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Short Communication

Relationship between Carotid Body Tumor and Thyroid Papillary Cancer

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Abstract: Carotid body tumor (CBT) represents a specific type of head and neck paraganglioma that is characteristically located at the bifurcation of the carotid artery. This tumor typically causes a separation of the external and internal carotid arteries. On the other hand, papillary thyroid carcinoma is recognized as the most common malignant neoplasm of the thyroid gland. In spite of the fact that they are distinctive pathologies, they both affect the neck region. Given the exceptionally low incidence of carotid body tumors (CBTs), the occurrence of an additional malignancy—whether synchronous or metachronous—in the same patient is expected to be an extraordinarily rare phenomenon. Within the literature, a genetic and syndromic relationship between carotid body tumor and papillary thyroid carcinoma is not however known. We describe two cases that could provide valuable insights into the limited body of evidence concerning the potential relationship between these distinct pathologies. The simultaneous presence of carotid body tumor and papillary thyroid carcinoma in a single patient might either represent a coincidental finding or stem from an unidentified genetic mutation.

Keywords: Carotid Body Tumor; Thyroid Cancer; Paraganglioma; Thyroidectomy

1. Introduction

Carotid body tumors (CBTs) are uncommon neuroendocrine neoplasms originating from paraganglionic cells situated within the carotid body. Representing approximately 0.5% of all head and neck tumors, they constitute the majority (65%) of paragangliomas in this region [1]. Given their infrequency, there remains limited understanding regarding their etiology, clinical characteristics, biological behavior, malignancy potential, and overall prevalence. The most frequently reported clinical manifestation is the presence of a gradually enlarging, painless cervical mass. Bilateral carotid body tumors (CBTs) occur in about 5% of cases; however, this proportion can rise to as high as 30% in familial cases. CBTs are categorized into three distinct types: the most common being sporadic, followed by familial and hyperplastic variants [2].

Carotid body tumors have a slow growth rate; lesions usually present as slowly growing, painless masses. Once they reach a certain size, symptoms are most regularly due to compression of the tenth and twelfth cranial nerves due to anatomic proximity and more often than not include symptoms secondary to neurologic deficits such as dysphagia, difficulty swallowing, and hoarseness. Carotid body tumors may show sudden drops and increases in blood pressure, sudden onset of facial rash, and palpitations due to catecholamine discharge. The majority of carotid body tumors (CBTs) are classified as benign, with malignant forms representing a small fraction, estimated at 2% to 8% of cases [3]. Only a limited number of these tumors have the potential for secretion.

Papillary thyroid carcinoma (PTC) stands as the most common type of thyroid cancer, affecting individuals across both adult and pediatric age groups. While radiation exposure is a well-established risk factor for PTC, ad-

ditional environmental contributors include dietary iodine intake, obesity, hormonal influences and exposure to environmental toxins. Familial PTC is encountered in approximately 5% of cases and may present at an earlier age. Some familial cases have been found related to germline mutations. BRAF mutations are frequently observed in cases of sporadic papillary thyroid carcinoma and hold significant value as both clinicopathological and prognostic indicators. There is no mutation defined yet between papillary thyroid cancer and carotid body tumor [4]. We present two cases involving patients diagnosed with carotid body tumor (CBT) in conjunction with papillary thyroid carcinoma (PTC), either concurrently or at different intervals. To the best of our knowledge, this rare coexistence of the two tumors constitutes a novel clinical entity.

2. Case 1

A 57-year-old woman presented to our department with slowly growing right-sided neck swelling for 2 years. She had a history of left mastectomy in 2008 and total thyroidectomy with central neck dissection in 2023. Classical variant of papillary carcinoma with non-metastatic lymph nodes was documented. Physical examination revealed right-sided cervical masses with noticeable pulsation. Laboratory evaluations demonstrated that serum levels of calcium, parathyroid hormone (PTH), phosphorus, free thyroxine (FT4), calcitonin, and thyroid-stimulating hormone (TSH) were within normal reference ranges. Neck USG revealed a solid mass of 17 × 12 mm on the right carotid bifurcation. Enhanced magnetic resonance images (MRI) showed an irregular solid, T1 hypointense and T2 hyperintense lesion located in the carotid artery bifurcation suggesting a glomus tumor. The radiology department performed DSA imaging, and they reported a mass supplied from the right ascending pharyngeal artery (**Figure 1**). The patient was identified as having a Shamblin type I non-secretory carotid body tumor (CBT). Genetic analysis revealed no evidence of alterations in the RET proto-oncogene, von Hippel-Lindau (VHL) gene, SDHB gene, or SDHD gene. Total surgical extraction was performed. No pre-operative embolization was applied. The patient is disease-free for 3 months. Her thyroid follow-up is done by the common surgery department.

