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The Value of Sentinel Lymph Node Biopsy in Oral Cavity Cancers

Original Investigation

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Abstract

Objective: The aim of this study was to establish the effectiveness of sentinel lymph node biopsy in the detection of metastasis in N0 necks of T1-T2 early-stage oral cavity cancers.

Materials and Methods: Twenty neck dissections were performed in 18 patients diagnosed with T1 and T2 oral cavity cancer, with an indication for elective neck dissection between November 2007 and January 2011. The male to female ratio was 12:8, with a mean age of 54.5 years (range 28-76). Eight of the dissections were performed for lower lip cancer, 7 for tongue cancer, and 5 for floor of the mouth cancer. Sentinel lymph node biopsy was used to detect metastatic lymph nodes. Tc99m radionuclide injection was administered to the periphery of the tumor 24 h before the operation, and a lymphoscintigraphy image was obtained 30 min after the injection. Sentinel lymph nodes were localized and excised on the day of surgery using static lymphoscintigraphy images and a gamma probe. Sentinel lymph nodes were sent for a frozen section examination, and either a selective or a comprehensive neck dissection was performed for each neck according to the results.

Results: After the final histopathological examination of the specimens, the negative predictive value, the positive predictive value, the accuracy of the sentinel lymph node biopsy, and frozen section accuracy were found to be 100%.

Conclusion: Sentinel lymph node biopsy was found to be an efficient method in the pathological staging and management of the N0 neck in early T-stage oral cavity cancers.

Keywords: Oral cavity, carcinoma, sentinel lymph node biopsy, lymphatic metastasis, neck dissection, squamous cell carcinoma

Introduction

Oral cavity cancer accounts for 3% of all new cancers in males and 2% in females. Oral cavity cancers generally require elective treatment of the neck because of a high rate of occult metastasis (1). Classical teaching suggests an elective treatment of the neck, where the risk of occult metastasis is 20%–30% or more (2). Although the wait-and-see method was used from time to time, it has never gained wide acceptance. The most important point for the implementation of this method is the high number of unnecessary elective neck dissections. However, follow-up of the patients with occult metastasis using the wait-and-see method may significantly worsen the prognosis after the treatment of patients who developed clinically evident metastasis (3). Neck metastasis is generally diagnosed at the N2 stage, and more aggressive treatments need to be applied in this case. Regardless of the treatment modality, the regional tumor control becomes more difficult. Regional control rates are reported to be 30%–50% in this situation (4, 5).

When patients with an occult metastasis risk higher than 20% undergoes neck dissection, a certain proportion of the patients are inevitably treated with unnecessary neck dissections Therefore, screening methods for occult metastasis have been investigated. Radiological screening methods constitute an important place among these methods. Because of the insufficient sensitivity and specificity values of these methods, accurate neck staging does not reach the desired level (6, 7). Sentinel lymph node biopsy (SLNB), which is recently being used on a routine basis in breast cancer and malignant melanoma, is now used to examine head and neck cancers.

This method is based on the idea of lymphatic flow from the cancerous tissue following a certain direction and draining to a certain lymph node or a group of lymph nodes. This lymph node or these lymph nodes are the first (sentinel) lymph nodes where the lymphatic metastasis will occur. Detection and evaluation of these lymph nodes for metastasis will provide us accurate information regarding the status of the neck (8).

Neck dissection is performed in most of the T3-T4 stage oral cavity cancers because a neck metas-

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tasis is generally present or the risk of occult metastasis is very high. The aim of this study was to establish the effectiveness of SLNB in the detection of metastasis in N0 necks of T1-T2 early stage oral cavity cancers.

Methods

This study was conducted at a tertiary medical center between November 2007 and January 2011 in concordance with the international ethical standards and the guidelines laid down by the World Health Organization and the Declaration of Helsinki. Twenty SLNBs of 18 patients with primary oral cavity squamous cell carcinoma were retrospectively reviewed.

