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J Case Rep Images Surg 2022 Jul-Dec;8(2):9–14.
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CASE REPORT PEER REVIEWED | OPEN ACCESS

Primary intrathyroidal paraganglioma: A case report of immunohistochemistry findings and a recommendation for surgical resection

Sara Izwan, Alfred Lam, Russell Manley

ABSTRACT

Introduction: Thyroid paragangliomas are very rare tumors. Awareness of its presentation is important to differentiate it from other common thyroid neoplasms. We present a care report of a primary intrathyroidal paraganglioma and its histopathologic findings.

Case Report: A 58-year-old asymptomatic female was referred to the General Surgery clinic following an incidental finding of thyroid nodules on imaging. She had no significant personal or family history of thyroid disease. Routine blood and thyroid function studies were within normal limits. Neck ultrasound demonstrated a multinodular goiter with a hypoechoic nodule in the right superior thyroid. Fine needle aspirate (FNA) showed atypia of unknown significance (Bethesda 3). She underwent a right hemithyroidectomy which confirmed on pathological examination to be a 19 mm intrathyroidal paraganglioma, which was positive for neuroendocrine markers and negative for calcitonin and cytokeratin. Serum metanephrine studies returned within normal limits.

Conclusion: Given the difference in management of paragangliomas compared to its cytology mimics and association with familial cancer syndromes, awareness of this rare tumor, and use of immunohistochemical stains are critical in arriving at the diagnosis, which has implications for clinical management and surveillance of these patients.

Keywords: Neuroendocrine, Paraganglioma, Thyroid tumors

How to cite this article

Izwan S, Lam A, Manley R. Primary intrathyroidal paraganglioma: A case report of immunohistochemistry findings and a recommendation for surgical resection. J Case Rep Images Surg 2022;8(1):9–14.

Article ID: 100106Z12SI2022

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doi: 10.5348/100106Z12SI2022CR

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Received: 07 May 2022
Accepted: 10 July 2022
Published: 29 August 2022

INTRODUCTION

Thyroid paragangliomas are uncommon neuroendocrine tumors, with less than 70 cases of primary thyroid paragangliomas being reported in the literature since its first description in 1964 [1]. They are thought to arise from the neural crest-derived paraganglia of the autonomic nervous system [2, 3]. Sympathetic paragangliomas usually secrete catecholamines and are located within the sympathetic chain in the thorax, abdomen, and pelvis; however, parasympathetic paragangliomas are non-functional and located along the vagal and glossopharyngeal nerves in the head and neck [4, 5]. Paragangliomas adjacent to, or inside the thyroid gland, are a subset of laryngeal paragangliomas,

most commonly the inferior laryngeal paraganglia [6, 7]. The normal inferior laryngeal paraganglia are located along the recurrent laryngeal nerve at the lateral margin of the cricoid cartilage in the cricothyroid membrane [3], and there are currently only two known cases of paragangliomas arising from recurrent laryngeal nerves [8, 9]. The thyroid gland is not considered a normal site for the occurrence of paraganglia, but the variable location of the inferior laryngeal paraganglia may be the origin of the rare cases of primary intrathyroidal paragangliomas. One hypothesis is that as a paraganglioma forms from the inferior laryngeal paraganglia, it is slowly dragged downward and ultimately rests lateral to the thyroid gland. It is possible that the inferior laryngeal paraganglia may form in the thyroid capsule itself, which could ultimately create an intrathyroidal paraganglioma [10].

Most patients are female, and present with an asymptomatic thyroid nodule; however, there have been published case reports of rare thyroidal paragangliomas in male patients [8, 11–15], with paragangliomas that were often misdiagnosed as carcinomas in the preoperative setting [12, 16]. After a diagnosis of paraganglioma has been confirmed, it is important to define any association with genetic disease. Up to 25% of paragangliomas may be present in the setting of hereditary systemic syndromes including multiple endocrine neoplasia (MEN) type 2, Von Hippel-Lindau disease, neurofibromatosis type I, or hereditary paraganglioma syndrome [5, 17, 18].

