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Evaluation of incidence of skip metastasis in patients of oral squamous cell carcinoma

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ABSTRACT

Aim: The aim of the present study was to detect the incidence of skip metastasis in sentinel lymph nodes of oral squamous cell carcinoma.

Method: Lymph nodes from level I to V were macroscopically isolated from the patients at the time of surgery, and stained to evaluate the incidence of skip metastasis.

Results: The incidence of skip metastasis in this study was 21.2% (17/80).

Conclusion: Skip metastases was seen in about 1/5 of our cases with increase incidence in subgoups of patients with tongue & floor of mouth.

Keywords: Skip metastases, occult metastases, lymph node

1. INTRODUCTION

Cancer results when cells grow out of control and form a tumor. It results because of an accumulation of mutations that render the cells insensitive to growth control. Squamous cell carcinoma of the head and neck (SCCHN) frequently metastasizes to the regional lymph nodes and this is the strongest predictor of disease prognosis and outcome (Ferris et al., 2005). Lymph nodes are the first site of arrest of tumor cells that have invaded the peritumoral lymphatics. Accurate staging of lymph nodes in the neck is essential for optimal patient management. Current preoperative clinical methods, including newer radiographic techniques, are suboptimal and misdiagnose the presence or absence of nodal metastasis in many patients (Ferris et al., 2005). Surgical resection of lymph node is always indicated for clinically N-positive disease, but clinically N0 disease presents a diagnostic dilemma, as more than 30% of these patients will have occult metastasis/ skip metastasis. So the importance of identifying and managing sentinel lymph node micrometastasis cannot be overemphasized. If left undetected this can at a later date, manifest as a metastatic disease.

The aim of the present study was to detect the incidence of skip metastasis in sentinel lymph nodes of oral squamous cell carcinoma.

2. MATERIALS AND METHOD

Eighty patients diagnosed as primary squamous cell carcinoma of the oral cavity by the Department of Oral Pathology and Microbiology, Sharad Pawar Dental College and Hospital & who underwent surgical resection along with neck dissection were included in the study. Approval was taken from the Institutional Ethical Committee, of Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha, Maharashtra. An informed consent was obtained from all the subjects included in the study.

Inclusion criteria: Patients undergoing radical neck dissection (RND)
Exclusion Criteria: Patient undergoing segmental dissection

Before surgery the lymph node was accessed by the surgeon from level I to level V clinically. The following levels of lymph nodes were identified and accessed sequentially during radical neck dissection (RND).

- Level I: Submental and submandibular nodes
- Level Ia: Submental triangle lymph node
- Level Ib: Submandibular triangle lymph node
- Level II: Upper jugular nodes
- Level III: Middle jugular nodes
- Level IV: Lower jugular nodes
- Level V: Posterior triangle group
- Level VI: Anterior triangle group
- Level VII: Upper mediastinal nodes.

Lymph nodes from level I to V were macroscopically isolated from the patients at the time of surgery, and stained by frozen section; hematoxylin and eosin method. The remaining tissues of the lymph node were processed for paraffin-embedded sections and were stained routinely.

Conventional H & E staining on formalin fixed tissue

Paraffin embedded block of the gross lymph node tissue were prepared and a single section from the centre of the lymph node was cut and stained by conventional H/E staining. The node was said to positive for malignancy if it showed epithelial cell infiltrating the node in the form of groups, islands, chords and sheets. Data pertaining to 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.

3. RESULTS & OBSERVATIONS

The largest number of patients with OSCC in the study was in the 5th decade of life followed by those in the 6th decade (27.5%). The least number of patients were in the 8th decade i.e. 6.25%.However no OSCC patient was not observed below 21 of years. In this study the buccal mucosa was the most frequently involved site, accounting for 48.75%, followed by gingivo-buccal sulcus at 23.75%. The incidence of skip metastasis in this study was 21.2% (17/80), (Tables 1-3). We also evaluated the incidence of Skip metastasis i.r.t. the site of the lesion and Brynes grading (Tables 4 & 5).

