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Sentinel Lymph Node Biopsy in Clinically Node-Negative Oral Cancer: A Review

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Abstract

Sentinel lymph node biopsy (SLNB) is an emerging technique for staging node-negative oral cancer, offering a less invasive alternative to elective neck dissection. By mapping the primary lymphatic drainage pathway, SLNB improves the detection of occult metastases while minimizing surgical morbidity. A combination of radiotracers and dyes facilitates sentinel node identification, followed by histopathological evaluation. Studies demonstrate high accuracy and negative predictive value, supporting its role in guiding management. SLNB reduces unnecessary neck dissections, preserving function without compromising oncological outcomes. As evidence grows, SLNB is increasingly recognized as a reliable staging tool in early-stage, clinically node-negative oral cancers. This review summarises the importance of sentinel lymph node biopsy in clinically node-negative oral cancer.

Keywords: biopsy, sentinel lymph node, oral cancer, metastases

Introduction

Oral cavity squamous cell carcinoma (SCC) is the most common oral cancer, and many treatments have been evaluated. [1-3] Approximately half of all patients who present with oral cavity squamous cell carcinomas (OCSCC) are diagnosed with clinical stage I/II OCSCC without clinical or radiological evidence of cervical nodal metastasis. [4,5]

Patients who present with early OCSCC are usually treated with resection of the primary tumour. In terms of

neck staging, patients either undergo elective neck dissection (END) at the time or watchful waiting with therapeutic neck dissection (TND) if nodal relapse was to occur.[6]

Traditionally, elective neck dissection was considered for patients with early-stage oral cavity SCC. Several studies reported that this was better than watchful waiting (until metastasis developed). [7–9]

Elective neck dissection improved survival and reduced the recurrence rate. However, elective neck dissection may be an unnecessarily invasive approach for patients at low risk of lymph node involvement. [7,8] As elective neck dissection can affect shoulder motility and cause persistent pain and scarring, an alternative is desirable. Sentinel node biopsy represents a compromise between elective neck dissection and watchful waiting and has often been used to detect occult neck node metastases accurately. [10,11] Sentinel node biopsy involves the injection of a radiotracer or methylene blue dye to identify the lymph nodes that drain first from the primary cancer, [12,13] and sensitivity and accuracy are high. [14,15]

There are several factors to consider when performing and evaluating SLNB.

The current, 8th edition of the American Joint Committee on Cancer (AJCC) guidelines utilises depth of invasion (DOI) as a key parameter in tumour classification (T) with oral cavity T1 and T2 being ≤5 mm or ≤10 mm, respectively. [16,17]

Sentinel lymph node identification and nodal distribution

One of the key factors required for the widespread use of SLNB is the reliable identification of lymphatic drainage from the primary tumour. Depending on the primary site of the oral cancer, the common drainage pattern differs as the sentinel node does not always have to be the closest node to the primary.

Lower sensitivity has been demonstrated in floor-of-mouth tumours,[18] likely due to the "shine through" phenomenon.[19] In the floor of the mouth, first echelon nodes are often nearby (e.g. level IA & IB) to the primary tumour where the radiotracer may remain post-injection in a relatively high concentration, and the signal can "shine through" to obscure SLN detection in the adjacent nodal basin. Methods for mitigating this effect include resection of the primary lesion before SLN localization, cross-reference to multiple imaging studies modalities or use of injected dye adjuncts to help reduce this error. [20,21]

Another potential mechanism for false-negative sentinel nodes is the presence of skip metastasis which have been reported in OCSCC. [22,23] In such cases, nodal metastasis may travel beyond the likely first nodal basin, and be identified in the lower neck levels III & IV.

The result is not immediately available and therefore requires a two-stage surgery for a completion neck dissection if a positive sentinel node is identified. Furthermore, for improved accuracy for identification of subclinical micrometastasis, step-sectioning is recommended at 150 μm for sentinel lymph node evaluation, as performed in a multicenter study in 2015. [20]

Utilization of thin step sectioning at 150 μm significantly increases the pathologic sections, more than 10-fold compared to standard 2mm sections or bisection of nodes.

Post-operative complications

One of the main factors driving consideration of SLNB for early-stage OCSCC is the potential to reduce overall morbidity for patients with truly node-negative disease.

Potential complications from neck dissection, particularly to shoulder function, are well established.

Shoulder dysfunction was first described by Alan et al in 1961 as the "shoulder syndrome" where patients had trapezius palsy, shoulder pain, and limited abduction caused by damage to the spinal accessory nerve.[24] Other structures such as the internal jugular vein, hypoglossal nerve, vagus nerve and thoracic duct are also potential risk for injury and resultant morbidity. Postoperative sequelae can be exacerbated if adjuvant radiotherapy is recommended which can cause further scarring, lymphedema, and sensory dysfunction.[25] Due to the smaller incision needed for SLNB and minimal lymph node removal, a reduction in risk for these complications in node-negative patients undergoing SLNB may be expected.

Imaging

For SLNB, lymphoscintigraphy is a valuable diagnostic nuclear imaging tool that utilizes radiopharmaceutical agents in mapping the lymphatic system and was first introduced in the late 1900s. [26,27] This modality is coupled with a radiotracer injection at the primary site and imaging timed shortly thereafter. Although lymphoscintigraphy can visualize entire lymphatic drainage patterns, anatomical relationships can be difficult to distinguish with planar imaging. Therefore, dual SPECT imaging modality of lymphoscintigraphy superimposed on CT is becoming more frequently utilized preoperatively, particularly in the head and neck for visualization of sentinel nodes in relationship to known anatomical landmarks. [28,29]

Intraoperative tracers

In adjunct with the preoperative imaging, intraoperative dyes and radiotracers are often used to localize sentinel lymph nodes intraoperatively. Previously, a blue dye (brand name Lymphazurin, CT, USA) was commonly used to visually identify sentinel nodes. While sensitivity was good, a major limitation is the transient pass-through of dye that limits the time interval that the sentinel node can be visualized, leading to the potential for false-negative results. [30,31]

In the modern era, dye has been predominately replaced by radiotracers. Radiotracers are not only visible on preoperative nuclear imaging, but can also facilitate intraoperative sentinel node localization and confirmation using a gamma probe ^{99m}Tc-serum albumin nanocolloid (HAS) [32] is the most commonly used radiotracer in Europe and filtered or unfiltered ^{99m}Tc-sulfur colloid [33] in the United States.

A new intraoperative technology rising in popularity to counter the "shine through" phenomenon is the free hand SPECT (FhSPECT).[34] A dynamic, three-dimensional image is extrapolated based on the anatomical landmarks calibrated to the patient at the start of the procedure. This allows the surgeon to visualize the depth of the sentinel node, which the gamma probe could not provide.

Conclusion

Sentinel node biopsy, which has no life-threatening side effects, is preferable to elective neck dissection for patients with early-stage clinically node-negative oral cavity SCC. SLNB provides an accurate and technically feasible method of assessing nodal status in suitable patients with OCSCC provided strict quality control is maintained.

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