Original Article

Prevalence and pattern of nodal metastasis in pT4 gingivobuccal cancers and its implications for treatment

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Abstract

CONTEXT: The pattern of nodal spread in oral cancers is largely predictable and treatment of neck can be tailored with this knowledge. Most studies available on the pattern are from the western world and for early cancers of the tongue and floor of the mouth. **AIMS:** The present study was aimed to evaluate the prevalence and pattern of nodal metastasis in patients with pathologic T4 (pT4) buccal/alveolar cancers. **SETTINGS AND DESIGN:** Medical records of the patients with pT4 primary buccal and alveolar squamous cell carcinomas treated by single-stage resection of primary tumor and neck dissection at Gujarat Cancer and Research Institute (GCRI), Ahmedabad, a regional cancer center in India, during September 2004 to August 2006, were analyzed for nodal involvement. **MATERIALS AND METHODS:** The study included 127 patients with pT4 buccal/alveolar cancer. Data pertaining to clinical nodal status, histologic grade, pT and pN status (TNM classification of malignant tumors, UICC, 6th edition, 2002), total number of nodes removed, and those involved by tumor, and levels of nodal involvement were recorded. Statistical analysis was performed using the Chi-square test. **RESULTS:** Fifty percent of the patients did not have nodal metastasis on final histopathology. Occult metastasis rate was 23%. All of these occurred in levels I to III. Among those with clinically palpable nodes, level V involvement was seen only in 4% of the patients with pT4 buccal cancer and 3% of the patients with alveolar cancer. **CONCLUSIONS:** Elective treatment of the neck in the form of selective neck dissection of levels I to III is needed for T4 cancers of gingivobuccal complex due to a high rate of occult metastasis. Selected patients with clinically involved nodes could be well served by a selective neck dissection incorporating levels I to III or IV.

Key words: Elective and therapeutic neck dissections, gingivobuccal cancers, lymph node spread

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Introduction

Oral cancer accounts for 10.7% of all solid tumors in males and 5.4% in females in high incidence areas, such as India.[1] Metastases to the regional lymph nodes is the single most important prognostic factor in predicting local and distant failure as well as survival. The nodal metastasis reduces the survival by 50%.[2] Nodal metastasis in oral cancers is largely predictable with the levels I to III being most commonly involved. Skip metastasis to the levels IV or V in the absence of disease in the upper levels is around 4–5% except in the tongue where it approaches 16%.[3,4] The cancer of the buccal mucosa and lower alveolus together called the gingivobuccal complex cancer (Indian oral cancer) is the most commonly affected oral subsite in India.[5] Lymph nodal metastasis even with the mandibular involvement is less than 50%. Clinically enlarged nodes are often inflammatory or reactive.[6,7] Although a variety of tools are available for the detection of nodal metastasis, 20–50% of clinically negative patients are found to have metastasis on final histopathology.[8-10] They develop clinical disease usually within 2 years if the neck is not treated initially.[8,9] The incidence of occult metastases varies with the site, size, and thickness of the primary tumor. Currently, elective treatment of neck is indicated if this incidence reaches 15–20%.[11]

The standard treatment for patients with clinically palpable metastatic lymph nodes has been comprehensive neck dissection. Classical radical neck dissection involves resection of level I to V lymph nodes along with the tail of parotid, submandibular gland, sternocleidomastoid muscle, internal jugular vein and, spinal accessory nerve. Although it is an oncologically safe procedure that significantly reduces the risk of regional recurrences, it

produces significant postoperative morbidity—mainly shoulder dysfunction. Aiming to reduce the morbidity, several modifications to this procedure have been employed.[11] Several reports have suggested spinal nerve dysfunction with associated morbidity even in patients who undergo modified or selective neck dissections. Hence the option of omitting dissection at sublevels II B and V in patients with clinically negative neck is being considered by some investigators.[12-14]

Most of the literature available on the incidence and patterns of nodal metastasis is from the western world where tongue and floor of the mouth cancers are more common than gingivobuccal complex cancers. Prediction of the lymphatic spread could help in choosing the appropriate surgical procedure for both clinically positive and negative neck. Therefore, the present study was designed to look into the pattern of cervical lymph node metastasis in patients with pT4 gingivobuccal cancers, which is the most common oral subsite in India.

Materials and Methods

Medical records of 127 patients with pT4 buccal mucosa/lower alveolus primary squamous cell carcinoma who had undergone single-stage comprehensive neck dissection along with excision of the tumor between September 2004 and August 2006 in a regional cancer center were analyzed for nodal involvement. Data regarding clinical nodal status, histologic grade, pT and pN status, total number of nodes removed, and those involved by tumor and levels of nodal involvement were recorded. The primary site and nodal staging was done according to the TNM classification of malignant tumors, UICC, 6th edition, 2002.[15]

Statistical analysis

Statistical analysis was performed to compare the nodal involvement in the primary buccal mucosa and alveolar cancer groups, using the Chi-square test.

