CASE REPORTS

Case Report: Pulmonary Papillomatosis in a Patient Presenting with Cough and Hemoptysis

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ABSTRACT
A previously healthy patient was seen in the Emergency Department for evaluation of a one-month history of cough and one-day history of hemoptysis. A computed tomography scan of the thorax found a mass on the right lower pulmonary lobe and a mass on the left upper lobe. A biopsy specimen of the right lobe lung mass, obtained during bronchoscopy, demonstrated papilloma. This case report, from a pulmonologist’s perspective, includes a comprehensive review of the patient’s clinical presentation and outcome, as well as a discussion of recurrent respiratory papillomatosis.

INTRODUCTION
Recurrent respiratory papillomatosis (RRP) is an uncommon clinical entity. The incidence rate is 1.8 cases per 100,000 adults and 4.3 cases per 100,000 children. Recurrent respiratory papillomatosis is caused by human papillomavirus (HPV) serotypes 6 and 11 (the same serotypes responsible for more than 90% of genital condylomata) and serotypes 16, 18, 31, and 33 (the serotypes associated with genital and aerodigestive tract malignancies). A double-stranded DNA virus in the Papovaviridae family, HPV infects the mucosal basal layer and induces cellular proliferations via activation of host replication genes through the epidermal growth factor receptor pathway. This results in thickening of the basal layer. Papilloma appears grossly as velvety or exophytic “cauliflower.”

CASE REPORT
A 43-year-old man presented to the Emergency Department with a 1-day history of dark burgundy-colored sputum and a cough. The patient had the cough as well as a 2.7-kg (6-pound) weight loss in the month before admission. He denied fever, night sweats, or change in the tone of his voice. He had no remarkable medical history and no prior surgery. He was not taking any medications. He did not know his family history because he is adopted. His social history included substantial secondhand smoking exposure. He had multiple drug use in the past that included marijuana, cocaine, lysergic acid diethylamide, and amphetamine. He had multiple female sexual partners.

A chest x-ray film obtained on admission showed a right-sided lung mass. Computed tomography scan of the chest was subsequently performed for better visualization. Chest computed tomography (Figure 1) demonstrated a right lung mass measuring 5.4 cm × 5.2 cm × 6.1 cm at the superior segment of the right lower lobe with associated “tree-in-bud” nodularity, as well as a lesion in the left upper lobe measuring 1.7 cm in diameter. The inpatient pulmonary team was consulted for assistance with the diagnosis. The patient underwent bronchoscopy, which identified a polypoid lesion on the right vocal cord (Figure 2) and an endobronchial mass at the right lower lobe (Figure 3). The right lung mass was biopsied. Pathologic findings revealed squamous cell papillomatosis.

Figure 1. Computed tomography scan of chest showing masses in right lower and left upper pulmonary nodes.

Figure 2. Bronchoscopy demonstrating polypoid lesion on right vocal cord.

Figure 3. Bronchoscopy showing view of endobronchial mass at right lower lobe.

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The patient had 4 hospitalizations for treatment of recurrent pneumonia in the next 6 months, with 19 inpatient days accounted for by this complication. A thoracic surgeon was consulted, and the decision was made to perform a right-sided lobectomy via video-assisted thoracoscopic surgery. A biopsy was performed from the gross specimen obtained at the lobectomy (Figure 4). Results demonstrated squamous cell carcinoma. The patient was subsequently referred to an oncologist for a discussion of treatment options for squamous cell carcinoma of the lung.

DISCUSSION

The incidence of RRP is bimodal, with the juvenile-onset form typically first occurring in children aged 2 to 4 years and adult-onset RRP typically occurring in adults aged 20 to 40 years. Juvenile-onset RRP is thought to be caused from peripartum exposure through an infected birth canal. Cesar-ean delivery appears to lower the risk of RRP in newborns but does not eliminate the risk. Risk factors for juvenile-onset RRP include being firstborn, being born via normal spontaneous vaginal delivery, and being born to a teenage mother. Risk factors for adult-onset RRP include multiple lifetime sexual partners as well as a high frequency of oral sex. There was no statistically significant difference in illicit drug use between patients with adult-onset RRP vs a control group in a study by Ruiz et al.

Human papillomavirus has a predilection for the junction between squamous and ciliated epithelium. RRP affects, from the most common site to the least common site, the true vocal cord, oral cavity, trachea, bronchi, and esophagus. Therefore, patients present most commonly with hoarseness followed by stridor, cough, and dyspnea. Pediatric patients may present with failure to thrive as well. Talierco et al reported 100% of patients with adult-onset RRP had concurrent HPV infection of the oral cavity; however, our patient had no evidence of oral cavity HPV infection on physical examination or bronchoscopy findings.

The diagnosis of lesions typically is first made through visualization by imaging modalities such as computed tomography of the chest, followed by biopsy of suspicious lesions through laryngoscopy, nasopharyngolaryngoscopy, or bronchoscopy. The gross appearance of papilloma is exophytic, with white or pink lesions with frondlike projections. Histologically, papilloma is described as projections of nonkeratinized stratified squamous epithelium over a fibrovascular core (Figure 5).

The primary treatment of RRP is surgical removal of the papilloma to reduce the tumor burden. Surgical techniques include cold steel excision, carbon dioxide or argon laser, endoscopic microdebrider, and pulsed dye laser. Potential side effects of carbon dioxide or argon laser include active viral DNA in the laser smoke, which potentially can expose the practitioner performing the procedure and the staff to HPV and spread HPV to the patient’s previously unaffected body parts. Other side effects of laser therapy include damage to surrounding tissue causing vocal glottis edema or vocal cord scarring, as well as the potential for the laser to cause an explosion when mixed with oxygen-rich supply from the
endotracheal tube. Tracheostomy might be needed for patients with airway obstruction. However, tracheostomy is to be avoided if at all possible because of a risk of activating or contributing to the spread of RRP because tracheostomy creates a squamocolumnar junction.

Medical therapy is considered adjuvant to surgical therapy. The criteria for medical therapy include more than 4 surgeries performed per year, spread of the disease to a distant site, or rapid growth of lesions. Medical therapy includes interferon, ribavirin, acyclovir, and intraläsional injection of cidofovir. Additional new adjuvant medical therapy under investigation includes bevacizumab and HPV vaccine. Injection of bevacizumab to vocal cord RRP lesions enhanced photoangiolytic laser treatment of RRP and was found to be safe without additional complications related to laser treatment. For patients who had rapidly growing laryngeal papilloma, adjuvant therapy with 3 doses of quadrivalent prophylactic HPV vaccine (Gardasil, Merck Co, New York, NY) was approved in the US for prevention of cervical cancer caused by HPV infection. Gardasil theoretically should prevent RRP and future studies should focus on the role of vaccination to prevent RRP.

A literature review of RRP case reports revealed that patients usually have the diagnosis of RRP many years before evidence of malignant transformation. In contrast, our patient had evidence of malignant transformation about six months after diagnosis of respiratory papillomatosis. Our patient received primary therapy for RRP which was surgical removal of papilloma that was causing infectious complications. However, once malignant transformation to squamous cell carcinoma was diagnosed in the surgical specimen, adjuvant therapy for RRP would have been inappropriate, and the focus was therefore shifted toward treatment of squamous cell carcinoma.

Disclosure Statement
The author(s) have no conflicts of interest to disclose.

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