Int. J. Oral Maxillofac. Surg. 1995; 24: 356–360
Printed in Denmark . All rights reserved

International Journal of
Oral & Maxillofacial Surgery
ISSN 0901-5027

Pitfalls in the treatment of delayed lymph-node metastases after control of small tongue carcinomas

Hiroshi Kurita, Kenji Kurashina, Toshikazu Minemura, Akira Kotani
Department of Dentistry and Oral Surgery, Shinshu University School of Medicine, Matsumoto, Japan

H. Kurita, K. Kurashina, T. Minemura, A. Kotani: Pitfalls in the treatment of delayed lymph-node metastases after control of small tongue carcinomas. Int. J. Oral Maxillofac. Surg. 1995; 24: 356–360. © Munksgaard, 1995

Abstract. Between 1985 and 1992, 13 patients were treated for delayed lymph-node metastases that developed after obtaining control of primary lesions of the tongue. These lesions were treated primarily by radiotherapy or surgical resection; cervical metastases were treated mainly by delayed radical neck dissection (RND). Seven of the 13 patients survived with no evidence of recurrence. The other six patients developed tumors in the neck, and five of these patients died due to uncontrollable disease. In all but one patient, recurrence appeared between the site of the primary lesion and the region of RND, the oral floor and/or the parapharyngeal space. None of the patients with recurrence received radiotherapy in the area between the primary lesion and the site of RND. In contrast, there was no recurrence in patients who received external irradiation to the primary lesion and upper cervical lymph nodes. This review emphasizes the need to direct more attention to the area between the site of the primary lesion and the regional lymph nodes in patients receiving treatment for delayed metastases associated with small carcinomas of the tongue.

Key words: tongue; carcinoma; lymph-node metastasis; radical neck dissection; radiotherapy.

Accepted for publication 15 June 1995

Because of the rich lymphatic drainage of the tongue, occult lymph-node metastases occur in 23% to 66% of patients with small tongue carcinomas (stages I or II), and the salvage rate in these patients is poor[3,6,8,12,17,18].

Stage I or early stage II primary tumors of the tongue often can be treated with radioactive implants. Delayed lymph-node metastases are frequently treated by radical neck dissection (RND), independently of the primary lesion. However, little attention has been paid to the area between the primary lesion in the tongue and the regional lymph nodes, the site of the local lymphatic drainage system ("untreated area", Fig. 1). We previously reported

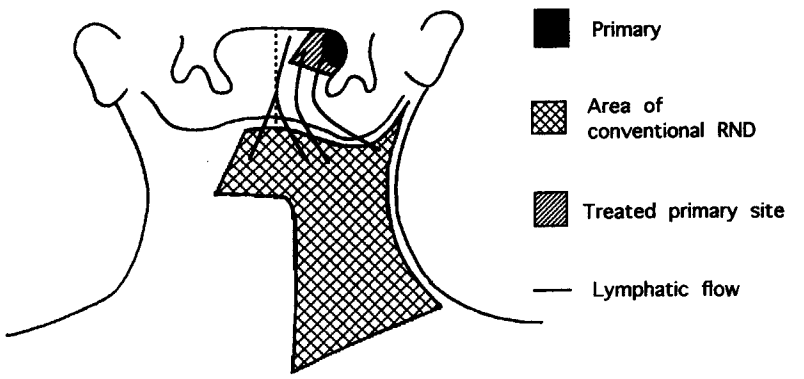

Fig. 1. Schematic representation of treated primary site, surgical area of conventional radical neck dissection (RND), and regional lymphatic flow. When primary lesion and neck metastases are treated separately, area between them remains "untreated".

the recurrence of stage I tongue carcinomas in the cervical region of patients who underwent delayed RND[10]. All recurrence appeared in the "untreated area" (the oral floor and/or the parapharyngeal space). These results suggest "pitfalls" in procedures currently employed to prevent cervical recurrence. We therefore retrospectively analyzed the duration of survival and the causes of recurrence in patients who developed delayed lymph-node metastases after obtaining control of small primary lesions of the tongue.

