CASE REPORTS

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Triple Primary Malignancy (Synchronous Papillary and Follicular Thyroid Carcinomas and Diffuse B-Cell Lymphoma of the Submandibular Gland and Cervical Lymph Nodes) in a 70-Year-Old Woman

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ABSTRACT

Objective: To report a case of triple primary malignant neoplasms in a 70-year-old woman diagnosed with follicular and papillary thyroid carcinoma and diffuse B-cell lymphoma of the right submandibular gland and cervical lymph nodes.

Methods:

Design: Case Report
Setting: Tertiary Government Training Hospital
Patient: One

Results: A 70- year-old woman presented with a four-year history of gradually enlarging anterior neck mass, associated with a right submandibular mass and neck nodes for one year. The gradual progression of her symptoms made the patient think that it was a benign condition. This led to a delay in medical consultation. The patient underwent total thyroidectomy with functional neck dissection of the ipsilateral right neck. Histopathology revealed simultaneous follicular and papillary thyroid carcinoma, and diffuse B-cell lymphoma of the cervical lymph nodes. The patient was referred to medical oncology and nuclear medicine for further management.

Conclusion: Our patient was incidentally diagnosed with follicular and papillary thyroid carcinoma and diffuse B cell lymphoma of the cervical lymph nodes after surgery. Such triple primary malignant neoplasms in a single individual are rare, and as in our case, may only be diagnosed in hindsight.

Keywords: *multiple primary malignant tumors; follicular thyroid carcinoma; papillary thyroid carcinoma; submandibular gland diffuse b cell lymphoma*

Multiple primary malignant tumors (MPMT) are defined by two or more distinct malignancies occurring in the same patient.[1] Such MPMTs may be diagnosed synchronously (the second primary cancer is diagnosed within 6 months after the detection of the first primary cancer) or metachronously (the second primary cancer is diagnosed more than 6 months after the detection of the first primary cancer).[2] Based on a search using HERDIN Plus, Directory of Open Access Journals (DOAJ), PubMed and PubMed Central using the search terms "Multiple

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Primary Malignancies", "Synchronous Thyroid Tumors", "Synchronous Malignancies" and "B Cell Lymphoma", we found no reported case of a combined papillary thyroid carcinoma with follicular thyroid carcinoma and a diffuse large B cell lymphoma in a single patient. We report one such case.

CASE REPORT

A 70-year-old woman presented with a four-year history of gradually enlarging, approximately 2x2 cm non-painful right anterior neck mass with no signs and symptoms of hyperthyroidism, hypothyroidism and compression. She did not take any medication nor seek any consultation. However, a year prior to consult, there was an appearance of a non-painful mass in the right submandibular area and right lateral neck area with no associated signs and symptoms. The patient subsequently consulted in our department.

On physical examination, there was a 2 x 3cm, firm, non-erythematous, non-tender anterior neck mass that moved with deglutition. A 2.5 x 3 cm firm, well-circumscribed, non-tender mass was also noted in the right submandibular area together with a 6x8 cm, soft to firm, non-movable, non-tender mass in the right lateral neck area, levels II-IV. There were no palpable neck nodes on the left. *(Figure 1)*

Thyroid function tests revealed low TSH at 0.005 uIU/ml (normal value: 0.27-4.20 uIU/ml) and elevated FT4 at 1.85 ng/dl (normal value: 0.93-1.71 ng/dl). Ultrasound imaging of the thyroid gland showed a solid right thyroid nodule with rim calcification, measuring 2.45 cm in greatest dimension, and a mild solid-cystic left thyroid nodule, 3.78 cm in greatest dimension. Multiple enlarged cervical lymph nodes were also noted in levels I-IV, right. Fine needle aspiration cytology of the thyroid nodule on the right was classified Bethesda system category V (suspicious for papillary thyroid carcinoma). However, fine needle aspiration cytology of the right lateral neck node on level III revealed nonspecific malignant findings.

Repeat thyroid function tests were normal after two weeks of medication with Methimazole and the patient was cleared to undergo surgery. Thinking that this is a typical case of papillary thyroid carcinoma with right neck node involvement, we initially intended to perform a total thyroidectomy with right functional neck dissection.

