Submandibular Gland Invasion in Oral Cavity Cancers: Should We Really Remove the Gland?

Oral Kavite Kanserlerinde Submandibular Gland İnvazyonu; Bezi Gerçekten Almalı mıyız?

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ABSTRACT

Objective: Neck dissection and resection of the primary tumor are still the most effective treatments for oral cavity cancer (OCC). The excision of the submandibular gland is routinely performed during neck dissection. The present study aimed to review the stages, risk factors, and incidence of submandibular gland metastases in patients treated for OCC and discuss whether the submandibular glands could be preserved in this patient group.

Material and Methods: This study was performed retrospectively with the data of patients diagnosed and treated with oral cavity squamous cell carcinoma at the Otorhinolaryngology and Head and Neck Surgery Department of Akdeniz University School of Medicine between 2014 and 2019.

Results: Of the 44 patients included in the study, 26 were male. A total of 57 neck dissections were performed. Tumor invasion was observed in only 1 (2.27%) of 57 submandibular glands. The tumor localized to the floor of the mouth invaded the submandibular gland by direct invasion.

Conclusion: SMG can be preserved in selected patients with OCC according to the tumor location and suspected level I metastasis when planning treatment.

Key Words: Oral cavity cancer, Metastasis, Head and neck cancer

ÖZ

Amaç: Oral kavite kanserleri tedavisinde primer tümörün rezeksiyonu ve boyun diseksiyonu halen en etkin tedavi olark kabul görmektedir. Boyun diseksiyonu sırasında submandibuler glandın eksizyonu rutin olarak yapılmaktadır. Çalışmanın amacı oral kavite kanseri nedeni ile tedavi edilen hastaların evreleri, risk faktörleri ve submandibuler gland metastaz insidansı açısından gözden geçirilmesi ve bu hasta grubunda submandibuler glandın korunup korunamayacağının tartışılmasıdır.

Gereç ve Yöntemler: Çalışma Akdeniz Üniversitesi Tıp Fakültesi KBB ve Baş-Boyun Cerrahisi kliniğinde 2014-2019 yılları arasında, oral kavite yassı hücreli karsinom tanısı alıp tedavi edilen hastaların verilerinin retrospektif incelenmesi ile gerçekleştirildi.

Bulgular: Çalışmaya dahil edilen 44 hastanın 26'sı erkek, 18'i kadındı. Toplam 57 boyun diseksiyonu uygulanmıştır. İncelenen 57 submandibuler glandın sadece 1 tanesinde (%2.27) tümör invazyonu izlendi. Ağız tabanına lokalize tümörün bu hastada submandibuler glandı direkt yayılım yolu ile invaze ettiği görüldü.

Sonuç: Tedavi planlanırken, tümör konumuna ve şüpheli seviye I metastazına göre seçilmiş OCC'li hastalarda SMG korunabilir.

Anahtar Sözcükler: Oral kavite kanseri, Metastaz, Baş-boyun kanseri

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INTRODUCTION

Oral cavity cancers (OCCs) account for about 3% of all cancers. Squamous cell carcinoma is the most common histopathologic diagnosis in these cancers. Smoking and alcohol consumption are among the leading etiological factors. Large resection of the primary area and neck dissection are the currently accepted treatment options for oral cavity squamous cell carcinomas (OCSCCs) (1). Neck dissection can be performed unilaterally or bilaterally as selective or radical neck dissection depending on the localization of the disease and involvement of the neck. In neck dissections for OCCs, the submandibular gland (SMG) is routinely removed. The risk of level I metastasis is high in these cancers. However, SMG metastasis is very rare (2).

Saliva plays an important role in bringing food to taste, chewing, swallowing, preserving teeth, and speaking. The majority of salivation (65%) is provided by both SMGs. In OCCs, the removal of SMGs during dissection and the radiotherapy of patients after the surgery results in severe xerostomia. This problem leads to secondary consequences, considerably decreasing the quality of life (3-6). The aim of the present study was to review the stages, risk factors, and incidence of SMG metastases in patients treated for OCC and discuss whether SMGs could be preserved in this patient group.

MATERIALS and METHODS

This study was carried out at the Department of Otorhinolaryngology and Head and Neck Surgery. Ethics committee approval was obtained from the Akdeniz University School of Medicine Ethics Committee for the study performed retrospectively with the data analysis of patients with OCSCC (26.12.2018/907).

Forty-four patients who underwent primary surgery and/or radiotherapy–chemoradiotherapy for OCC between 2014 and 2019 were included in the study. Further, 57 neck dissections were performed in 44 patients. SMGs were excised in all patients who underwent neck dissection. A total of 57 SMGs were analyzed histopathologically.

