EPIDERMOID CANCER OF THE ORAL CAVITY: A RETROSPECTIVE ANALYSIS

ORAL KAVİTE EPİDERMOİD KANSERLERİ: BİR RETROSPEKTİF ANALİZ

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ABSTRACT

Purpose: To present our results with respect to TNM classification, stage, surgical pathology, locoregional recurrence and survival rate of patients with epidermoid cancer of the oral cavity. *Methods:* The medical records of 34 patients treated with surgery alone or surgery with postoperative radiotherapy and followed up for at least 3 years are reviewed. Number and percentage of the patients according to the stage were as follows: Stage I: 5 (14.7%), Stage II:6 (17.6%), Stage III:14 (41.1%), Stage IV: 9 (26.7%). *Results:* The 3-year survival rate for the complete series was 67.6%. 3-year survival rates with respect to the size of the primary tumor were 83.3% for T1, 73.3% for T2, 55.5% for T3, and 50.0% for T4 tumors. Survival rates for N0, N1 and N2 patients were 80%, 72.7% and 37.5% respectively. 3-year survival rates according to the stage of the patients were 80% for Stage I, 83.3% for Stage II, 71.4% for Stage III, and 44.4% for Stage IV patients. Local relapse occurred in 6 patients (17.6%), nodal recurrence in 5 patients (14.7%) and both in 1 patient (2.9%). The 3-year survival rate for local relapse and nodal recurrence were 33.3% and 40% respectively. There was a statistically important decrease in the survival rate with advanced lymph node involvement of the tumor. *Conclusion:* Diagnosis of intraoral cancers before any neck metastasis occurs is of critical importance for improved outcomes. Survival rates get worse in cases with neck metastasis.

Key Words: Intraoral, Epidermoid, Cancer, Tumor, Survival, Recurrence

ÖZET

Amaç: Oral kavite epidermoid kanserli hastalarımıza ait TNM klasifikasyonu, evre, cerrahi patoloji, lokorejyonel nüks ve sağkalı oranları sonuçlarını sunmak. *Gereç ve Yöntem:* Cerrahi veya cerrahi ve sonrasında radyoterapi ile tedavi edilmiş ve üç yıl süreyle takip edilmiş 34 hastanın tıbbi kayıtları incelendi. Hastaların evre dağılımına göre sayı ve yüzdeleri şöyleydi: Evre I: 5 (%14.7), Evre II: 6 (%17.6), Evre III:14 (%41.1), Evre IV: 9 (%26.7). *Sonuçlar:* Serinin toplam 3 yıllık sağkalı oranı %67.6 olarak bulundu. Primer tümörün boyutuna göre 3 yıllık sağkalı oranları T1 tümörler için %83.3, T2 için %73.3, T3 için %55.5, T4 için 50.0% olarak saptandı. N0, N1 ve N2 hastalar için 3 yıllık sağkalı sırayla %80, %72.7 ve %37.5 bulundu. Evreye göre sağkalı ise Evre I tümörler için %80, Evre II için %83.3, Evre III için %71.4, Evre IV için %44.4 idi. 6 hastada lokal nüks (%17.6), 5 hastada (%14.7) rejyonel nüks görüldü, Hem lokal hem rejyonel nüks 1 hastada (2.9%) vardı. Lokal ve rejyonel nüks için 3 yıllık sağkalı sırasıyla %33.3 ve %40 olarak bulundu. Tümörün boyun lenf nodu tutulumunun artmasıyla istatiksel olarak önemli derecede sağkalının düştüğü gözlendi. *Sonuç:* İntraoral skuamöz kanserlere boyun metastazı olmadan önce tanı konması daha iyi tedavi sonuçları için kritik önem taşımaktadır. Boyun metastazı oluştuğunda sağkalı belirgin derecede düşmektedir.

Anahtar Kelimeler: İntraoral, Epidermoid, Kanser, Tümör, Sağkalı, Nüks.

