Initial CT findings in early tongue and oral floor cancer as predictors of late neck metastasis

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Abstract

Background. Detecting the risk factors for late neck metastasis (LNM) in early tongue and oral floor cancer is important for establishing an accurate prognosis, as well as for increasing survival rates.

Methods. Patients with either stage I or II tongue and oral floor cancer underwent either a resection of the primary tumor or interstitial radiotherapy without neck dissection. We measured the short- and long-axis diameters of lymph nodes on initial CT images.

Results. Of the 38 patients, 20 had LNM and 18 did not. CT images showed a total of 161 lymph nodes. Twenty-five “occult lymph nodes” developed into LNM, whereas the remaining 136 “reactive lymph nodes” did not. Comparison between “occult” and “reactive” lymph nodes revealed significant differences in the short-axis diameters (p=0.01).

Conclusions. The measure of short-axis diameters of neck lymph nodes on initial CT images is a useful predictor of LNM in patients with early tongue and oral floor cancer.

Introduction

The presence of neck metastasis is the single most adverse independent prognostic factor in head and neck squamous cell carcinoma[1]. Early tongue and oral floor cancer is known for its propensity for subclinical lymph node metastasis, and the incidence of late neck metastasis has been reported at 20-30%[2,3,4]. It has been reported[5,6] that patients with neck lymph node metastasis tend to develop distant metastasis, even though the regional control is maintained by neck dissection. Identifying the risk factors for late neck metastasis in early tongue and oral floor cancer is important for providing an accurate prognosis and thus achieving higher survival rates.

Histopathologic factors, such as tumor size, depth, degree of differentiation, mode of invasion, microvascular invasion and histologic grade of malignancy, have been reported to be reliable parameters for determining neck metastasis[2,7,8,9]. However, as these are commonly unavailable prior to definitive surgical exploration and/or treatment, making a decision about regional treatment is not possible based on histologic findings.

Although many investigators have attempted to detect occult neck metastasis using various imaging methods, such detection of small occult metastasis has limitations. Certain authors do not accept the usefulness of preoperative imaging such as CT, MRI and ultrasonography[7,10]. In the pre-treatment setting, there exists an obvious need for more reliable imaging parameters that would diminish the risk of occult neck metastasis. This study was thus aimed at identifying a more useful predictor of late neck metastasis on initial contrast-enhanced CT findings.

Materials & Methods

We reviewed the medical records of 144 patients who were treated for squamous cell carcinoma of the tongue and oral floor at the Department of Otolaryngology-Head & Neck Surgery at Hokkaido University Graduate School of Medicine between 1997 and 2006. All patients were initially evaluated by a multidisciplinary team consisting of otolaryngologists and radiation oncologists, and tumors were classified according to the 2002 Union Internationale contre le Cancer (UICC) staging system. The stage of the tumor was determined on the basis of patient history, physical examination, chest x-rays, and CT, MRI and/or ultrasonographic findings. Neck lymph node status of the patient was considered N0 when there were no palpable lymph nodes by physical examination, and the size of any lymph nodes was <1 cm by CT and/or MRI, taking into account the shape of the lymph node and the presence of hilar echoes that were identified on ultrasonography. We also excluded patients with nodes, irrespective of their size, when they exhibited central necrosis on CT imaging.

This study was limited to 38 patients who had either stage I or II carcinoma of the tongue and oral floor and had underwent contrast-enhanced CT scanning before receiving initial treatment. The initial treatment consisted of either primary tumor resection or interstitial radiotherapy without neck dissection. Two patients with late neck metastasis received preoperative (40 Gy) and postoperative (50 Gy) external radiotherapy, respectively. One patient underwent a pull-through procedure with bilateral selective neck dissection (ipsilateral level I, II, III and contralateral level I, II). In this patient, late neck metastasis occurred from outside the dissected area (ipsilateral level IV and contralateral level III). Two patients without late neck metastasis had preoperative external radiotherapy (40 Gy). All of the patients who underwent primary tumor resection had a negative surgical margin, and no patients had local recurrence at the primary site. All patients were closely observed during follow-up, usually at 4-week intervals for the first 2 years. The mean follow-up period was 35 months.

CT examination was performed in the presence of a contrast agent delivered by an IV bolus injection. We obtained axial images of 3-mm thickness from 32 patients, and of 5-mm thickness from the remaining 6 patients, who subsequently had late neck metastasis. When a patient was suspected of having late neck metastasis after the initial treatment, neck dissection was indicated. The metastatic lymph nodes were pathologically identified in the dissected tissue samples. All lymph nodes on initial CT imaging had their area classified according to the criteria proposed by Som et al.[11] On initial CT, the lymph nodes that had subsequently developed neck metastasis were labeled as "occult lymph nodes", while the lymph nodes which had not developed neck metastasis were labeled as "reactive lymph nodes". Topographical correlation was accessed between occult nodes in the initial CT and metastatic nodes in the CT obtained after late neck metastasis was suspected. Metastatic nodes appeared on the CT images were confirmed by surgeons who dissected the neck. We first measured the long-axis diameters of the nodes in the whole neck on these CT images. The short-axis diameter recorded was the length that crossed perpendicular to the long axis of the node. The ratio of long- to short-axis diameter was calculated.