In this report, we present a case of an intrathyroidal paraganglioma in an asymptomatic female. We discuss the clinical and histopathologic features, as well as the problems related to the differential diagnosis, treatment, management, and surveillance of intrathyroidal paragangliomas.

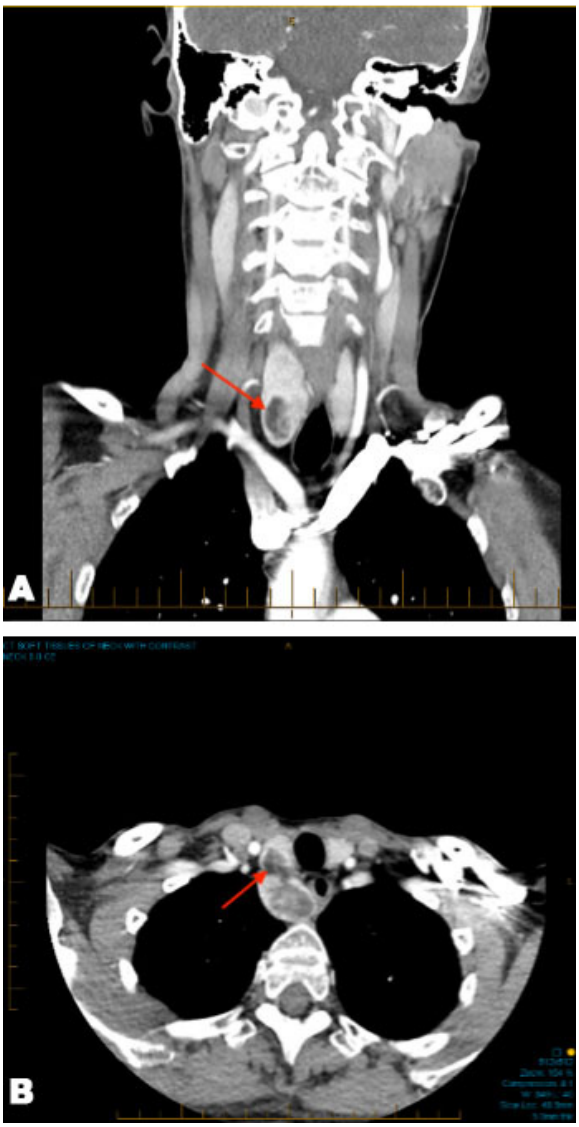

Figure 1: (A) CT neck and chest demonstrating a goitrous nodule (see red arrow) in the right hemithyroid with mild displacement of the trachea and esophagus in coronal view. (B) CT neck and chest demonstrating a goitrous nodule (see red arrow) in the right hemithyroid with mild displacement of the trachea and esophagus in axial view.

CASE REPORT

Clinical history

A 58-year-old asymptomatic Caucasian female was referred to the General Surgery clinic for review of two non-tender right-sided thyroid nodules, of unknown duration, which were incidentally discovered on plain film spine X-ray following a spinal fracture. Computed tomography (CT) of the neck demonstrated a goitrous nodule within the right lobe of the thyroid with no retrosternal extension, but with impingement and mild displacement of the trachea and esophagus (Figure 1). The patient had no history of thyroid disorders or irradiation, no significant family history of thyroid cancer or disease, and no history of autoimmune disease. Physical examination demonstrated a mildly enlarged thyroid with no palpable nodules, negative for Pemberton's sign, without palpable cervical lymphadenopathy, and normal laryngeal motility.