Material and methods

Between 1985 and 1992, 16 patients were treated for delayed lymph-node metastases that developed after control of stage I or II squamous cell carcinomas of the mobile part of the tongue. All tumors were less than 4 cm in diameter, and there were no clinically palpable lymph nodes. The patients included seven men and nine women, ranging in age from 44 to 87 years (mean: 66.3 years). Seven patients had T1 lesions (tumor diameter: ≤2 cm), and nine had T2 lesions (tumor diameter: 2–4 cm). The primary tumors were well-differentiated in 10 patients, moderately differentiated in five, and poorly differentiated in one. For treatment of the primary lesion, 11 patients received radioactive needle implants alone. Four patients with somewhat advanced T2 tumors (tumor diameter: 3–4 cm) received a combination of interstitial irradiation and external irradiation. The external radiation field included the site of the primary lesion and the high cervical lymphatic chain, and each patient received a dose of 18–36 Gy before interstitial irradiation. Only one patient underwent surgical resection alone.

Latent lymph-node metastases were detected between 1 and 24 months after initial treatment. Twelve of the 16 patients (75.0%) developed cervical nodal metastases within less than 6 months. All lesions except one were located in the area of the ipsilateral level I or level II nodes. One patient simultaneously developed contralateral neck metastases. According to the N-classification (UICC, 1987), four patients were N1 (ipsilateral side, less than 3 cm and solitary), three were N2a (ipsilateral side, 3–6 cm and solitary), eight were N2b (ipsilateral side, multiple lymph-node involvement and less than 6 cm), and one was N2c (both sides or contralateral side and less than 6 cm). On examination, most nodes had decreased mobility.

Several methods were used to treat the metastatic nodal lesions. Seven patients underwent conventional RND alone. Five patients underwent RND with external radiotherapy. Preoperative radiation (dose: 20–50 Gy) was administered to the site of the primary lesion and the entire ipsilateral neck in two patients until the time of RND. Postoperative radiation was administered to three patients because of close proximity of the tumor to the resection margin. A total dose of 50–60 Gy was delivered to the surgical field alone. The primary site and higher cervical lymphatics were not included in the radiation field. One patient underwent *en bloc* resection of the cervical lymph nodes and primary lesion by the pull-through technique, because there was a risk of remaining primary tumor. However, there was no evidence of recurrence on histopathologic examination of surgical specimens. Three patients, including one with bilateral metastases, could not be treated satisfactorily because of other diseases (double cancer in two, severe diabetes mellitus in one), and they died from their neck tumors. The remaining 13 patients were closely followed until death (or the last available record). The patients underwent a mean follow-up period of 32.5 months after the second treatment. The characteristics of the patients are shown in Table 1.

Results

Seven of the 13 patients are currently well with no signs or symptoms of disease. Cervical recurrence developed in the other six patients after they received treatment for metastatic neck disease. Only one patient with recurrence survived; all others died of their neck disease. In all but one of these patients, cervical recurrence was located in the oral floor and/or parapharyngeal space (Fig. 2). In the other patient (no. 11), recurrence appeared at the site of cervical resection.

Treatment algorithms and outcomes are shown in Fig. 3. Nine patients received no treatment of the area between the primary and regional lymph nodes, either at the time of their initial treatment or their recurrences ("untreated" patients: nos. 1–6, 9–11). Of these pa-

