Asymptomatic p16 Positive Oropharyngeal Squamous Cell Carcinoma—An Emerging Trend

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ABSTRACT

The incidence of oropharyngeal squamous cell carcinoma (OPSCCa) is on the rise in the United States largely attributed to human papillomavirus (HPV). While the other types of head and neck cancers have decreased with the declining prevalence of tobacco use, the rapid increase of HPV-associated oropharyngeal cancer has demonstrated a need for new strategies in prevention, diagnosis, evaluation, staging and treatment of this disease. Despite patients frequently presenting with advanced disease and poorly differentiated histology, HPV-related oropharyngeal cancer is typically associated with a favorable prognosis as it responds well to treatment.

The epidemiology of HPV-associated oropharyngeal cancer is distinctly different than that of HPV-negative oropharyngeal cancer. The HPV-associated disease often affects younger cohorts with sexual behavior risk factors, minimal alcohol or tobacco use, and is diagnosed at an early T stage with frequently advanced N stage. These epidemiologic changes in HPV-associated head and neck cancers may also lead to an emerging trend of identifying incidentally noted asymptomatic early stage HPV-associated oropharyngeal cancer if detected prior to development of nodal metastasis. Early stage tumors are typically associated with an excellent prognosis and are frequently treated with single modality therapy. For oropharyngeal squamous cell carcinoma, p16 is most reliably associated with advanced stage disease, with frequent involvement of the tonsils which are not accessible to surface cytology collection methods. Thus, p16-positive oropharyngeal premalignant lesion has not yet been identified. Additionally, these cancers are thought to initiate in the deep crypts of the tonsils which are not accessible to surface cytology collection methods. This produces a clinical scenario with a high rate of malignancy on evaluation of incidentally identified lesions leading to a diagnosis of HPV-related oropharyngeal premalignant lesion which has not been done.

Incidentally identified lesions found during routine physical exam or with imaging and can lead to the diagnosis of early stage disease. This has led in incidental findings of the kidney, brain, adrenal gland, lung, thyroid, and liver. Incidental findings of the head and neck also occur, and are even noted in otherwise healthy individuals undergoing routine radiologic evaluation as a second-look evaluated high-risk HPV associated lesions identified during positron emission tomographic scanning. Identifying an HPV associated high-risk HPV lesion in the head and neck area. Further workup of these incidental lesions ultimately led to a diagnosis of malignancy in 21% of the patients. Tonsil asymmetry is another frequently encountered clinical situation with a rate of malignancy on pathological analysis reported as 5%, leading to a number needed to treat of twenty. This produces a clinical scenario with a high rate of malignancy on examination of incidentally identified lesions with associated morbidity will need to be done for a relatively low prevalence of disease.

We present 5 patients who were identified with asymptomatic p16 positive oropharyngeal carcinomas discovered by a variety of methods: clinical exam, radiologic studies, and pathology. Four of these patients were found to have early stage disease. One patient was identified with advanced stage disease and had been evaluated by several practitioners for tongue leukopla. His asymptomatic contralateral p16 positive tonsil cancer, however, was not noted until his appointment with the Head and Neck Surgeon. The emergence during the past few years of the incidence of incidentally identified p16 positive OPSCCa is likely the result of the changing epidemiologic landscape in oropharyngeal cancer.

CONCLUSIONS

The epidemiology of oropharyngeal squamous cell carcinoma is changing which has led to an increase in the incidence of p16 positive OPSCCa. There are currently no available screening technologies to detect early primary site disease. Because of this, purely incidentally diagnosed HPV-associated OPSCCa might increase in incidence, as we have experienced. During the previous 2 years, this has accounted for 3.7% of all patients evaluated at our institution for p16 positive OPSCCa. These data will be used as a baseline for tracking incidence of this phenomenon in the upcoming years. Early observations suggest that patients with incidentally identified disease can present at an early stage and have a favorable prognosis, potentially with unimodality therapy.

REFERENCES


INTRODUCTION

Early experience suggests that these asymptomatic oropharyngeal squamous cell carcinomas are associated with a low rate of nodal metastasis, and underwent surgical treatment as a single modality. One patient had an advanced stage disease and underwent chemoradiotherapy. At a mean follow-up of 11.6 months, four patients remained disease free and the fifth patient is currently undergoing chemoradiotherapy.

RESULTS

A total of 134 patients, derived from multidisciplinary head and neck tumor board patient listings, were treated at Washington University School of Medicine/Siteman Cancer Center with p16 positive OPSCCa during the time period included. Of these patients, 3.7% (n=5) had their cancers identified incidentally and were asymptomatic. A summary of the patients is included in Table 1. The median age of the five patients was 58 years (range 56-73 years). Three of the five patients had their tumors discovered by physical exam either in the office or during an unrelated operative procedure. One patient was identified in a pathology specimen during a tonsillectomy performed as part of an obstructive sleep apnea procedure. One patient’s tumor was identified based on a radiologic finding. Four of the five patients were T1 stage tumors and were treated with transoral surgical resection and elective neck dissection. These patients were all found to have pT1N0M0 stage disease. Additionally, these individuals did not receive any subsequent adjuvant therapy and have remained disease free at a median of 14 months follow up (range 6-24 months). The fifth patient was referred for a large leukoplakia lesion on the right ventral oral tongue, but was found by physical exam to have an asymptomatic and previously unrecognized cT3N2b left tonsil cancer. This patient is currently being treated with chemoradiation therapy.

Table 1: Incidentally identified p16 positive oropharyngeal squamous cell carcinoma patient characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Presenting Problem</th>
<th>Method of Detection of OPSCCa</th>
<th>Tumor Location and Clinical Stage</th>
<th>Treatment</th>
<th>Outcome following treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57</td>
<td>Left tonsil impaction</td>
<td>Physical exam</td>
<td>Right tonsil, pT1N0M0</td>
<td>Transoral resection + neck dissection</td>
<td>No evidence of disease at 24 months</td>
</tr>
<tr>
<td>2</td>
<td>56</td>
<td>Obstructive sleep apnea</td>
<td>Pathology of tonsil specimen</td>
<td>Right tonsil, pT1N0M0</td>
<td>Transoral resection + neck dissection</td>
<td>No evidence of disease at 6 months</td>
</tr>
<tr>
<td>3</td>
<td>73</td>
<td>Lung nodule</td>
<td>Radiology</td>
<td>Right tonsil, pT1N0M0</td>
<td>Transoral resection + neck dissection</td>
<td>No evidence of disease at 10 months</td>
</tr>
<tr>
<td>4</td>
<td>58</td>
<td>Vocal fold paralysis following spine surgery</td>
<td>Physical exam</td>
<td>Left tonsil, pT3N2M0</td>
<td>No evidence of disease at 18 months of follow up</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>73</td>
<td>Right oral tongue leukopla</td>
<td>Physical exam</td>
<td>Left tonsil, pT3N2M0</td>
<td>Chemoradiotherapy</td>
<td>Currently undergoing therapy</td>
</tr>
</tbody>
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