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Incidental Thyroid Tissue in Sentinel Nodes From Oral Squamous Cell Carcinoma

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Objective: Sentinel node biopsy (SNB) is a surgical staging test in which sentinel nodes (SNs) undergo intensive histological analysis. SNB diagnoses early cancer spread, but can also reveal unexpected findings within the SNs. We review cases of incidental thyroid cells (TC) found in SNs from patients with oral squamous cell carcinoma (OSCC) to assess the prevalence of TC, and the clinical significance of these.

Methods: Multicenter retrospective review of SNB performed for cT1-T2N0 OSCC. Incidental TC were identified by TTF-1 or thyroglobulin positivity. Anatomical location of nodes containing TC, TC morphology, and ongoing management/follow up of this incidental finding was recorded. Neck dissections performed during the same period were reviewed to establish the expected incidence of TC in neck nodes without serial sectioning analysis.

Results: 278 SNB cases were reviewed. Ten procedures detected TC in nine patients (10/278, 3.6%). During the same time period 725 neck dissections were performed, six containing TCs (6/725, 0.8%). One patient underwent SNB twice with TC identified on both occasions. Three patients had both OSCC metastasis and thyroid cells. All SNB patients with TC identified underwent thyroid USS with no primary tumours identified. Three patients underwent thyroidectomy, in all cases no primary thyroid tumour was found.

Conclusion: Prevalence of incidental TC in SNs appears to be higher than that reported in neck dissections, these are not likely to be clinically relevant and can be managed on a conservative basis in the absence of clear metastatic features.

Key Words: cervical metastasis, neck dissection, sentinel node biopsy, thyroid cancer, thyroid inclusion.

Level of Evidence: Multicentre retrospective cohort study, Level 3

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INTRODUCTION

Management of thyroid tissue discovered incidentally within the lateral cervical lymph nodes is a contentious issue. Some authors believe that these always represent metastatic deposits even without an identifiable primary tumor, whereas others support the hypothesis of thyroid inclusions which may be embryologically occurring and do not represent a disease process.[1]

Thyroid cells are a rare but well-recognized finding in cervical lymph nodes in neck dissection specimens from patients with head and neck squamous cell carcinoma. Rates are reported between 0.6% and 1.7%.[2–5] Further management will typically include ultrasound scanning (USS) of the thyroid gland and surgery (partial or total thyroidectomy) based on the presence of identifiable primary tumor. Tumor board/multidisciplinary team (MDT) review may recommend serial surveillance USS or clinical examination only if no primary tumor is detected.[2,4]

Sentinel node biopsy (SNB) for oral squamous cell carcinoma (OSCC) is increasing in popularity as a staging technique with a high sensitivity of detecting occult disease within cervical lymph nodes. The SNB procedure firstly maps lymphatic flow to cervical lymph nodes (LN). Peritumourally injected radiotracer preferentially accumulates within LN with high lymphatic vessel density (LVD). Increased LVD is seen in pre-metastatic and metastatic LN because of signaling from the primary tumor, resulting in reliable identification of the nodes at risk of metastasis.[6,7] Radiologically identified nodes are excised and submitted for histological examination by serial step sectioning with immunohistochemistry. Both lymphatic mapping and serial sectioning will detect changes in the pathophysiology of cervical lymph nodes with the possibility of detecting synchronous tumors either by means of intensive pathological assessment, or by mapping

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changes in the flow to LN because of influence from additional malignant tumors.

The purpose of this article is to review cases of incidental thyroid cells (TC) found in sentinel nodes (SNs) from patients undergoing SNB for OSCC within the South of England SNB consortium.[8] We aim to assess if there is a higher than expected rate of TC within SNB cases, and to understand if identification is aided by lymphatic mapping and/or pathological examination. Furthermore, we will provide advice regarding ongoing management of TC in the context of SNB patients.

MATERIALS AND METHODS

Retrospective case note review of SNB procedures performed for cT1-T2 OSCC within South of England SNB consortium between 2017 and 2021.[8] All SNs within the five-center consortium were analyzed by a central specialist Head and Neck pathology service based at Guys Hospital, London (Viapath). A previously published analysis[8] showed that the consortium had an SNB positive rate of 28% with sensitivity, negative predictive value, and false negative rate of 92.8%, 97.0% and 6.8%.

SNs and clinical data including location of hotspots seen on lymphatic mapping, staging and outcome from OSCC, size and morphology of incidental thyroid tissue and subsequent management of thyroid cells were analyzed on a case-by-case basis.

To estimate the expected rate of TC in non-SN cases an additional cohort of patients who underwent neck dissection for OSCC of any clinical stage during the same time period were analyzed.