Table 1

Baseline characteristics of the study participants (N=80)

Variable		
Mean age (SD) in years	52.3 (10.7)	
Sex M:F	7:3	
Location	**Frequency**	**Percent**
Buccal mucosa	39	48.75
Floor of mouth	1	1.25
Gingivo-buccal sulcus	19	23.75
Labial mucosa	12	15
Lip & labio-gingival sulcus	2	2.5
Retromolar area	2	2.5
Tongue	5	6.25
Total	80	100.0

Table 2

Showing the distribution of cases according to Bryne's Grading

Brynes Grading	No. of Patients
Good	26
Moderate	31
Poor	23

Table 3

Showing the frequency of cases with skip metastasis

Skip Metastasis	Frequency	Percent
Absent	63	78.8
Present	17	21.2
Total	80	100

Table 4

Showing the frequency of cases with skip metastasis according to site of lesion

Location	Level of Lymph node	Skip metastasis case	Percentage	
Labial mucosa	I-III	5/23	21.7%	1 level was skipped
Bucco gingival sulcus	II	8/50	16%	
Tongue	I- V	2/4	50%	2 levels were skipped
Floor of mouth	I-IV	2/3	75%	

Table 5

Brynes Grading & Skip metastasis Cross tabulation

		Skip metastasis		
		Absent	**Present**	**Total**
Brynes Grading	Good	18	8	26
	Moderate	28	3	31
	Poor	17	6	23
	Total	63	17	80

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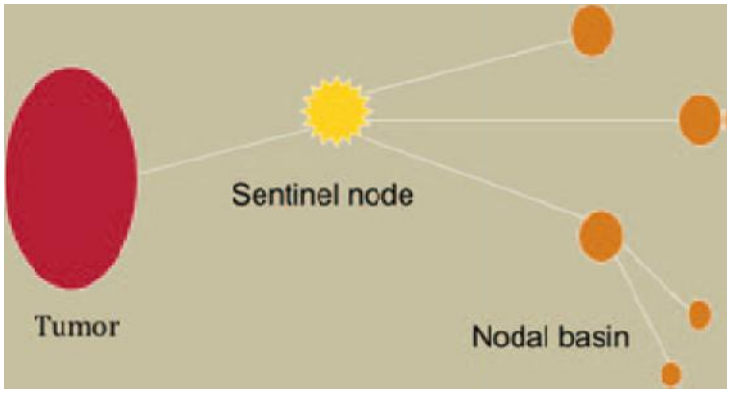