Patients were informed about SLNB before the procedure, and their informed consents were obtained. Demographic data and data regarding the detection of the SLN, localization, number of lymph nodes, results of the histopathological examination of the frozen section, results of the histopathological examinations of both SLNs and neck dissection specimens, type of neck dissection, and treatment of the primary tumor was obtained from patient records.

The selection criteria for SLNB were as follows:

1. Histopathologically proven oral cavity cancer
2. Clinical N_0 stage
3. Indication to perform an ipsilateral or bilateral elective neck dissection

Patients showing the presence of any contraindication to the use of radionuclide injection or those not giving their consent to undergo SLNB were excluded from the study. Patients were designated as clinically and radiologically N_0, with no palpable neck nodes during manual palpation, ultrasound, and/or computed tomography (CT) of the neck.

While choosing the type of neck dissection, our routine management of the N_0 neck was used by taking the localization and stage of the primary lesion into consideration. According to our protocol, levels I–III are dissected in lower lip and floor of the mouth cancers, whereas levels I–IV are dissected in tongue cancers.

For the injection of radionuclide to the oral cavity lesions, Tc99m-labeled nanocolloid (Nanocoll, Nycomed Amersham Sorin®, particle diameter 95% <80 nm) was injected 24h before the operation. Four radionuclide injections were administered to the periphery of the tumor by taking the lymphatic drainage pattern of the anatomic localization into account. In total, 0.4 MCurie (0.2 mL) Nanocoll injection was administered to each point with a 1-cc tuberculin syringe. The injection was administered submucosally, and to prevent the agent from passing into the microcirculation, the plunger of the syringe was withdrawn to check for a false entry to a vessel. In addition, care was taken to avoid creating a high submucosal pressure therefore causing this high pressure for the agent to leak into the capillary vessels. Pain during the injection was considered as the most important finding of high submucosal pressure. Because the injected agent partially leaks through the needle insertion point with some bleeding, patients were asked to rinse their mouth with cold water for 10 min and not to swallow the agent. No local anesthetics were used to limit the increase in the submucosal interstitial pressure of the Tc99m-labled nanocolloid injection site. To standardize the procedure, all the injections were administered by the same investigator.

Procedures were conducted according to the radiation safety rules. Radiotracer injections were made in the nuclear medicine department, where favorable conditions for the use of radioactive material were present.

Preoperative lymphoscintigraphy was performed 30 min after the injection procedure was conducted. Lymphoscintigraphy was acquired in the anterior–posterior projection in the nuclear medicine department with the Toshiba GCA602A (Toshiba Co, Tokyo, Japan) scintigraphy device. Preoperative static lymphoscintigraphy images were acquired. SLNs were localized and excised on the day of surgery using static lymphoscintigraphy images and a gamma probe (Crystal Photonics GmbH, Berlin, Germany). The primary lesion was resected before SLNB. The purpose of this was to eliminate the shadowing effect of the primary lesion. Thus, we aimed to facilitate the search for the SLN with the gamma probe. A scan was performed in the Tc99m window. Lymph nodes were considered as a sentinel node if they were in the same localization area as the scintigraphy image and having radiation over 400 firings or higher detected by the gamma probe and 10% of the brightness was remained in the region of removal.

Detected SLNs were sent for frozen sections. Neck dissection was extended as necessary if the frozen pathology was reported positive for malignancy and if the patient was N positive.

Histopathological examination of every SLN was performed with two sections using hematoxylin and eosin stain during frozen sections and sections of 0.10 mm during permanent paraffin examination using hematoxylin eosin stain and immunohistochemistry.

For the effectiveness of the method, parameters such as the histopathological examination results of the SLNs sent for frozen biopsy, paraffin results of the SLNs, and final histopathological examination results of the neck dissection specimens were evaluated. Using these criteria, this method's detection rate of the SLNs, negative predictive value, positive predictive value, and the consistence of the histopathological examination results of frozen and permanent paraffin sections were calculated. Statistical analysis was performed using a computer software [Statistical Package for the Social Sciences (SPSS) version 22.0, SPSS Inc. Chicago, IL, USA].