Table 1. Patients, treatments, and survival status

Patient no.	Age (years)	Sex	T-classification	Histologic grade of primary tumor	Initial treatment	Duration between end of initial treatment and delayed metastasis	N-classification	Treatment of metastatic neck	Status after treatment of metastatic neck follow-up period)
1	51	F	T1	Well	Brachy	6 months	N2a	RND	NED(4Y)
2	68	M	T1	Well	Brachy	3	N2b	RND	NED(4Y1M)
3	83	F	T2	Well	Brachy	3	N1	RND	NED(1Y2M)
4	54	M	T1	Well	Brachy	5	N2b	RND	NeckRel→Ao(7Y1M)
5	45	M	T1	Mode	Brachy	4	N2b	RND	NeckRel→Dn(1Y4M)
6	87	F	T1	Mode	Brachy	7	N2b	RND	NeckRel→Dn(4M)
7	61	F	T2	Well	Brachy	2	N1	ExtRad→RND	NED(2Y6M)
8	78	F	T2	Well	Brachy	6	N2b	ExtRad→RND	NED(1Y4M)
9	77	F	T1	Well	Brachy	24	N1	RND→ExtRad	NeckRel→Dn(1Y7M)
10	51	M	T2	Poor	Brachy	6	N2b	RND→ExtRad	NeckRel→Dn(3M)
11	75	M	T1	Mode	Resection	3	N2a	RND→ExtRad	NeckRel→Dn(5M)
12	74	F	T2	Well	ExtRad→Brachy	9	N1	RND	NED(7Y1M)
13	63	F	T2	Well	ExtRad→Brachy	2	N2b	EnblocRes	NED(4Y1M)
14	59	M	T2	Well	Brachy	1	N2b	Not fully treated	
15	62	M	T2	Mode	ExtRad→Brachy	4	N2c	Not fully treated	
16	73	F	T2	Well	ExtRad→Brachy	8	N2a	Not fully treated	

Brachy: brachytherapy; ExtRad: external irradiation; EnblocRes: *en bloc* resection of both tongue and metastatic neck (pull-through); NED: no evidence of disease; NeckRel: neck relapse; Ao: alive free of carcinoma; Dn: died of neck failure; Well: well-differentiated type; Mode: moderately differentiated type; Poor: poorly differentiated type.

Fig. 2. Computed tomogram showing neck recurrence in parapharyngeal space (arrow) after therapeutic radical neck dissection.

tients, five developed neck recurrences in the oral floor and/or parapharyngeal space. In contrast, no recurrence appeared in the patients who received external radiation to both the primary lesion and upper cervical chain or the patient who underwent a "pull-through" operation ("treated" patients: nos. 7, 8, 12, 13). The difference in the incidence of the secondary neck recurrence between the "treated" and "untreated" patients was statistically significant (Fisher's exact probability test, $P=0.0485<0.05$).

The distribution of the T- and N-classifications and the histologic grades of these 13 patients are also shown in Fig. 3. "Treated" and "untreated patients" did not differ significantly in the distribution of histologic grades and N-classification. However, there was a statistically significant difference in the distribution of T-classification (Fisher's exact probability test, $P=0.021<0.05$). Five of seven patients with T1 tumors had secondary neck tumor, in contrast to only one of the six patients with T2 tumors. Four T2 patients who received external irradiation to the upper cervical area remained free of neck disease.

According to histologic grade, four of five patients with poorly or moderately differentiated tumors suffered secondary neck disease, in contrast to two of eight patients with well-differentiated tumors. With one exception, all patients with poorly or moderately differentiated tumors had not received any treatment to the oral floor or parapharyngeal space, and died from their neck tumors. According to N-classification, neck recurrence appeared in four of seven patients with N2b lesions, as compared with one of four patients with N1 lesions. The two patients with N2b lesions who received treatment of the oral floor and/or parapharyngeal space showed no signs of neck disease. On the other hand, four of the five patients with N2b lesions who received no treatment to that area suffered a second neck tumor.

Discussion

In this series, 16 patients developed delayed lymph-node metastases after control of a stage I or II primary tongue lesion. These patients accounted for approximately 10% of those who underwent RND in our department during the study period.

