell death. The mechanism of cellular transformation contrasts strikingly with that of smoking-related malignancy, and is associated with upregulation of p16, which has been used as a surrogate biomarker for HPV-related oropharyngeal cancer.

The mechanism of HPV-mediated cellular transformation of respiratory papillomatosis in the setting of immunosuppression is unknown. It is also unclear if laryngeal cancer arising from respiratory papillomatosis in this population would have a more favorable prognosis than smoking-related laryngeal cancer, or have a grave prognosis secondary to immunosuppression, comparable to cutaneous squamous cell malignancies in transplant patients.

We suggest the upper airway of transplant patient with respiratory papillomatosis be examined closely every several months for early detection of malignant transformation, in the larynx, as well as the tracheobronchial tree. As immunodeficiency may raise the risk of malignant transformation of respiratory papillomatosis, the dose of immunosuppression should be tailored appropriately to both reduce the risk of organ rejection and to possibly minimize the risk of cancer formation.