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Papillary thyroid carcinoma in cervical lymph node found in a patient of primary tongue squamous cell carcinoma: Ectopic thyroid versus metastatic deposits; A diagnostic dilemma

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Abstract

Background: The incidental discovery of papillary thyroid carcinoma (PTC) in cervical lymph nodes during neck dissection for tongue squamous cell carcinoma (SCC) is an exceedingly rare finding, reported in approximately 0.3 - 1.6% of head and neck squamous cell carcinoma (HNSCC) cases. Differentiating between metastatic PTC and papillary carcinoma arising in aberrant thyroid tissue poses a diagnostic challenge, especially in the absence of a detectable thyroid mass.

Case Presentation: A 35-year-old male presented with a rapidly growing ulcero-proliferative lesion on the lateral border of the tongue for four months. Biopsy revealed moderately differentiated SCC. The patient underwent hemiglossectomy with supraomohyoid neck dissection. Histopathology confirmed SCC with clear margins and no nodal metastasis; however, one cervical lymph node revealed thyroid follicles with cells showing optically clear nuclei. Immunohistochemistry was positive for TTF1 and HBME-1, confirming metastatic PTC. No palpable thyroid nodule was identified, and computed tomography demonstrated only hypodense colloid nodules. Thyroid function tests were normal, and the patient remains disease-free on follow-up without thyroid surgery.

Conclusion: The coexistence of tongue SCC and metastatic PTC in cervical lymph nodes is exceptionally uncommon. The absence of a primary thyroid lesion raises questions regarding the origin - occult metastasis versus transformation in aberrant thyroid tissue. The literature supports conservative management with vigilant follow-up when thyroid imaging shows no evidence of malignancy. Meticulous histopathological examination of neck dissection specimens in HNSCC is vital. Management should be individualized, balancing surgical intervention and surveillance based on clinic radiologic findings.

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Introduction

Patients diagnosed with oral cancers often exhibit the occurrence of multiple primary cancers in various organs (1). In this context, detecting papillary thyroid carcinoma (PTC) within cervical lymph nodes during neck dissection for tongue squamous cell carcinoma (SCC) is a rare occurrence. Such incidental metastatic deposits from thyroid carcinoma have been documented in only a small proportion - about 0.3% to 1.6% - of neck dissections performed for head and neck squamous cell carcinoma (HNSCC) (2).

Some patients may have primary lesions in the thyroid gland, while others may not manifest any evident malignant thyroid lesions. The factors contributing to this clinical phenomenon and the connection between tongue SCC and PTC identified in the cervical lymph nodes remain unclear. Furthermore, surgeons continue to face a clinical dilemma in deciding between thyroid surgery and opting for follow-up care (3).

It is challenging for a pathologist to determine whether to report it as PTC arising in lateral aberrant thyroid tissue or as metastatic PTC, especially in the absence of any obvious thyroid mass. Occult metastatic PTC frequently arises in the setting of more aggressive squamous cell carcinomas, and the clinical significance and optimal management of incidentally detected metastatic PTC remain uncertain. This is particularly challenging when imaging findings are negative, as the focus may be extremely small on gross examination, leading to difficulties in identifying the primary thyroid tumor in certain cases (4). We present a case of PTC metastasis identified incidentally in a cervical lymph node obtained during neck dissection for tongue SCC.

Case Report

A 35-year-old male presented to the otolaryngology outpatient department (OPD) with a rapidly growing ulcero-proliferative lesion over the lateral border of the tongue for 4 months. He had a history of smoking for 15 years. There was no significant past or family history. Physical examination, as well as his hematological and biochemical parameters, were within normal limits. Histopathological examination of the preliminary punch biopsy suggested Moderately Differentiated Squamous Cell Carcinoma (MDSCC). Thereafter, hemiglossectomy with supraomohyoid neck dissection was performed.

Gross examination showed a tumor measuring 3 × 2 × 1 cm in size with grossly clear margins. A total of 7 lymph nodes were dissected from the supraomohyoid neck dissection, the largest measuring 1.5 × 1 × 0.5 cm in size (Level II). Histopathology was consistent with MDSCC with free surgical margins and lymph nodes (Figure 1A). The Depth of Invasion (DOI) was 4 mm. Interestingly, the largest lymph node showed thyroid tissue with its usual follicular arrangement and central colloid. A few cells showed optically clear nuclei; however, nuclear grooving was not seen (Figure 1B). An immunohistochemistry (IHC) panel was applied to confirm the metastatic nature of the thyroid deposits and to differentiate them from ectopic/heterotopic thyroid tissue. These cells were immunopositive for Thyroid Transcription Factor-1 (TTF1) and Human Bone Marrow Endothelial Marker-1 (HBME 1) (Figure 1C). A diagnosis of MDSCC tongue (pT1N0) with incidental metastatic Papillary Thyroid Carcinoma (PTC) in the cervical lymph node was rendered.