RESULTS

Between 2017 and 2021, 278 cases of SNB were performed. Ten SNB procedures revealed TC in nine patients (10/278, 3.6%) (Table I). The SNB cohort without TC had a male:female ratio of 1.6 and mean age of 58 years (range 36–66). Of the nine patients with TC in the SNs, three were female (M:F ratio 3), mean age was 58 years (range 36–66).

One patient had SNB performed 4 years apart for two primary OSCCs. On both occasions thyroid cells were present in the SNs. Another patient had two SNB surgical episodes, in the first procedure a level VI node was identified on imaging but was not excised as it was judged to be a second echelon node due to location and timing of its appearance. In the second procedure 18 months later the same node was identified in level VI, this time it was excised and found to contain thyroid cells.

Three patients had both OSCC metastasis and thyroid cells, but these were never found in the same lymph node. One patient had TC present in three SNs.

During the same time period 725 neck dissections were performed and submitted for routine histopathological evaluation. Six neck dissections contained thyroid cells, a prevalence of 0.8%.

Imaging and Location of Lymph Nodes Containing TCs

In nine cases TC were found in nodes located in neck levels III–VI, with one in level IIa. Figure 1 shows distribution of lymph nodes containing thyroid cells and the location of metastatic OSCC SN.

Figure 2 shows case 8 imaging from SNB in 2019 and 2021. In these images, drainage is shown in level VI on both occasions. The node was only retrieved at the second procedure and contained TC.

TABLE I.
Sentinel Node Cases with Incidental Thyroid Cells.

Case Number	Primary Tumour Location (OSCC)	OSCC Pathological Staging (TNM8)	Thyroid Deposit Morphology
1	Midline FOM	T1N0	Follicular
2	Left lateral tongue	T1N0	Follicular
3	Left ventral tongue	T1N0	Papillary (3 nodes)
4	Midline FOM	T1N1(sn)	Follicular
5	Left lateral tongue	T1N0	Follicular
6	Left lateral tongue	T1N0	Follicular
7	Right tongue	T1N0	Follicular
8	Left lateral tongue	T1N0	Follicular
9	Left ventral tongue	T1N1(sn)	Follicular
10	Left lateral tongue	T1N1(sn)	Follicular

FOM = floor of mouth; OSCC = oral squamous cell carcinoma.

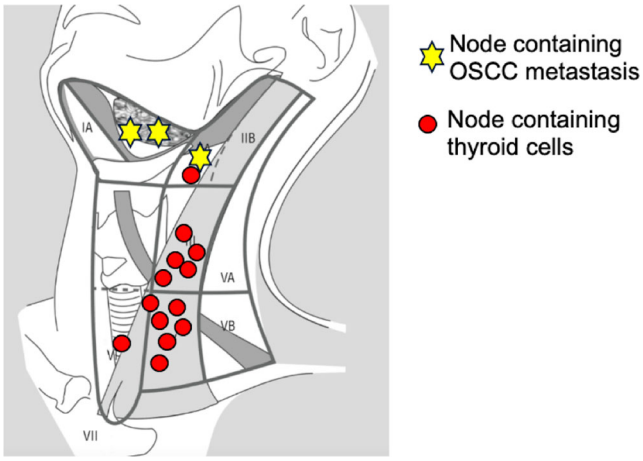

Fig. 1. Location of lymph nodes containing metastatic oral squamous cell carcinoma and thyroid cells. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

SN Thyroid Cell Identification and Morphology

The size of TC deposits ranged from 0.1 to 3.3 mm and identification was confirmed with TTF-1 and/or thyroglobulin positivity. Thyroid cell deposit was reported as wedge shaped in one case and in six cases TCs were located in the peripheral sinus or subcapsular location, one with suggestion of extranodal extension.

Diagnosis of definitive thyroid metastasis was made in one case where three nodes contained multifocal papillary thyroid cancer cells. In all other cases, TC were of follicular morphology and none showed definite or unequivocal nuclear features of papillary carcinoma.

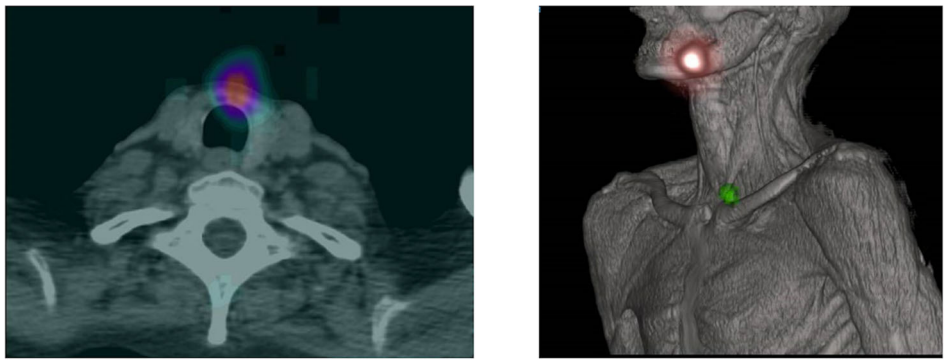

Fig. 2. Single photon emission computed tomography imaging from patient undergoing sentinel node biopsy for tongue cancer. On both occasions tongue tumour was injected and scan showed hot spot in level VI. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

