



SENTINEL NODE BIOPSY: METHOD AND ITS ROLE IN SQUAMOUS CELL CARCINOMA OF ORAL CAVITY

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ABSTRACT

Sentinel node biopsy (SNB) is the method in which first-echelon nodes of regional basin is biopsied to see the metastasis by malignant neoplasm. It has been studied extensively in malignant melanoma and breast carcinoma with excellent results. The first application of SNB for Oral cancer was reported by Koch and colleagues and Pitman and coworkers. For oral cancer patient's accurate diagnosis and staging is needed to select proper treatment modality and estimate prognosis. Cervical metastasis is the single most important prognostic factor in patients of oral cancer with its presence reducing the five years disease survival rate by 50%. The greatest problem is with clinically N0 neck in which sometimes after histopathologic examination of dissected lymph nodes it is felt by the clinician that there was no need of elective neck dissection (END). To reduce the cost burden and morbidity associated with END and simultaneously to properly treat the patients, SNB may play an important role in the management of oral cancer patients. Although this technique is under investigation for staging oral cancer patients, sufficient experience with SNB is available to discuss the method, diagnostic efficacy and challenges associated with this technique.

INTRODUCTION

Sentinel lymph node (first echelon node) is the first lymph node/ groups of lymph nodes draining a cancer. Sentinel lymph node biopsy (SNB) is the procedure in which first echelon lymph nodes are biopsied to see the metastasis due to primary. Initially SNB was used in cases of malignant melanoma and later it was used in breast carcinoma cases. For effective management of oral cancer patients accurate staging is required to determine the prognosis and to select appropriate management. Cervical metastasis is the single most important prognostic factor in oral cancer patients, with its presence reducing the five years disease survival rate by 50%.^[1,2,3]

Although there are definitive indications of neck dissection in patients of clinically positive neck metastasis but those patients who have clinically N0 neck various treatment modalities have been proposed in the literature. Approximately 30% patients with head and neck squamous cell carcinoma having clinically N0 neck are found to have subclinical metastases.^[4] and knowledge of lymph node disease alters management. Currently computed tomography (CT) and magnetic resonance imaging (MRI) scans are used to classify the neck, but their overall accuracy is limited to approximately 70%, and hence highly accurate means of

identifying lymph node disease is needed to perform a correct staging of lymph node.^[5]

At present there are three modalities of management for clinically N0 neck.^[1] Selective neck dissection (most commonly Supraomohyoid neck dissection) with the aim of regional staging and elective treatment,^[2] radiotherapy of neck as elective treatment, and,^[3] clinical follow-up with therapeutic neck dissection or irradiation reserved for patients who develop detectable disease.

The benefit of elective neck dissection (END) is realized when dissected lymph nodes are found to contain metastatic tumor cells upon histopathologic examination. This also helps in proper staging based on which adjuvant radiotherapy is given. However in up to 65% to 75% of case of selective neck dissection for N0 neck, no disease is found and hence morbidity and additional cost associated with it is unjustified⁶. Similarly radiotherapy as an elective treatment of N0 neck over treats a patient and at the same time does not provide any staging which is essential to estimate prognosis and guide further treatment. Elective radiotherapy also makes future surgery difficult if second primary tumor develops. Likewise those patients who are kept on follow-up to see the detectable disease in neck and then to provide treatment, this may lead to development of more advanced stage in the neck hence making management

more complicated.^[7,8] Thus, more precise staging before treatment is needed to prevent the consequences of inappropriately selected management strategies for the clinically N0 neck in oral cancer.

SNB is used to identify micrometastatic disease within a sentinel node considered most likely to drain the tumor bed and receive initial metastatic deposits from the primary malignancy. SNB thus provides a less invasive means of providing staging information for the patient with oral cancer with N0 neck. Hence unwanted morbidity and cost can be minimized.

The first successful identification of sentinel node in head and neck squamous cell carcinoma was done by Alex and Krag in 1996^[9]. Later, the procedure was applied for oral cancer by Koch and colleagues^[10] and Pitman and coworkers.^[11]

Application of sentinel node biopsy for staging oral cancer

The concept of SNB for oral carcinoma is based on the drainage of primary tumor by collecting vessels that reach first echelon nodes of regional basin (Fig. 1).

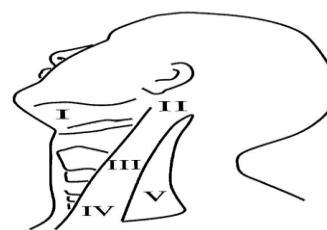


Fig.1: Location of cervical lymphatic metastases

For patients having small primary tumors of oral cavity it is easier to perform SNB as compared to bulky invasive tumors. Also the status of regional lymph nodes in patients with small primary tumor is less uncertain. Likewise, the success of SNB is high in patients without clinical evidence of regional disease as compared to clinically positive nodes and even grossly positive nodes that are missed on clinical evaluation. Such diseased nodes often uptake tracer poorly or divert lymphatic flow altogether, resulting in the labeling of downstream nodes.^[10]

Therefore, in patients with T1 or T2 oral cavity carcinoma, SNB is most applicable for staging the following: (1) the ipsilateral clinically N0 neck drained by a unilateral primary tumor, (2) the bilateral clinically N0 neck drained by a midline tumor or tumor crossing the midline, and (3) the contralateral clinically N0 neck drained by a midline tumor or tumor crossing the midline in the presence of a clinically positive ipsilateral neck (Table 1)

