Papillary thyroid carcinoma associated with non-functioning parathyroid carcinoma with Warthin's tumor of the parotid gland: A case report and brief literature review

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Abstract. Multiple neck pathologies occurring simultaneously are a rare condition. The present study describes an extremely rare case of papillary thyroid carcinoma, non-functioning parathyroid carcinoma (PC) and Warthin's tumor of the parotid gland. A 59-year-old male presented with a 3-month history of anterior neck swelling. The neck ultrasound revealed a left-sided thyroid nodule associated with pathological lymph nodes. There was a parotid gland mass. A fine-needle aspiration of the left parotid mass was not diagnostic, although the left thyroid nodule revealed a malignancy with metastasis to the left cervical group lymph nodes. The patient underwent total thyroidectomy, left central and left lateral cervical lymph node dissection. A superficial parotidectomy was also performed. A histopathological examination revealed three different pathologies: Papillary thyroid microcarcinoma, PC and Warthin's tumor. The simultaneous occurrence of a Warthin's tumor, papillary thyroid microcarcinoma and PC is an unusual condition. The concurrent findings of these three pathologies have not yet been reported in the literature, at least to the best of our knowledge. The synchronous findings of PTC, non-functioning PC and Warthin's tumor are extremely rare, yet possible. Surgical intervention remains the most appropriate treatment strategy.

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Introduction

Thyroid carcinomas (TC) account for <1% of newly diagnosed malignancies. Of the cases of primary hyperparathyroidism (PHPT), <1% are caused by parathyroid carcinoma (PC) and such cases are rarely observed in patients with normal blood calcium and parathyroid hormone (PTH) levels (1). PC is commonly a sporadic disease and less frequently presents as a genetic syndrome (2).

Concurrent PC with thyroid carcinoma is extremely uncommon, with only a few cases reported in the literature to date (3-5). On the other hand, tumors of the salivary glands are uncommon and the majority of these are benign; only 20% are malignant. The parotid gland is the most common site of occurrence, with >80% of major salivary gland tumors arising from an unknown etiology (6). The clinical and epidemiological characteristics include a history of tobacco smoking, old age, multicentricity and a male predominance (7). Primarily, it affects males in their fifth decade of life (8). However, a comprehensive review of the literature has not revealed any documented reports of synchronous thyroid and salivary gland tumors.

The present study describes an extremely rare case which involved the occurrence of papillary thyroid microcarcinoma (PTC), PC with Warthin's tumor of the parotid gland.

Case report

Patient information. A-59-year-old male presented to Smart Health Tower (Head and neck center) with anterior neck swelling with a duration of 3 months. He had a known history of hypertension and had been smoking for >30 years. He had a negative family history of cancer.

Clinical findings. A physical examination revealed a left sided non-tender anterior neck mass, as well as a non-tender swelling on the left side of the face.

Diagnostic assessment. The hematological analyses revealed normal levels of thyroid stimulating hormone, free T4 and

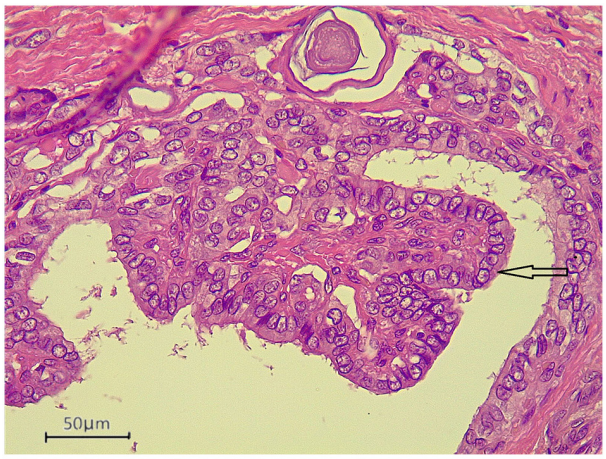

Figure 1. Results of the histological examination revealing a Thyroid carcinoma with papillary structures and typical nuclear features (black arrow).

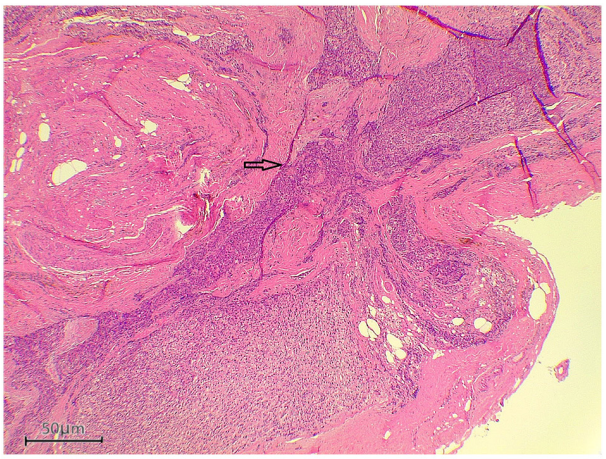

Figure 3. Results of the histological examination revealing a parathyroid tumor (black arrow) with infiltration of the surrounding fibroadipose tissue (yellow arrow). Magnification, x400.

