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Synchronous Primary Head and Neck Tumors: Follicular Thyroid Carcinoma and Squamous Cell Carcinoma of The Tonsil

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Simultaneously occurring malignancies may be detected in different organs or tissues at any given time. Patients diagnosed with a tumor may be found to have another tumor or second primary cancer. Second primary cancers (SPCs) may be further classified as synchronous or metachronous. Synchronous SPCs are lesions detected simultaneously or within 6 months after the diagnosis of the primary tumor while metachronous SPCs are tumors diagnosed 6 months after primary tumor diagnosis.¹

There is an increased risk of having second primary cancer in Head and Neck Squamous Cell Carcinoma (HNSCC) patients.¹ In a study by Strojan *et al.* in 2013, among 2,106 head and neck cancer patients, 2.4% developed synchronous second primary cancers.² A systematic review by Coco-Pelaz *et al.* in 2020, showed that second primary tumors most frequently occur in the head and neck area followed by the lungs and esophagus.³

We present a case of follicular thyroid carcinoma with an incidental finding of cervical lymph-node metastatic squamous cell carcinoma from the tonsil and discuss the clinical presentation, ancillary procedures and management.

CASE REPORT

A 54-year-old woman consulted due to a firm and non-tender anterior neck mass that she palpated three months earlier associated with enlarged lymph node on the right lateral neck. She had no sore throat or dysphagia. She had a family history of thyroid disease (hypothyroidism and hyperthyroidism) but no history of malignancy. She was an occasional cigarette smoker and alcoholic beverage drinker.

Nasal endoscopy showed unremarkable nasal cavities and nasopharynx; the oral cavity examination appeared normal with unenlarged, unremarkable faucial tonsils and non-hyperemic

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posterior pharyngeal wall. A firm, non-tender anterior neck mass measuring 2 x 2.5 cm that moved with deglutition and a firm, movable, non-tender right level II jugulodigastric lymph node measuring 4 x 2 cm were palpated. Video laryngoscopy showed normal-appearing symmetrical vocal cords with no masses that were mobile on phonation.

A neck CT scan revealed a 2.1 x 2.3 x 1.5 cm enhancing hypodense mass in the right thyroid lobe with multiple cervical lymphadenopathies (level IB bilaterally, and levels II and III, right) with the largest at level II measuring 4.0 x 2.3 x 2.1 cm. (Figure 1) Fine needle aspiration biopsy of the right thyroid lobe revealed atypical thyrocytes with oncocytic and anaplastic features (Bethesda V). The clinical impression was thyroid malignancy.

She underwent total thyroidectomy with right lateral neck dissection. Intraoperative findings revealed a solitary firm nodule measuring 2.0 x 2.0 cm in the right thyroid lobe. Enlarged right lateral neck nodes at Levels II and III were identified and removed during the operation. Histopathology revealed minimally invasive follicular carcinoma, right thyroid lobe, and metastatic squamous cell carcinoma, keratinizing, Level II and III lymph nodes. (Figure 2A)

Due to the findings of metastatic squamous cell carcinoma to cervical lymph nodes, a second primary tumor was sought. Re-evaluation showed no other significant primary lesions on physical examination and on CT scan. A Positron Emission Tomography (PET) scan showed a hypermetabolic enhancing right palatine tonsil and right cervical lymphadenopathy. (Figure 3) Wide resection of the right palatine tonsil with right modified radical neck dissection was done followed by radiation therapy 6 weeks post-surgery. Final histopathology revealed moderately differentiated squamous cell carcinoma and no malignant cells were found in the 17 lymph nodes from levels II-V. (Figure 2B) The hospital stay of the patient was unremarkable and she was discharged well.

