CLINICAL VIGNETTE

Adult-Onset Recurrent Respiratory Papillomatosis: A Rare Manifestation of HPV

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Case

A 33-year-old male with a past medical history of gastroesophageal reflux disease, Helicobacter pylori infection, vaping, cannabis use and nicotine dependence presents to otolaryngology with progressive hoarseness for the past year. There was no associated dyspnea, wheezing, sore throat, dysphagia or neck pain. Vitals signs included blood pressure 118/79, pulse 70, temperature 36.5°C, SpO2 97%, height 6'5" and weight 211 lbs. General physical exam was unremarkable. Flexible fiberoptic nasopharyngoscopy showed bilateral vocal cord nodules (L>R) with associated Reinke's edema. The vocal cords were otherwise mobile and symmetric. No masses or lesions were identified. The nodules were initially thought to be due to poor vocal hygiene, smoking and acid reflux. Microdirect laryngoscopy was performed and showed a large left posterior vocal cord lesion that appeared papillomatous under magnification. This lesion was biopsied and pathology showed a squamous papilloma without high-grade dysplasia or malignancy consistent with recurrent respiratory papillomatosis.

It was recommended that the patient avoid activities that exacerbate vocal cord trauma and treat the acid reflux. The human papilloma virus (HPV) vaccination series and indole-3-carbinol supplementation were also recommended. The patient was treated with microdirect laryngoscopy with carbon dioxide laser ablation and excision of the left vocal cord papilloma. He did well post-operatively with significant improvement in dysphonia. He returned to clinic two months later reporting that the hoarseness had returned as before. Laryngostroboscopy showed sessile, mild diffuse papillomatosis (L>R) with lesions in the operative area. A microdirect laryngoscopy with true blue laser ablation and subtotal excision was performed. Unfortunately, the patient had mild recurrent lesions post-operatively. Laryngoscopy with ablation of lesions with potassium titanyl phosphate laser was performed in clinic. His voice improved for a few days following the ablation then worsened. He continued to follow with otolaryngology for surveillance and ablation therapy every few months.

Discussion

Recurrent respiratory papillomatosis (RRP) is a rare disease of the respiratory tract caused by HPV.[1] HPV types 6 and 11 are the most common serotypes in RRP.[2] The most frequent site of involvement is the larynx, but papillomas can also be found in the trachea, nose, nasopharynx, oral cavity, oropharynx and lungs.[1] Although RRP is a benign disease, it can cause significant morbidity and infrequent mortality due to airway obstruction.[2] There is a <1% risk of the lesions becoming malignant.[2] Patients initially present with progressive dysphonia but can develop stridor and respiratory distress with worsening airway obstruction.[1] Other symptoms including chronic cough, dyspnea and recurrent upper respiratory infections can delay diagnosis.[3]

RRP is categorized into juvenile-onset (JoRRP) and adult-onset (AoRRP) based on age at presentation. JoRRP is acquired at birth from the mother's genital tract, and AoRRP is thought to be sexually transmitted.[1] A case-control study found patients with AoRRP more likely to have more lifetime sexual partners and increased frequency of oral sex than adult controls.[2] Since HPV has the ability to form latent infection in healthy mucosa, AoRRP could be the reactivation from HPV infection acquired at birth rather than from exposure in adulthood.[2] The juvenile type is more aggressive and recurs more often.[3] Across both types, the disease incidence is higher in children and men.[3] A study in Europe suggested a trimodal distribution in the age at diagnosis with peaks at 7, 35 and 64 years.[1,3] The incidence is similar in developed and developing countries, and the disease severity does not appear to be impacted by socioeconomic factors.[3]

Diagnosis is made by flexible fiberoptic laryngoscopy or direct laryngoscopy with biopsy.[3] Histopathologic findings confirm the diagnosis of RRP.[3] Although there is no cure, the goal of treatment is to control the disease through papilloma removal, voice preservation and prevention of major complications until the disease spontaneously resolves.[1,2] Treatment involves repeated microlaryngoscopic procedures, which can lead to complications including glottic stenosis and granuloma formation.[1] Adjuvant therapies include indole-3-carbinol, MMR and HPV vaccinations, interferon-alpha, cidofovir, retinoids, cyclooxygenase-2 inhibitors, programmed cell death protein 1 (PD-1) inhibitors and bevacizumab.[1,3,4]

HPV vaccinations that protect against serotypes 6 and 11 have led to reduction in the incidence of JoRRP by reducing maternal infection.[1] These vaccines may also reduce the incidence of AoRRP, but it is important to note that only quadrivalent and nonvalent HPV vaccinations target serotypes 6 and 11.[1]

Conclusion

RRP is a benign manifestation of HPV affecting both children and adults that can result in significant morbidity and rare mortality. Given the prevalence of HPV, clinicians should have a high clinical suspicion for the disease when patients present with symptoms of progressive dysphonia. RRP should also be considered in patients presenting with chronic cough or recurrent upper respiratory infections to reduce time to diagnosis. Disease management is supportive rather than curative, so the clinician's efforts are best focused on disease prevention with HPV vaccination recommendation.

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