Results

Age range in the study group was 21–90 years. The study included 99 males and 28 females (male:female ratio 3.5:1). Seventy-one patients had exclusive bone involvement (primary lower alveolus tumor), 43 had external skin involvement, and 13 had both skin and bone involvement (buccal mucosa) on final histopathologic examination (HPE). A total of 127 comprehensive neck dissections were performed; 90 patients underwent modified neck dissection and 37 patients underwent classical radical neck dissection. Average nodal yield was 28 for the modified radical neck dissections and 32 for the classical radical neck dissections.

Distribution of pN category is shown in Table 1. Nearly 50% of the patients in each group had no nodal metastasis. In all, 63 of 127 patients (50%) had no nodal disease on final HPE. Next common category was pN2b with multiple involved nodes. A Chi-square test to find out the difference between the lower alveolus and buccal lesions in the development of nodal involvement was performed and no significant difference was observed. Occult metastasis is defined as metastasis in lymph nodes on final HPE in the absence of clinically detectable enlarged lymph nodes. Of the 56 patients with buccal cancer, 25 had clinical N0 neck of whom 7 had proven metastasis on final HPE. Hence, prevalence of occult metastasis was 28%. Similarly, 6 of 26 patients with lower alveolar cancer (23%) who were clinically node negative had metastasis on final HPE. All of these metastases occurred in levels I to III. None of these 13 occult metastases was seen in level IV or V. Among those with pathologically involved nodes (pN+), levels I and II cervical nodes were the most commonly involved sites. The prevalence of nodal metastasis to level V was 4% for buccal cancers (1 of 27) and 3% for alveolar cancers (1 of 36). There was no case with isolated level IV or V involvement in the absence of nodal disease at level I to III [Table 1].

Table 1: Summary of the prevalence and pattern of nodal metastasis in pT4 buccal and alveolar cancers

Primary site	Buccal mucosa	Lower lveolus	Total
No. of patients	56	71	127
cN0	25	26	51
pN+	07	06	13
Occult metastasis (%)	28	23	26
pN status[15]			
pN0	29	34	63
pN1	06	10	16
pN2a	01	01	02
pN2b	19	19	38
pN2c	01	06	07
pN3	00	01	01
Pattern of nodal involvement (%)			
Level I	96	86	
Level II	42	53	
Level III	19	31	
Level IV	11	14	
Level V	04	03	

Discussion

The cervical node metastasis in head and neck squamous cell carcinoma is the most important prognostic factor.[1,2,4,11] The prevalence of nodal involvement in pT4 cancers of the buccal mucosa/lower alveolus was 50% in the present series. This is comparable to earlier findings.[4,16] In a recently published histopathologic study of 526 neck dissections by Woolgar (56 of 78 primary cheek/lower aloveolus patients were pT4), pathologic nodal involvement among pT4 buccal and lower alveolar cancer patients was only 30%.[17]

Several clinical and pathologic studies have demonstrated that the pattern of lymph node metastases is largely predictable in patients with oral squamous cell carcinomas.[9,18-20] The use of selective neck dissection I to III supraomohyoid neck dissection (SOHND) for the elective treatment of the neck is now well established.[10] However, its role in the treatment of patients with clinically positive neck is controversial. Some authors have advocated this type of selective neck dissection for patients with limited neck disease at the upper levels of the neck, without compromising local control. The main factors supporting this approach are the usually good prognosis in patients with single levels I or II metastasis independent of the extent of neck dissection, and the low rates of level V involvement in the oral cavity tumors. Furthermore, the high incidence of clinically false-positive lymph nodes in oral cavity cancer patients is well recognized. In selected cases, SOHND could be extended to level IV, and followed by radiotherapy when indicated.