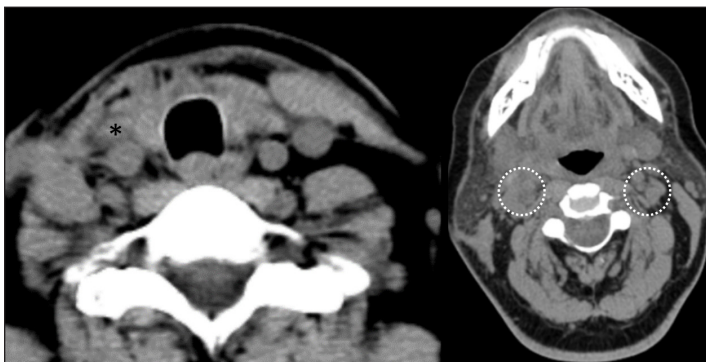


Figure 1. Contrast-enhanced CT scan of the neck. Enhancing hypodense mass in the right thyroid lobe (black asterisk) and multiple enlarged right cervical lymphadenopathies (white dashed circles)

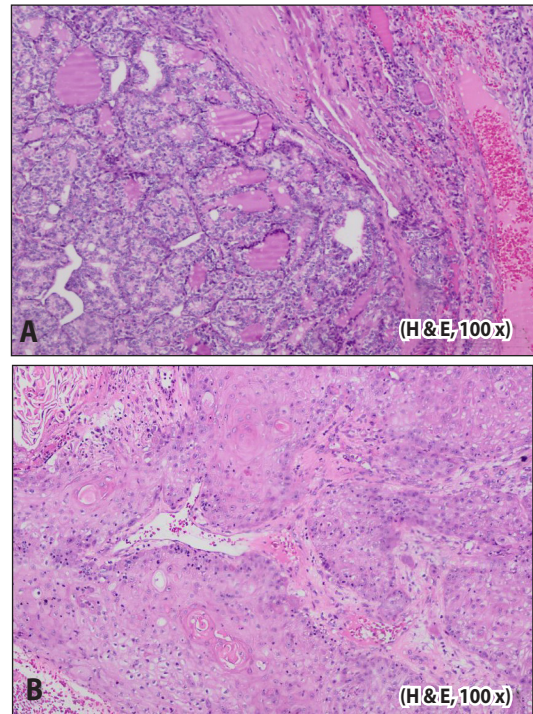


Figure 2. Histopathology slides, Hematoxylin – Eosin, low-power views (100x), showing **A.** Follicular carcinoma of the thyroid showing capsular invasion; and **B.** Squamous cell carcinoma of the right tonsil showing well differentiation characterized by keratinization

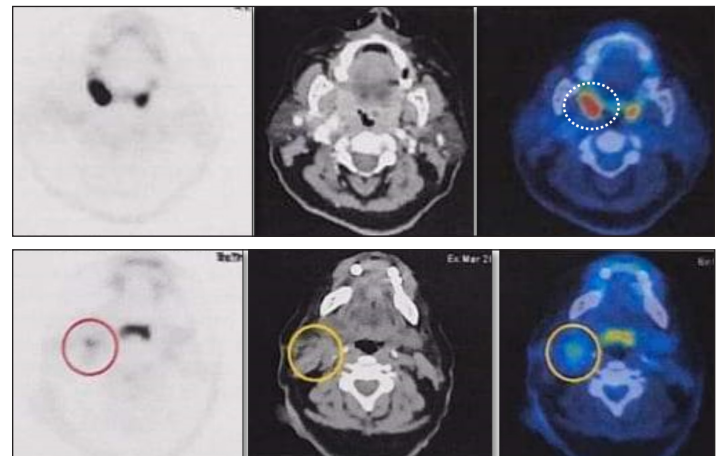


Figure 3. PET-CT scan showing enhancing right palatine tonsil (dashed circle) and right level II lymph nodes (solid circles)