Intraoperatively, the sizes of the right lobe, isthmus, and left lobe were 5×3×1.5 cm, 2 × 1.5 × 0.3 cm, and 4.5 × 3 × 2.2 cm, respectively. Both thyroid lobes were noted to have multiple firm and cystic nodules, the largest of which was a cystic nodule in the middle to inferior portion of the left thyroid lobe approximately 3 x 2 cm in size and a firm nodule on the middle portion of the right thyroid lobe, approximately 2 x 1.5cm. *(Figure 2A)* What we initially thought to be the right submandibular lymph node turned out to be the right submandibular gland which

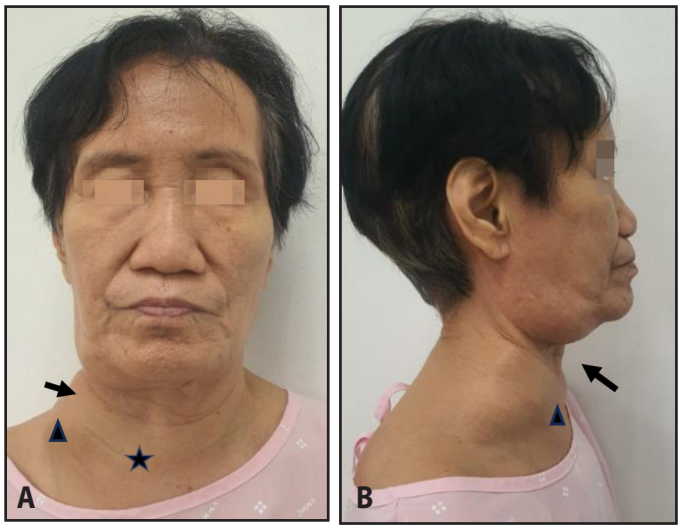
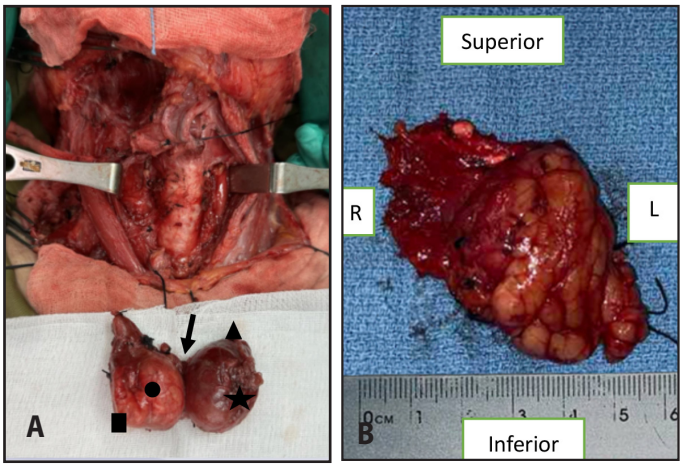


Figure 1. Pre-operative photographs. **A.** frontal; and **B.** lateral views; showing 2x3cm, firm non-erythematous non-tender anterior neck mass that moves with deglutition (star); 2.5 x 3 cm firm, well circumscribed, non-tender right submandibular mass (arrows) also noted, together with a 6 x 8 cm soft to firm non-movable non-tender right lateral neck mass, levels II-IV (triangle). Photos published with permission.



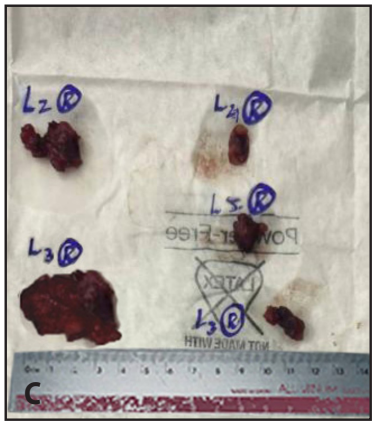
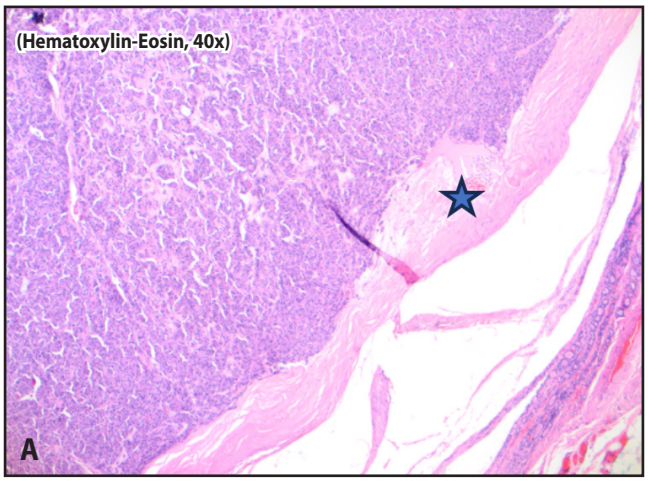
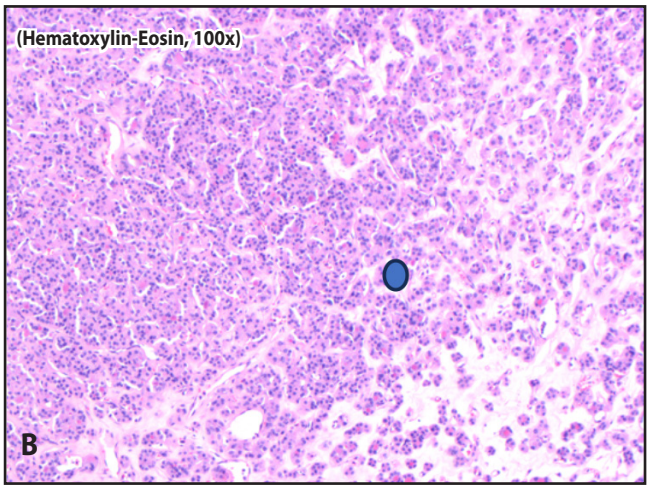