Unfortunately, we cannot estimate the incidence of occult neck metastasis associated with small tongue carcinomas because most of the patients already had neck metastasis at the time of presentation to our department. Poor salvage rates, ranging from 11 to 40%, have been reported after the devel-

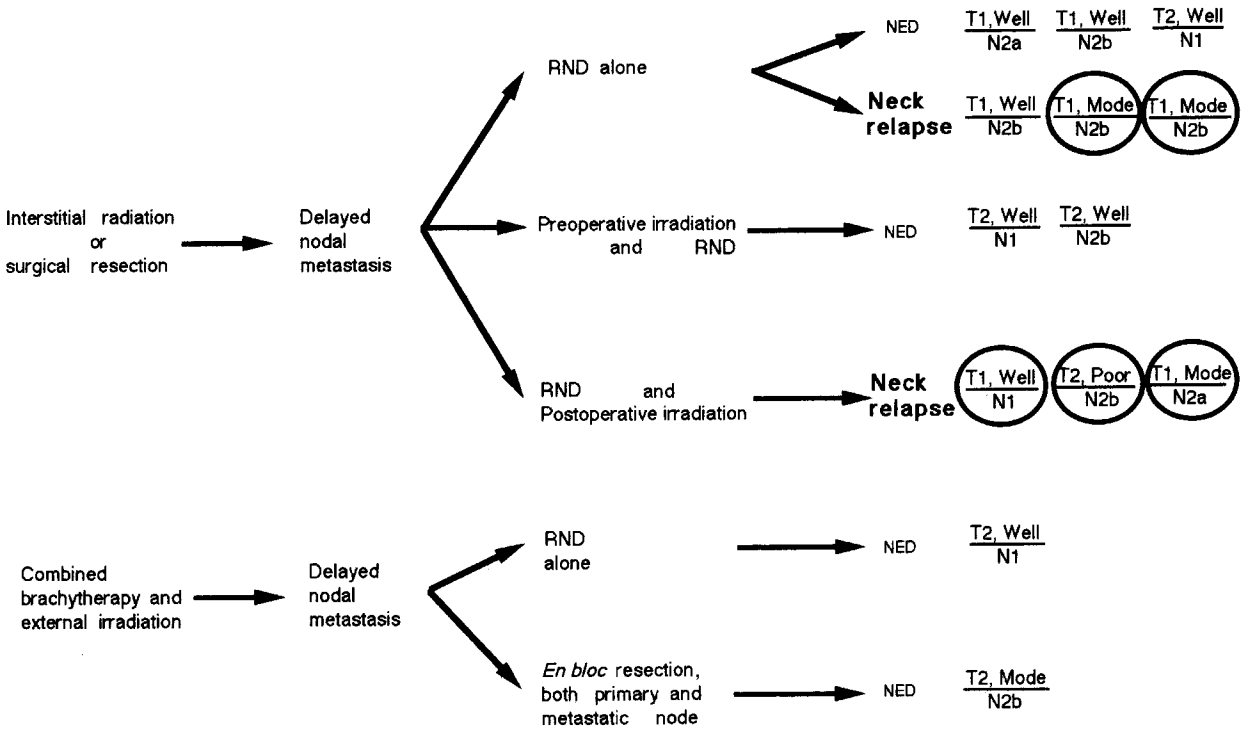

Fig. 3. Treatment algorithms, outcomes, and distribution of T- and N-classifications (UICC, 1987) and histologic differentiation of primary tumor. Numerator shows T-classification and tumor differentiation; denominator shows N-classification. NED: no evidence of disease; O: death from neck failure; Well: well-differentiated type; Mode: moderately differentiated type; Poor: poorly differentiated type.

opment of nodal metastasis[3,6,8,12,17,18]. In this study, the salvage rate of delayed node metastasis was 50.0% (8/16), slightly higher than in previous reports.