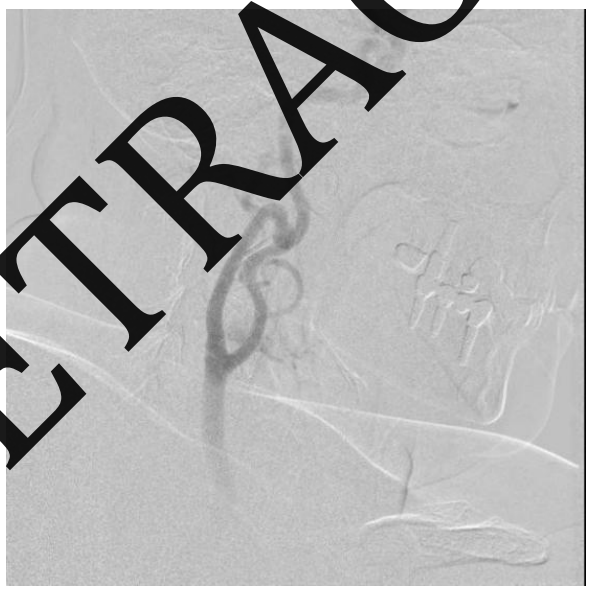
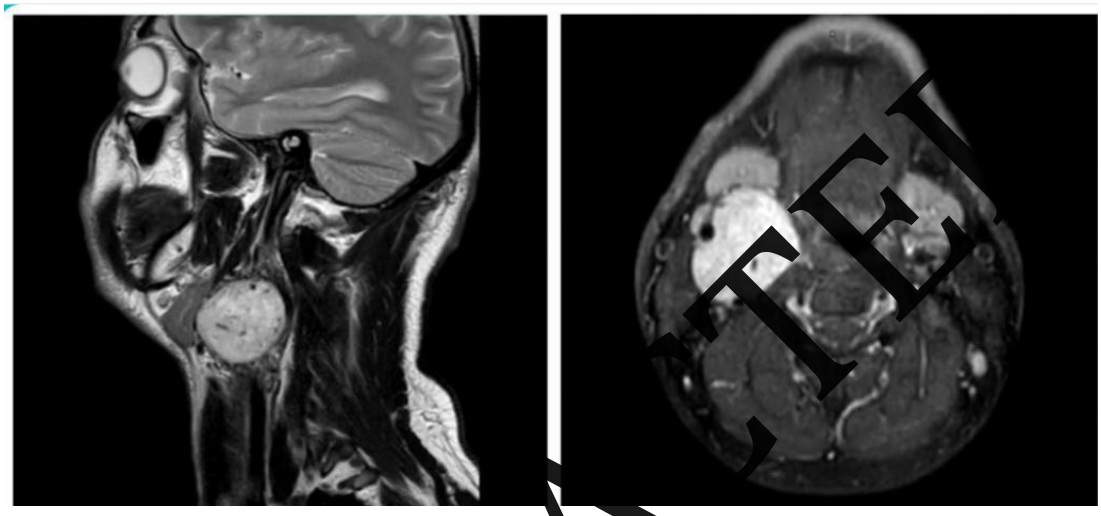


Figure 1. DSA imaging showed a mass supplied from the right ascending pharyngeal artery.

3. Case 2

The patient was a 29-year-old male in otherwise good health, who presented with an asymptomatic mass located on the right side of his neck, which had been noticeable for the past 14 months. A prior diagnostic workup included a neck ultrasound, which identified a heterogeneous, hypoechoic solid lesion measuring 40 × 35 × 55 mm. The lesion demonstrated moderate vascularity and was located at the bifurcation of the common carotid artery (CCA), adjacent to the right thyroid lobe. Thyroid USG was also performed, and multiple nodules, the biggest on the right lobe (28 × 18 mm) with cystic components and a 12 × 9 mm nodule with microcalcifications on the left

lobe, were reported. A fine needle aspiration biopsy was performed and a papillary carcinoma diagnosis was reported. Enhanced MRI revealed diffuse enhancement of solid masses of 40 × 30 × 43 mm, T1 hypointense and T2 hyperintense suggesting a glomus tumor (**Figure 2**). DSA imaging showed a mass supplied from the right ascending pharyngeal artery (**Figure 3**). The serum levels of calcitonin, free thyroxine (FT4), thyroid-stimulating hormone (TSH), parathyroid hormone (PTH), phosphorus, and calcium were all found to be within normal reference ranges. The patient was determined to have a Shamblin type III non-secretory carotid body tumor (CBT) in conjunction with papillary thyroid carcinoma (PTC). Genetic analysis showed no evidence of mutations in the SDHD gene, SDHB gene, von Hippel-Lindau (VHL) gene, or RET proto-oncogene. Embolization was performed 24 hours before the operation. Total excision of the glomus tumor and total thyroidectomy with central neck dissection were performed. No complications were observed after the surgeries.