Results

Eighteen patients were included in the study. Because two of the patients underwent bilateral neck dissections at the time of surgery, a total of 20 neck dissections were performed. Examina-

Table 1. Data of the 18 patients who underwent 20 neck dissections

Patient number	Gender	Age (years)	Tumor localization	T stage	Neck dissection levels	Frozen section: Number of metastatic lymph nodes/number of dissected SLN	Final histopathological examination: Metastatic lymph nodes/ number of dissected lymph nodes for each specimen
1	M	33	Lower lip	2	I–III	0/3	0/12
2	M	64	Lower lip	2	I–III	0/5	0/2
3	F	76	Tongue	1	I–IV	0/3	0/26
4	F	28	Tongue	1	I–IV	0/3	0/14
5	F	76	Floor of the mouth	2	I–III	0/5	0/19
6	F	46	Floor of the mouth	2	I–III	0/3	0/5
7	F	46	Floor of the mouth	2	I–III	0/3	0/4
8	M	59	Tongue	2	I–V	3/5	2/23
9	F	50	Tongue	2	I–V	1/4	0/13
10	F	63	Lower lip	2	I–III	0/4	0/20
11	M	68	Lower lip	2	I–III	0/3	0/15
12	M	47	Lower lip	2	I–III	0/2	0/9
13	M	55	Lower lip	2	I–III	0/2	0/12
14	M	70	Lower lip	2	I–III	0/3	0/16
15	M	70	Lower lip	2	I–III	0/1	0/16
16	M	59	Tongue	2	I–III	2/3	0/18
17	F	59	Tongue	2	I–III	1/2	0/15
18	M	47	Tongue	2	I–V	2/4	0/17
19	M	53	Floor of the mouth	2	I–III	0/4	0/22
20	M	54	Floor of the mouth	2	I–III	0/4	0/17

M: male; F: female; T: tumor; SLN; selective neck dissection

tions were performed according to the number of neck dissections to prevent confusion because SLNBs were performed for each side of the neck dissections. Male to female ratio was 12:8, with a mean age of 54.5 years (range 28–76).

Eight of the dissections were performed for lower lip cancers, 7 for tongue cancers, and 5 for floor of the mouth cancers. All of the lower lip cancers were T2 lesions. Two of the tongue cancers were T1 and five were T2 lesions. Five floor of the mouth cancers had T2 lesions. Data regarding the cases are presented in Table 1.

Peroperative SLNs could be dissected in all of the included patients. Fifteen patients were pathologically N0, and five of the patients were N positive.

The minimum and maximum number of lymph nodes (excluding SLNs) harvested from the specimens were 2 and 26, respectively (mean 18.05, total 361 nodes). Eleven (3%) were malignant. Four out of 18 patients (22%) and 5 out of 20 necks (20%) had positive regional lymph nodes. All of the patients with positive lymph nodes had tongue cancer.

Sixty-six SLNs were excised from 20 necks. One to five SLNs were found in each patient. Of these nodes, 26 (39%) were in level I, 26 (39%) in level II, 11 (16%) in level III, and three (4%) in level IV. Nine (13%) of these SLNs were malignant. Two of the malignant lymph nodes were in level I, five in level II, one in level III, and one in level IV. The occult metastasis rate was found to be 22% in our series, and it was possible to establish an accurate staging using only the SLNB and frozen section method.

No false-positive or false-negative results were found in any of the patients. One patient out of the five positive necks had a positive lymph node other than the SLNs. The other four only had SLN positivity. The negative predictive value was 100%, positive predictive value was 100%, and accuracy of the frozen results were 100% in our study (Table 2).

