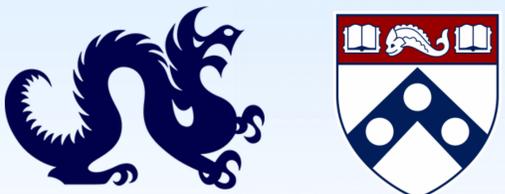


# Do You See What Eye See? A Complex Case of Recurrent p16+ HPV-Associated Oropharyngeal Squamous Cell Carcinoma Resulting in Orbital Exenteration in an Elderly Male

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Oropharyngeal squamous cell carcinoma (OPSCC) accounts for 90% of all malignancies of the oral cavity. It is strongly linked to alcohol consumption, cigarette smoking and infection with high-risk human papillomavirus (HPV) strains 16 and 18. If detected early, oropharyngeal squamous cell carcinoma can often be resected and many patients reach remission, with an overall 5-year survival rate of 68.5%; however, when OPSCC is detected in later stages, it can often lead to large, complex resections with multiple recurrences of disease<sup>1</sup>.

The patient is an elderly male in his 60s with a history of p16+, HPV-associated T3N1 OPSCC of the left neck and tonsil. He is status post left soft palatectomy, base of tongue resection, pharyngectomy, and tracheostomy. Additionally, the patient underwent a left neck dissection at the time of initial resection, which revealed multiple positive lymph nodes. Several years later, the patient experienced a recurrence of disease in his left maxilla. Subsequently, a partial maxillectomy was performed. Just months after his maxillectomy, the patient began to experience increased facial and oral swelling. While hospitalized for suspected post-surgical infection, magnetic resonance imaging (MRI) revealed local recurrence at the superior and anterior margins of the previous maxillectomy. Due to his history of multiple recurrences and the proximity of the lesion to the orbit, the patient underwent an extended maxillectomy with orbital exenteration. The case was received in the anatomic pathology laboratory in six parts. The primary specimen consisted of an oriented resection of the left upper portion of the face, including the entire eye, skin, soft tissue, and portion of bone. Tissue sections, including relevant margins, were selected by the pathologists' assistant (PA) to submit for microscopic review. **Microscopically, both bone and perineural invasion were identified, but all margins were negative for carcinoma.**

Due to the infrequency of orbital exenterations, these specimens can prove to be challenging. This case illustrates the importance of pathologists' assistants in initiating a collaborative approach to grossing and ultimately, the role of PAs in achieving positive patient outcomes. Furthermore, this case study serves as a reference for other pathologists' assistants who may encounter similar specimens in the future. **So, do you have what it takes to be a PA? Do you see what I see?**

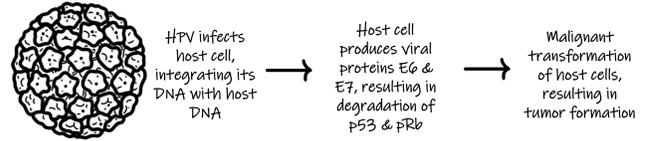


Figure 1. HPV carcinogenesis

## Patient History & Hospital Course

- Patient is an elderly male in his 60s with a history significant for p16+ HPV-associated T3N1 squamous cell carcinoma (SCC) of the left tonsil and left neck
- Status post left soft palatectomy /base of tongue resection/ partial pharyngectomy, with left neck dissection and tracheostomy in 2019
- Chemoradiation in 2020 with recurrence and subsequent maxillectomy in 2023



- Patient presented to the ED 5 months post maxillectomy with persistent worsening facial and oral swelling
- Symptoms had been ongoing 2 weeks despite treatment with Augmentin and clindamycin for suspected infection
- Recent MRI of the head demonstrated increasing abnormal soft tissue within the left maxillary sinus and in the left premaxillary soft tissues
- Patient was admitted to the hospital under the care of ENT for suspected infection
- Labs were within normal limits (WBC of 9.4, Hgb of 14.6)
- Started on IV vancomycin and cefepime, but then transitioned to Levaquin due to an upper respiratory culture positive for Citrobacter, Pseudomonas, and Klebsiella

Figure 2. An MRI of the neck during admission revealed: "Local recurrence at the superior and anterior margin of the graft reconstruction which measured approximately 3.7 x 3.0 cm." This was confirmed with a left oral cavity biopsy which showed superficial fragments of exophytic keratinizing squamous cell carcinoma with stromal invasion. The patient returned approximately two weeks later for surgical resection of the recurrence.