The prevalence of occult metastases depends on the diagnostic modalities, the kind of study (retrospective or prospective), the number of lymph nodes removed and examined, and the histologic technique of lymph node analysis (number of sections, immunohistochemistry, molecular analysis, and others). The prevalence reported in retrospective single-section hematoxylin and eosin lymph node analysis is in the range of 11–33%, whereas prevalence reported in prospective studies is between 35% and 48%. Although serial sectioning analysis, immunohistochemical methods, molecular and genetic analyses further enhance detection rates, significance of such a finding is yet to be determined.[9, 10] Prevalence of the clinically occult metastasis in the present study was 26%. Hence elective treatment of the neck is needed for all advanced tumors of buccal mucosa/lower alveolus. Since none of the metastases occurred in the levels IV or V, a suitable approach would be selective neck dissection I to III (SOHND) for patients with clinically negative neck. Similar to our findings, Diaz *et al.* have reported an occult metastasis rate of 26% for all stage buccal cancers.[7] However, other researchers have reported significantly low (3.5%) involvement of the level IV or V and skip metastasis rate of 1.5-5% in the clinically negative neck.[18-20]

A majority of the involved nodes were in the levels I and II. Isolated skip metastasis to the levels IV or V was not seen in the present study. Rao *et al.* in their series of 181 cases of neck dissection for T3/T4 lesions of alveolobuccal complex, reported nodal involvement of 85% in level I (91% in the present series), 51% in level II, 19% in level III, 18% in level IV, and 5% in level V. They also reported a 4.4% chance of skip metastasis at levels IV and V.[3] It is interesting to note that Woolgar has reported no metastasis at levels IV and V among 78 patients with cancers of buccal mucosa and lower alveolus (56 of 78 patients were pT4 status) in his study of 439 patients with oral and oropharyngeal cancers.[17] Even Shah *et al.* in their classical study of 516 radical neck dissections reported the absence of metastasis in level V in patients with cancers of buccal mucosa, retromolar trigone, and tongue and 6% involvement in alveolar lesions in patients who underwent immediate therapeutic neck dissection.[18] Therefore, it is possible that in a carefully selected group of patients, a selective neck dissection of either the levels I to III (SOHND) or I to IV (anterolateral neck dissection) would be to remove a major part of the nodal disease. But this has to be proved in a large randomized clinical trial before advocating for routine clinical practice. Among pN+ category, most common group was N2b.

Several reports have confirmed the usefulness of minimally invasive sentinel lymph node biopsy in cutaneous melanoma and breast cancer.[21] However, only preliminary data testing the feasibility of the method exist regarding the management of oral and oropharyngeal squamous cell carcinoma. The complexity of lymphatic drainage and the presence of deep lymphatics of the neck make application of this method difficult. This attractive concept has recently been explored by several investigators who examined the feasibility of identifying the sentinel lymph node in primary echelons of drainage from oral cavity squamous carcinoma.[22-24] The current knowledge of sentinel lymph node biopsy does not allow avoiding the indication of elective neck dissection in clinical practice. Sentinel lymph node biopsy cannot be considered the standard of care at this time. However, there are multiinstitutional clinical trials testing this approach.[25] Management of occult neck node metastasis continues to be a matter of debate. The role of imaging methods, such as ultrasound-guided needle biopsy, sentinel node biopsy, and positron emission tomography–computed

tomography are still being evaluated as alternatives to elective neck dissections. Whether one of these techniques will change the current management of cervical node metastasis remains to be proved in the coming days.[9]

Since the present study is a retrospective, histopathologic study with inherent weaknesses, no definite recommendations can be made with respect to the type of neck dissection for clinically palpable nodes. At the same time, the study validates current approach of selective neck dissection for advanced primary oral cancers with clinically N0 neck. Nevertheless, information on the pattern of cervical lymph node metastases is important for not only the clinicians but also for pathologists. An awareness of the pattern of spread allows pathologists to concentrate their assessment on specific nodal groups and to produce standardized pathology reports. This is fundamental to the postsurgical management of the patient, including the planning of adjuvant radiotherapy. Further studies in the form of prospective randomized controlled trials comparing selective neck dissections to comprehensive neck dissections in addressing nodal disease in advanced oral cancers are warranted.

