CLINICAL STUDY

MANAGEMENT OF SQUAMOUS CELL CARCINOMA OF THE LOWER LIP: ANALYSIS OF FIVE YEARS' EXPERIENCE (78 PATİENTS) AND REVIEW OF THE LITERATURE

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SUMMARY

The most frequent type of all oral cavity tumors, squamous cell type (SCC) has currently been reported to account for 90% of all malignant oral tumors. Lips are the most common localization after skin in the head and neck region for the squamous cell carcinomas to involve. Among the pivotal risk factors having impact on the prognosis are as follows: size of the tumor, histopathological type and grade, perineural invasion, regional lymph node metastasis, and local recurrences. The present retrospective study included a total of 78 patients with SCC of the lower lip who had been treated in the second Plastic Surgery Clinic in Ankara Numune Training and Research Hospital between 2007 and 2011. Such characteristics as age, gender, lesion localization, presence of palpable lymph nodes in the physical examination, ultrasonographic presence of cervical metastasis, pathology reports, cervical lymph node dissection and the results of the reconstructive operations undertaken were compared, thus proposing an algorithm in the light of the collected data. When diagnostic and treatment modalities are implemented appropriately and in the early period, the survival period and the quality of life change in a positive way. Particularly, we have concluded that lymph node dissections have a positive impact on the survival and reduce the recurrence rates.

Keywords: Lower lip, squamous cell carcinoma, lip

ALT DUDAK SCC Lİ HASTALARDA TANI VE TEDAVİ 5 YILLIK DENEYİM (78 HASTA) VE LİTERATÜRÜN GÖZDEN GEÇİRİLMESİ

ÖZET

Son zamanlarda oral kavite tumorleri arasında en sık olan yassı hücreli tipin (scc) oral kavite tümörlerinin %90'ini teşkil ettiği belirtilmiştir. Scc için baş ve boyun derisinden sonraki en sık tutulum lokalizasyonu dudaklardır. Bilinen risk faktörleri arasında prognoza etkisi olan faktörler şunlardır: tümor boyutları, histopatolojik tip ve evre, perinöral invazyon, bölgesel lenf nodu metastazi ve lokal rekürrensler. Yapılan retrospektif çalısmada kliniğimizde 2007-2011 yılları arasında alt dudak scc tanısıyla tedavi edilmiş 78 hasta dahil edilmiştir. Yapılan çalısmada yaş, cinsiyet, lezyonun lokalizasyonu, fizik muayenede palpe edilebilir lenf nodu varlığı, ultrasonografik servikal metastazi mevcudiyeti, patoloji raporları, lenf nodu disseksiyonu ve yapılan rekonstruktif operasyonun sonuçları gibi nitelikler karşılaştırılmış böylece toplanmış olan verinin ışığında bu tip hastaların tedavisinde bir algoritma önerilmektedir. Tanı ve tedavi metodları özellikle de erken dönemde uygun şekilde uygulandığında hayatta kalım süresi ve yaşam kalitesi olumlu yönde değişmektedir. Tarafımızdan özellikle lenf nodu disseksiyonunun hayatta kalım üzerine pozitif etkisi olduğu ve rekurrens oranlarını azalttığı sonucuna varılmıştır.

Anahtar Sözcükler: Alt dudak, skuamöz hücreli karsinom, dudak

INTRODUCTION

Lip cancers are among the most common malignancies observed in the head-neck region, and constitute 25% of all cancers encountered in the oral cavity. As the most frequent type of all oral cavity tumors, squamous cell type (SCC) has currently been reported to account for 90% of all malignant oral tumors. Lips are the most common localization after skin in the head and neck region for the squamous cell carcinomas to involve[1]. The incidence increases with age, reaching a peak in the seventh and eighth decades.5,9 The lower lip is affected far more frequently (80% to 95%) than the upper lip (2% to 12%) or commissure (1% to 15%)[2]. The majority of SCCs of the lower lip stems from the vermillion border.

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Lip cancers have a common predilection for white races especially in the 6th decade of life. The etiology of lip cancer is multifactorial, with exposure to the sun, previous radiotherapy, genetic predisposition (mutation of the p53 suppressor gene), and tobacco smoke playing important roles[2]. Although the SCCs localized on the lips have been regarded among the most common malignancies, higher cure rates are achieved compared with the other malignancies of head-neck region. In conjunction with the boosting rates of diagnosis and treatment especially in the initial stages in recent years, cure rates have been progressively increasing (83-96%); moreover, the significance of a meticulous evaluation for probable presence of metastasis in the regional lymph nodes have also been emphasized[4].