(**a**) (**b**)

Figure 2. MRI revealed diffuse enhancement of solid masses of 40 × 30 × 43 mm (**a**) T1 hypointense and (**b**) T2 hyperintense, suggesting a glomus tumor.

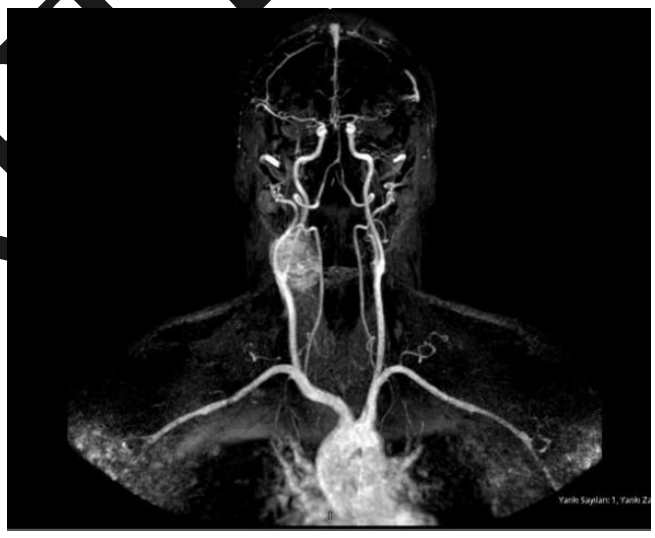


Figure 3. DSA imaging showed a mass supplied from the right ascending pharyngeal artery.

4. Discussion

Paragangliomas (PGLs), a type of neuroendocrine tumor, originate from ganglia associated with either the parasympathetic or sympathetic nervous systems. Among all PGLs, those in the head and neck region account for approximately 65% to 70% and represent about 0.6% of malignancies within this anatomical area. Of these, carotid body tumors constitute the majority, comprising 60% of head and neck PGLs [5]. Although most of these tumors are benign, between 6% and 19% of head and neck paragangliomas have the potential to metastasize beyond their original site [6]. Carotid body tumors typically present as slow-growing, rounded masses located at the bifurcation of the common carotid artery, causing a separation of the external and internal carotid arteries.

Malignant paragangliomas in the head and neck region are commonly associated with increased mitotic activity, central necrosis, and hypervascularity. Nevertheless, these characteristics alone are insufficient for reliably distinguishing malignant cases from benign ones. Although metastases are predominantly restricted to the regional lymph nodes, distant spread can also take place, most often involving the skeletal system or lungs, with reported rates ranging from 6% to 13% [7]. Chronic hypoxia is the only identified acquired risk factor for paraganglioma, with an increased risk observed in individuals residing at high altitudes [8]. This association may be attributed to the connection between sequence variations in pseudo-hypoxia-related pathways and the development of paraganglioma.

Research suggests that genetic predisposition, along with prolonged exposure to chronic hypoxia, may contribute to the prevalence of CBTs. This is particularly evident in individuals residing at high altitudes or those with chronic heart or lung conditions [9]. Histologically, the gland is composed of several lobules, each containing three distinct cell types, all of which exhibit a marked sensitivity to hypoxic conditions [10].

It is frequently observed unilaterally, but in most cases with a familial predisposition it tends to be bilateral. Familial cases constitute a substantial portion of carotid body tumors and have been associated with genetic mutations identified through mapping studies.

Mutations in the succinate dehydrogenase (SDH) gene family are primarily responsible for the hereditary forms of these tumors [11]. Interestingly, these genetic mutations tend to manifest more frequently in younger patients [12]. Familial tumors are characterized by an autosomal dominant inheritance pattern and are commonly associated with conditions such as multiple endocrine neoplasia (MEN), tuberous sclerosis complex, and Von Hippel-Lindau syndrome [13]. The typical age of onset for these hereditary tumors ranges between 30 and 40 years [14]. Women are affected by this condition more frequently than men. When pheochromocytoma (PHEO) or paraganglioma occurs alongside medullary thyroid carcinoma (MTC), it is a strong indicator of multiple endocrine neoplasia (MEN). In these instances, mutations in the succinate dehydrogenase subunits D (SDHD) and B (SDHB) are often identified [15]. Nevertheless, cases involving papillary thyroid carcinoma remain exceedingly rare.

