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Rare Presentation of Oral Squamous Cell Carcinoma of the Tongue with Ectopic β-hCG Secretion: A Case Report and Literature Review

Al Hassan T[1]*, Bender-Heine A[2] and Giese RA[3]

[1]University of Texas, Rio Grande Valley, USA

[2]Department of Ear, Nose & Throat and Head & Neck Surgery, University of Texas, Rio Grande, USA

[3]Department of Ear, Nose & Throat and Head & Neck Surgery, University of Texas Health Science Center, USA

***Corresponding author:** Taha Al Hassan, University of Texas Rio Grande Valley; 1214 W. Schunior St. Edinburg, TX 78541, USA, Tel: 9564786713; Email: taha.alhassan01@utrgv.edu

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Abstract

Background: Squamous cell carcinoma (SCC) is the most common form of cancer in the oral cavity and oropharynx. Early detection is amongst the most crucial factors for effective treatment and disease-free survival. Recent studies have explored potential prognostic indicators and screening markers, such as β-hCG antibody, to enhance clinical decision-making and prioritize therapeutics. β-hCG levels have been found to be associated with poorer outcomes and shorter survival time in various carcinomas, including oral squamous cell cancer.

Case Presentation: This case uniquely presents a 47-year-old woman with a poorly differentiated squamous cell carcinoma of the oral tongue. The patient presented with a large bleeding tumor, bilateral hypoglossal nerve weakness, lymphadenopathy, and dysarthric speech. Despite a history of bilateral tubal ligation, the patient tested positive for pregnancy due to ectopic β-hCG secretion by the tumor. Biopsy confirmed the diagnosis of invasive oral squamous cell carcinoma with increased serum levels of β-hCG. Palliative immunotherapy was initiated due to the advanced stage of the tumor, and tracheostomy and percutaneous endoscopic gastrostomy were performed to maintain the patient's airway and nutrition during treatment.

Conclusion: This case report highlights the potential use of β-hCG as a prognostic indicator for oral squamous cell carcinomas. Further research is needed to establish the relationship between β-hCG secretion and tumor growth rate, as well as to determine threshold levels, and possible eventual incorporation into guidelines. Utilizing β-hCG as a clinical tumor marker could represent a novel method to diagnose, monitor treatment, and surveil for recurrence. Evaluation of salivary and serum levels of β-hCG should also be considered in future studies to explore their potential clinical significance. Lastly, given the advanced stage at presentation in this case our study advocates for increased screening and education on the signs, symptoms, and risks for oral cancer.

Keywords: Oral Squamous Cell Carcinoma; β-hCG

Abbreviations: OSCC: Oral Squamous Cell Carcinoma; SEER: Surveillance, Epidemiology, and End Results Program.

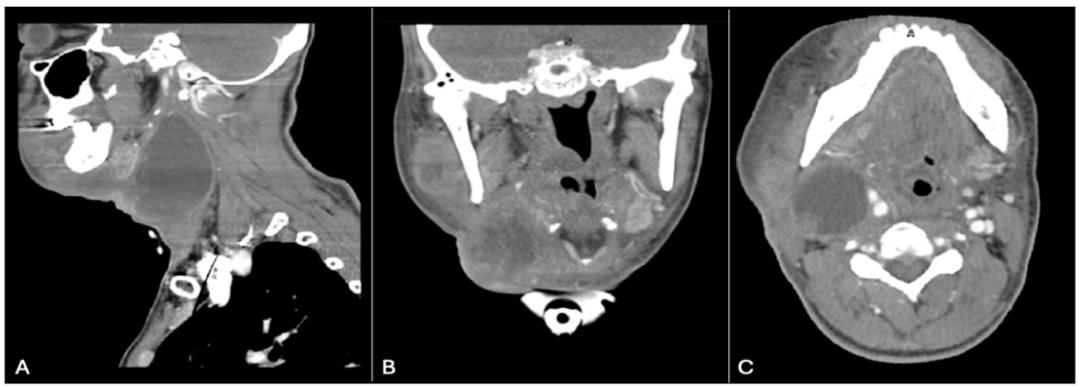
Introduction

Squamous cell carcinoma of the oral cavity (OSCC) is the most common type of cancer affecting the upper aerodigestive tract and its various subsites approximating more than 90% of all presentations [1]. According to data from the National Cancer Institute Surveillance, Epidemiology, and End Results Program (SEER), approximately two-thirds of all oral cavity and pharynx cancers present with regional lymph node spread (51%) or distant metastatic disease (15%) at the time of diagnosis. Early detection is critical as the 5-year relative survival rates plummet with later stage disease; literature demonstrates survival rates of 86.6%, 69.1%, and 39.3% for localized disease vs regional metastasis vs distant metastasis respectively [2]. To potentially enhance survival, Healthy People 2030 has taken these figures into consideration and made it a national objective to increase the proportion of oral and pharyngeal cancers detected at the earliest stage [3]. Additionally, recent studies have investigated potential prognostic indicators and screening markers, like β-hCG antibody, that may improve how clinicians' approach and prioritize therapeutic algorithms.