Management of TC

Three patients with positive OSCC SNB had completion neck dissection with no further thyroid deposits found. All patients had thyroid USS with no primary tumors identified although minor glandular abnormalities (e.g., U2 thyroid nodule, thyroid microcalcification and generalized thyroid nodularity) were described. Three patients went on to have thyroidectomy after review at thyroid MDT (two with minor changes on USS), including the patient with metastatic papillary thyroid cancer, in all cases no primary tumor was found.

DISCUSSION

Thyroid cells in lymph nodes can pose a diagnostic dilemma, evidenced by conflicting opinion and nomenclature in the literature. Benign inclusions, parasitic thyroid nodules, or aberrant lateral thyroid tissue are all terms used to describe non-malignant lateral neck thyroid tissue. Thyroid inclusions are typically described to be small in size, wedge shaped and/or located in the subscapular region and present in two or less lymph nodes.[3]

Conversely some authors argue that there is no embryological origin for thyroid tissue within lateral lymph nodes and thus all should be treated as metastasis.[9–11] Indeed, it has been shown that thyroid metastasis can occur without the identification of a primary source within the thyroid gland and so this theory cannot be disputed in the absence of a definitive thyroid malignancy.[1,2,12,13]

What is certainly agreed is that many thyroid malignancies are clinical indolent and there is a risk of overtreatment with removal of the thyroid gland condemning patients to life-long replacement therapy.[14]

The incidence of undiagnosed thyroid cancer in the general population is estimated at 0.7% although this varies geographically,[14,15] and the incidence of thyroid inclusions/metastasis in our cohort of 725 neck dissection patients falls within the published expected range.

This review of 278 SNB patients shows a prevalence of 3.6%, there are no other published series with which to compare this figure. Undoubtedly serial sectioning analysis at 150μn intervals will allow detection of extremely small deposits of abnormal tissue—this is the principle by which the process of diagnosing occult metastasis from OSCC is based. It is therefore possible that the pathological nodal analysis is uncovering the "true" rate of thyroid tissue within cervical lymph nodes. However, we know that on average 2–3 sentinel lymph nodes are submitted per patient where as a thorough neck dissection should contain at least 18 and often will consist of many more than this. Unless the neck dissections are also subjected to serial sectioning (an extremely laborious and costly endeavour) we will not be able to confirm this theory.

What is striking in this cohort of patients is the identification lymph nodes containing thyroid cells in neck levels that are infrequently mapped from oral cancers. In half of these cases the lymph nodes were in level IV or VI. In the two patients that underwent SNB twice for separate oral cancers the drainage patterns to these unusual sites were constant over time. The reliability of lymphatic mapping to metastatic and pre-metastatic lymph nodes was explained by Harrell et al.[7] In their murine model of metastatic melanoma where primary tumor cells injected into mouse foot pads induced increased lymphatic flow to the SNs prior to the development of a metastatic deposit. This suggests that mapping lymphatic flow within the neck may reflect a physiological process that is affected not only by the presence of OSCC metastasis but is potentially influenced by other non-lymphoid cells within the lymph nodes.

In SNB for oral cancer, the procedure involves injecting radiotracer closely around the tumor but in other tumor sites, for example breast, the radiotracer is injected in the vicinity of the tumor and still drains reliably to the "at-risk" lymph nodes. Our case series may show us the injection technique within the oral cavity is not critical, as the radiotracer will flow to lymph nodes which have an increased flow pattern. In turn this suggests that lymph nodes which contain thyroid cells have in some way been altered by the presence of thyroid cells and that these are not simply inactive inclusions. In a

sense, this may alter our definition of a SN from an LN that has a direct drainage pathway with the primary tumor to regional lymph nodes which have shown flow alterations because of the influence of signals from outside the node itself.

In this cohort none of the three patients who had a positive SNB OSCC leading to completion neck dissection had further TC in the neck dissection specimen. No primary thyroid lesion has been found in any of our patients with TC in the neck by imaging or thyroidectomy. However, these cases are at an early stage of follow up and they will continue long-term review.

CONCLUSION

Our study demonstrates that the prevalence of incidental TC in SNs is greater than that reported in neck dissections. Our observations would support the overarching conclusion for patient management in the discovery of incidental thyroid cells within SNs for OSCC. TC are not likely to be clinically relevant and can be managed on a conservative basis in the absence of clear metastatic features.

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