While the coexistence of medullary thyroid carcinoma (MTC)—a neuroendocrine malignancy — and pheochromocytoma (PHEO) or paraganglioma (PGL) is well-recognized within the framework of MEN2, the simultaneous presence of single or multiple PGLs/PHEOs alongside papillary thyroid carcinoma (PTC), the most prevalent thyroid malignancy originating from follicular cells, has been reported in only a few cases. It remains uncertain whether this coexistence is purely coincidental or indicative of an underlying genetic connection [8]. Genetic testing in the current cases demonstrated no detectable mutations in the RET proto-oncogene, SDHB, SDHD, or von Hippel-Lindau (VHL) genes.

The prevalence of PTC has shown a consistent rise over the last decade, likely attributable to advancements in and widespread use of diagnostic tools, including MRI, CT, and ultrasound. For example, papillary thyroid carcinoma was detected incidentally in radiological examinations in our second patient who presented with a neck mass caused by glomus caroticum. Whereas PTC and CBT can be seen at the same time within the same patient, they can also occur at different times. In the first patient, CBT and PTC were diagnosed and treated eight years apart. In the second patient, CBT and PTC were diagnosed at the same time and the surgeries were performed at different times after discussing them with the patient. When an endocrine gland tumor is identified, it is essential to consider and screen for multiple endocrine neoplasia (MEN). Elevated serum calcitonin levels, exceeding 1000 pg mL^{-1}, serve as a specific marker for diagnosing medullary thyroid carcinoma (MTC).

Doppler ultrasound, computerized tomography (CT), magnetic resonance imaging (MRI), and angiography are essential in diagnosing carotid body tumors (CBTs). However, ultrasonography and fine needle aspiration biopsy

are more dependable in identifying thyroid tumors. Cross-sectional imaging techniques, such as CT angiography or magnetic resonance angiography, offer valuable insights into how the tumor interacts with the artery bifurcation and the potential positioning of cranial nerves, providing crucial information to guide surgical planning [16].

The onset of the condition often involves multiple organ systems, necessitating a multidisciplinary approach to treatment. In this case, surgical removal of both the paraganglioma and the papillary thyroid carcinoma was identified as the optimal treatment strategy. However, it was crucial to first rule out the presence of pheochromocytoma (PHEO), as alternative interventions could have triggered a hypertensive crisis. Notably, the resection of paragangliomas located at the carotid bifurcation presents a significant challenge for surgeons due to the tumor's extensive vascularity. Our first patient did not undergo embolization before surgery, but the second patient underwent embolization by the interventional radiology team 24 hours before surgery. Although embolization is controversial in carotid body tumors, we prefer to perform embolization in Shamblin type 2 and 3 tumors. After CBT excision, 27% of cases experience postoperative complications of the Shamblin type. The most significant complications associated with total thyroidectomy include permanent hypoparathyroidism, occurring in approximately 1.6% of cases, and permanent vocal cord paralysis, observed in 1.7% of cases. Notably, none of our patients experienced postoperative complications [17]. Advances in modern diagnostic techniques now allow for the accurate preoperative identification of both lesions in most cases. Even when these lesions are detected concurrently, complete and effective surgical excision can often be achieved with minimal risk of morbidity.

5. Conclusions

The cases we presented highlight the possibility that the simultaneous occurrence of carotid body tumors and papillary thyroid carcinoma could be either coincidental or due to an unidentified genetic mutation. As far as we are aware, there is no recognized syndrome or documented interrelation between these tumors that can explain this unusual presentation. Further research is required to clarify the association between CBT and PTC.

Author Contributions

Conceptualization, M.D.E. and B.A.E.; methodology, B.A.E.; software, M.D.E.; validation, M.D.E., B.A.E.; formal analysis, M.D.E.; investigation, M.D.E.; resources, B.A.E.; data curation, B.A.E.; writing—original draft preparation, M.D.E.; writing—review and editing, B.A.E.; visualization, M.D.E.; supervision, B.A.E.; project administration, M.D.E., B.A.E.; funding acquisition, none. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

Because the study was conducted as retrospective case series, it did not require ethical approval.

Informed Consent Statement

Written informed consent has been obtained from the patients to publish this paper.

Data Availability Statement

Governmental hospital database was used for retrieval of patient demographics. No new data were created.

Conflicts of Interest

The authors declare no conflict of interest of any manner.

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