

The Relationship between the Localization, Size, Stage and Histopathology of the Primary Laryngeal Tumor with Neck Metastasis

Primer Larenks Tümörünün Lokalizasyon, Büyüklük, Evre ve Histopatolojisi ile Boyun Metastazı Arasındaki İlişki

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Abstract

Objective: In this study we aimed to investigate the laryngectomy (partial and total) and neck dissection (functional, radical) in patients undergoing larynx identified as a result of the operation of primary tumour localization, size, stage and histopathology of the relationship between neck metastasis.

Materials and Methods: The files of 118 patients who have had operation of laryngectomy (partly, total) and neck dissection (functional, radical) because of larynx cancer in the Ear Nose and Throat (ENT) Clinic in the last ten years (1997-2007) have been evaluated retrospectively.

Results: 116 of them were male and 2 of them were female. Age average was 56±22. 189 neck dissections have been applied to 118 patients. While in supraglottic tumours, 55.2% cervical metastasis and 28.9% occult metastasis have been determined, in transglottic tumours 35.1% cervical metastasis and 18.9% occult metastasis have been determined. It has been seen that while the cervical metastasis ratio of tumours bigger than 4 cm is 55.8%, the tumours smaller than 4 cm is 27.27% (p=0.002). The cervical metastasis rate has been determined as 26.3% in T1 cases, 25.8% in T2 cases, 40.6% in T3 cases and 58.3% in T4 cases. In tumours with advanced T stage, the rate of cervical metastasis has been seen more than the ones with early T stage (p=0.027). Cervical metastasis has been determined as 27.3% in good differential (G1) tumours, 53.4% in medium differential (G2) tumours, and 74.1% in bad differential (G3) tumours (p=0.005).

Conclusion: Considered in the light of clinical parameters specified in the cervical lymph node metastasis, N₀ patients with laryngeal cancer, tumour, according to the anatomical location as unilateral or bilateral elective neck dissection should be performed and histopathological specimens taken in the event of a positive detection of metastases concluded that postoperative radiotherapy should be performed.

Key Words: Larynx cancer, localization, size, T stage, histopathological grade, cervical lymph node metastasis

Özet

Amaç: Bu çalışmada larenjektomi (parsiyel, total) ve boyun diseksiyonu (fonksiyonel, radikal) yapılan hastalarda, operasyon sonucu larenkste tespit edilen primer tümörün lokalizasyonu, büyüklüğü, evresi ve histopatolojisi ile boyun metastazı arasındaki ilişkiyi araştırmayı amaçladık.

Gereç ve Yöntem: Kulak Burun Boğaz Kliniği'nde 1997-2007 yılları arasında larenks kanseri nedeni ile larenjektomi (parsiyel, total) ve boyun diseksiyonu (fonksiyonel, radikal) uygulanan ardışık 118 hastanın dosyaları retrospektif olarak değerlendirildi.

Bulgular: Olguların 116'sı erkek, 2'si kadındı. Yaş ortalaması 56±22 idi. 118 hastaya 189 boyun diseksiyonu operasyonu yapıldı. Supraglottik tümörlerde %55,2 oranında servikal metastaz, %28,9 oranında occult metastaz tespit edilirken, transglottik tümörlerde %35,1 oranında servikal metastaz, %18,9 oranında occult metastaz tespit edildi. 4 cm'den büyük tümörlerin servikal metastaz oranı %55,8 iken 4 cm'den küçük tümörlerin servikal metastaz oranı %27,27 olarak bulundu (p=0,002). T1 evreli vakalarda %26,3, T2 evreli vakalarda %25,8, T3 evreli vakalarda %40,6, T4 evreli vakalarda ise %58,3 servikal metastaz oranı tespit edildi. İleri T evreli tümörlerde servikal metastaz oranı, erken T evreli tümörlerden daha yüksek bulunmuştur (p=0,027). İyi diferansiye (G1) tümörlerde %27,3, orta diferansiye (G2) tümörlerde %53,4, kötü diferansiye (G3) tümörlerde %71,4 oranında servikal metastaz tespit edildi (p=0,005).