Surgery and radiotherapy stand for the therapeutic approaches known to be effective in the treatment of cancers of the lower lip, with successful results reported for both of the treatment modalities. In addition, evaluation of the cervical lymph nodes

and the tumor resection borders seem to be the most significant advantages of a tumor surgery. The incidences of local recurrence and second primary tumors were both reported to be 5% following treatment. Among the pivotal risk factors having impact on the prognosis are as follows: size of the tumor, histopathological type and grade, perineural invasion, regional lymph node metastasis, and local recurrences. Nevertheless, the prognosis of the carcinomas of the lower lip has been reported to be better than that of all other cancers of the oral cavity[5].

In the present retrospective study, the diagnostic and treatment modalities were assessed in the patients who had been admitted with lower lip cancer to our clinic.

MATERIAL and METHODS

The present retrospective study included a total of 78 patients with SCC of the lower lip who had been treated in our clinic between 2007 and 2011. Such characteristics as age, gender, lesion localization, presence of palpable lymph nodes in the physical examination, ultrasonographic presence of cervical metastasis, pathology reports, cervical lymph node dissection and the results of the reconstructive operations undertaken were compared, thus proposing an algorithm in the light of the collected data.

In addition to routine biochemical and hematological tests, the patients were evaluated ultrasonographically in the cervical and parotid lymph nodes; tomographically for probable pulmonary and cranial metastasis; and scintigraphically for probable bone metastasis. Preoperative staging was performed based on the pathological diagnosis and presence or absence of lymph node and/or distant metastasis. In this regard, cervical dissection and parotidectomy, along with reconstructions including local or regional flaps, or free tissue transfer were preferred.

The patients were all followed up at 3, 6, 12 month postoperative intervals. Cervical ultrasonography was undertaken on a routine basis during follow-up. Local recurrences, if any, were treated by excision and repair, whereas modified radical (ipsilateral and/or contralateral) lymph node dissections were the preferred treatment modality in case of lymph node recurrences.

Although presence of palpable lymph node represents an unreliable marker of a disseminated cancer in the physical examination, the bilateral cervical ultrasonographic evaluation implemented in all patients, indeed, has long been a diagnostic method gaining wide acceptance all over the world. Once all diagnostic tests were completed, each patient was clinically staged according to the TNM[6] classifications upon being discussed on the clinical council. Preceded by the definitive diagnosis established through incisional biopsy in all patients, radical surgical excision and repair appropriate for their stages were undertaken.

RESULTS

The ages of the patients included in the study ranged between 22 and 81 years, with the mean age of 62.1 years. Of all patients, 38 (77%) were male and 11 (23%) were female. 72.9% of the cases had the history of tobacco use, 85.7% of whom were heavy smokers (20 sticks/day for an average of 15 years). 40% of the patients had poor oral hygiene. Moreover, 15% had history of alcohol intake.

The localizations of the lesions on the lower lip were identified to be as follows: 22 lesions (28.2%) on the 1/3 left side; 7 lesions (8.9%) on the 1/3 right side; 37 lesions (47.43%) on the 1/3 midline; 5 lesions (6.4%) at the left oral commissure; and 7 lesions (8.9%) at the right oral commissure.

A thorough physical examination revealed clinically palpable lymph nodes in 26 (33.3%) of the patients. 38 patients (48.7%), on the other hand, were observed through bilateral cervical ultrasonography to possess pathological lymph nodes.

Table-1 gives the distribution of the patients according to their TNM classifications. Clinical stages of the patients on the basis of the TNM classification were as follows: 30 patients (38.4%) with stage 1; 6 patients (7.6%) with stage 2; 13 patients (16.6%) with stage 3; 29 patients with stage 4 (37.1%).