Although human chorionic gonadotropin (β-hCG) levels are commonly recognized for detecting early pregnancy, they can also be used as a tumor marker in diagnosing gestational trophoblastic disease, neuroendocrine tumors, and other carcinomas. The research thus far suggests that the expression of β-hCG by these tumors, compared to β-hCG negative variants, is associated with poorer outcomes and statistically shorter survival time [4]. Recent studies correlating β-hCG antibody and OSCC showed that 50% of the tumors were found to positively stain for β-hCG antibody, which closely aligns with the results of two earlier independent studies demonstrating positivity rates of 64% and 43.3% [5,6,7]. Furthermore, in each of these studies, the specimens that were histologically less differentiated were also more likely to demonstrate β-hCG expression with the antibody detectable in increased levels in urine and saliva [5,6,7]. In this case report the patient had sufficiently high β-hCG levels that there was confusion regarding possible underlying pregnancy.

Report of Case

A 47-year-old woman presented to the emergency room with a large, firm, bleeding tumor of the oral tongue. Physical examination revealed bilateral hypoglossal weakness with paralysis on the right side and paresis on the left. Patient demonstrated bilateral submandibular and cervical lymphadenopathy and dysarthric speech. Medical history was significant for previous right lateral tongue leukoplakia treated with antibiotics and steroids. Patient denied history of smoking or alcohol consumption. CT neck showed enhancement of right oral tongue with tumor extending to the right floor of mouth musculature including the anterior belly of the digastric (Figure 1). In addition, there were pathological lymph nodes in right level 1b and bilateral level 2. The patient was pre-menopausal and despite a prior tubal ligation she had a routine urine pregnancy test which was positive. The oral squamous cell carcinoma was suspected to have increased serum levels of β-hCG since the patient was confirmed to be not pregnant. The tumor was biopsied and final pathology revealed a right lateral oral tongue poorly differentiated stage 4 SCC T4N2cMx. Treatment was limited to palliative immunotherapy due to the size, extension of the tumor, and advanced stage. Additionally, to maintain the patient's airway and nutrition both tracheostomy and percutaneous endoscopic gastrostomy were placed to facilitate treatment.



Sagittal (A), coronal (B), and axial (C) tomographic slices showing tumor expansion

Figure 1: Computed Tomography.

Discussion

Based on our review of the literature in the English language this case is the first to document oral squamous cell carcinoma ectopically producing sufficient β-hCG detectable by a urine pregnancy test (hCG 6.3-12.5 mIU/mL) [8]. Previous studies have shown saliva and urine β-hCG levels in the setting of poorly differentiated OSCC cases at levels of 1.47 mIU/mL [5]. These lower levels are not sufficient to trigger a concern for possible underlying pregnancy. Although the mechanism of β-hCG production by non-trophoblastic tumors is not fully understood, our case report supports the hypothesis that production is associated with dedifferentiation and aggressive growth potential. More research is needed to determine the relationship between β-hCG secretion and OSCC tumor growth to make it more useful for prognosis and treatment algorithms. In this case, the patient presented to the emergency department with stage 4 diseases and patient was determined to be a poor surgical candidate. It remains to be determined how patients with elevated levels of β-hCG respond to surgical and non-surgical treatments and if that differs significantly from non β-hCG secreting tumors. This case study suggests two important clinical questions: can β-hCG immune-expression serve as a prognostic indicator and does urine β-hCG have a role in pre and or post treatment surveillance? The research to date suggests that urinary β-hCG levels as well as salivary and serum levels of β-hCG may be future markers to diagnose and monitor disease course [5,9,10].

Conclusion

This case reports represent the first recorded instance of markedly elevated β-hCG in a patient with stage 4 oral tongue SCC. Further research on the potential use of urine β-hCG as well as serum and salivary β-hCG is needed to determine its role in the diagnosis, prognosis, and treatment efficacy of OSCC. Given the advanced stage at presentation of this patient's oral cancer, our study also emphasizes the importance of and advocates for increasing access and frequency of cancer screenings as well as enhanced population education on the risk factors, signs, and symptoms regarding oral cancer - aligning with objectives set by the Office of Disease Prevention and Health Promotion Healthy People 2030 [3]. Not only is survival drastically enhanced in those patients with earlier detection, but outcomes are just as equally impacted as well. That being said, through more investigation β-hCG may demonstrate potential to development new methods or enhance already established forms of oral cancer screening and surveillance.

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