References

1. Sunny L, Yeole BB, Hakama M, Shiri R, Sastry PS, Mathews S, *et al*. Oral cancers in Mumbai, India: a fifteen years perspective with respect to incidence trend and cumulative risk. Asian Pac J Cancer Prev 2004;5:294-300.
2. Johnson JT, Barnes EL, Myers EN, Schramm VL Jr, Borochovitz D, Sigler BA. The extracapsular spread of tumors in cervical node metastasis. Arch Otolaryngol 1981;107:725-9.
3. Rao RS, Deshmane VH, Parikh HK, Parikh DM, Sukthankar PS. Extent of lymph node dissection in T3/T4 cancer of alveolo-buccal complex. Head Neck 1995;17:199-203.
4. Byers RM, Weber RS, Andrews T, McGill D, Kare R, Wolf P. Frequency and therapeutic implications of "skip metastases" in neck from squamous cell carcinoma of oral tongue. Head Neck 1997;19:14-9.
5. Pathak KA, Das AK, Agarwal R, Talole S, Deshpande MS, Chaturvedi P, *et al.* Selective neck dissection (I-III) for node negative and node positive necks. Oral Oncol 2006;42:837-41.
6. Dhawan IK, Verma K, Khazanchi RK, Madan NC, Shukla NK, Saxena R. Carcinoma of buccal mucosa: incidence of regional lymph node involvement. Indian J Cancer 1993;30:176-80.
7. Diaz EM Jr, Holsinger FC, Zuniga ER, Roberts DB, Sorensen DM. Squamous cell carcinoma of the buccal mucosa: one institution's experience with 119 previously untreated patients. Head Neck 2003;25:267-73.
8. Kane SV, Gupta M, Kakade AC, D' Cruz A. Depth of invasion is the most significant histological predictor of subclinical cervical lymph node metastasis in early squamous carcinomas of the oral cavity. Eur J Surg Oncol 2006;32:795-803.
9. Zbären P, Nuyens M, Caversaccio M, Stauffer E. Elective neck dissection for carcinomas of the oral cavity: occult metastases, neck recurrences, and adjuvant treatment of pathologically positive necks. Am J Surg 2006;191:756-60.
10. Ferlito A, Silver CE, Rinaldo A. Elective management of the neck in oral cavity squamous carcinoma: current concepts supported by prospective studies. Br J Oral Maxillofac Surg 2009;47:5-9.
11. Kowalski LP, Sanabria A. A Elective neck dissection in oral carcinoma:a critical review of evidence. Acta Otorhinolaryngol Ital 2007;27:113-7.
12. Lim YC, Song MH, Kim SC, Kim KM, Choi EC. Preserving level IIb lymph nodes in elective supraomohyoid neck dissection for oral cavity squamous cell carcinoma. Arch Otolaryngol Head Neck Surg 2004;130:1088-91.
13. Elsheikh MN, Mahfouz ME, Elsheikh E. Level IIb lymph nodes metastasis in elective supraomohyoid neck dissection for oral cavity squamous cell carcinoma: a molecular-based study. Laryngoscope 2005;115:1636-40.
14. Villaret AB, Piazza C, Peretti G, Calabrese L, Ansarin M, Chiesa F, *et al*. Multicentric prospective study on the prevalence of sublevel IIb metastases in head and neck cancer. Arch Otolaryngol Head Neck Surg 2007;133:897-903.
15. Sobin LH, Wittelund C. TNM Classification of Malignant Tumors. International Union Against Cancer (UICC). Geneva, Switzerland: Wiley-Liss; 2002.
16. Pathak KA, Gupta S, Talole S, Khanna V, Chaturvedi P, Deshpande MS, *et al*. Advanced squamous cell carcinoma of lower gingivobuccal complex: Patterns of spread and failure. Head Neck 2005;27:597-602.
17. Woolgar JA. The topography of cervical lymph node metastases revisited: the histological findings in 526 sides of neck dissection from 439 previously untreated patients. Int J Oral Maxillofac Surg 2007;36:219-25.
18. Shah JP, Candela FC, Poddar AK. The patterns of cervical lymph node metastasis from squamous carcinomas of oral cavity. Cancer 1990;66:109-13.
19. Byers RM, Wolf PF, Ballantyne AJ. Rationale for elective modified neck dissection. Head Neck 1988;10:160-7.
20. Spiro JD, Spiro RH, Shah JP, Sessions RB, Strong EW. Supraomohyoid neck dissection: A critical assessment. Am J Surg 1988;156:286-9.
21. Scoggins CR, Chagpar AB, Martin RC, McMasters KM. Should sentinel lymph-node biopsy be used routinely for staging melanoma and breast cancers? Nat Clin Pract Oncol 2005;2:448-55.
22. Shoaib T, Soutar DS, Macdonald DG, Gray HW, Ross GL. The nodal neck level of sentinel lymph nodes in mucosal head and neck cancer. Br J Plast Surg 2005;58:790-4.
23. Calabrese L, Bruschini R, Ansarin M, Giugliano G, De Cicco C, Ionna F, *et al*. Role of sentinel lymph node biopsy in oral cancer. Acta Otorhinolaryngol Ital 2006;26:345-9.
24. Stoeckli SJ, Alkureishi LW, Ross GL. Sentinel node biopsy for early oral and oropharyngeal squamous cell carcinoma. Eur Arch Otorhinolaryngol 2009;266:787-93.
25. Alkureishi LW, Burak Z, Alvarez JA, Ballinger J, Bilde A, Britten AJ, *et al*. Joint practice guidelines for radionuclide lymphoscintigraphy for sentinel node localization in oral/oropharyngeal squamous cell carcinoma. Eur J Nucl Med Mol Imaging 2009;36:1915-9.

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