None of the patients in our study who developed secondary neck recurrences had received any treatment to the area between the primary site and the first-echelon lymph node. With one exception, all sites of recurrence were in the oral floor and/or the parapharyngeal space. HATA & OKUDA[4] have reported similar cases and have suggested that these recurrences might be due to tumor emboli from lymphatic ducts penetrating the "oral diaphragm". After RND is performed, the centrifugal spread of regional lymphatic drainage is interrupted just below the "oral diaphragm". Tumor cells remaining in the lymphatics of the oral floor may start to proliferate locally or may metastasize to the contralateral side and/or para- or retropharyngeal lymph nodes through alternative pathways. Most of the delayed metastases occurred within 6 months of treatment of the primary site. This supports the hypothesis that occult disease may be present in the lymphatics between the site of the primary lesion and the regional lymph nodes. Lingual lymph nodes are also located outside the range of RND, and the possibility of lingual nodal metastasis must be considered[14,15].

No secondary neck recurrences were noted in patients who received irradiation to the primary lesion and upper cervical chain. Several reports have advocated elective neck irradiation to lower the incidence of neck metastasis[7,11,13]. Elective irradiation is based on the need for treatment during the subclinical stage, when the results are expected to be better and the morbidity lower. Thus, upper neck irradiation as an initial treatment or at the time of neck metastasis may eliminate occult microscopic foci remaining in untreated areas. In our series, such an effect was substantiated by the fact that those who received external irradiation to the upper neck (either as an initial treatment or secondary treatment) remained free of neck disease. On the other hand, all three patients who received postoperative radiation died of neck failure. This may have resulted from insufficient coverage of the upper radiation field. Because our study involved small numbers of patients, we cannot make firm recommendations regarding the optimal dose of radiation and the dimensions of the irradiation field. As there are alternative lymphatic pathways on the contralateral side, the sites of the primary lesion and both sides of the upper cervical lymphatic chains should be included in the radiation field. However, high radiation doses and a broad field may induce changes that preclude physical detection of lymph-node involvement, thereby decreasing the surgical salvage rate. Of interest is a study that showed that elective neck irradiation decreased the incidence of neck metastasis without an improvement in survival[11].

Survival of the patients with poorly or moderately differentiated tumors was poor, as was that of the patients with multiple lymph-node involvement[1,2,9]. In our study, patients with poorly or moderately differentiated primary lesions and/or multiple lymph-node involvement tended to have secondary neck disease. However, there was no statistically significant difference in distribution of histologic grades and N-classification between the "treated" and "untreated" patients. In the "untreated" patients, all patients, except one, with moderately or poorly differentiated tumors and/or N2b lesions developed secondary neck recurrences. In contrast, all patients with moderately differentiated tumors and/or multiple nodal involvement who underwent preoperative irradiation or *en bloc* resection did not develop secondary neck recurrence. Recently, several indicators of high-risk patients, such as lesion thickness[16], mode of invasion[19], and DNA ploidy[5], have been proposed. The relatively few patients in this study and the lack of adequate information concerning the primary tumor precluded an assessment of these factors.

This study emphasizes that in the treatment of delayed lymph-node metastases associated with small primary carcinomas of the tongue, more attention should be directed to the area between the site of the primary lesion and the regional lymph nodes, especially when metastasis occurs within 6 months after treatment of the primary site. We believe that irradiation of this area might decrease treatment failures due to recurrence in the neck. Improvement of the outcome in high-risk patients requires aggressive treatment, such as *en bloc* resection (either electively or delayed) or a combination of surgery and irradiation.

Acknowledgment. We thank Prof. W. Yoshioka (Department of Dentistry and Oral Surgery, Hyogo College of Medicine, Hyogo, Japan) for his help.