Stage	Gross Criteria
T1	Primary tumor < 2 cm
T2	Primary tumor > 2 cm but < 4 cm
T3	Primary tumor > 4 cm or extends to the lingual surface of the epiglottis
T4a	Moderately advanced local disease; primary tumor invades the larynx, extrinsic muscles of the tongue, medial pterygoid, hard palate, or mandible
T4b	Very advanced local disease; primary tumor invades the lateral pterygoid muscle, pterygoid plate, lateral nasopharynx, or skull base or encases the carotid artery

Figure 3. Oropharyngeal squamous cell carcinoma tumor (T) staging criteria<sup>2</sup>

## Photographs



Figure 4. Anterior aspect of primary specimen; specimen was received inked and oriented by the surgeon as follows: green-lateral, blue-superior, yellow-medial, black-inferior, orange-not true margin



Figure 5. Posterior aspect of primary specimen

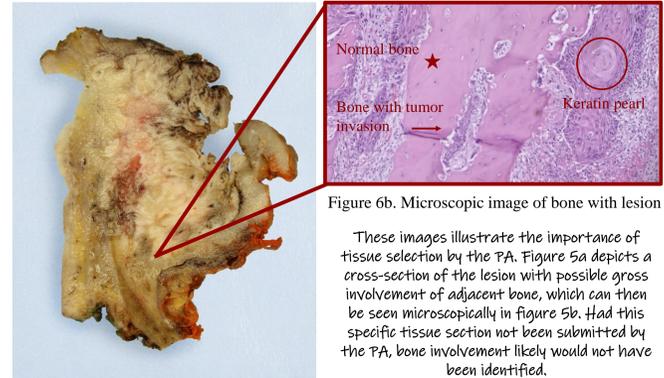


Figure 6a. Gross image of bone with lesion

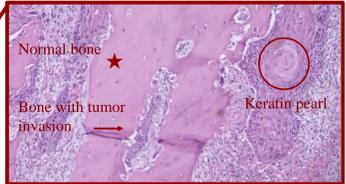


Figure 6b. Microscopic image of bone with lesion

These images illustrate the importance of tissue selection by the PA. Figure 5a depicts a cross-section of the lesion with possible gross involvement of adjacent bone, which can then be seen microscopically in figure 5b. Had this specific tissue section not been submitted by the PA, bone involvement likely would not have been identified.

What is a Pathologists' Assistant (PA)? A PA is a highly trained allied healthcare professional who quite literally serves as the 'eyes' of the pathologist in the gross room. The primary role of a PA is to examine surgical specimens and determine which tissue to submit to the pathologist for microscopic review!