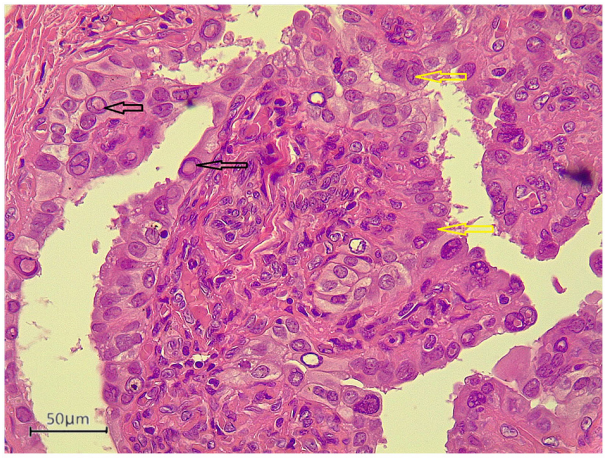

Figure 2. Results of the histological examination, with areas exhibiting typical nuclear features of papillary thyroid carcinoma, intranuclear pseudoinclusions (black arrows), and nuclear grooves (yellow arrows). Magnification, x400.

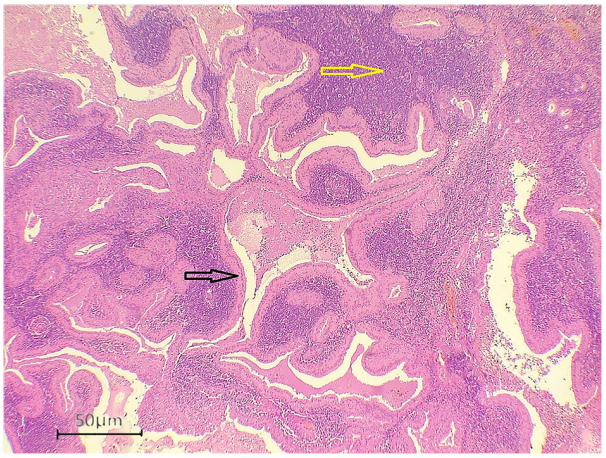

Figure 4. Results of the histological examination revealing a Warthin's tumor with double-layer benign-looking oncocytic epithelial cells (black arrow) with prominent benign lymphoid cells in the stroma (yellow arrow). Magnification, x400.

serum calcium. The neck ultrasound examination revealed a well-defined solid nodule of 17x15x13 mm in size in the middle left-sided thyroid gland with microcalcifications and groups II, III and IV lymph nodes were suspected to be pathological, the largest of which was 26x15 mm in size. An ultrasound of the left parotid gland revealed an ill-defined complex mass of 36x30 mm, involving the deep and superficial lobes. A computed tomography (CT) scan of the neck and chest with contrast imaging revealed multiple pathological cervical lymph nodes and superior mediastinal lymph nodes, the largest being 15 mm in size in the pre-aortic area with a 25x23-mm-thick wall structure in the left parotid gland. A fine needle aspiration from the left thyroid nodule was positive for malignancy with left cervical lymph node metastasis, but was non-diagnostic for the left parotid tumor.

Therapeutic intervention. After proceeding with a total thyroidectomy, the patient's left central and left lateral cervical lymph nodes were dissected. Subsequently, during the same session, the left superficial parotid gland and lymph nodes were also removed. The surgical specimen was analyzed in the histology laboratory of Smart Health Tower. The result of the histopathological examination was multifocal bilateral papillary thyroid microcarcinoma (PTMC) of conventional type (Figs. 1 and 2) with an incidental finding of PC in the left thyroid lobe (Fig. 3). The PC was associated with perineural and capsular invasion. The third pathology was a Warthin's tumor of the left parotid gland (Fig. 4). A total of 10 of the 30 lymph nodes dissected from the lateral groups (levels 2, 3, 4 and 5) and ipsilateral central were involved (one from the Delphian group, three from left the central group, and six from left the lateral group) with minimal extra-thyroidal extension in the left lobe tumor.

Patient follow-up. The post-operative period was uneventful. The patient was discharged on the first post-operative day.

