Clinical Paper
Head and Neck Oncology

First signs of late-presenting cervical lymph node metastasis in oral cancers during follow-up

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Abstract. One of the most important prognostic factors in oral squamous cell carcinoma (OSCC) is the presence of lymph node metastasis. Therefore, the early detection of late-presenting cervical lymph node metastasis is important. Although many studies have assessed diagnostic modalities for detecting metastatic cervical lymph nodes, no study has evaluated the process, especially first signs, for detecting late-presenting cervical lymph node metastasis. A retrospective analysis comparing methods for detecting the first signs of late-presenting lymph node metastasis was performed. A total of 65 OSCC patients were assessed. These patients were identified retrospectively as having presented late metastasis during follow-up after initial treatment with curative intent. The findings of four detection methods were analyzed: palpation, ultrasonography, computed tomography, and subjective symptoms. The numbers of cases identified by each method were as follows: palpation, 31 (47.7%); ultrasonography, 17 (26.1%); computed tomography, 12 (18.5%); and subjective symptoms, 5 (7.7%). Palpation played a major role in the discovery of late-presenting lymph node metastasis. In contrast, metastatic lymph nodes were detected by other methods in about half of the cases. The results suggest a possible stratification of the various methods used for metastatic lymph node detection, depending on the characteristics of individual cases.

The presence of lymph node metastasis is the most important prognostic factor in squamous cell carcinoma of the head and neck region (HNSCC),[1] including oral squamous cell carcinoma (OSCC). It is generally accepted that cervical lymph node metastasis in patients with OSCC indicates a poor prognosis.[2] Survival is poorer in patients with cervical lymph node metastasis than in those without, and the possibility of distant metastasis increases when there is cervical node involvement.[3] Thus, optimal management of cervical lymph node metastasis is very significant in improving survival. Follow-up examination of the neck after primary treatment is particularly important. The National Comprehensive Cancer Network (NCCN) guidelines version 1.2015 for head and neck cancers provide recommendations only for the duration of follow-up.[4] There are no recommendations regarding modalities for the detection of cervical lymph node metastasis;

moreover, it has been observed that the patients themselves report most recurrences.[4]

Generally, the existence of late-presenting cervical lymph node metastasis is suspected based on palpation and is subsequently confirmed by computed tomography (CT), magnetic resonance imaging (MRI), ultrasonography (US), or positron emission tomography (PET). Neck dissection is then planned and performed based on these findings. However, not all cases of late-presenting cervical lymph node metastasis are detected using palpation as the only method. In some cases, metastatic lymph nodes are diagnosed for the first time by modalities other than palpation. Many studies have addressed the accuracy, specificity, and sensitivity of each mode of diagnosis of cervical lymph node metastasis in oral cancers.[5–8] However, no study has examined the process leading to the discovery of late-presenting cervical lymph node metastasis in these malignancies. In the present study, a retrospective analysis was conducted with emphasis on the process, especially first signs, for detecting late-presenting cervical lymph node metastasis.

Patients and methods

A total of 65 patients with OSCC were assessed. These patients were identified retrospectively as having presented late metastasis during follow-up after initial treatment with curative intent. They had undergone neck dissection for late-presenting cervical lymph node metastasis in the Department of Maxillofacial Surgery, Tokyo Medical and Dental University (Tokyo, Japan) between 2008 and 2012. All study protocols were reviewed and approved by the Research Ethics Committee of Tokyo Medical and Dental University. Informed consent was obtained from all participants in accordance with the institutional guidelines. The cohort comprised 42 men and 23 women, with an average age of 61.4 years.

In the study department, oral cancer patients are usually followed up by a team of doctors, rather than by a single oral surgeon, as per the following protocol: once every 1–2 weeks from the time of hospital discharge to 6 months after discharge; once every 2–4 weeks from 6 months after discharge to 1 year after discharge; once every 1–2 months from 1 year to 2 years after discharge; and once every 2–6 months at more than 2 years after discharge.