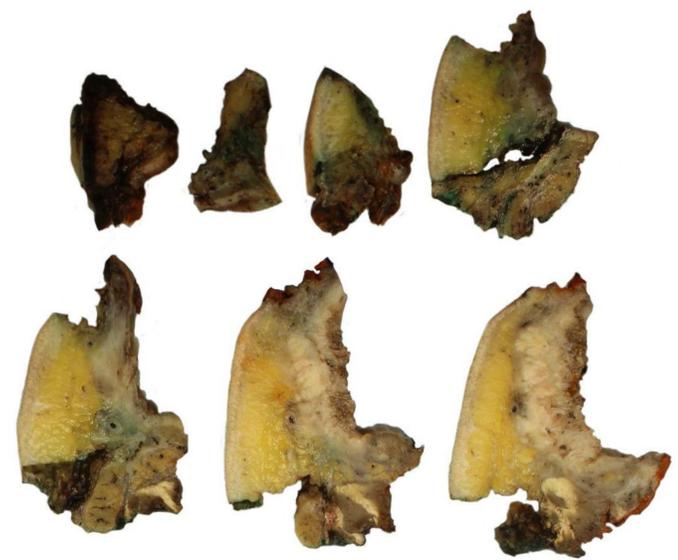


Figure 7. Sequential cross-sections of lesion

## Dissection & Gross-to-Scope

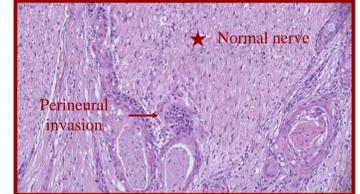


Figure 8. Microscopic perineural invasion

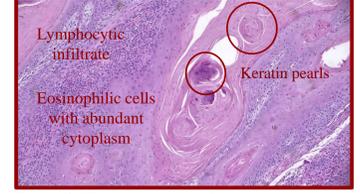


Figure 9. High-power view of lesion



Figure 10. Low-power view of lesion

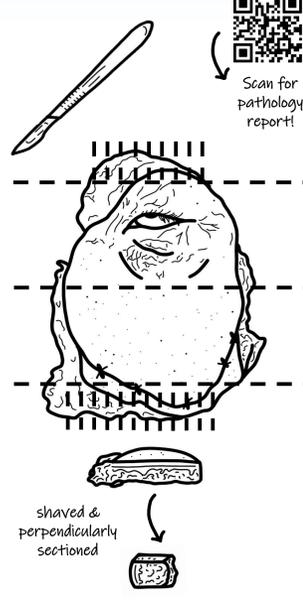


Figure 11a. Specimen grossing scheme

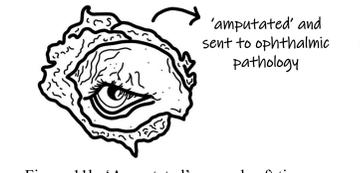


Figure 11b. 'Amputated' eye and soft tissue

The specimen was approached as a modified lumpectomy specimen. The superior and inferior 'caps' were shaved and perpendicularly sectioned. The eye was amputated from the specimen and the remainder of the specimen was then serially sectioned. Relevant margins, including all soft tissue, bone, and nerve margins were submitted in addition to numerous representative sections of the lesion.

## Conclusions

- 7.0 x 6.0 x 3.0 cm irregular, tan-white, friable lesion with irregular and infiltrative borders (lesion measured only 3.7 cm in greatest dimension on MRI)
- Lesion grossly involved the previously inked orange "not true margin"
- Possible gross involvement of adjacent bone
- Eye and skin were grossly unremarkable
- On microscopy, all soft tissue and bone margins were negative for carcinoma
- Microscopic perineural and bony invasion identified
- Eye grossly unremarkable and negative for carcinoma as per ophthalmic pathology
- Patient appears to be recovering well post-surgery and will follow with his care team to discuss further treatment based on pathology report

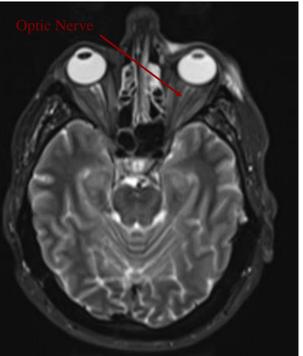


Figure 12. MRI of head prior to resection

Can HPV-related OPSCC be prevented? Yes, it can! Although most commonly associated with the prevention of cervical cancer, the HPV vaccine is 90% effective at preventing ALL HPV-related malignancies<sup>3</sup>.

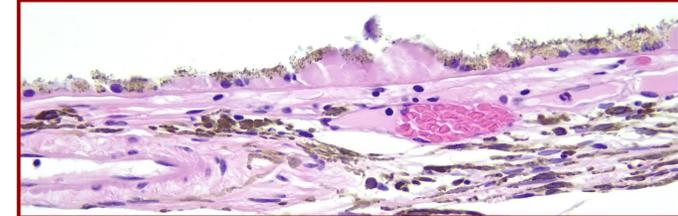


Figure 13. Microscopic image of lipid accumulation in the eye

Reference: 1. Glass SH. SCC-general. PathologyOutlines.com website. <https://www.pathologyoutlines.com/topic/oralcavitysc.html>. Accessed April 18th, 2024.  
 Reference: 2. Jamal Z, Anjum F. Oropharyngeal Squamous Cell Carcinoma. [Updated 2023 Apr 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK563268/>  
 Reference 3: Centers for Disease Control and Prevention. (2021, November 16). HPV vaccination: What everyone should know. Centers for Disease Control and Prevention. <https://www.cdc.gov/vaccines/vpd/hpv/public/index.html>