Statistical Analysis. All data were tabulated, and unpaired double-sided t-tests were performed using the Stat View software (version 5.0, Abacus Concepts, Inc., Berkeley, CA) to compare the long-, short-axis diameter and ration of long- to short-axis diameter between 25 "occult" and 136 "reactive" lymph nodes. Results were considered significant when the p value was < 0.05.

Results

Initial CT images of 38 patients (27 male and 11 female, mean age 58 years) were reviewed, and of the 38 patients, 20 had late neck metastasis and 18 did not. Patient characteristics are summarized in Table 1. Eighty-five percent of late neck metastasis had occurred within 2 years of the initial treatment. The average interval was 10 months. All patients without late neck metastasis were followed over 12 months. CT images showed a total of 161 lymph nodes. The number of lymph nodes examined from each patient on CT imaging ranges from 0 to 16, with a median of 4. The number of lymph nodes was not significantly different between patients with and without late neck metastasis (p=0.8). Twenty-five of the 161 lymph nodes developed into late neck metastasis and were labeled the "occult lymph nodes" on the initial CT images. Most of them resided in ipsilateral level I, II and III. Table 2 summarizes the distribution of these lymph nodes. The remaining 136 lymph nodes that did not develop into neck metastasis were considered "reactive lymph nodes". Forty-five metastatic lymph nodes were pathologically identified in the neck dissection. Table 3 summarizes the distribution of these lymph nodes. Therefore, 56% (25/45) of the lymph nodes that were shown to be metastatic by pathologic examination were detected as the "occult lymph nodes" on initial CT images. We labeled 14 (70%) patients as having "occult lymph nodes" on the initial CT images, out of the total of 20 patients who had late cervical metastasis. Comparison between the 25 "occult" and 136 "reactive" lymph nodes revealed significant differences in the short-axis diameters on the initial CT images (p=0.01), as shown in Figure. Setting a criterion of 6 mm in short-axis diameter as being an "occult lymph node" had a sensitivity of 64%, a specificity of 81%, a positive predictive value of 38% and a negative predictive value of 92% for the development of late neck metastasis (Table 4).

Discussion

Previously, it had been reported that the late neck metastasis was one of the risk factors of loco-regional failure for patients with early tongue and oral floor cancer[8,12,13,14]. However, late neck metastasis has recently been successfully salvaged by neck dissection due to advances in imaging and operating technique. Goto et al.[3] examined 90 previously untreated patients with stage I or II tongue cancer who underwent surgical treatment. Thirty-three patients underwent synchronous elective neck dissection (END) at initial surgery, while the other 57 did not. As a result, late neck metastasis had a strong impact on disease-specific survival, whereas loco-regional recurrence failed to have any statistical impact on survival, when the management of the loco-regional area was followed by early diagnosis and adequate salvage surgery. Furthermore 70% of cancer-related deaths were due to distant metastasis. These results indicate that the most important problem to be addressed is the control of patients with distant metastasis, who are free of disease in loco-regional sites. Considering that the possibility of distant metastasis might increase when there is neck node involvement[5,6], identifying the risk factors for late neck metastasis in early tongue and oral floor cancer is important for providing an accurate prognosis and for achieving higher survival rates.

The role of supraomohyoid neck dissection as a prophylactic dissection is widely accepted as the appropriate elective procedure for patients with early oral cancer[15,16,17]. In addition, it can provide precise pathologic staging of the neck nodes and other important information, such as the presence of metastatic lymph nodes and extracapsular spread in the patients who have the greatest risk and need for postoperative radiotherapy and/or chemotherapy. Duvvuri et al.[18] reported on 359 previously untreated patients with T1/T2N0 cancer of oral cavity and oropharynx, who were treated with resection of primary tumor, followed by either observation or END. This study indicated that END significantly improved regional control and regional recurrence-free survival, but, when compared with observation of the neck, END did not improve overall survival. Though Weiss et al.[19] recommended END when the risk for occult metastasis is estimated to exceed 20%, given that END itself entails low morbidity, it produces unnecessary morbidity in some patients without occult metastasis. Therefore, we prefer to use “wait-and-see” policy rather than prophylactic neck dissection.

Many authors reported the pre-treatment evaluation of neck lymph nodes in patients with head and neck cancer using CT, MRI, ultrasonography, positron emission tomography (PET) or a combination thereof. Ultrasonography is the most appropriate imaging to depict the lymph nodes because of its improved ability to delineate not only shape and size, but also changes in the internal architecture of the nodes. Furthermore, the lack of a requirement for radiation and low cost may be major advantages. It is also the only available imaging technique that can be used for frequent routine follow-up. However, it takes more time than CT and the accuracy of diagnosis is operator dependent. van den Brekel et al.[19,20] obtained a sensitivity of 73% and a specificity of 100% in N0 necks with the use of ultrasound with ultrasound-guided fine-needle aspiration biopsy. However, in a multicenter study Takes[22] and others[23,24] could not achieve such good results. In addition, these techniques are time-consuming. Therefore, these findings led us to investigate whether we could identify a more useful predictor of late neck metastasis with early tongue and oral floor cancer in initial contrast-enhanced CT imaging.