Sonuç: Belirtilen klinik parametreler ışığında servikal lenf nodu metastazı düşünülen, N₀ larenks kanserli olgularda; tümörün anatomik olarak yerleşim yerine göre unilateral veya bilateral elektif boyun diseksiyonu yapılmalı ve alınan spesmenlerde histopatolojik (+) metastaz tespit edilmesi durumunda postoperatif radyoterapi mutlaka uygulanmalıdır kanaatine varılmıştır.

Anahtar Kelimeler: Larenks kanseri, lokalizasyon, büyüklük, T evresi, histopatolojik diferansiyasyon derecesi, servikal lenf nodu metastazı

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Introduction

The most important factors which define the prognosis in laryngeal cancers are the place of primer lesion, the size of lesion, whether or not there is a cervical metastasis, and cellular differentiation [1]. The risk of metastasis to cervical lymphatics has a crucial importance in laryngeal carcinoma. The presence of lymph node decreases the probability of local control and survival [2]. In this study, we aimed at making a survey of the relationship between the localization, the size, the phase, and the histopathology of the primer tumour, determined in larynx by operation, and neck metastasis in the patients who was operated (functional and radical) neck dissection and (partial, total) laryngectomy in our clinic in the last decade.

Materials and Methods

The files of 118 successive patients treated with (functional and radical) neck dissection and (partial, total) laryngectomy operations because of laryngeal cancer in our clinic in the years between 1997-2007 were retrospectively analysed. Patients whom neck dissection was not operated were excluded from the study. Ages and sexes of the patients, localization of the tumour, whether or not there was a lymph node in the neck before the operation, operations performed, operation findings and histopathological results of the postoperative specimen were retrospectively analysed. The results of preoperative neck examination were compared with the histopathological examination results of the postoperative neck dissection specimen. As a result of preoperative clinic examination and postoperative pathological evaluation, necks with positive tumour metastasis were evaluated as N (+); and, the necks, accepted as N₀ (no palpable lymph node) in preoperative clinic examination and getting N (+) (tumour metastasis positive and lymph node presence) in postoperative pathological evaluation were evaluated as N false (-) (occult metastasis). Patients who were determined to have node by preoperative palpation and determined not to have metastasis in pathological examination of postoperative specimen were accepted as N false (+) (false +).

Lymphadenopathy (LAP) bigger than 1.5 m in the neck was accepted as clinically N (+) in physical examination. Neck metastases were evaluated with regard to the level of lymph node. We had no case of laryngeal cancer having isolated subglottic location. T1, T2, T3, and T4 phases, differentiation degrees, and sizes of supraglottic, glottic and transglottic tumours and the presence of cervical metastasis in these tumours were examined in each case separately. The relationship between localization, size, phase, and histopathological differentiation degree of the tumour and neck metastasis was evaluated.

Statistical Analysis

The figures attained after the study were statistically evaluated in a computer working under Microsoft® Windows XP operating system, using SPSS package software (SPSS 13.0 for Windows). Performing the Chi-Square test, ordinal figures, the relationship between them and the relationship between them and the shared figure were determined.

Results

Of 118 patients with laryngeal cancer included in the study, 116 were male, and 2 were female. The youngest patient was 34, and the oldest was 78.

For primary focus, total laryngectomy was operated on 82 (69.5%), supraglottic laryngectomy on 24 (20.3%), vertical haemilaryngectomy on 6 (5%), frontolateral laryngectomy on 5 (4%), and frontal anterior laryngectomy on 1 (0.8%) of our cases.

As for the surgical treatment operated on the neck, 118 patients were operated 189 neck dissections. 173 of these were functional neck dissections, and 16 were radical neck dissections. Also, 71 patients were operated bilateral neck dissections.

According to the place of the tumour, 38 cases (32.3%) were supraglottic, 6 cases (5%) were glottic, and 74 cases (62.7%) were transglottic. We had no case with subglottic localization only.