Ultrasonography of the neck confirmed the largest individual nodule inferiorly measured at 25 × 21 × 13 mm and appeared heterogeneous echotexture with mixed cystic and solid components with well-defined margins and some internal vascularity. A second hypoechoic nodule superior to this measured 16 × 11 × 13 mm with some vascularity. Routine blood and thyroid function studies including serum thyroid stimulating hormone (TSH), corrected calcium, parathyroid hormone (PTH) were within normal limits. Ultrasound-guided fine needle aspiration (FNA) cytology of the large inferior thyroid nodule returned as non-diagnostic (Bethesda 1), and the superior nodule returned as atypia of unknown significance (Bethesda 3). Consecutive FNAs returned indeterminate, and the patient opted to undergo elective surgical resection of the right hemithyroid, with an unremarkable intraoperative and postoperative course.

Intraoperative findings

Intraoperatively, a multinodular goiter was appreciable, with a 10 mm nodule in the upper pole, a ~15 mm inferior pole nodule, and a 1 cm mid-upper pole nodule. Nodules were soft, with no obvious extrathyroidal extension or Level VI lymphadenopathy. Both parathyroids were seen in conventional position, and the right recurrent laryngeal nerve was identified and preserved.

Pathological findings

Sectioning of the right lobe of the thyroid confirmed the presence of two discrete lesions. Lesion 1 in the upper pole measured 19 × 13 11 mm and was a solid cream well-defined unencapsulated lesion. Lesion 2 occupied most of the lower mid-poles and measured 36 × 35 × 15 mm. It was an encapsulated multilobulated cream-to-hemorrhagic lesion with a focus of severe calcification in the center. Microscopic examination of the thyroid showed nodular hyperplasia of the thyroid. Parathyroid tissues were noted near the nodule. Lesion 1 was vascular, with an alveolar pattern of spindle and epithelioid cells (Figure 2).

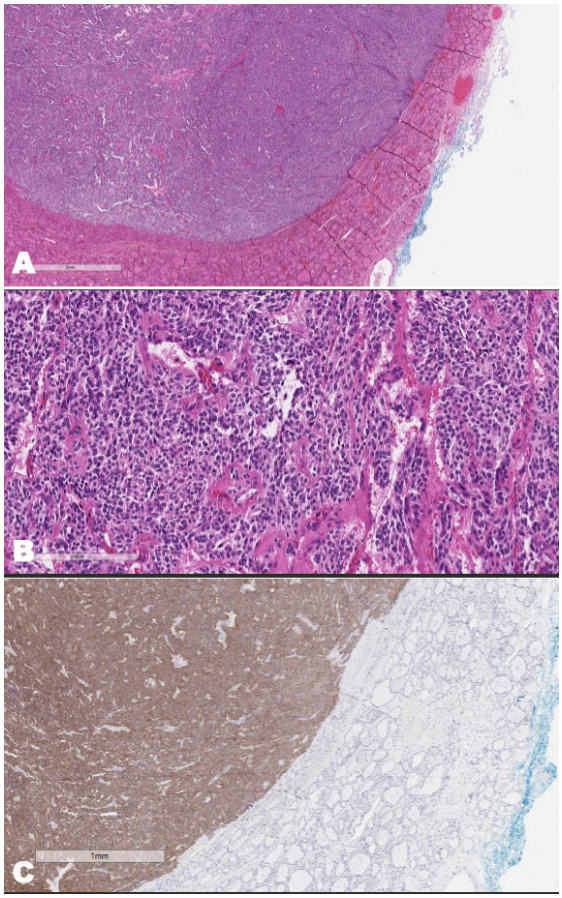

Figure 2 (A) Thyroid paraganglioma: showing a well demarcated nodule in the thyroid (× 2). (B) Thyroid paraganglioma: showing alveolar pattern of tumor cells with granular cytoplasm with highly vascular stroma (× 20). (C) Thyroid paraganglioma: positive for synaptophysin.

Immunohistochemical findings

Immunohistochemistry was performed on lesion 1. The tumor was positive for neuroendocrine markers synaptophysin and CD56, and weakly positive for chromogranin. It was negative for cytokeratin (AE1/3), calcitonin, C-Kit, and CD5. The Ki67 index was less than 1%.

