A 16-Year-Old Boy with a Rare Respiratory Papillomatosis Complication

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A 16-year-old boy with a medical history of recurrent tracheolaryngeal papillomatosis along with significant lung involvement was admitted for a 2-week history of nausea and vomiting. Other major complaints included subjective fever, excessive fatigue, weakness, constipation, and a 5-lb weight loss.

He was well known to our otolaryngology team because they had been treating him since he was child and he had been hospitalized numerous times for airway management requiring surgical excisions of laryngeal papillomas due to the recurrent nature of this disease.

On the day of his latest admission, the emergency department’s initial laboratory screening revealed a marked hypercalcemia of 14.2 mg/dL (ionized calcium of 2.02 mm/L). A chest X-ray was obtained and showed a cystic lesion in the right lower lobe with an air-fluid level that was concerning for a bacterial infection (Figure 1).

Figure 1. Chest X-ray showing a large cavitary lesion in the superior segment of the right lower lobe that demonstrates an air-fluid level.

Editor’s note: Each month, this department features a discussion of an unusual diagnosis. A description and images are presented, followed by the diagnosis and an explanation of how the diagnosis was determined. As always, your comments are welcome via email at pedann@Healio.com.

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Lung Squamous Cell Carcinoma in Respiratory Papillomatosis

Subsequent diagnostic imaging with a computed tomography (CT) scan illustrated worsening cystic lung disease as well as a larger heterogeneous soft tissue mass in the right lower lobe, confirming a suspected cancerous lesion. The CT scan also revealed evidence of metastasis to the kidneys and pancreas (Figure 2).

During his hospitalization, the patient underwent a right lower lobe needle biopsy of the soft tissue mass, and the pathology report confirmed the presence of well-differentiated squamous cell carcinoma. His hospital course was notable for an acute episode of total body tremors associated with a tingling sensation and postictal right hemiparesis, which was concerning for seizure-like activity. A diagnostic magnetic resonance imaging scan of the head demonstrated a left-sided parietal metastatic mass (Figure 3).

After completion of an 8-day palliative chemotherapy regimen with cisplatin and gemcitabine, the patient was discharged home with an antiepileptic drug regimen (levetiracetam).

DISCUSSION
Recurrent respiratory papillomatosis (RRP) is a viral infection caused by the human papilloma virus (HPV) and is characterized by the formation of numerous squamous papillomas in the respiratory system. It most commonly affects the larynx but can be present anywhere along the respiratory tract. It is thought that infants acquire HPV transvaginally during delivery from mothers with genital lesions. Of the more than 120 subtypes, viral subtypes 6 and 11 account for more than 90% of all RRP cases. Direct pulmonary involvement is not common, being seen in <1% of RRP cases, mostly in the pediatric population.

Children with recurrent respiratory papillomatosis usually present with progressive hoarseness, stridor, dyspnea, or acute respiratory distress and chronic cough. The clinical course for patients with RRP is characterized by numerous surgical excisions of the papillomas, as well as multiple hospitalizations due to respiratory distress and superimposing infections. RRP causes significant morbidity and mortality, but the clinical history is variable. RRP can regress, persist (leading to airway obstruction and infections), and very rarely transform into carcinoma.
Extensive pulmonary involvement of RRP is seen more commonly in male patients than female patients, and is often associated with a more aggressive course. Rarely, RRP has been shown to transform into cancerous lesions, and there are few published cases reporting the progression of RRP to cancer. In these reports, the patients are male, were diagnosed at a young age (<5 years), and had extensive pulmonary involvement of their RRP. In all the reported cases, HPV 11 was identified as the subtype present in the cancerous lesions, suggesting that it may play a major role in RRP’s transformation to cancer. The exact mechanism leading to this transformation and the role HPV 11 plays is presently unknown. Lele et al. proposed that changes in specific protein production (p21 and p53) may contribute to the development of cancer and may prove to be useful markers for patients at an increased risk of developing cancer.

Treatment options involve management necessary to alleviate associated respiratory symptoms, prevent spread of disease, and maintain patent airways. Currently, there is no curative treatment, and the mainstay therapy has been surgical excision of large papillomas that compromise the airway. This treatment often poses a challenge because of the recurrence of papillomas once initially excised. Adjunctive therapy to prevent spread of the disease and progression of papilloma growth includes immunomodulators, disruption of molecular signaling cascades and HPV replication, and antivirals. Interestingly, Katsenos and Becker recommended a trial of interferon-alpha for 6 months in attempts to obtain partial or complete remission of RRP, but they noted that this therapy had no significant effect when there was lung involvement. Presently, there is no routine treatment for carcinoma associated with RRP. Chemotherapy and radiotherapy, although not curative, are performed in attempts to slow the progression of the disease, but the prognosis is usually grim.

REFERENCES