The patient was further investigated for any thyroid tumor. There was no palpable mass; therefore, Fine Needle Aspiration Cytology (FNAC) could not be attempted (Figure 1D). However, Computed Tomography (CT) revealed multiple hypodense nodules in the left lobe of the thyroid, suggestive of colloid nodules (Figure 1E). His thyroid function tests were normal. On follow-up, he has not undergone any thyroid surgery and remains clinically stable.

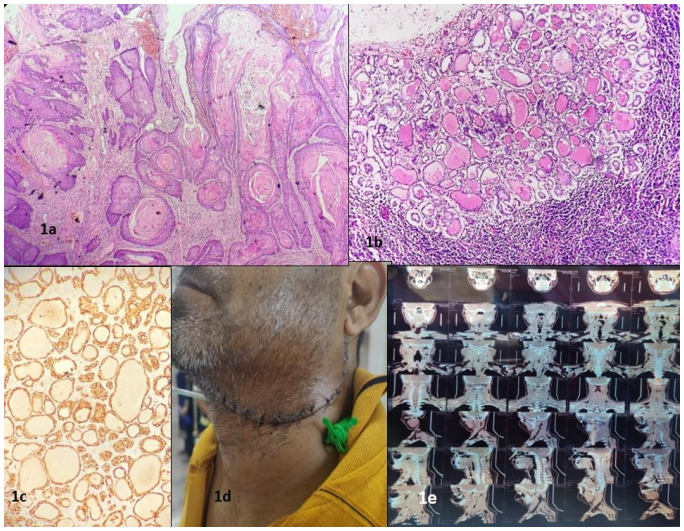

Figure 1. (A) Moderately differentiated squamous cell carcinoma of the tongue (H and E; 100×), (B) Metastatic papillary thyroid carcinoma in a lymph node (H & E; 200×), (C) HBME1-positive tumor cells (IHC; 100×), (D) Post-hemiglossectomy with modified radical neck dissection, showing no palpable thyroid mass, and (E) CT scan showing multiple hypodense nodules in the left lobe of the thyroid, consistent with colloid nodules.

Discussion

The incidental discovery of thyroid inclusions during elective or therapeutic neck dissection for non-thyroid cancers, such as head and neck squamous cell carcinoma (HNSCC), is an uncommon occurrence (5). The inadvertent identification of papillary or follicular thyroid tissue during the histological examination of neck dissections (NDs) performed for non-thyroid cancers, such as HNSCC, is described under the term “lateral aberrant thyroid.” The possibilities range from heterotopia to metastasis from an occult primary tumor or malignant transformation of ectopic thyroid tissue within the cervical lymph nodes (3,6). A comprehensive review in 1981 concluded that benign thyroid follicles may be present in cervical lymph nodes (7). Willis's doctrine suggests that any “lateral aberrant thyroid” represents metastasis from a small or unsuspected thyroid carcinoma (8). However, it remains a gray zone whether to classify such findings as benign or metastatic, and thorough evaluation is required.

The reported prevalence of thyroid ectopy is approximately 1 in 10,000, with over 99% of thyroid cancers originating within the thyroid gland itself. Ectopic thyroid tissue can manifest in several anatomical locations, with the lingual, sublingual, thyroglossal, laryngotracheal, and lateral cervical areas being the most frequently encountered sites. However, during embryonic development, thyroid tissue may also aberrantly appear in more distant structures, including the esophagus, mediastinum, heart, aorta, adrenal glands, pancreas, gallbladder, and even the skin. Notably, ectopic thyroid tissue is susceptible to the same pathological conditions as orthotopic thyroid tissue, including inflammation, hyperplasia, and tumor development, highlighting the clinical significance of recognizing and managing such occurrences (9,10).

The thyroid gland develops adjacent to the base of the tongue, between the first and second pharyngeal pouches. Around the third week of gestation, endodermal cells within the primitive pharynx proliferate to form the thyroid diverticulum. This invagination arises at the foramen cecum and descends to form the thyroid parenchyma, initially remaining connected by the thyroglossal duct. The duct later degenerates around the seventh week of gestation. Ectopic thyroid tissue arises due to abnormalities in the descent of the median anlage of the thyroid or the ultimobranchial bodies, often combined with incomplete closure of its vertical tract (9).