The relationship between the localization of the tumour and cervical metastasis has been shown in Table 1, and the

Table 1. Comparison with the localization of the tumour, cervical metastasis

Tumour localization	Number of cases	Number of cervical metastasis	Cervical metastasis %	Number of occult metastasis	Occult metastasis %	Number of false (+)	False (+) %
Supraglottic	38	21	55.2	11	28.9	-	-
Glottic	6	-	-	-	-	-	-
Transglottic	74	26	35.1	14	18.9	6	8
Subglottic	-	-	-	-	-	-	-

relationship between the anatomic region the tumour has occupied in laryngeal parts has been shown in Table 2. It has been determined in our study that the supralaryngeal tumours are much more metastatic to the neck.

When the contralateral cervical metastasis was compared with the anatomic localization the primary tumour occupied, it was determined that 6 (13.3%) of 45 tumour cases which were reaching the other side crossing the midline, showing ipsilateral localization, 3 (25%) of 12 piriform sinus located tumour cases, 6 (18.7%) of 32 tumour cases with epiglottis involvement, 1 (5.3%) of 19 tumour cases showing anterior commissural involvement, and 1 (50%) of 2 tumour cases with tongue base involvement did contralateral cervical metastasis.

The relationship between the histopathological differentiation degree of the tumour and cervical metastasis has been

shown in Table 3. This relationship was found very meaningful in our study ($p=0.005$; $p<0.01$).

According to Tumor Node Metastasis of American Joint Committee on Cancer (AJCC TNM) classification, the relationship between the T phase of the tumour and cervical metastasis has been shown in Table 4. While cervical metastasis was found in 13 (26%) and occult metastasis was found in 9 (18%) of 50 advanced-phase (T_1 - T_2) cases, cervical metastasis was found in 34 (50%) and occult metastasis was found in 16 (23.5%) of advanced-phase (T_3 - T_4) 68 cases. In our study, there was a meaningful relationship between the T phase of the tumour and the risk of cervical metastasis ($p=0.027$; $p<0.05$). However, the relationship between the T phase of the tumour and the risk of occult metastasis was not found to be meaningful ($p=0.639$; $p>0.05$).

Table 2. Comparison metastasis of the tumour in cervical with anatomic region holds

Anatomic site of the tumour kept	Number of cases	Number of metastasis	Metastasis %
Epiglot	64	31	48.4
Ariepiglottik plica	26	14	53.8
Ventricular band	90	37	41
Ventricular	27	12	44.4
Vocal cord	69	22	31.8
Arytenoid	26	14	53.8
Anterior comissure	38	15	39.4
Tyroid cartilage	26	13	50
Piriform sinus	16	11	68.7
Base of the tongue	2	2	100
Preepiglottic space	11	6	54.5
Cricoid cartilage	6	3	50
Subglottic area	18	6	33.3

Table 3. In our series of 118 cases of cervical metastasis compared with histopathologic differentiation

Histopathologic differentiation of tumour	Number of cases	Number of cervical metastasis	Cervical metastasis %
G ₁ Well differentiated	66	18	27.3
G ₂ Moderately differentiated	45	24	53.4
G ₃ Poorly differentiated	7	5	71.4
$X^2=10.683$; $p=0.005$ ($p<0.01$)			

The relationship between the size of the tumour and cervical metastasis is shown in Table 5. The reason for the use of 4 cm as limit value in the size of the tumour was that the diameter of the primary lesion was found between 2-4 cm in the most of the cases and that value of 4 cm was median as of the distribution of the cases. As a result of our study, there was a very meaningful relationship between the size of the tumour and cervical metastasis ($p=0.002$; $p<0.01$).

The relationship between the localization of the tumour and the level of cervical metastasis it did is shown in Table 6.

In 6 (12.7%) of our 47 cases showing cervical metastasis, perinodal invasion was seen. In our study, it has been determined that perinodal invasion is not connected with the localization, the T phase, and the differentiation degree of the tumour.

Discussion

The presence of cervical lymph node is an important factor in terms of the prognosis in head and neck cancers [3-5].

It has been stated that while 5-year survival is between 29-54% in patients who have laryngeal cancer with nodal metastasis, it changes between 64-94.5% in patients who do not have local metastasis [6, 7]. Size and number of the involved lymph node, and whether there is extracapsular spread or not affects survival [8, 9]. It has been stated that, if the size and number of the involved lymph node increase, if there is lymph node involvement in more than one level, and if extracapsular spread exists, there is a significant decrease in survival [3, 8, 9]. Therefore, it is important to know the factors which affect the neck metastases and to determine the treatment to be operated on the neck [10].