Diagnosis

The overall features of the tumor were consistent with a primary intrathyroidal paraganglioma. There was no coagulative necrosis, vascular invasion, capsular invasion, or hypercellularity to suggest high metastatic potential. The patient was seen in the Endocrinology outpatient clinic with normal vitals and serum metanephrines, and a surveillance ultrasound demonstrating a stable multinodular goiter without evidence of recurrence within the right hemithyroidectomy bed. Magnetic resonance imaging (MRI) of the skull and neck, chest, abdomen, and pelvis was negative for synchronous paragangliomas. At seven months post-surgery, she is well. She is currently awaiting follow-up with genetics testing.

DISCUSSION

Primary paragangliomas of the thyroid gland are very rare, with difficulty in both preoperative and postoperative differential diagnoses. The first reported thyroid paraganglioma was described in 1964 by Van Miert [1]. All other cases reported to date occurred in women between the ages of 9 and 73 years old [3], and thyroid paragangliomas accounted for 3 out of 6782 (0.04%) patients undergoing thyroidectomy in three decades [19]. The diagnosis of intrathyroidal paragangliomas is rarely established preoperatively by FNA biopsy or intraoperative frozen section. Differential diagnoses of these tumors in pathological examination include medullary thyroid carcinoma, hyalinizing trabecular tumor, and metastatic neuroendocrine neoplasms. True thyroid paragangliomas are characterized by positive immunohistochemical staining for chromogranin A, synaptophysin, S-100, and neuron-specific enolase, and negative staining for calcitonin, carcinoembryonic antigen, thyroglobulin, and cytokeratin [20]. The histopathological diagnosis of a paraganglioma can be straightforward when the lesion is in an expected location, and supplemented by confirmation by immunohistochemistry. Chromogranin and synaptophysin yield cytoplasmic positivity in tumor cells, and S100 provides a specific intense positivity that highlights sustentacular cells within these neoplasms [2, 21].

It is important to distinguish paragangliomas from metastatic neuroendocrine neoplasms, as prognosis and management are very different. Surveillance of these patients includes biochemical testing, including metabolites of catecholamines [21, 22]. The accurate determination of catecholamine profile is crucial in the

clinical management and surveillance of these patients, as they are at risk of lability of blood pressure, cardiac dysfunction, and acute vascular catastrophes [21]. Surgical resection is the recommended standard treatment [2, 23]. The prognosis of thyroid paragangliomas appears to be favorable, provided that surgical excision is complete. There is currently no evidence to suggest that elective neck dissection or adjuvant radiation therapy is indicated in order to improve outcomes for these patients. However, given its rarity, it is important for the clinician to be familiar with its characteristics, prognosis, and options for management.

CONCLUSION

Intrathyroidal paragangliomas are rare and can be mistaken for metastatic neuroendocrine neoplasms. Often, they are confirmed on histology and serum biochemical markers. The accurate diagnosis of these paragangliomas helps guide appropriate management, whereby surgical resection is the current recommended standard treatment, leading to favorable outcomes for patients.

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Author Contributions

Sara Izwan – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Alfred Lam – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Russell Manley – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission
The corresponding author is the guarantor of submission.

Source of Support
None.

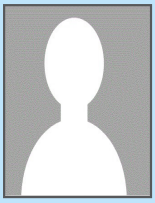
Consent Statement
Signed informed consent was obtained from the patient prior to publication of this case report.

Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

ABOUT THE AUTHORS

Article citation: Izwan S, Lam A, Manley R. Primary intrathyroidal paraganglioma: A case report of immunohistochemistry findings and a recommendation for surgical resection. J Case Rep Images Surg 2022;8(1):9–14.



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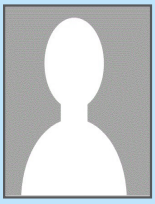

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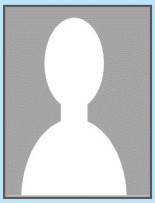

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