Statistical Analysis

Descriptive statistics are presented with frequency, percentage, mean, and standard deviation values. The Pearson chi-square test was used to analyze the relationships between variables. The Mann–Whitney *U* test and Kruskal–Wallis tests were used to examine whether the invasion depth values were different according to the clinical characteristics of the patients. Correlation analysis was performed to investigate the relationship between level I metastasis and tumor size. *P* values less than 0.05 were considered statistically significant. The SPSS 22.0 software was used for analysis.

RESULTS

The mean age of the 44 patients included in this study was 60.36±13.06 years; 26 (59%) patients were male. Also, 20% of the patients were PEG/NG dependent and 30% were tracheotomy dependent. Twenty-four patients underwent flap repair after primary surgery. The examination of the T stages of the patients revealed that 31.81% were T2 and 27.27% were T1 (Table I).

The mean tumor size was 3.15±1.31 cm, and the depth of invasion was 1.57±1.31 cm. Perineural invasion (PNI) was found in 41% and lymphovascular invasion (LVI) was found in 11% of patients. When the tumor differentiation of the patients was examined, 22 patients had well-differentiated, 15 had moderately differentiated, and 7 had poorly differentiated tumors. The records showed that the most common primary tumor site was the tongue followed by the floor of the mouth (Table II). Twenty-three patients received chemoradiation after surgery (Table III).

Level I lymph node metastasis was not seen in 27 patients. Tumor invasion was detected in only 1 of the 57 SMGs (2.27%). SMG invasion developed as a result of direct dissemination in the patient with the tumor located in the floor of the mouth (Figure 1,2). The records showed that PNI, LVI, and level I metastasis were also present, and the tumor was poorly differentiated.

The analysis showed a high correlation between the depth of invasion and tumor size (r=0.66, P=0.03, P< 0.05). Another important finding revealed by the analysis was that patients

Table I: T stage of lesions.

Stage of Primary Tumor	Number of Cases	%
T1	12	27.27
T2	14	31.81
T3	7	15.90
T4	11	25
Total	44	

Table II: Sites involved among the study population.

Site Involved	Number of Cases
Tongue	17
Floor of Mouth	16
Buccal Mucosa	4
Retromolar Trigone	4
Alveolus	3
Total	44

Table III: Patient information about adjuvant therapy after surgery.

	Number of Patients	%
Patients who received RT*	8	18.1
Patients who received RT*+CT**	23	52.2
Patients who didn't received any treatment	13	29.5
Total	44	

*Radiation Therapy, **Chemotherapy

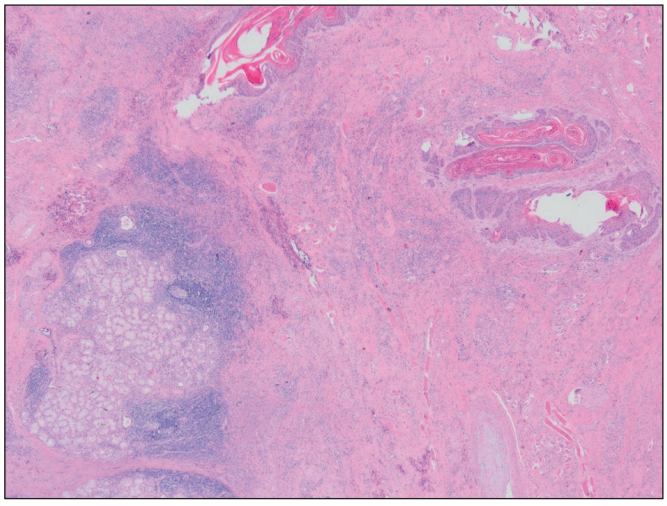

Figure 1: Microscopic image of SMG invasion of case, Haematoxylin and Eosin, x20.