In our study, cervical metastasis was discovered in 21 (55.2%) of 38 supraglottic tumours. The neck was evaluated as N0 in physical examination in 10 cases, although metastasis (occult metastasis) was found in the neck dissection specimen. No cervical metastasis was found in any of the 6 glottic cancer cases. In 26 (35.1%) of 74 glottic cancer patients, cervical metastasis was found, and occult metastasis was found in 14 (18.9%) of these 74 patients. We had no

Table 4. In our series of 118 cases of cervical metastasis compared with T stage of the tumour

T stage of the tumour	Number of cases	Number of metastasis	Cervical metastasis %	Number of occult metastasis	Occult metastasis %
T1	19	5	26.3	2	10.5
T2	31	8	25.8	7	22.5
T3	32	13	40.6	8	25
T4	36	21	58.3	8	22.2

$X^2=9.143$; $p=0.027$ ($p<0.05$) (Cervical metastasis); $X^2=1.689$; $p=0.639$ ($p>0.05$) (Occult metastasis)

Table 5. The relationship between cervical metastasis and size of the tumour in our series of 118 cases

Size of the tumour	Number of cases	Number of cervical metastasis	Cervical metastasis %
4 cm ≤	52	29	55.8
4 cm >	66	18	27.27

$X^2=9.855$; $p=0.002$ ($p<0.01$)

Table 6. Evaluate the relationship between the level of the cervical metastasis and the localization of the tumour

Tumour localization	Level II	Level III	Level IV	Level I - II	Level I and III	Level II-III	Level II and IV	Level III-IV	Level I- III	Level I- V	Total
Supraglottic	9	1	1	2	-	4	1	-	3	-	21
Transglottic	6	3	4	-	1	7	1	2	1	1	26
Total	15	4	5	2	1	11	2	2	4	1	47

any isolated subglottic located case. It has been determined in our study that the results obtained are in accord with the literature [3, 5]. In our study, in keeping with the literature again, the rates of cervical metastasis have been determined as 48.4% for epiglottis, 53.8% for aryepiglottic plica, 41% for ventricular band, 44.4% for ventricular, 31.8% for cord vocal, 50% for thyroid cartilage, 68.7% for piriform sinus, 100% for tongue base involvement and 54.5% for preepiglottic area involvement [11].

In our study, there was contralateral cervical metastasis in 17 patients. Of these patients, 8 patients had midline located tumour, and 6 had the tumour crossing the other side reaching the midline. In addition, 3 patients had piriform sinus located tumour while 16 of 17 contralateral metastases had also ipsilateral lymph node metastasis and these results are considered to be accordant with the literature [11].

The T phase of the primary lesion also affects the risk of cervical metastasis [12]. According to the T phase of the primary tumour, Papparella found metastasis incidence as 15-40% in T1-phase tumours, 35-42% in T2-phase tumours, 50-65% in T3-phase tumours, and 65% in T4-phase tumours [8]. In our study, cervical metastasis in supraglottic located tumours were found in 5 (35.7 %) of 14 cases for T1, in 2 (33.3%) of 6 cases for T2, in 4 (66.6%) of 6 cases for T3, and in 10 (83.3%) of 12 cases for T4. No cervical metastasis was found in any of 6 glottic tumour cases. Of transglottic tumours, 6 (24%) of 25 cases having T2 transglottic lesion, 9 (34.6%) of 26 cases having T3 transglottic lesion, and 11 (47.8%) of 23 cases having T4 transglottic lesion were determined to have cervical metastasis. Totally, while of early-phase (T1-T2) 50 cases, cervical metastasis was found in 13 cases (26%) and occult metastasis was found in 9 cases (18%), cervical metastasis was found in 34 (50%) and occult metastasis was found in 16 (23.5%) of advanced-phase (T3-T4) 68 cases ($p < 0.05$).