References

1. ARTHUR JF, FENNER ML. The influence of histological grading on prognosis in carcinoma of the tongue: a computer analysis of 299 cases. Clin Radiol 1966: **17:** 384–96.
2. DECROIX Y, GHOSSEIN NA. Experience of the Curie Institute in treatment of cancer of the mobile tongue. II. Management of the neck nodes. Cancer 1981: **47:** 503–8.
3. FAKIH AR, RAO RS, PATEL AR. Prophylactic neck dissection in squamous cell carcinoma of oral tongue: a prospective randomized study. Semin Surg Oncol 1989: **5:** 327–30.
4. HATA T, OKUDA M. Tongue cancer. Problems associated with cervical lymph node metastasis. Otologia Fukuoka 1988: **34:** 1338–42.
5. HEMMER J, SCHON E, KREIDLER J, HAASE S. Prognostic implication of DNA ploidy in squamous cell carcinoma of the tongue assessed by flow cytometry. J Cancer Res Clin Oncol 1990: **116:** 83–6.
6. HO CM, LAM KH, WEI WI, et al. Occult lymph node metastasis in small tongue carcinoma. Head Neck 1992: **14:** 359–63.
7. HORIUCHI J, ADACHI T. Some consideration on radiation therapy of tongue cancer. Cancer 1971: **28:** 335–9.
8. JOHNSON JT, LEIPZIG B, CUMMINGS CW. Management of T1 carcinoma of the anterior aspect of the tongue. Arch Otolaryngol 1980: **106:** 249–51.
9. KALNIS IK, LEONALD AJ, SAKO K, RAZACK MS, SHEDD DP. Correlation between prognosis and degree of lymph node involvement in carcinoma of the oral cavity. Am J Surg 1977: **134:** 450–4.
10. KURITA H, TAKEDA S, NEBASHI S, et al. Problems associated with a radical neck dissection for patients with a tongue carcinoma: four cases of a stage I tongue carcinoma that recurred in the cervical area after the dissection. Jpn J Cancer Clin 1990: **36:** 2563–7.
11. LEBORGNE F, LEBORGNE JH, BARLOCCI LA, ORTEGA B. Elective neck irradiation in the treatment of cancer of the oral tongue. Int J Radiat Oncol Biol Phys 1987: **13:** 1149–53.
12. MENDELSON BC, WOODS JE, BEAHRS OH. Neck dissection in the treatment of carcinoma of the anterior two-thirds of the tongue. Surg Gynecol Obstet 1976: **143:** 75–80.
13. MEOZ RT, FLETCHER GH, LINDEBERG RD. Anatomical coverage in elective irradiation of the neck for squamous cell carcinoma of the oral tongue. Int J Radiat Oncol Biol Phys 1982: **8:** 1881–5.
14. OMURA K, TAKEMIYA S, SHIMADA F, HAYASHI N. Lingual node metastasis from tongue cancer: report of a case. Jpn J

Oral Maxillofac Surg 1989: **35:** 996–1000.
15. Ozeki S, Tashiro H, Okamoto M, Matsushima T. Metastasis to the lingual lymph nodes in carcinoma of the tongue. J Max-Fac Surg 1985: **13:** 277–81.
16. Spiro RH, Huvos AG, Wong GY, Spiro JD, Gnecco CA, Strong EW. Predictive value of tumor thickness in squamous cell carcinoma confined to the tongue and floor of the mouth. Am J Surg 1986: **152:** 345–50.
17. Eichgraeber JF, Clairmont AA. The incidence of occult metastases for cancer of the oral tongue and floor of the mouth: treatment rationale. Head Neck Surg 1984: **7:** 15–21.
18. Whitehurst JO, Droulisa CA. Surgical treatment of squamous cell carcinoma of the oral tongue. Arch Otolaryngol 1977: **103:** 212–15.
19. Yamamoto E, Miyasaka A, Kohama G. Mode of invasion and metastasis in squamous cell carcinoma of the oral cavity. Head Neck Surg 1984: **6:** 938–47.

Address:
Hiroshi Kurita, DDS
Department of Dentistry and Oral Surgery
Shinshu University School of Medicine
Asahi 3-1-1, Matsumoto 390
Japan