Table 1. Application of sentinel lymph node biopsy for the staging of oral cancer.^[12]

T1 or T2 tumors	Clinically N0 neck
Tongue	Ipsilateral neck for a unilateral primary tumor
Retromolar trigone	
Buccal mucosa	Bilateral neck for a midline tumor or tumor crossing the midline
Lip	
Alveolar ridge	Contralateral neck for a midline tumor or tumor crossing the midline in the presence of a clinically positive ipsilateral neck
Hard palate	
Floor of the mouth	

In oral cancer, staging of the clinically N0 neck by SNB can be done in two ways 1) SNB assisted elective neck dissection and 2) Use of SNB as a stand-alone procedure, potentially replacing elective neck dissection. In the second method excision of only the sentinel nodes are done and sent for pathologic evaluation to check the metastasis. The advantage of this approach is that it is minimally invasive and can potentially be more sensitive in pathologic staging. On the basis of the sentinel node status, patients then undergo a therapeutic neck dissection or clinical follow-up.

Technique of SNB In oral cancer patients, SNB is performed along with excision of primary tumor and END.

a) Preoperative lymphoscintigraphy: Under local anesthesia radiocolloid (technetium-99m-labeled sulfur colloid) is injected into submucosa around the periphery of entire primary tumor. Particles of radiocolloid travels rapidly to first echelon lymph nodes where they are entrapped before reaching the downstream lymph nodes. The advantages of using 99mTc-SC are, low level exposure of radiation, short half-life and energy peak within the range that is easily detected by most gamma cameras and handheld gamma probes. After injection of colloid lymphoscintigraphic imaging is taken which identify the nodal basins at risk for metastasis and location of sentinel lymph nodes. These lymph nodes are marked on the patient's skin.

- b) Intraoperative lymphatic mapping: After lymphoscintigraphy, the patient is prepared under general anesthesia and first primary tumor is excised to reduce the back ground radioactivity. The handheld gamma probe is calibrated to detect $^{99m}\text{Tc-SC}$. The neck is then probed to identify the lymph nodes that were marked on the skin. The radioactivity of hot spot relative to background level is recorded. A skin incision is designed in such a fashion that helps in removal of sentinel node as well as it can be further extended if END is needed. Addition of vital blue dye (isosulfan blue in 1% aqueous solution) injection before primary tumor resection along with lymphoscintigraphy, increases the probability of success in identifying sentinel lymph nodes.
- c) Excision of sentinel lymph node: the skin incision is deepened and subplatysmal flap is elevated to provide sufficient access. Hand held gamma probe is used to direct deeper dissection and identification of sentinel lymph nodes. Blue stain may further aid identification. A sentinel node is defined as a node with an activity ratio of 3:1 or higher in vivo (at least three times the background levels). Once identified the sentinel node is removed by sharp dissection. Surrounding nonsentinel lymph nodes can also be removed to provide internal control. The radioactivity level of all excised nodes is measured with the probe and recorded. A ratio of radioactivity in an excised sentinel node relative to a nonsentinel lymph node (ex vivo activity ratio) of 10:1 or higher further confirms correct identification of the sentinel node.
- d) Pathologic examination of sentinel lymph nodes: For pathologic evaluation, fixed lymph node is bisected through long axis and divided into slices of 2.5mm. These sections are sent for H&E stain and immunohistochemical analysis. Intraoperative frozen section of specimen helps to decide immediately whether to perform neck dissection during the procedure.

Problems associated with SNB

There are various complicating factors associated with SNB

1. Rich lymphatic system in the head and neck may produce bilateral drainage pattern on the lymphoscintigraphy images, creating problem in excising sentinel lymph nodes.
2. Due to complex anatomy of head and neck the precise localization of sentinel lymph nodes become difficult.
3. Finding of multiple radioactive lymph nodes leads to difficulty in identifying true sentinel nodes.
4. In cases of skip metastasis the tumor cells which metastasize at the lower levels escaping the first draining nodes, may go undetected in some patients undergoing SNB.

5. Bulky primary tumors that invades the adjacent structures pose difficulty in peritumoral injection of radioactive tracer, thus this technique is used mainly for staging of N0 neck with early stage primary tumors.
6. Because intraoperative frozen section analysis has not yet been proven accurate, a second procedure to perform therapeutic neck dissection may be required in the event of upstaging on final pathologic evaluation.

Diagnostic efficacy of SNB in oral cancer: Diagnostic efficacy of SNB should be evaluated based on the feasibility of SNB to identify sentinel lymph nodes, the extent to which metastasis can be detected within those nodes, and the accuracy of the procedure in determining the status of the neck¹².

Sentinel lymph node identification rate

- 96%–98% for SNB-assisted elective neck dissection
- 91% for SNB alone

Detection of occult metastasis

- 34%–60% of patients upstaged

Accuracy

- Sensitivity: 86%–100%
- Negative predictive value: 83%–99%

CONCLUSION

it can be concluded that SNB is feasible in detecting occult metastases in patients of oral cancer with clinically N0 neck and it offers significant advantages over elective neck dissection for staging. However still the concept is invalidated because of biologic behavior of squamous cell carcinoma of oral cavity and complex anatomy of head and neck. Also most of the studies available are from single institution pilot study or are ongoing trials, so larger studies are needed to correctly evaluate its role in oral cancer patients.

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