The increase in grade of the primary tumour increases the risk of neck metastasis [5, 13, 14]. It has been emphasized that the rate of cervical metastasis is higher in tumours with poor histopathological differentiation (grade= G_3) than those with good differentiation (grade= G_1) [13, 15]. In our study, out of 118 patients cervical metastasis was found in 27.3% (18 of 66 cases) of cases with good differentiation (G_1), in 55% (25 of 45 cases) of cases with moderate differentiation (G_2), and in 71.4% (5 of 7 cases) of cases with poor differentiation (G_3) ($p < 0.01$).

The relationship between the size of the tumour and cervical metastasis is disputable. Kirchner and friends [16], in a study of 50 cases, have found metastasis at the rate of 55% in transglottic cancers, bigger than 4 cm, and at the rate of 25% in tumours, smaller than 4 cm. It has been stated in this study that cervical lymph node metastases depend on the localization of the primary tumour rather than its size. In our study, cervical metastasis was found in 29 (55.8%) of 52 laryngeal

tumours, bigger than 4 cm and in 18 (27.27%) of 66 laryngeal tumours, smaller than 4 cm ($p < 0.01$).

It has been emphasized that cervical lymph node metastasis is at I and II neck level at the most in many supraglottic and glottic located laryngeal carcinoma cases [17]. In a study consisting of 40 patients with clinic N0, the main localizations of all occult metastases been determined to be ipsilateral II and/or III. Occult metastasis could not be found in the lymph nodes on the levels of I, IV, and V [18]. Following the directions which can be early lymph node metastasis in laryngeal carcinomas that are clinically N0, it has been emphasized that lateral neck dissection which has been operated on is an acceptable treatment method [19, 20]. It has been stated that involvement of the area I increases in the case of the involvement of the areas II-IV as well as the probability of isolated involvement is rarely seen [19, 20]. In our study, being accordant with the literature, of 47 cases which were laryngeal cancer and being cervical metastatic, 15 cases (31.9%) were metastatic to level II, 4 cases (8.5%) to level III, 5 cases (10.6%) to level IV, 11 cases (23.4%) to level II and III, 2 cases (4.25%) to level III and IV, 4 cases (8.5%) to level I, II, and III, and 1 case to all the levels. Also, it was determined that 80% of the cases which had involvement with area IV had cartilage invasion.

When the patients with extracapsular spread were compared with the patients of the same phase who had cervical metastasis limited to lymph node, a meaningful decrease in survival was determined [21]. Extracapsular spread was seen in 6 cases in our study.

It has been stated that the probability of pathological (+) lymph node presence in the neck specimen obtained by operation changes between 13.6% and 37% in the laryngeal cancer patients whose necks are clinically non-palpable to lymph nodes [19, 20]. Probably, it will never be possible to be able to determine micrometastases in neck lymph nodes correctly with imaging methods. The risk of cervical metastasis, concerning the characteristic features of the primary tumour (localization, size, grade, infiltration degree), is at stake [22]. Therefore, the treatment of the neck should be handled sprily, even if the neck is clinically negative [23].

Treatment of the neck is compulsory during the first treatment of cases with a positive lymph node in clinic examination [13]. However, there is no consensus about performing elective neck dissection on laryngeal cancer patients [10, 12, 13, 16, 19, 24-27].

The debates increase especially on the neck examination and patient group accepted as N₀. In this case, there are three options: elective radiotherapy, elective neck dissection and neck follow-up until encountering a metastatic disease [28, 29].

Some of the authorities advocate elective neck dissection because of the fallibility of palpation and the high risk of lymph node metastasis of supraglottic tumours [30, 31].

Also, some authorities have adopted and recommended elective neck dissection as standard treatment because it decreases recurrence rates in clinically negative necks [32-34]. Nowadays, detailed histopathological evaluation of the lymph nodes removed during the neck dissection is the most reliable method available for the diagnosis of the correct locations of lymph nodes [35].

Consequently, the risk of cervical metastasis to be associated with the characteristic features of the primary tumour (localization, size, T stage, histopathological differentiation degree), was determined. We believe that, in N0 laryngeal cancers, it is necessary to do unilateral or bilateral elective neck dissection according to anatomic localization of the tumour, in cases where positive cervical lymph node is thought to exist considering clinical parameters (tumour size, T stage and histopathological differentiation degree), and to do postoperative radiotherapy in case that histopathological (+) metastasis is found in taken specimens.

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