Figure 1

Shows concept of skip metastasis

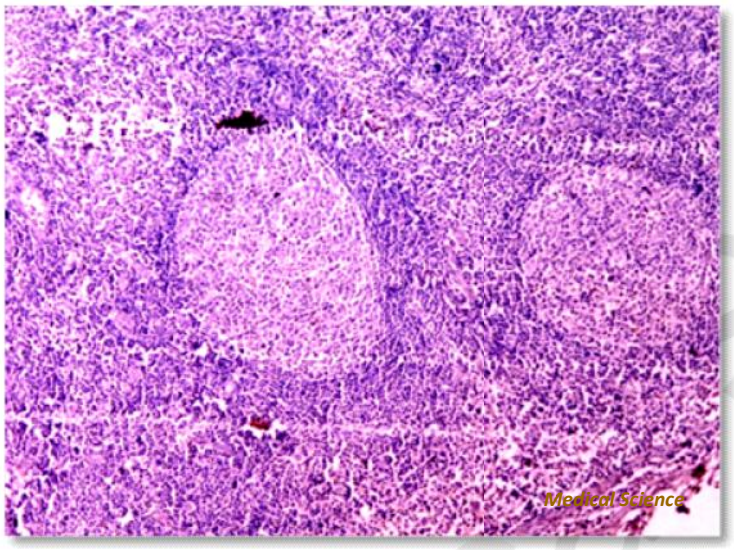

Figure 2

Photomicrograph under 10X view of Level I lymph node

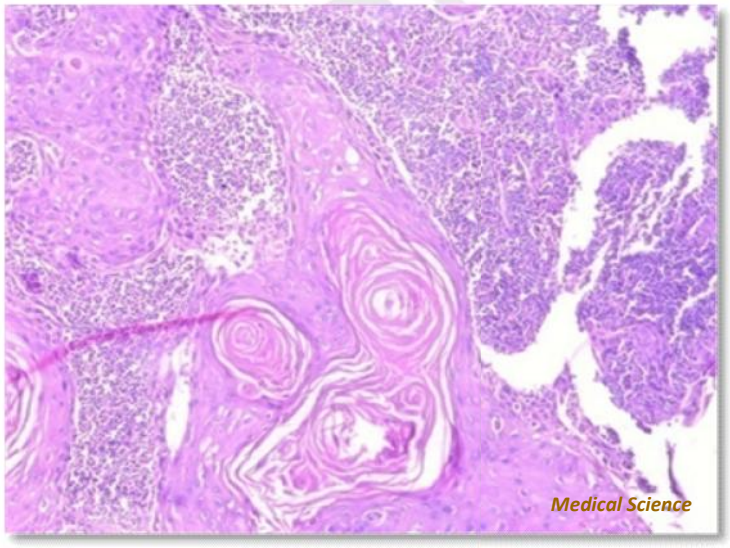

Figure 3

Photomicrograph under 10X view of Level II lymph node

4. DISCUSSION

The deleterious effect of cervical metastases on prognosis is so great that even a 20% chance of metastases in an otherwise clinically and radiographically negative neck pushes most clinicians toward its treatment. By definition, treatment subjects, 80% of patients to therapy-related morbidity despite the fact that these patients have No neck disease. The current management of the clinically node negative (cN0) neck commonly includes routine elective neck dissection (END) with pathologic examination of the removed lymph nodes. END or cervical lymphadenopathy done at the time of primary surgery for SCCHN for a cN0 neck, is associated with a significantly improved regional recurrence-free survival and lower incidence of distant metastases (Byers et al., 1997). But on the other hand the patient, who is treated unnecessarily for lymphadenectomy, bears the needless postoperative complications like pain, numbness, motor dysfunction and lymphoedema.

Tumor recurrence must reflect the presence of malignant cells which are not detected by current diagnostic procedures. This residual cancer may be present at the surgical margins, in lymph nodes or disseminated throughout the body (Ferlito et al., 2001). Histopathological examination of the neck dissection provides important information for staging and prognosis. Sentinel lymph nodes, are a variable, but limited, set of nodes and are the first sign of spread in most human cancers. The term ''skip metastasis'' refers to nodes involved with cancer which are not in the orderly progression of the disease, or what we refer to as ''the first echelon of nodes'' (Byers et al., 1997). The clinical significance of skip metastasis in head and neck cancer is not well established (Figure 1).

Using radioactive colloid gold, Seaman and Powers in 1955 for the first time demonstrated the concept of the first echelon node and nodal basin. Gould et al., subsequently coined the term 'SLN' in a case of malignant parotid tumor. The term skip metastasis was first coined by Byers et al for oral tongue cancers (Masafumi & Hiroyuki, 2007). Due to the rich lymphatic network of the majority of intra oral anatomic sites, the probability for the development of occult and skip metastasis varies from 6% to 46% in patients with stage I/II SCC of the oral cavity (Fernando et al., 2006), (Figure 2 & 3).

This study was carried out on 80 patients with OSCC treated with surgical excision to evaluate the prevalence of skip metastasis. The incidence of skip metastasis in this study was 21.2% (17/80), (Figure 4). Our results are similar with those presented by Ferlito et al., (2001) but not with Woolgar et al., (1995) who reported a 10% incidence of skip metastasis. It is historically documented that a pathologically negative sentinel lymph node predicts the absence of metastasis to the remainder of the regional lymph node basin with about a 98% degree of certainty. However, in this study this is underestimated (21%). Another term often used synonymously is Occult metastasis, which is different from skip metastasis. It includes micrometastasis & isolated group of cells which are not detected by routine histopathological techniques.