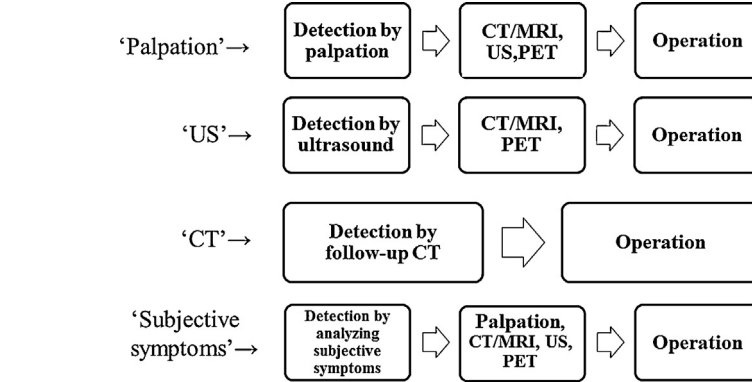Palpation was performed at every follow-up visit and by more than one oral surgeon. Palpation of the neck was done thoroughly, first anteriorly to screen for levels Ia and Ib, and then posteriorly to screen for levels IIa, IIb, and III, after exposing the neck down to the level of the clavicle bilaterally. This was done to determine the presence or absence of enlarged lymph nodes.

CT examinations were performed using a Somatom Sensation 64 scanner (Siemens AG, Forchheim, Germany). All patients received 1 mg/kg non-ionic water-soluble iodine-containing contrast agent. Contiguous axial CT sections (3/3 mm) were taken from the base of the skull to the level of the clavicles. The lymph nodes were assigned similar levels to those of clinical examination. Criteria for the CT assessment of lymph nodes based on the presence or absence of central nodal necrosis and a minimal axial diameter of 10 mm were followed[9]. During follow-up, CT examinations were performed at 1, 3, 6, and 12 months postoperative. After 1 year, patients underwent CT once or twice per year.

Ultrasound examinations were performed using an Aloka model SSD-5500 ultrasound system (Aloka, Tokyo, Japan) with a 7.5-MHz probe. Metastatic lymph nodes were diagnosed according to the ultrasonographic lymph node metastasis criteria proposed by Furukawa and Furukawa.[10] These criteria included the thickness of the lymph node (>6 mm or not) and existence or not of intra-lymph node space-occupying lesions suspected of having a metastatic focus. US examinations were performed at the time of discharge and between CT examinations.

The detection of occult cervical lymph node metastasis in oral cancer patients was performed using the following four methods: palpation, US, CT, and subjective symptoms. 'Palpation' refers to the cases in which palpation gave the first sign of occult metastasis. In such cases, the findings were confirmed using imaging modalities, including CT, US, or PET. Accordingly, 'US' refers to cases in which lymph node metastasis was first detected by US. 'CT' indicates the first detection of lymph node metastasis by CT. 'Subjective symptoms' refers to cases where subjective symptoms such as pain and swelling were the first sign of the occurrence of metastatic lesions (Fig. 1). In this study, the four methods were compared using clinical parameters including the region of the metastatic lymph nodes,[11] the minor axis of the metastatic node, and body mass index (BMI).[12,13] All four of these clinical parameters may affect the diagnosis of late cervical lymph node metastasis.

Whenever lymph node metastasis was first detected by US or CT, the minor axis of the metastatic lymph node was measured in each image. When lymph node metastasis was first detected by palpation or subjective symptoms, CT or US was performed as soon as possible, and the minor axis of the lymph node metastasis measured. In this study, a lymph node minor axis measurement cut-off value of 10 mm was used.[10] All diagnoses of lymph node metastasis were confirmed histopathologically after neck dissection. A BMI cut-off value of ≥ 25 kg/m^2 was used in this study, based on the reference values determined by the Japan Society for the Study of Obesity (JASSO).[14]

Results

On assessing the first signs for the discovery of occult cervical lymph node metastasis, the numbers of cases identified by each method were as follows: palpation, 31 (47.7%); US, 17 (26.1%); CT, 12 (18.5%); and subjective symptoms, 5 (7.7%) (Fig. 2).

Fig. 1. The four methods used for the detection of late-presenting cervical lymph node metastasis in oral cancer: palpation, ultrasound (US), computed tomography (CT), and subjective symptoms.