Table I: TNM classification of the patients

T	N	Stage
3	2C	4A
1	1	3
3	1	3
1	0	1
is	0	0
2	1	3
4a	2b	4a
1	0	1
2	1	3
1	0	1
2	2b	4a
2	1	3
1	0	1
2	0	2
3	2c	4a
1	0	1
2	2b	4a
2	1	3
2	0	2
4a	2c	4a
3	2a	4a
3	2c	4a
2	0	2
4a	2c	4a
1	0	1
2	0	2
1	0	1
1	0	1
1	0	1
1	0	1
4a	2b	4a
3	2b	4a
1	0	1
3	2c	4a
1	0	1
3	1	3
1	0	1
3	2b	4a
1	0	1
1	0	1
2	1	3
1	1	3
1	0	0
1	0	0
1	2c	4a
3	1	3
3	2C	4A
1	0	1
1	0	1
1	0	1
1	0	1
1	0	1
1	0	1
2	0	2
1	0	1
1	0	1
1	0	1
1	0	1
4a	2b	4a
3	2b	4a
1	0	1
3	2c	4a
1	0	1
is	0	0
2	1	3
4a	2b	4a
1	0	1
2	1	3
1	0	1
2	2b	4a
4a	2c	4a
3	2a	4a
3	2c	4a
2	0	2
4a	2c	4a
1	0	1
3	2C	4A
1	1	3

Pathological analysis yielded results compatible with well-differentiated SCC in 48 patients (61.5%); moderately differentiated SCC in 17 patients (21.7%); early invasive SCC in 2 patients (2.5%); and poorly differentiated SCC in 11 patients (14.1%).

Resection was carried out with minimum 10-mm excision margins. The resultant defects were reconstructed using V-Y mucosal advancement flaps in 2 patients (2.5%); Abbe flap in 10 patients (12.8%); double-barrel flap in 4 patients (5.1%); primary repair following Wedge excision in 5 patients (6.4%); Gillies fan flap in 8 patients (10.2%); Karapandzic flap in 10 patients (12.8%); Nakajima flap in 16 patients (20.5%); Webster Bernard modification in 13 patients (16.6%); radial forearm flap in 6 patients (7.6%); and, fibula osteocutaneous free flap in 4 patients (5.1%). No complication associated with the flaps occurred in the patients. However, local infections complicated in 11 patients and they were treated with an antibiotherapy commenced based on the recommendations of the hospital's infection committee. 5 patients underwent re-excision due to positive surgical margins.

Lateral cervical lymph node involvement was evaluated by palpation and ultrasonography. At diagnosis, 9 patients were N+ and 69 were N0. Of the 9 patients with N+ disease (all N1), 6 had stage T3 and 3 stage T2. Of the 69 patients with N0 disease at presentation, 5 developed lymph node metastasis 8 to 16 months after treatment of the tumor, of whom 2 had had T3 and 3 had had T2 disease.

In accordance with the clinical stages, cervical dissection was undertaken in the patients with stage-3 and stage-4 SCC of the lower lip. While elective cervical dissection was generally performed in stage-3 patients, modified radical cervical dissection was the procedure preferred in stage-4 patients. Moreover, superficial parotidectomy was performed as an additional process to the cervical dissection in 3 patients with pathological lymph node in the parotid glands.

As for the radiotherapy, it was planned to be implemented following the surgical repair in 9 patients in an attempt to prevent development of local recurrences. Although changing depending on the modality selected, total tumor doses ranged from 50 to 60 Gy.

DISCUSSION

Lower lip cancers are among the tumors with the most straightforward diagnosis and treatment owing to their origination in transitional zone of the face and to their conspicuous localization[7]. Despite a common ulcerative appearance in the suffering patients, a scene resembling to a cutaneous horn was encountered in 2 of our cases in the present series.

The demographic, clinical and histological characteristics of the patients with lower lip SCC and the surgical procedures implemented in this study shared similarities with the other studies in the literature[4-9].

The multiplicity of techniques reported in the literature states that there is no ideal method for reconstruction of the lower lip. It is generally agreed that reconstruction following resection of more than 60% of the lower lip gives poor results[9].

A number of treatment modalities, such as surgery, radiotherapy, chemotherapy, alone or in different combinations, have been reported in the treatment of SCCs of the lower lip. The ultimate gold standard in the treatment has been to reduce the tumor burden as much as possible, to prevent relapses, and to maintain the quality of life. Surgical resection and reconstruction of the residual defect are the most frequently recommended treatment modalities by a sizable number of centers[8]. The primary aim of the surgery is total excision of the tumor and to achieve an acceptable result both functionally and aesthetically, since lips not only make a significant contribution to the general outlook but they also possess quite significant functional features in both eating and speaking. Although many distinctive techniques exist regarding repair of the defect, what has been determinative is the size, localization and the need for repair of the tumor.