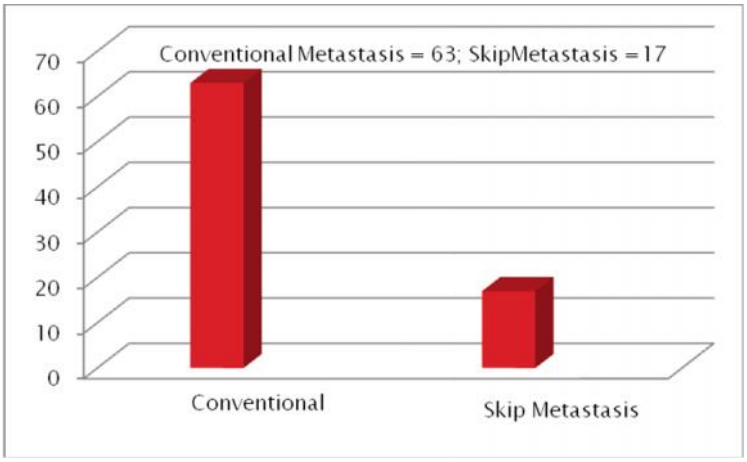

Figure 4

Frequency of cases with skip metastasis

Supraomohyoid neck dissection- includes level I, II, and III nodes is the routine surgical procedure recommended for tongue carcinoma patients. The nodes located below the inferior belly of the omohyoid muscle can be involved as the only manifestation of metastatic disease to the neck. So the question arise whether to include nodes below the level of the superior belly of the omohyoid muscle or not to include?. Study indicates that for floor of mouth and tongue, radical neck dissection beyond supraomohyoid i.e. till level V is justified as high incidence of skip metastasis is seen. While for cases involving labial & buccal mucosa clinical judgement by surgeon, depending on size & shape of the lymph node should be made. The precise mechanisms by which the tumor cells move preferentially toward particular lymph node(s) remain poorly defined. Recent evidence indicates that a more complex interaction between tumor cells and lymphatic endothelium may take place (Shayan et al., 2006). Thus lymph node involvement is no longer a passive phenomenon but indicator of the characteristic of aggressive phenotype of tumor cells. This also indicates that SLN biopsy cannot be relied upon as an indicator for spread of metastases. This might explain why skip metastases occur or why metastatic tumor cells or dormant metastasis at the initial presentation may lead to higher recurrences in high risk group.

The other probable causes for skip metastasis can be

- The elevated hydrostatic pressure due to tumor cells may compress the vessels in lymph node of sentinel node
- Tumor microenvironment (hypoxia, other stresses) can induce migration-related pathways
- Thus lymph node involvement is no longer a passive phenomenon but indicator of the characteristic of aggressive phenotype

5. CONCLUSION

Skip metastases was seen in about 1/5 of our cases with increase incidence in subgoups of patients with tongue & floor of mouth and alteration in surgical protocol is indicated in these patients. Dissection till level III lymph node should be done even in cases of labial & buccal mucosa so as to avoid failure. Every attempt should be made to detect metastasis in both sentinel and non sentinel lymph nodes.

CONFLICTS OF INTEREST

No conflicts of interest. No disclosures

REFERENCES

1. Byers RM, Weber RS, Andrews T, mcgill D, Kare R, Wolf P. Frequency and therapeutic implications of "skip metastases" in the neck from squamous carcinoma of the oral tongue. *Head Neck*, 1997, 19(1), 14-9 [PMID: 9030939]
2. Ferlito A, Partridge M, Brennan J, Hamakawa H. Lymph node micrometastases in head and neck cancer: a review. *Acta Otolaryngol.*, 2001 ,121(6), 660-5 [PMID: 11678163]
3. Fernando LD, Roberto AL, Jacob K, Terence PF, Jose RNS, Gabriel M, Geraldo MS. Relevance of skip metastases for squamous cell carcinoma of the oral tongue and the floor of the mouth. *Otolaryngology–Head and Neck Surgery*, 2006, 134(3), 460-465 [PMID: 16500445]
4. Ferris RL, Xi L, Raja S, Hunt JL, Wang J, Gooding WE, Kelly L, Ching J, Luketich JD, Godfrey TE. Molecular staging of cervical lymph nodes in squamous cell carcinoma of the head and neck. *Cancer Res.*, 2005, 15, 65(6), 2147-56 [PMID: 15781625]
5. Masafumi K, Hiroyuki T. Significance and problems of histopathological examination and utility of Real-Time Reverse Transcriptase-Polymerase Chain Reaction method for the detection of sentinel lymph node metastasis in breast cancer. *Breast Cancer*, 2007, 14(4), 342-349 [PMID: 17986798]
6. Shayan R, Achen MG, Stacker SA. Lymphatic vessels in cancer metastasis: bridging the gaps. *Carcinogenesis,* 2006, 27(9), 1729-38 [PMID: 16597644]
7. Woolgar JA, Beirne JC, Vaughan ED, Lewis-Jones HG, Scott J, Brown JS. Correlations of histopathological findings with clinical and radiologic assessments of cervical lymph-node metastases in oral cancer. *Int. J.Oral Maxillofac.Surg.*, 1995, 24 (1 pt 1), 30-37 [PMID: 7782638]