Figure 2. Intraoperative photographs showing **A.** thyroid gland gross specimen: the right lobe (square), isthmus (arrow), and left lobe (triangle). Both thyroid lobes were noted to have multiple firm and cystic nodules, largest of which was a cystic nodule on the middle to inferior portion of the left thyroid lobe (star) and a firm nodule on the middle portion of the right thyroid lobe (dot); **B.** right submandibular gland; and **C.** right lateral neck nodes from levels II-V.





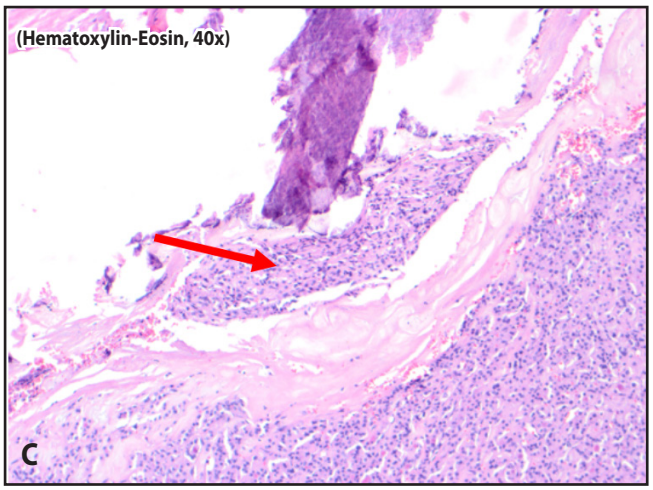
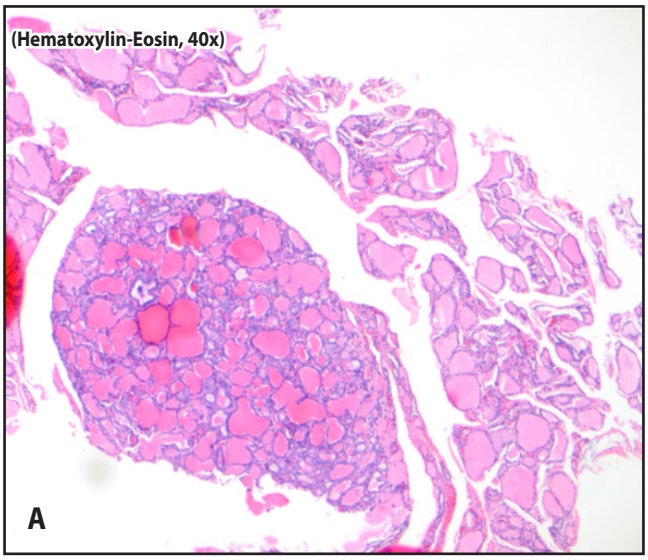


Figure 3. Histopathologic sections from the right thyroid lobe, hematoxylin and eosin (H&E) stain. **A.** scanning view (40x); **B.** low power view (100x); and **C.** scanning view (40x) showing monomorphic appearance of thyroid cells with formation of micro follicles (dot) within a capsule (star) with identified angioinvasion (arrow), diagnostic of follicular thyroid carcinoma.