INTRODUCTION

Malignant tumors of the oral cavity make up 4% of the cancers in males and 2% of those in females with deaths related to oral cancer occurring in 2% of males and 1% of females with

the disease (1). The stage of the lesion at presentation tends to be greater due to the negligence of the patient and the lack of experience and knowledge of the physician. Tumors of the oral cavity are usually first diagnosed during dentistry visits for periodontical problems. Referral to a head and neck surgeon at an advanced stage results in wider tumor resection and increased mortality and morbidity.

The purpose of this study was to report our clinic's treatment outcomes and discuss the significance of tumor size, lymph node involvement and stage at the initial presentation on 3-year-survival rates.

MATERIALS AND METHODS

Medical records and pathologic specimens from 34 patients with diagnosed squamous cell cancer of the oral cavity were reviewed. Patients were treated with surgery at Gazi University's Faculty of Medicine, Department of Otorhinolaryngology, Ankara, between 1983 and 1997. The patients were followed up for at least 3 years and results with respect to stage, histopathological examination findings, treatment complications and outcome are presented.

Patients who did not meet the following selection criteria were excluded from the study:

1-The patient must have epidermoid carcinoma of the oral cavity documented via biopsy.

2-The pathology report of both the diagnostic biopsy and the resection material must be available.

3-Primary therapy to the lesion must have been completed before September 1994.

4-The patient must have been followed up for at least 3 years.

Thirty-four patients meeting the criteria were selected. Table 1 presents the primary tumor sites of the patients.

Patients were treated with surgery alone or surgery with postoperative radiotherapy and/or adjuvant chemotherapy according to their clinical status. We performed radical neck dissection (8 patients) or modified radical neck dissection (11 patients) in cases with palpable lymph node involvement (N+ necks). Fifteen patients who had no clinically palpable lymph nodes (N0 necks) were treated by selective neck dissection (supraomohyoid neck dissection). Criteria for using radiotherapy were: (i) advanced tumor stage (Stage III and IV cases); (ii) presence of more than one histologically positive lymph node or extracapsular spread; (iii) neural, cartilaginous, muscular, vascular, skin and connective tissue invasion by the tumor; and (iv) therapy to the contralateral side of the neck for high risk tumors reaching midline. The dosage for radiotherapy was a total of 5000 cGy with 150-200 cGy daily boluses.

Resection material from the primary tumor site and the neck dissection material were examined histopathologically. Presence of tumoral tissue in the material, adequacy of the resection margins, tumoral differentiation and neural, cartilaginous, muscular, vascular skin and connective tissue invasion by the tumor were determined. The neck regions of lymph nodes with tumor metastatis were noted.

After resection of the lesion, the resulting defect was reconstructed with flaps. Pectoralis major myocutaneous flap was used in 5 patients, sternocleidomastoid flap in 3 patients, pediculated temporalis muscle flap in 1 patient and free skin flap in another. Mandibulectomy was necessary for 3 patients with oral tongue tumor, 2 for floor of the mouth and 1 for gingival tumor. Mandibulectomy defects were reconstructed using mandibular reconstruction plates constructed of stainless steel (AO plates),

Maxillectomy was performed in 2 patients; one with gingival and another with hard palate tumor. Obturator and dental prosthesis was used for the reconstruction of the palatal defect.

In cases of recurrence, patients were treated by salvage surgery. Salvage surgery was accepted as being successful if the patient had spent at least 1-year disease free after surgery.

Table-1: Sites of the tumor involvement.

Site of involvement	Number & Percentage
Anterior 2/3 tongue	19 (55.8%)
Floor of the mouth	8 (23.5%)
Gingiva	4 (11.7%)
Buccal mucosa	2 (5.6%)
Hard palate	1 (2.8%)
Total	34 (100%)

T, N and stage groups were analyzed as pairs with respect to survival using the Wilcoxon matched-pairs test. Results were analyzed using SPSS for Windows, version 9.0 and P<0.05 was considered to be statistically significant.

RESULTS

The mean age was 50 years (range: 35 to 65 years) with a 3:2 male to female ratio. Table 2 presents the TNM classification of the patients.

The number and percentage of the patients according to stage were as follows: Stage I: 5 (14.7%), Stage II: 6 (17.6%), Stage III: 14 (41.1%), Stage IV: 9 (26.7%).