CT criteria for assessing neck lymph node metastasis are based on nodal size and shape, presence of central necrosis and presence of a localized group of nodes in an expected node-draining area for a specific primary tumor[25]. Central necrosis is the most reliable finding on contrast-enhanced CT, and it has been reported to have a specificity of 100%[26]. However, this finding is considered to be a biologically late event in the evolution of a tumor within a lymph node[27], and it occurs primarily in lymph nodes approximating 20.0 mm or greater[28]. It is also quite rare and not often visible in small lymph nodes[29,30]. The generally used upper limit of normal for the greatest nodal diameter is 1.5 cm for level I and II nodes, and 1 cm for all other levels. van den Brekel et al.[26] measured the short- and long-axis diameters, and the longitudinal diameter for all dissected lymph nodes of 71 necks from 55 patients with carcinoma of the upper aerodigestive tract. The short-axis diameter proved to be the most valid size criterion in predicting a metastatic node. They proposed that the most effective size criterion was a short-axis diameter exceeding 11 mm in level II and 10 mm in all other levels. However, these size criteria were defined for all stages of disease in patients with head and neck cancer, and not limited to the patients with a clinical N0 stage neck. Subsequently, van den Brekel et al.[31] measured lymph node sizes of 184 patients with head and neck cancer using preoperative ultrasonography, In this study, the patients underwent a total of 248 neck dissections. Comparing the short-axis diameter of the 117 patients with and 131 patients without palpable neck metastasis, the best adjustment of the size criteria for all 248 necks was not appropriate for patients without palpable neck metastasis. This result indicated that lymph node size criteria for patients with clinically N0 necks should be discussed separately from those for patients with clinically positive necks.

In our analysis of patients with early tongue and oral floor cancer, short-axis diameter of lymph nodes showed a statistically significant difference between “occult” and “reactive” lymph nodes. The other size criteria tested, such as long-axis diameter and ratio of long- to short-axis diameters, were not found to be statistically significant predictors. Therefore, we propose that a short-axis diameter of 6 mm on CT findings represents the optimal compromise between sensitivity and specificity in patients with early tongue and oral floor cancer. Furthermore, our results also make it likely that these optimal size criteria of a short-axis diameter will detect a difference between patients with all N stages and those with a clinical N0 stage on CT imaging.

The intention of this article is not to suggest that decision regarding the treatment plan should be based on one approach over another, but rather to encourage clinicians to refer to these results during follow-up. The use of any single imaging modality by itself is neither sensitive nor specific enough to reliably identify the patients most likely to develop late neck metastasis. It remains important that patients with early tongue and oral floor cancer are observed closely, and not lost to follow-up. This will allow early detection of metastatic lymph nodes and reduce the likelihood of the existence of very advanced neck disease at first detection.

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Figure Legend.

Comparison of lymph node size. This Box Plots indicate the distribution of 25 “occult (solid circles)” and 136 “reactive (open circles)” lymph nodes in the long-, short-axis diameter and ration of long- to short-axis diameter. Note a significant difference in short-axis diameter (p=0.01).

Table 1
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Table 1: Descriptive statistics of study cohort

	No. in group (%)		
	Patients with LNM*	Patients without LNM*	Total
Number of patients	20	18	38
Gender			
Male	14 (70)	13 (72)	27 (71)
Female	6 (30)	5 (28)	11 (29)
Age			
Range	60	56	58
Median	28-82	33-78	28-82
T Stage			
I	9 (45)	8 (44)	17 (45)
II	11 (55)	10 (56)	21 (55)
Primary Subsite			
Tongue	17 (85)	17 (94)	34 (89)
Oral floor	3 (15)	1 (6)	4 (11)

*late neck metastasis

Table 2
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Table 2: Distribution of lymph nodes on CT

	Ipsilateral		Contralateral	
Level	No. Lymph node	No. (%) Occult	No. Lymph node	No. (%) Occult
I	43	6 (14)	-	-
II	31	8 (26)	19	2 (11)
III	22	7 (32)	17	1 (6)
IV	14	1 (7)	13	0 (0)
V	2	0 (0)	0	0 (0)

Table 3
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Table 3: Distribution of metastatic lymph nodes

	Ipsilateral	Contralateral
Level	No. Lymph node	No. Lymph node
I	8	-
II	16	2
III	14	2
IV	2	0
V	1	0

Table 4
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Table 4: Sensitivity, specificity, PPV and NPV of different size criteria

Minimum Axial Diameter, mm	Sensitivity, %	Specificity, %	PPV*, %	NPV**, %
5	80	43	20	92
6	64	81	38	92
7	20	91	29	86

* Positive predictive value

** negative predictive value

Figure
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