SQUAMOUS CELL CARCINOMA OF THE UVULA: DIAGNOSIS, PROGNOSIS, AND TREATMENT

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Chief Complaint: UVular Mass

History of Present Illness: A 47-year-old male with a history of smoking presents with three-month history of a mass on his uvula. The mass has grown in size since he first noticed it. Patient describes the mass as “multicolored.” He reports difficulty swallowing, voice changes, dry cough and frequent throat clearing. Patient denies shortness of breath and pain with swallowing. Nothing aggravates or alleviates these symptoms. He is worried he has cancer.

Past Medical History: none
Past Surgical History: none
Medications: none
Allergies: ND/NA

Social History: 20 pack-years history of cigarette smoking. Use of marijuana every other day for approximately 10 years. Frequent use of heroin and other opioids, both IV and intranasally. Alcohol consumption of 4 drinks/week. Patient lives with his son’s family of 4 and is currently unemployed. Patient reports economic and transportation barriers regarding access to healthcare. Patient is sexually active with one female partner and uses protection intermittently.

Review of Systems: 12-system ROS negative apart from findings noted in HPI.

OBJECTIVE

Vital Signs: Temp 37°C, Pulse 100, BP 140/70, HR 16, O2 sat 98%, BMI 21.3.

Physical Exam: Exophytic uvular mass – 1.5x1.5cm extending up to the base of the uvula at the soft palate. No masses or lesions noted in the tongue, buccal mucosa, tonsils, posterior oropharyngeal wall, vallecula, base of tongue, epiglottis, subglottis, posterior.

Labs/Imaging: CBC and BMP within normal limits, INR 1.1, PT 12 seconds

CT report: 1. 2.2cm exophytic uvular mass without obvious expansion onto soft palate 2. No evidence of cervical lymphadenopathy

Excisional Biopsy of the uvula was performed under general anesthesia and the results were sent to pathology for frozen section

Pathology results: Squamous cell carcinoma pT1 + with negative margins. Tumor ulcerated with 1 cm closest margin on the anterior aspect

Diagnosis

2.2cm pT1b, primary squamous cell carcinoma (SCC) of the uvula

Discussion of Disease Process/Clinal Correlations

1. Human Papillomavirus and the Increase in Oropharyngeal HPV+ SCC
   a. Prevalence
   i. Over the past decade, there has been a steady increase of oropharyngeal squamous cell carcinoma (OPSCC) and a decline in cancers of the larynx and hypopharynx, largely due to the identification of exposure to high-risk oncopgenic human papillomavirus (HPV) as a risk factor for development of OPSCC.
   ii. Other risky behaviors (smoking, illicit drug use) correlate with an increased risk for HPV infection and other STIs.
   iv. HPV-16 testing is now routinely performed on most HNSCC tumors.

b. Prognostic
   i. HPV+ tumors are documented to be more responsive to therapies and produce better outcomes as compared to HPV− tumors.
   c. Clinical significance
   i. De-escalation of chemoradiation regimens is often advised for patients presenting with HPV+ OPSCC (case-dependent) – can help avoid negative side effects of treatment

2. Common Genetic Landmarks of OPSCC
   a. Background
   i. Cancer is caused by an accumulation of mutations within a cell. Once a cell has reached a particular mutation load burden, it loses control of its growth, proliferation, and cell cycling to become cancerous
   ii. Commonly mutated pathways in HNSCC (chosen based on clinical significance - target therapies)
   a. Oncogenes (Upregulated)
      1. EGFR – Growth, proliferation, and cell cycle regulation
      2. PTEN
      3. CDK4 – Growth arrest or apoptosis
   b. Tumor Suppressor Genes (Downregulated)
      1. TP53 – loss of the cell to cell growth arrest or apoptosis
      2. CDKN2A – controls the orderly progression through each stage of the cell cycle

1. Contributions of HPV Infection to Development of OPSCC

Current Research and New Treatments

1. For locally advanced stages of OPSCC (III and IV), combined chemotherapy and radiation (CRT) has proven to be superior to radiation alone.
   a. A meta-analysis revealed that 60% reported patients receiving CRT achieved significantly improved regional control and significant progression-free survival compared to radiation alone. CRT patients had a 22.4% 5-year overall survival rate as opposed to 15.8% for radiotherapy alone (P=0.05).
   b. Selective neck dissection surgery (SNM) is often performed on the nodes of non-positive HNSCC, including OPSCC.
   c. Transoral laser microsurgery (TLM) and transoral robotic surgery (TORS) are performed on the primary tumor for oncologic resection. These cause minimal cosmetic deformity, and facilitate optimal speech and swallowing after completion of therapy.
   a. For TORS: overall survival for HPV-associated and HPV-negative groups was 97.2% and 90.9% at 1-year, and 81.0% and 80.0% at 2-year follow up, respectively. Both groups had favorable outcomes with primary TORS with and without adjuvant CRT, but the small sample size failed to demonstrate a significant difference in outcomes associated with HPV status.
   b. There is a severe long-term sequelage of aggressive CRT: late onset toxicity, particularly acute mucositis and severe dysphagia, with a major negative impact on patient quality of life. TLM and TORS are therefore predicted to recapture the role as the primary treatment modality for OPSCC.

Conclusions

Chronic illicit drug use, tobacco use, and other risky behaviors can contribute to the development of OPSCC; risk of laryngeal cancer is 10–20-fold higher in current smokers than in non-smokers alone. HPV status is becoming increasingly important in both the diagnosis and treatment of SCC in the head and neck; HPV+ tumors are typically more responsive to treatment and patients can benefit from a de-escalated chemoradiation regimen in addition to surgical excision.

References


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