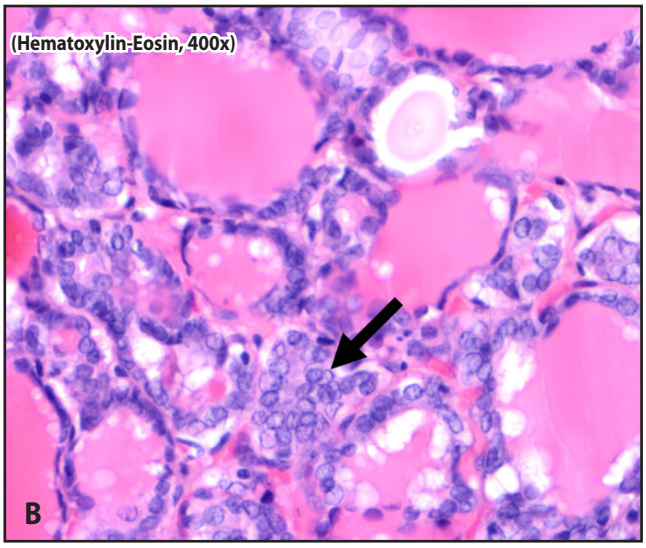


Figure 4. Microsections of the isthmus, hematoxylin and eosin (H&E) stains; **A.** scanning view (40x); and **B.** high power view (400x), exhibiting nuclear enlargement and overlapping, chromatin clearing and irregular nuclear contour and nuclear grooves (arrow), diagnostic of papillary thyroid carcinoma.

presented as a gray-white appearance with a soft texture lobulated external surface. The right submandibular gland measured 5.5 x 5 x 3cm *(Figure 2B)* and the right cervical lymph nodes in levels II-V were enlarged, largest of which was in level III, measuring 5 x 3.5cm in largest diameter *(Figure 2C)*, with firm attachment to the right carotid sheath and resultant compression of the adjacent segment of the right internal jugular vein. The patient tolerated the procedure and was subsequently discharged in good condition.

On follow-up, histopathological studies revealed follicular thyroid carcinoma in the right thyroid lobe *(Figure 3)* while the thyroid isthmus

had papillary thyroid carcinoma. *(Figure 4)* The right submandibular gland and right lateral neck nodes revealed numerous monotonous populations of large, round blue cells with prominent nucleoli, suggestive of a neoplastic process. *(Figure 5)* Immunohistochemical staining of the right submandibular gland was positive for CD20 and Ki-67, while CD3 tested negative, *(Figure 6)* confirming the diagnosis of diffuse B-cell lymphoma. The patient was referred to medical oncology and nuclear medicine for further management. However, she temporarily refused to continue her treatment and was lost to follow-up. The patient decided to continue her treatment in another institution, where she subsequently completed 16 fractions of external beam radiation therapy totaling 480 cGy and awaits chemotherapy for her diffuse B-cell lymphoma and RAI for the thyroid carcinomas. Post surgery, they had to prioritize the treatment for lymphoma, hence, radiation therapy. As of this writing, she is scheduled for a fluoro-D-glucose positron emission tomography with computed tomography (FDG PET/CT) scan to re-evaluate the status of her cancer prior to further oncologic treatment and to determine whether RAI is still warranted.