The 3-year survival rate for the complete series was found to be 67.6%. Survival rates for the male and female patients were 65.0% and 71.4% respectively. Three-year survival rates with respect to the size of the primary tumor were 83.3% for T1, 73.3% for T2, 55.5% for T3, and 50.0% for T4. Survival rates for N0, N1 and N2 patients were 80%, 72.7% and 37.5% respectively. Three-year survival rates according to the stage of the patients were 80% for Stage I, 83.3% for Stage II, 71.4% for Stage III, and 44.4% for Stage IV .

Upon paraffin section analysis surgical margins were positive in 4 patients (11.7%) and negative in 30 (88.3%). Three-year survival rates with positive and negative margins were 25.0% and 76.6% respectively. The pathologic tumor types of the specimens were well differentiated (26 patients 76.4%), intermediate (5 patients 14.7%) and poorly differentiated squamous cell carcinoma (3 patients 8.8%). Three-year survival rates according to tumor type were 69.2%, 60.0% and 67.0% respectively. In neck dissection there were 12 patients (35.3%) with nodal involvement of tumoral cells. 3-year survival rate for patients with and without nodal involvement were 41.6% and 81.8% respectively. Patients who had no clinically palpable lymph nodes (N0 necks) were treated by selective neck dissection (supraomohyoid neck dissection). Metastatic squamous cell carcinoma was identified in 4 of 15 prophylactic neck dissections (26.6%).

The T, N and stage groups were analyzed as pairs with respect to survival using Wilcoxon matched pairs test. Only the N0-N2 and N1-N2 pairs showed a statistically important difference with respect to survival (P<0.05). There is a statistically important fall in survival rates according to the advanced lymph node involvement status of the tumor. We did not find any statistically important difference between T and stage pairs. When the patients with tumor involvement of the surgical boundaries were compared to those without involvement, we did not find any statistically important difference between the two groups. This might have been due to the inadequacy of the number of cases in the tumor involvement group (4 cases). In addition, all patients with positive margins received subsequent postoperative irradiation, and this might have improved the local recurrence rate.

The complications of reconstruction with pectoralis major myocutaneous flaps included partial necrosis in 1 patient and suture opening in another. Total necrosis or major fistula development was not observed.

Thirteen (38.2%) patients completed a course of radiotherapy after surgery; 7 of them were Stage III and 6 were Stage IV patients. The 3-year survival rate of the surgery for the postoperative radiotherapy group was 61.5%, although it was 71.4% for the surgery group.

Local relapse occurred in 6 patients (17.6%), nodal recurrence in 5 patients (14.7%) and both local relapse and nodal recurrence in 1 patient (2.9%). Distant metastasis occurred in 2 patients (5.8%). One patient developed a secondary primary tumor (thyroid papillary carcinoma). The 3-year survival rate for local relapse and nodal recurrence were 33.3% and 40% respectively. Patients with distant metastasis and secondary tumors died from these evolutions.

Table-2: TNM classification of the patients.

	N0	N1	N2	N3	Total
T1	5	1	0	0	6 (17.6%)
T2	6	6	3	0	15 (44.1%)
T3	3	4	2	0	9 (26.4%)
T4	1	0	3	0	4 (11.7%)
Total	15(44.1%)	11(32.3%)	8(23.5%)	0(0%)	34

DISCUSSION

As in all other regions of the head and neck, the vast majority of malignancies of the oral cavity are squamous cell carcinomas. In our series, the oral tongue was the most common primary site of tumoral involvement, just as it was in the literature (2,3).

Patients were treated with surgery alone or surgery with postoperative radiotherapy and or adjuvant chemotherapy according to their clinical status. Radiotherapy is an alternative therapeutic approach that provides results as successful as surgery for T1 and small T2,N0 patients (4-7). However, sequels of radiotherapy are inevitable after its application. These complications vary in severity from mild mucosal membrane atrophy and dryness in the mucosa with xerostomia to the development of ulcers, from decreased bone density to the more severe osteoradionecrosis, spontaneous fractures and malunion (4-8). Larson et al. found the ratio of the life-threatening complications (ulceration, spontaneous fractures and malunion) as high as 58% (8). Fein et al. reported the development of mild complications in 33% of their patients, mostly consisting of connective tissue necrosis and disclosure of the bone for T1 and T2 lesions treated primarily with radiotherapy (4). In our clinics we prefer surgery as the primary modality for treatment in order to avoid such complications, although radiotherapy would be the alternative modality for patients ineligible for surgery and for those who reject surgery.