It is important to consider the possibility of metastatic malignancy when a cervical lymph node exhibits an atypical histological pattern. Secondary deposits in cervical lymph nodes may arise from primary tumors in diverse organs, including the esophagus, breast, stomach, lung, prostate, head and neck region, and thyroid gland - as demonstrated in the present case. Evaluating the likelihood of synchronous malignancies before initiating oral cancer therapy is essential, as it can significantly influence patient prognosis. Moreover, occult PTC is not uncommon and has been reported in up to 10% of the general population and in 8%-35% of autopsy studies (1).

In a 2005 study, León and colleagues identified unsuspected thyroid tissue within lymph nodes in 11 out of 752 patients who underwent neck dissection for head and neck carcinoma. Among these, five cases showed features consistent with metastases from occult PTC, while the remaining six exhibited benign thyroid follicular inclusions located beneath the lymph node capsule (11).

PTC and SCC have been identified in the same cervical lymph node as a collision metastasis (3). Collision tumors refer to the concurrence of two histologically distinct neoplasms originating from separate primary sites, physically abutting and intermixing with each other. The primary site for this intermingling is typically the lymph node (2). However, the diagnosis of a collision tumor in the present case is not applicable, as there was no palpable thyroid mass and the patient did not undergo any prophylactic thyroid surgery.

Similar to the present case, Xu et al., in 2018, reported patients who underwent surgery for tongue SCC with incidentally detected thyroid tissue in cervical lymph node dissections. Neither preoperative physical examinations nor USG detected significant nodules in the thyroid glands of these patients. Consequently, none of the individuals underwent thyroid surgery or chemo-radiotherapy as part of their treatment plan. Xu et al. observed an absence of apparent malignant lesions in the thyroid glands and no evidence of related metastatic disease in these patients during follow-up. Their findings led them to propose that the occurrence and progression of PTC in cervical lymph nodes may not be significantly influenced by tongue SCC. Consequently, they suggested that immediate thyroid surgery may not be necessary in such cases. Instead, they emphasized the importance of regular follow-up examinations to monitor the patients’ health status over time (3).

Beyond the characteristic nuclear features of papillary thyroid carcinoma, which include intranuclear grooves, intranuclear cytoplasmic inclusions, and a ground-glass appearance, the use of immunohistochemical staining is helpful in differentiating metastatic lesions from ectopic thyroid tissue (12). In the current case, histomorphology revealed exclusively clear nuclei without inclusions or grooving. Consequently, IHC analysis was performed to establish the diagnosis. Notably, one study reported that PTC cells exhibit strong and diffuse immunoreactivity for keratin, CK7, thyroglobulin, TTF1, and PAX8. In contrast, other markers such as HBME-1, Galectin-3, S100 protein, CITED1, and CK19 have shown variable results (13). In another study, IHC, particularly with markers such as HBME-1 and CK19, proved valuable in distinguishing intranodal benign thyroid tissue from metastatic PTC within lymph nodes. In the present case, a definitive diagnosis of metastatic papillary thyroid carcinoma in the cervical lymph node was established, supported by strong positive staining for TTF1 and HBME-1 (11,14).

The predominant genetic alteration found exclusively in PTC and its variants, and absent in benign thyroid lesions, is the BRAF V600E gene mutation. IHC staining for BRAF V600E serves as a reliable alternative to molecular detection techniques, thereby facilitating an accurate diagnosis (4).

The optimal strategy for managing incidentally discovered metastatic PTC during neck dissection for primary oral tongue SCC remains controversial. This consideration is influenced by the generally favorable prognosis associated with thyroid cancer and the challenges in identifying the primary tumor, which is often small and not grossly apparent. Management of such cases requires careful evaluation and appropriate therapeutic guidance. In cases where papillary thyroid carcinoma coexists with HNSCC, overall survival is primarily determined by the stage of SCC (2).

When thyroid ultrasonography does not reveal any features suggestive of malignancy, many patients may opt for regular clinical follow-up as a suitable approach. This strategy enables close monitoring without immediate intervention unless further evidence of malignancy emerges (4).

Conclusion

Thorough scrutiny of dissected lymph nodes in non-thyroid surgeries, such as those performed for HNSCC, is crucial to identify the possibility of incidentally discovering foci of PTC in lymph nodes. It is noteworthy that identification of a primary PTC within the thyroid is not consistently achieved, even in specimens obtained from partial or total thyroidectomy. The choice between surgical intervention and surveillance in clinical management depends on the findings of clinical and radiological evaluation of the tumor.

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Ethical Statement

Informed consent was obtained from the patient.

Conflicts of Interest

None

Author Contributions

All authors contributed equally to the manuscript.

Data Availability Atatement

Not applicable

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