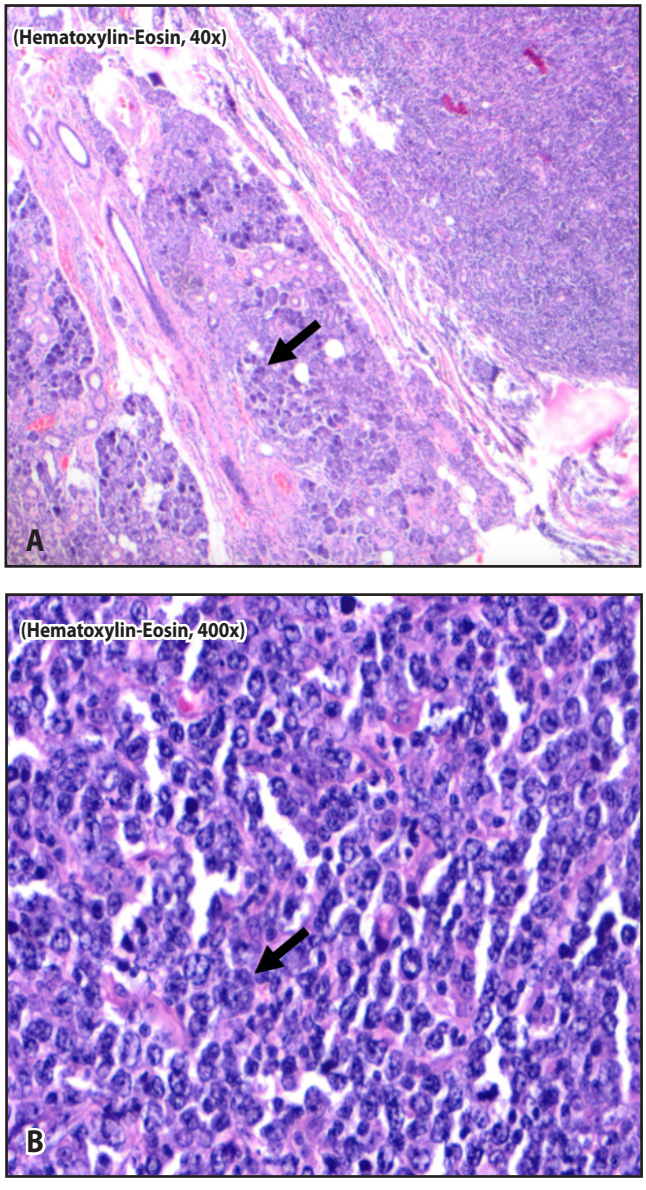


Figure 5. Microsections of the right submandibular gland, hematoxylin and eosin (H&E) stain; **A.** scanning view (40x); and **B.** right lateral neck nodes, hematoxylin and eosin (H&E) stain, high power objective (400x) showing numerous monotonous populations of large, round blue cells with prominent nucleoli (arrow), findings suggestive of a neoplastic process.

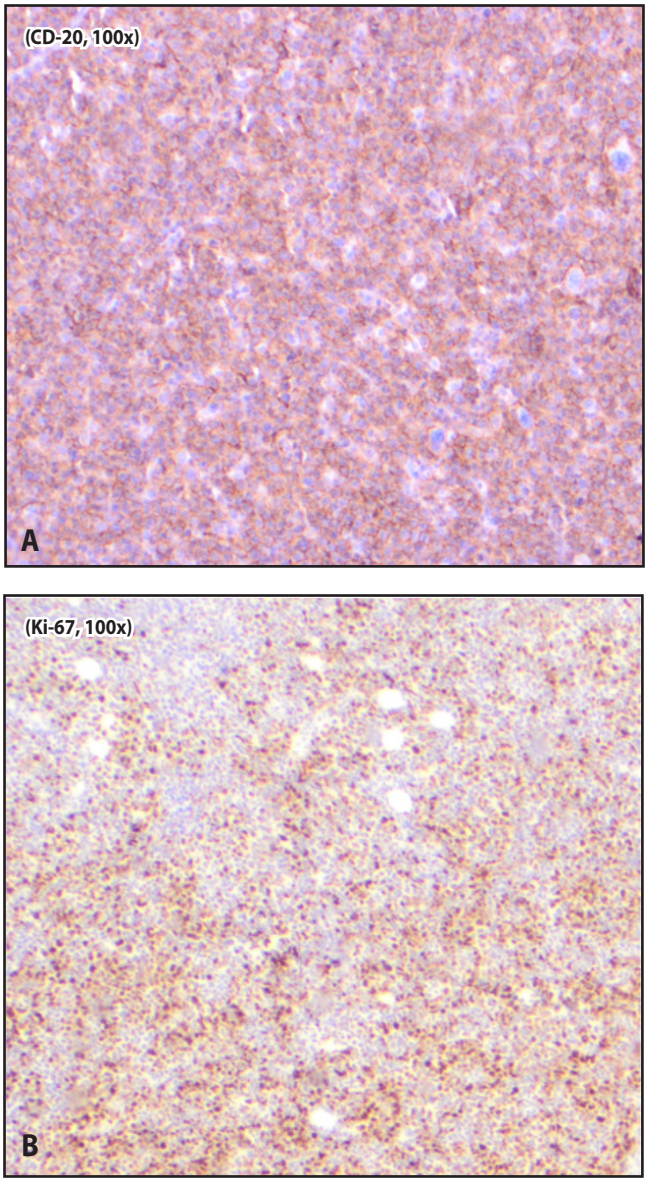


Figure 6. Microsections of the right submandibular gland, immunohistochemical stains, low power views (100x). The specimen tested positive for **A.** CD-20; and **B.** Ki-67;