The 3-year survival rate was 67.6% in our study. In a review of the literature, we found similar rates (9-13). Mohr et al. found a 72% 3-year survival rate for a group of 141 patients, treated surgically for cancer of the oral cavity (10). Brennan et al. reported a 69% 3-year survival rate for a similar group consisting of 548 patients (11). Pitman et al., in their meta-analysis, stated that the 3-year disease-free survival in the group of patients aged less than 40 was 53.3% for a total of 122 patients (14). Olasz et al. treated 50 patients with squamous cell cancer of the oral cavity with telecobalt preoperative irradiation followed by appropriate surgery, and another matching group of 50 patients with preoperative chemotherapy consisted of bleomycin, vincristine, mitolactol and methotrexate. The overall 3-year survival rate was 66% in the chemotherapy group and 57% in the radiation therapy group, with no statistical difference between the groups being noted (15).

According to the literature 90-95% of all recurrent tumors are diagnosed in the first 2 years following treatment (9-13). Lefebvre et al. reported the total (regional and local) recurrence rate as 32.1% after 5-year follow-up. The survival rate for the patients with recurrent tumors was 25% (13). Mohr et al. reported a 31% total recurrence after a 3-year follow-up (10). Rudoltz et al reported the local recurrence rate to be 22% after a 3-year follow-up (16). Zelefsky followed his patients for 7 years and found the total recurrence rate to be 18% (17). Mohit-Tabatabai found the regional recurrence rate to be 16% (18). We found the total recurrence rate of tumors in our patients to be 35.2%. While the overall survival rate was found to be 67.6%, the rate for patients with recurrent tumors was as low as 33.3%.

Kaya et al. found 28% of the N0 necks had metastatic disease in his series of 72 oral tongue cancer patients (19). In our series, metastatic squamous cell carcinoma was identified in 4 of 15 prophylactic neck dissections (26.6%). It is necessary to perform prophylactic neck dissection for N0 necks due to the high rate of occult metastasis in oral cavity squamous carcinomas (19-21).

There are many factors determining the rate of locoregional recurrences. Hoşal et al. stated that besides T-stage and nodal involvement, histopathologic parameters of tumor thickness, perineural invasion and lymphovascular space invasion, the extent of lymphocyte infiltration and the invasion pattern statistically correlated with locoregional recurrences (22).

There are some recent studies that aimed to evaluate the prognostic value of tumor thickness in the prediction of nodal metastasis, local recurrence, and survival of oral tongue carcinoma (21,23,24). Yuen et al. in his series of 85 glossectomy specimens of oral tongue carcinoma found that tumors up to 3-mm thick had 10% nodal metastasis, 0% local recurrence, and 100% 5-year actuarial disease-free survival rates; tumor thickness of more than 3 mm and up to 9 mm had 50% nodal metastasis, 11% local recurrence, and 77% 5-year actuarial disease free survival rates;

tumors of more than 9 mm have a 65% nodal metastasis, 26% local recurrence, and 60% 5-year actuarial disease-free survival rates (23). Gonzalez-Moles similarly stated that patients with a tumor thickness of < or = 3 mm had a 5-year survival of 85.7%, significantly greater (p<0.05) than the rates of 58.3% and 57% for patients with a tumor thickness of 4-7 mm and >7 mm, respectively (24). Similarly Ünal et al. found tumor thickness either < 9 mm or > 9 mm was correlated statistically with locoregional recurrence (p<0.05) (25).

There is a statistically important fall in the survival rate according to the advanced lymph node involvement status of the tumor. The diagnosis of intraoral cancers before any neck metastasis occurs is of critical importance for improved outcomes. Survival rates decline in cases with neck metastasis. When a neck metastasis is found, treatment is of primary importance as it is for that of the primary tumor.

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