DISCUSSION

Patients with head and neck malignancy are at an increased risk of developing second primary cancers although recent studies suggest a slightly reduced risk compared to previous estimates.¹ Over time, this risk becomes a significant concern for patients surpassing the threat posed by tumor recurrence.¹ Advanced patient age, inadequate oral hygiene and excessive tobacco and alcohol consumption are



common risk factors that heighten the likelihood of developing second primary tumors.³ Furthermore, head and neck cancer patients may be genetically susceptible to changes occurring in cancer development.⁴ Based on Global Cancer Data, the occurrence rates of second primary cancer in various regions of the head and neck are as follows: 4.3 cases per 100,000 population for the oral cavity, 2.2 for the larynx, 2.0 for the pharynx, and 1.2 for the nasopharynx.⁵ Head and neck cancers are reported to have 2.4 to 7% probability of having synchronous tumors.⁶ Synchronous tumors present unique challenges compared to metachronous tumors with the latter generally having a more favorable prognosis.⁷ This will depend upon the location of the tumors involved and stage at the time they were diagnosed and identified.

Initially, papillary thyroid carcinoma was considered in our patient due to its common occurrence with lymph node metastasis. However, histopathology revealed minimally invasive follicular thyroid carcinoma which is less likely to metastasize to lymph nodes. The presence of enlarged neck nodes raised suspicions of a possible second primary tumor, particularly from the tonsil, since nasal and laryngeal endoscopic evaluation did not show any suspicious tumor.

Follicular thyroid carcinoma (FTC) is considered the second most common thyroid cancer and typically presents as encapsulated lesions with varying degrees of invasion.⁸ Owing to its morphologic difference, FTC is divided into minimally invasive without vascular invasion which is more common in younger patients compared to invasive FTC which has vascular invasion or tumor capsule infiltration.⁹ Although metastasis to neck nodes is uncommon, since FTC is regarded as more aggressive than papillary thyroid carcinoma, the presence of multiple nodes prompted total thyroidectomy with selective neck dissection. In our case, histopathology revealed minimally invasive follicular neoplasm which has a ~97% 20-year survival.⁸ However, one of the lymph nodes revealed the presence of metastatic squamous cell carcinoma. Although a good survival rate may be expected in minimally invasive FTC, presence of a second primary tumor in our case certainly affects the patients otherwise good prognosis. The simultaneous occurrence of metastatic squamous cell carcinoma in the cervical lymph nodes suggested a second primary tumor, highlighting the importance of thorough investigation.⁸

Cervical metastasis of an unknown primary lesion comprises 5 to 10% of head and neck cases.¹⁰ In cases of metastatic squamous cell carcinoma with an unknown primary site, clinical examination and imaging are crucial for localization.¹¹ PET-CT has emerged as a valuable tool in identifying primary sites, particularly in cases where other modalities have failed.¹¹ However, interpretation pitfalls and false positive results must be considered.

In our case, the tonsils were not enlarged with no episodes of sore throat or complaints pertaining to problems in swallowing. Typically, individuals diagnosed with oropharyngeal squamous cell carcinoma often experience foreign body sensation in their throat, difficulty swallowing, ear pain, and in more severe instances, restricted movement of the jaw.¹² In contrast, our patient was asymptomatic at the outset except for the nodular goiter and enlarged neck nodes. Clinical manifestations of oropharyngeal SCC vary depending on the extent of the lesion wherein cranial nerve palsies may be present for patients with extensive tumors involving the parapharyngeal space while others may be primarily asymptomatic with no obvious lesion such as a submucosal tumor.¹² In these cases, additional imaging modalities may be requested. Over the last decade, there has been notable progress in evaluating carcinoma with unknown primary due to the introduction of Positron Emission Tomography-Computed Tomography (PET-CT). PET-CT proves valuable in cases where other imaging methods have fallen short, as it can guide surgeons toward potential primary sites.¹³