SCCs of the lower lip, especially those observed in younger patients, are frequently associated with immune deficiency. A young patient followed up with the provisional diagnosis of Xeroderma Pigmentosum underwent a constellation of operations for poorly differentiated SCC on the lower limp, which encompassed excision of the lesion, repair and bilateral cervical dissection due to bilateral lymph node involvement. At the same time, radiotherapy was undertaken in the patient in an attempt to prevent relapses.

Frequently accompanying the SCCs of the lower lip localized at the oral commissures, parotid lymph node involvement can be observed in lower lip SCCs of any localization. Ultrasonographic evaluation revealed pathological parotid lymph node in 2 patients with SCC at the left commissure of the lower lip and 1 patient with midline tumor. Modified

radical cervical dissection together with parotidectomy was undertaken in the former patients.

The reported incidence of regional metastases ranges from 0% to 15% for T1 tumors and between 11% and 35% for T2 tumors.[7,10]. In our study, however, physical examination revealed lymphadenopathy in 33% of the cases, while presence of pathological lymph node was evident through ultrasonography in 48.7% of the cases, which contradicted the other studies.

Many studies have indicated that at diagnosis, 75% to 80% of lip carcinomas are stage T1 which improves the survival rate[2]. In the present study, however, 46% of the cases were detected to be of grade 1 and 2, which was ascribed to the omission of the disease during lower stages due to low socioeconomic status of the patients and our clinic's being a tertiary healthcare facility.

Although implementation of the radiotherapy in early-stage SCCs of the lower lip has been recommended by a number of authors, our clinical view in this regard is as excision of all lower lip SCCs with appropriate safety margins, followed by early reconstruction. Surgery has been regarded in our clinic as a method providing rapid diagnosis and treatment, as well as a comprehensive evaluation by identifying the tumors histologically. We believe that the adjuvant radiotherapy would be more eligible for patients with T3-T4 stage tumors of low differentiation; for the patients with N3-N4 nodal metastasis; for the inoperable patients; and, for the patients carrying a substantial surgical risk.

As was also proposed by Bilkay et al.[4], tumor continuity was observed after en block resection with surgical margins of 10 mm in only 5 patients, which was interpreted as oncologically acceptable. Reconstruction was performed in all patients immediately after tumor resection, without any delay. Repair was achieved in the majority of the patients by use of random local or axial pattern flaps. A method of repair comprising hemimandibulectomy and osteocutaneous fibula flap transfer was undertaken due to mandibular infiltration in 4 patients, while the defect occurring as a result of wide resection was repaired by use of free radial forearm flap in 6.

Although ultrasonography has been able to differentiate pathological lymph nodes, a previous study confirmed the presence of pathological lymph node in only 20% of the patients in whom prophylactic lymph node dissection was performed[4]. It is clear that cervical involvement occurs at moderate rates. Yet the difficulty in predicting and in pinpointing at-risk patients still prevents elective neck dissection from being the treatment of choice for N0 necks of patients with carcinoma of the lower lip[11]. As such, we believe that one should pay meticulous attention in determination of patient's eligibility for cervical lymph node dissection. The patients were recommended in our clinic to undergo screening encompassing physical examination and bilateral cervical ultrasonography at 3 month intervals in the postoperative period. Furthermore, we encourage such approaches as elective lymph node dissections in the presence of pathological lymph node especially in the patients with stage-3 SCC of the lower lip and modified radical cervical lymph node dissection in stage-4 patients, considering that the former procedures are likely to abolish the metastatic lesions not yet diagnosed.

A substantial ratio of all local recurrences (23% (n=18) in the present study) was observed on the area where the primary tumor was localized, namely, on the primary site of involvement. Wide resection and repair operations were performed in these patients.

That distant metastasis occurs, on a rare basis, only at the end-stage of the disease in patients with SCC of the lower lip and that the lungs and the bones constitute the two sites where the majority of metastasis occur were reported in previous literatures[6]. Of all patients with SCC of the lower lip who were admitted to our clinic, 4 had lung metastasis and 1 had both pulmonary and bone metastasis; the patients were referred to radiation oncology clinic following resection and repair.

In conclusion, lower lip is a common site of involvement for squamous cell carcinoma. When diagnostic and treatment modalities are implemented appropriately and in the early period, the survival period and the quality of life change in a positive way. Particularly, we have concluded that lymph node dissections have a positive impact on the survival and reduce the recurrence rates.

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