Discussion

Thyroid nodules are a significant public health concern. Thyroid neoplasms arise from either follicular or

parafollicular cells (C cells) (9). Differentiated thyroid carcinomas (DTCs) arise from thyroid follicular cells. The most common variants of DTCs are Hürthle cell carcinoma, follicular thyroid carcinoma and PTC, which account for >90% of all thyroid cancer cases (10). PTC is the most common malignant thyroid tumor in countries where iodine is sufficient or excessive. The majority of tumors are discovered between the third and fifth decades of life (11). According to the World Health Organization (WHO), PTMC is a specific type of PTC with a maximum tumor diameter of ≤10 mm, accounting for 30-40% of all PTC cases (12,13). There are various well-known risk factors that contribute to the growth and progression of PTC, with ionizing radiation exposure being the most well-documented environmental cause of this disease. Other risk factors have been identified, including diabetes, sex, obesity, smoking, alcohol consumption, genetic factors, and the excessive consumption of dietary nitrates and iodine (14). The case in the present study had no family history of thyroid cancer; however, he had been a heavy smoker for >30 years.

It is uncommon for salivary glands and thyroid tumors to synchronize (15). The WHO classified parotid tumors histologically into >30 types. Warthin's tumors originate from both epithelial and lymphatic tissue (16,17). Salivary gland neoplasms are primarily treated by surgical resection, either with or without post-operative radiotherapy. There are also palliative treatment options available for patients who present with locally advanced, recurrent, or metastatic disease (18). Thyroid carcinomas have been reported to occur concurrently with breast, colon and stomach cancers, as well as with non-Hodgkin's lymphoma (15). The case described herein was diagnosed with a synchronous occurrence of thyroid cancer, PC and Warthin's tumor.

PHPT is a rare disorder that has increased in incidence in recent decades (3). PC can develop independently or as part of a genetic syndrome. Isolated familial hyperparathyroidism, multiple endocrine neoplasia (MEN)2A and MEN1 are examples of these syndromes. Furthermore, hyperparathyroidism jaw tumor syndrome, an autosomal dominant form of familial hyperparathyroidism causes PC in 15% of patients (4,19). There is a strong association between PC and hyperparathyroidism (HRPT)2 mutations (20). There have also been reports of PC arising within an adenoma or hyperplastic gland in patients who have had external irradiation (21,22).

In both MEN and non-syndromic cases, parathyroid and thyroid disorders frequently co-exist; however, synchronous thyroid cancer and PC cases are rare (2). Some researchers have classified these concurrent diseases as coincidental, while others have identified the rising of endogenous calcium levels, growth factors such as insulin-like growth factor and epithelial growth factor to play a role in synchronous diseases (5,23). In the case in the present study, there was no history of neck irradiation or any other known risk factors for PC and the HRPT2 genetic test was not performed.

The diagnosis of PC is difficult in the absence of regional or distant metastases (24). Biochemistry and imaging in the form of dual-phase sestamibi scintigraphy and ultrasonography are typically used as part of the pre-operative investigation for PHPT. Patients with parathyroid adenoma typically have elevated adjusted serum calcium and PTH levels; however, these biochemical markers may be abnormally elevated in PC (23). The common symptoms of patients with PC are the following: i) Severe primary hyperparathyroidism symptoms; ii) serum calcium levels of ≥14 mg/dl in >50% of patients; and iii) significantly elevated (typically five-fold the upper limit of normal) serum PTH levels (25). Only a few cases of non-functioning PCs with histological diagnoses have been reported to date (2). The case described herein had normal serum levels of calcium and no symptoms of hyperparathyroidism; however, the patient's pre-operative PTH levels were not investigated, as it was an incidental finding.

The surgical treatment of simultaneous parathyroid and thyroid carcinomas varies and has not always been fully described (26). A single operation of resecting both the thyroid and involved parathyroid glands is one of the choices (27). Superficial or total parotidectomy with preservation of the facial nerve is one of the treatments for Warthin's tumors (28). The case in the present study underwent total thyroidectomy, left central and left lateral cervical lymph node dissection, and the removal of the left superficial parotid gland and lymph nodes.

In conclusion, the synchronous findings of PTC, non-functioning PC and Warthin's tumor are extremely rare, yet possible. Surgical intervention remains the most appropriate treatment strategy.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

AMS was a major contributor to the conception of the study, as well as in the literature search for related studies. SHH and FHK were involved in the literature review, in the writing of the manuscript, in the follow-up of the case, as well as in the analysis and interpretation of the literature data to be included. AMA was the pathologist examining the specimen. YAS, SK and OAA were involved in the literature review, in the design of the study, as well as in the revision of the manuscript and in the processing of the figures. AJQ was the radiologist who performed the assessment of the patient. SAN and SHM were involved in the conception and design of the study. SAN and SHM confirm the authenticity of all the raw. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from the patient in the present study.

Patient consent for publication

The patient signed an informed consent form for the publication of his personal information and any related images.

Competing interests

The authors declare that they have no competing interests.

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