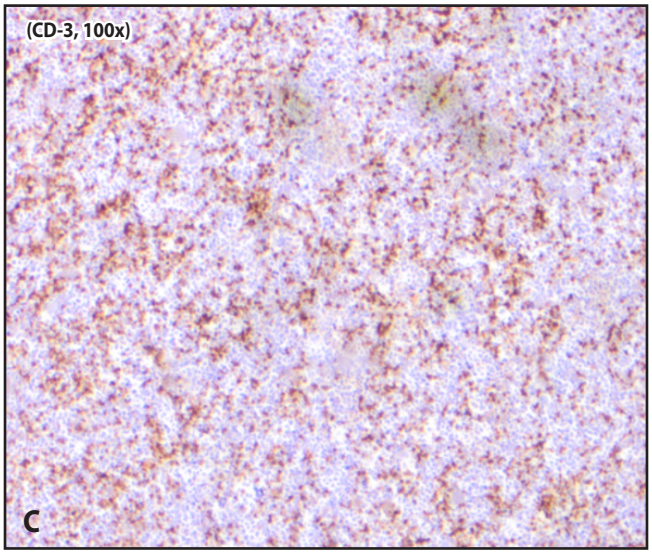


Figure 6 C. while testing negative for CD-3; confirming the diagnosis of diffuse large B-cell lymphoma.

DISCUSSION

We reported a case of triple primary malignant neoplasms in a 70-year-old woman diagnosed with follicular and papillary thyroid carcinoma and diffuse B-cell lymphoma of the cervical lymph nodes.

Multiple primary malignant tumors are quite uncommon. The reported prevalence of multiple primary malignant neoplasms (MPMN) varied between 0.734% and 11.7% (out of 1,104,269 cancer patients).[3] A similar study revealed that the prevalence of multiple primary malignancies is 1.09% (167 out of 15,321 cancer patients).[2]

Thyroid cancer accounts for about 1% of all cancers. Papillary thyroid cancer (PTC) and follicular thyroid carcinoma (FTC) account for 70–90 and 15% of all thyroid cancers, respectively.[4] However, the simultaneous occurrence of different types of thyroid carcinomas in the same patient is an unusual event, with simultaneous existence of FTC and PTC placed at 19%.[4]

While both types are considered to be relatively quiescent, papillary carcinoma shows a predilection for lymphatic metastasis while follicular carcinoma tends to metastasize hematogenously.[5] Having both poses a potential risk for both lymphatic and hematogenous metastasis from these individual pathologies. Lymph node metastases of papillary thyroid carcinoma are almost as often found in the ipsilateral cervicolateral compartment. However, in our case, the histopathological studies of lymph nodes revealed different malignant findings.

Since our patient presented with an anterior neck mass with ipsilateral right neck node involvement, we performed a fine needle aspiration biopsy that revealed papillary thyroid carcinoma. Her presentation did not give us any clue that she had multiple malignancies, and we did not anticipate the probability of occurrence of multiple malignant tumors.

Although many kinds of malignant tumors occur in the major and minor salivary glands, primary lymphomas arising in salivary glands are very uncommon.[6] Non-Hodgkin malignant lymphoma in the salivary glands is very rare, and accounts for about 1-5% of all salivary gland neoplasms.[7] Schmid *et al.* reported that of 25 salivary gland lymphomas, 21 were parotid gland lymphomas and 4 were submandibular gland lymphomas.[8]

Lymphomas originating in the submandibular salivary glands are a rare but well-documented occurrence.[9] In our patient, the histopathological study of the right submandibular gland revealed Diffuse B-Cell lymphoma. The submandibular gland lacks intraglandular lymph nodes and, therefore, the incidence of extranodal parenchymal lymphomas of the submandibular glands is very rare.[9] In our case, aside from the diffuse B-Cell lymphoma of the right submandibular gland, the ipsilateral neck nodes revealed the same findings.

The outcome is poorer for patients with multiple primary cancers than for those with a single primary cancer and treatment should be planned to achieve the best outcome for each cancer.[4] Hence, our patient was referred to Oncology and Nuclear Medicine for further evaluation and treatment planning, allowing the malignancies to be accurately assessed and appropriately prioritized.

In conclusion, our patient was incidentally diagnosed with follicular and papillary thyroid carcinoma and diffuse B cell lymphoma of the cervical lymph nodes after surgery. Such triple primary malignant neoplasms in a single individual are rare, and as in our case, may only be diagnosed in hindsight.

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