In a 10-year retrospective study done by Sokoya *et al.*, PET-CT was reported to have a sensitivity of 73.1% and negative predictive value of 68.9% in determining the primary site of unknown primary head and neck squamous cell carcinoma.¹⁴ Among the tumors identified, tonsillar cancer represents 56% of the cases.^{2,14} According to Kothari *et al.*, tonsillar carcinoma is the 3rd most common silent primary tumor, with an incidence of 18 - 47%, but is likely to be missed during clinical examination especially if the lesion is submucosal.¹⁰ According to Ridge, *et al.*, most common sites of silent primary tumors are the tonsils, base of the tongue and piriform sinuses.¹⁵ In our case, the tonsillar lesion was submucosal since no gross or apparent manifestations of malignancy were observed. Initial CT imaging did not reveal any suspicious lesion in the tonsils hence we requested PET-CT scan to evaluate for a possible second primary cancer. PET-CT scan aided the surgeons of this case since it revealed the hypermetabolic enhancing right palatine tonsil.

Submucosal squamous cell carcinomas are typically located in the base of the tongue and the tonsils. While the exact cause is not fully understood, some theories suggest that they might originate from a small mucosal tumor that regresses and emerges from the ducts of minor salivary glands, subsequently losing its surface connection.¹² In our case, the final histopathology of the right palatine tonsil revealed keratinizing moderately differentiated squamous cell carcinoma.

Cervical lymph nodes are considered the most common area of metastasis for malignant tumors from primary sites in the head and neck region. For the head and neck region, jugulodigastric (Level II) lymph nodes are referred to as sentinel nodes being the primary site of drainage in the upper neck region, including the nasopharynx, larynx,

and oropharynx.¹⁶ Level II nodes serve as primary lymphatic drainage for tonsillar neoplasms such as in our case but they may also involve retropharyngeal and parapharyngeal nodes and level III and IV nodes.¹⁶ The level of lymphatic drainage involvement depends on the stage at presentation. Tonsillar squamous cell carcinoma has high incidence of nodal metastasis at 76% of cases with level II node as the most common site.¹⁷ This may explain the prominently enlarged jugulodigastric node in our case.

In cases of oropharyngeal carcinoma, neck dissection depends on the primary, the clinical status and pathologic status of the neck. Modified radical neck dissection is usually done but supraomohyoid and lateral neck dissection also proves to have oncological safety.¹⁸ Neck dissection is beneficial to patients mainly due to the reduction of incidence of disease recurrence, thereby avoiding further surgeries.¹⁸ Hence, when the second primary was localized in the tonsils, wide excision and modified radical neck dissection was performed in our patient.

Tonsillar squamous cell carcinoma and minimally invasive follicular thyroid carcinoma synchronously occurring is a rare event. A search of HERDIN Plus, the ASEAN Citation Index (ACI), the Western Pacific Region Index Medicus (WPRIM), the Directory of Open Access Journals (DOAJ), MEDLINE (PubMed and PubMed Central), and Google Scholar

using the search terms “tonsil,” “squamous cell carcinoma,” “thyroid follicular carcinoma,” and “synchronous head and neck cancer” revealed no English language reports of such a synchronous occurrence. Recognition of both malignancies allows for proper management which offers the best chance of cure for the patient.

In retrospect, the presence of enlarged jugulodigastric lymph nodes in a follicular thyroid neoplasm should have alerted us to the possibility of a primary or secondary tumor of the oropharynx especially the palatine tonsils. In our case, the second primary tumor was in the oropharynx involving the right palatine tonsil. The normal looking mucosa overlying the tonsil gave no clue and made it difficult to determine the presence of underlying malignancy especially in the submucosal area. This was coupled with the absence of throat symptoms such as pain and odynophagia. The presence of an enlarged lymph node in the right jugulodigastric area may be misinterpreted as a red herring attributed to FTC which was eventually unmasked when histopathologic examination showed metastatic lymph nodes coming from the tonsils confirmed by PET scan.

Although rare, synchronous follicular thyroid carcinoma and occult tonsillar squamous cell carcinoma may occur. The presence of a second primary malignancy should be explored since it greatly affects the prognosis of patients with head and neck cancers.

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