**CLINICAL VIGNETTE**

**Squamous Cell Carcinoma of the Right Tonsil**

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**Introduction**

Primary care physicians commonly encounter symptoms of sore throat, dysphagia, and trouble swallowing. The majority of these cases are a result of reversible or benign disorders. The case presented below is an account of an uncommon cause of these same symptoms.

**Case Report**

The patient is a 50-year-old male with a twenty pack year smoking history and thirty year alcohol use history and who initially presented to his primary care physician with one year of intermittent throat pain, difficulty swallowing, and dysphagia. A chest radiograph and barium swallow were normal except for hiatal hernia. He was treated for GERD without significant improvement. The patient was referred for ENT consultation where no abnormalities were noted. As the patient continued to experience worsening symptoms, a second ENT consult was obtained, nearly six months from the first, and asymmetry of the right tonsillar pillar as well as paresis of the right vocal cord, firmness of the right tonsil, and thickening of the mucosa on the right oropharynx were noted. Oropharynx biopsy demonstrated moderately differentiated invasive keratinizing squamous cell carcinoma (SCCA). Human papillomavirus (HPV) status was negative. A CT scan of the neck demonstrated enlargement of the right palatine tonsil with asymmetry of the nasopharynx and multiple large cervical lymph nodes measuring up to 20 mm in diameter. Staging PET CT was consistent with the history of tonsillar cancer, with no locoregional or distant metastasis. Although clinically staged as T1N0Mx (Stage I), the SCC was radiographically staged as high as T1N2cMx (stage IVa). Following consultation with a multidisciplinary board, the patient elected to proceed with a transoral robotic surgical resection of the right tonsil and bilateral sentinel lymph node biopsy. Pathology revealed a poorly differentiated deeply invasive, keratinizing, squamous cell carcinoma measuring 6.0 cm. The depth of invasion was 1.3 cm with perineural invasion; p16 and HPV were negative. Multiple frozen sections showed negative surgical margins and 0/5 lymph nodes were involved with metastatic carcinoma. At the recommendation of the radiation oncologist, the patient agreed to complete a six week adjuvant radiation therapy course. Concurrent chemotherapy was not indicated because the tumor did not have positive margins.

**Discussion**

Oropharyngeal cancer is uncommon, and typically affects patients in the sixth to seventh decades of life; men are three to five times more often affected than women. Squamous cell carcinoma of the oropharynx (OSCCA) has an average incidence of 123,000 cases annually and can arise in the soft palate, tonsils, base of the tongue, pharyngeal wall, and vallecula. The anterior tonsillar pillar and tonsil are the most common locations for a primary tumor of the oropharynx. The most notable risk factors include smoking more than ten pack years and infection with HPV, especially HPV type 16. While types 16 and 18 are associated with cancers of the genital tract, type 16 is thought to be associated with 45-70% of oropharyngeal SCCA. It is postulated that HPV exerts its effect by integrating its genome into the host cell’s nucleus and inactivating the tumor-suppressant p53 and retinoblastoma proteins thus unrestricting cell proliferation. Other documented risk factors include a diet poor in fruits and vegetables, the consumption of maté (a stimulant beverage in South America), chewing betel quid (a stimulant used in Asia), and having a defective elimination of acetaldehyde due to an inactive mutant allele of alcohol dehydrogenase-2. No specific chromosomal or genetic abnormalities associated with OSCCA have been identified yet.

The diagnosis of and appropriate staging for OSCCA involves both clinical evaluation and imaging. Symptoms of tonsillar lesions often include pain, sore throat, dysphagia, odynophagia, weight loss, ipsilateral referred otalgia facilitated through Jacobson’s nerve, or simply a neck mass. Physical exam findings may include dysplasia, inflammation, or a superficial spreading lesion. Biopsies are done for tissue pathology as well as for HPV status. Histologically, OSCCA are often moderately to poorly differentiated. On immunohistochemistry, the presence of p16, a tumor
suppressor protein that plays an important role in cell cycle regulation, has shown to be the strong indicator of disease course; p16 positivity is highly predictive of lymph node metastasis. The initial imaging is a head and neck CT scan with IV contrast. If necessary, PET-CT can detect primary tumor, nodal disease, and distant metastatic disease and can guide radiation therapy.3

The most commonly used staging system is the TNM classification for oropharyngeal cancer as defined by The American Joint Committee on Cancer.

**T, tumor**
- Tx: primary site cannot be evaluated
- T0: no evidence of carcinoma
- Tis: carcinoma in situ
- T1: tumor ≤2cm in greatest dimension
- T2: tumor 2-4cm in greatest dimension
- T3: tumor >4cm in greatest dimension
- T4
  - T4a: invades larynx, deep/extrinsic tongue muscles, medial pterygoid, hard palate, or mandible
  - T4b: invades lateral pterygoid, pterygoid plates, lateral nasopharynx, skull base, or carotid

**N, node**
- Nx: lymph nodes cannot be evaluated
- N0: no evidence of nodal metastasis
- N1: single node involved, ≤3cm
- N2
  - N2a: single node involved, 3-6cm
  - N2b: multiple nodes involved unilaterally, ≤6cm
  - N2c: bilateral nodal involvement, ≤6cm
- N3: nodal involvement >6cm

**M, metastasis**
- Mx: distant metastasis cannot be evaluated
- M0: no distant metastasis
- M1: distant metastasis present

Table 1: Oropharyngeal Cancer Staging

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Distant metastasis automatically places an individual as Stage IVC regardless of the T or N status.4

Traditionally, surgery and radiation have been the treatment modalities of choice. As there are no current randomized data to compare surgery, radiation therapy, or combined treatment, no optimal therapeutic regimen is defined as having superior survival advantage over other regimens. OSCCA can be excised using the transpharyngeal, transmandibular or transoral approach, as limited by visualization and the ability to ensure a 1-2cm margin of normal tissue. With advances in robotic surgery, the transoral procedure has the added benefits of relative rapidity, decreased morbidity, and improved functional outcomes. More recently, chemotherapy has proven to be equally effective especially when combined with radiotherapy as treatment goals have shifted more towards organ preservation strategies.5

The prognosis for OSCCA is contingent upon HPV status, smoking history, tumor stage, and nodal stage. These criteria are used to determine if a patient has low, intermediate, or high-risk carcinoma. Low-risk patients are those with HPV-positive tumors, a smoking history of 10 or fewer pack years, and N0 to N2a nodal disease. Intermediate-risk patients include HPV-positive tumors, a smoking history of more than 10 pack years, and N2b–N3 disease; or, for those with HPV-negative tumors, a smoking history of 10 or fewer pack years, N2b or N3 disease, or T2–3 tumors. High-risk patients include those with HPV-negative tumors and a smoking history of more than 10 pack years; or, for those with HPV-negative tumors, a smoking history of 10 or fewer pack years, and T4 disease. The 3-year rates of overall survival are 93.0% in the low-risk group, 70.8% in the intermediate-risk group, and 46.2% in the high-risk group.6

**Conclusion**

Ninety percent of oropharyngeal malignancies are squamous cell carcinoma and most commonly afflict males in the sixth and seventh decades of life. Carcinogen exposure from tobacco and alcohol as well as infection with HPV, specifically type 16, are the most significant risk factors. The diagnosis of OSCCA is a multimodality process that includes clinical presentation, tissue biopsy, immunohistochemistry, and imaging with CT and PET scans. With advances in robotics, the transoral approach is an alternative to more invasive surgical options and in conjunction with radiotherapy and chemotherapy can achieve excellent results.

**REFERENCES**


Submitted on October 7, 2014