Discussion

Management of the N_0 neck in oral cavity squamous cell carcinoma is still controversial, similar to that in most of the head and neck squamous cell carcinomas. One of the reasons of this controversy is the frequent regional recurrence and the inadequacy of salvage surgery in the case of recurrence. On the other hand, the

Table 2. Comparison of the frozen section examinations of sentinel lymph nodes with the histopathological examination of the neck dissection specimens

		Sentinel lymph node + frozen section	
		Negative	**Positive**
Histopathological examination of the neck dissection specimens	Positive	0	5
	Negative	15	0

additional morbidity and cost by the unnecessary routine treatment of the clinical N_0 patients is another topic of debate (3). Developing a method that accurately distinguishes pathologic N_0 patients from clinically N_0 patients may be a solution to this issue (9). A technique to overcome this issue had been investigated in the field of radiology. However, none of the radiological techniques had adequate sensitivity and specificity for the detection of occult metastasis; thus, none of them could find a place in the routine screening protocols (6, 7). The most important feature expected from an ideal screening method for occult metastasis in head and neck cancers is a high negative predictive value. This value shows the error margin in a negative neck. This value has a mean of 96% according to the literature when all of the head and neck cancer SLNB reports were interpreted (10, 11).

In our study, the detection of SLN rate was found to be 100%, which supports the accuracy of our lymph node screening method. SLNB procedures used in oral cavity and oropharynx lesions have a reported SLN detection rate of 97% (12-16). Because there were no false-negative results in our study, we had a negative predictive value of 100%. This value has a reported rate of 95%, which is compatible with the previous reports (11).

We had no false-positive results, which makes a positive predictive value of 100%. This shows 100% avoidance from unnecessary treatments due to misstaging. Therefore, additional morbidity and cost is lowered, and a burden on the patient and on the healthcare system is reduced.

There had been six international meetings on head and neck SLNB. In the first one (Glasgow, May 2002), 22 institutions shared their SLNB experiences on 316 patients (17). SLN was found in 301 (95%) of the patients. Of these 301 cases, 76 were N positive and 225 were negative. The sensitivity of the SLNB was reported to be 90%. The sensitivity of the SLNB was found to be 57% in institutions with an experience of less than 10 patients and 94% in institutions with an experience of more than 10 patients. In conclusion, SLNB was accepted as an effective method of neck dissection in staging of the neck (11).

The Second International Conference on Sentinel Node Biopsy in Mucosal Head and Neck Cancer was held in September 2003 in Zurich. In this meeting, 20 institutions reported their experience with 379 clinically N_0 patients. SLN was found in 366 (97%) patients. Of the 366 patients, 103 (29%) were found to be N positive and 263 (71%) were found to be N negative. Eleven (4% false-negative results) of the 265 N negative patients were found to be N positive on definite pathology. The negative predictive value of the negative SLNB was found to be 96% (11). Pedersen reported the largest single-center study of 253 SLNB with a false-negative rate, sensitivity, and negative predictive values of 5%, 88%, and 95%, respectively (18). In another recent study, the neck control rate was as high as 97% in SLN-negative and 95% in SLN-positive patients (19). In addition, they reported a sensitivity rate of 80% and negative predictive value of 88%.

SLNB with frozen section could not detect all of the metastatic lymph nodes in our study. Therefore, neck dissection needs to be extended in SLN-positive cases. Because the high risk of metastasis in T3-T4 cases, we suggest that neck dissection is mandatory for oncologic safety. Therefore, we thought that it was appropriate to perform the SLNB only in patients with T1-T2 N0 oral cavity cancer.

Conclusion

In conclusion, SLNB could be used in the staging of the neck in oral cavity cancers. However, larger series are warranted for the routine application of this method. The predictive value of the sentinel sampling for regional spread can be assessed with a prospective study including the long-term follow-up results of the patients in further studies.

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Informed Consent: Written informed consent was obtained from patients who participated in this study.
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