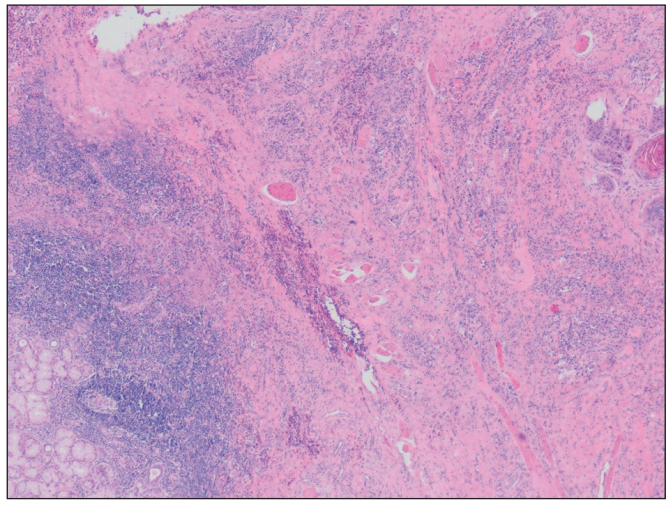

Figure 2: Microscopic image of SMG invasion of case, Haematoxylin and Eosin, x40.

with PNI had a greater depth of tumor invasion (P=0.04). In addition, no significant relationship was found between the depth of invasion and level I metastasis. In addition, the presence of PNI, LVI, and the degree of differentiation did not affect the presence of level I metastasis.

DISCUSSION

Cervical lymph node metastasis is one of the most important prognostic factors in OCC. The presence of metastatic lymph nodes reduces the prognosis by more than 50%. Even in early-stage OCC (T1–T2), the risk of cervical lymph node metastasis is high (7). Clinically, more than 30% occult metastasis was found in N0 necks. Therefore, the neck should also be treated when planning the treatment of patients with OCC. In all patients undergoing primary field surgery, classical neck dissection is always added to the treatment. In classical neck dissection, SMG is included in the specimen during level Ib dissection (8,9). The lymphatic and vascular network in SMG is not very dense (2, 10). In addition, it does not contain intraglandular lymph nodes (11). For these reasons, metastasis to SMG is not very common. SMG invasion is not very common in patients with OCC (12,13). In a study analyzing 183 patients with OCC, Cakir et al. (14) reported SMG invasion in 2 patients. They reported that both patients had primary oral floor tumors, and SMG metastasis developed by direct invasion.

Rouviere classified lymph nodes around SMG as preglandular, prevascular, retrovascular, retroglandular, and intraglandular (15). SMG metastasis may occur as a result of tumor infiltration from the metastases developing in these lymph nodes. Narayana et al. reported that they detected periglandular lymph node metastasis in 24% of 226 patients. In addition, 21 (9.3%) patients showed SMG invasion. The researchers reported that tumor localization was an important factor in the invasion of SMG, and the risk of oral floor tumors was very high. The same researchers reported that patients with a depth of invasion greater than 10 mm had a high risk of periglandular lymph node metastasis (10). In their study, Fives et al. reported a higher risk for tumors located in the floor of the mouth and also reported SMG invasion in 2 of 176 patients. They emphasized that both patients had oral base tumors (16). In the present study, no correlation was found between the depth of invasion and level I metastasis (Table IV).

Byeon et al. examined 316 specimens from 201 patients and showed that SMGs were infiltrated by tumors in 2 patients. They showed that level I metastasis was seen in 21.9%, whereas two patients with SMG infiltration did not have level I metastasis; the infiltration was caused by the direct spread of primary tumors (17). In another study, 294 SMGs were analyzed, and 13 patients had SMG involvement. Further, eight patients had direct invasion

Table IV: Literature review of SMG metastasis and level I metastasis in oral cavity SCC.

Study	SMG metastasis	Level I metastasis
Narayana	21 (9.3%)	38.5%
Chen	7 (1.8%)	No info.
Razfar	1 (0.39%)	11.5%
Panda	6 (3.68%)	No info.
Cakır	2 (1.09%)	30.9%
Naıdu	2 (2.9%)	21.4%
Ashfaq	2 (1.8%)	11%
Byeon	2 (1%)	21.9%
Fives	2 (1.2%)	15.9%
Malgonde	3 (3.06%)	No info.
Spiegel	9 (4.5%)	No info.
Present study	1 (2.27%)	36.3%

from the primary site and four patients had invasion by the periglandular metastatic lymph node. Only one patient had no infiltration from the primary site and no level I metastasis (18). In the present study, metastasis was detected in only 1 (2.27%) of 57 SMGs. The metastasis occurred by the direct spread in the patient with primary tumor localization. Dundar et al. reviewed 17 studies and found that only 58 (2.07%) of the 2792 SMGs had invasion. Also, 43 (17.2%) of these cases had direct invasion from the primary tumors and tumor infiltration by direct spread from the adjacent lymph nodes was found in 10 cases (19).

The major findings of this study were that the primary area was the most important factor in SMG involvement, and the presence of metastatic periglandular lymph node increased the risk of SMG involvement.

CONCLUSION

SMG can be preserved in selected patients with OCC according to the tumor location and suspected level I metastasis when planning treatment.

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