

Carcinoma arising from thyroglossal duct remnants

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Abstract. Thyroglossal duct cysts (TGDCs) are unusual remnants of the thyroid gland that are rarely observed in association with carcinoma. The present study aimed to showcase the clinical characteristics, diagnosis and management of patients with TGDC carcinoma. It was a single-center study conducted from February 2016 to February 2020. The study involved the retrospective analysis of a series of cases with TGDC carcinoma. A total of 10 patients were included in the study, of whom eight (80%) were females. Their age ranged from 25 to 48 years with a mean age of 39.1 years. A total of five cases (50%) underwent only Sistrunk's procedure, four patients (40%) underwent total thyroidectomy along with Sistrunk's procedure and one patient (10%) was treated by Sistrunk operation and lobectomy. In all of the cases (100%), histopathological examination confirmed papillary thyroid carcinoma in TGDCs. In addition, in the thyroid tissue, 2 cases (20%) also had papillary thyroid carcinoma and 3 cases (30%) had papillary thyroid microcarcinoma. Radioiodine was administered in one patient (10%) with suppressive thyroxine. A three-year follow-up with ultrasound revealed no suspicious lesions in any of the cases. Although rare, carcinoma may develop in the thyroglossal cysts. In this situation, both the thyroid gland and different lymph node compartments should be evaluated for malignancy. Surgical intervention is the cornerstone of management.

Introduction

Thyroglossal duct cysts (TGDCs) are unusual remnants of the thyroid gland that can arise anywhere along the thyroid migration pathway (1). This phenomenon is the most prevalent type of congenital neck mass in children, with a frequency of ~7% in the general population (1). During embryonic development, in the first six weeks of pregnancy, the thyroid gland begins to descend toward its definitive anatomical position, and afterward, the thyroglossal duct normally undergoes complete atrophy by the tenth week (1). However, failure to undergo atrophy can lead to the formation of TGDC, which can be in the form of a cyst, fistula, duct, tract or ectopic thyroid tissue (2). The cyst manifests as a solid, clearly delineated, painless mass that ascends with the protrusion of the tongue and during swallowing, connecting to the foramen caecum through the embryonic duct (3). In the pediatric population, TGDCs have been reported to primarily affect male individuals, while in adults, the prevalence is notably higher among females. The area beneath the hyoid bone emerges as the predominant site of origin for the anomaly. Complications associated with this congenital anomaly may include severe infection, localized inflammation, pain, swelling, malignancy and the development of fistulas (1). According to the literature, cancer rarely develops from TGDCs. The incidence of primary carcinoma within TGDCs among all cases subjected to TGDC removal was documented to vary between 0.7 and 6%. (1,4-7). This rare but significant occurrence presents a diagnostic and management challenge due to its rarity and our limited understanding, as the majority of the available data are from case reports, with some small case series (1,2,4,5,7). The present study aims to showcase the clinical characteristics, diagnosis and management of patients with TGDC carcinoma.

Materials and methods

Study design. This was a retrospective single-center study conducted at the thyroid clinic of the Smart Health Tower (Sulaimani, Iraq) from February 2016 to February 2020. It involved the retrospective analysis of a series of cases who had

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undergone a Sistrunk operation or thyroid operation (partial or total thyroidectomy) for the removal of TGDC.

Participants. Patients with a proven histopathological examination of thyroglossal carcinoma (TGC) were included in this study. Patients under 18 years of age, those who presented with neck swelling due to other causes than thyroglossal abnormalities and those with incomplete data were excluded.

Data collection. All the required data were collected from the center's electronic health records, including demographic data, presentations, physical examination, pre-operative thyroid state, neck US finding, radiation history, fine needle aspiration cytology (FNAC) results, histopathological examination report, surgery indication, type of operations, postoperative need for receiving radioactive iodine, complications, size of the cyst, a postoperative suppressive dose of thyroxine and recurrence.

Intervention. All cases underwent the Sistrunk procedure, which is a standard surgical operation for TGDC. In addition, all cases that had both TGDC with carcinoma and carcinoma in the thyroid gland underwent a thyroidectomy or thyroid lobectomy for managing thyroid cancers. All operations were conducted under general anesthesia in a supine position with the neck extended, after skin preparation and disinfection. A transverse incision was made in the neck over the mass of suspected TGC or along the incision for a thyroid operation. After opening the skin and platysma, dissection was done, including strap muscles as much as needed to avoid rupture of the cyst to avoid recurrence. The cyst was removed, including the anterior horn of the hyoid bone. If there was an extra-cystic extension of papillary carcinoma, careful dissection was undertaken to ensure complete removal of the tumor extension. In cases of proven thyroid cancer with positive cervical lymph nodes, total thyroidectomy with cervical lymph node dissection was performed after ligating the upper pole of the thyroid artery and then exploring and preserving the recurrent laryngeal nerve. All lymph nodes from levels II, III, IV and VI were removed. The close-vacuum drain was inserted, and then, the strap muscle and skin were sutured.

Histopathological procedure. After labeling, the surgical specimens were stored in neutral buffered formalin (10%) for a duration of 10 h at 25°C. Subsequently, Histo-Tek® VPI-(Sakura Finetek Europe) was used for fixation and dehydration of the tissue samples for 18-22 h. By using Histo Core Arcadia H (Leica Microsystems GmbH), the samples were embedded in paraffin wax to form blocks. The staining was performed using hematoxylin and eosin (H&E) for 1-3 min, according to the manufacturer protocol (Leica Microsystems).

Results

Patient demographics and clinical findings. A total of 10 patients were included in this study. The clinicopathological characteristics of the cohort are presented in Table I and individual information of each patient is in Table II. The mean and median age of the patients was 39.1 and 40 years, ranging from 25 to 48 years. The majority of the cases were female (n=8,

Table I. Summary of demographic data and clinical characteristics of included patients.

Variable	Value
Mean and median age (range), years	39.1, 40 (25-48)
Gender	
Male	2 (20)
Female	8 (80)
Family history of thyroid cancer	1 (10)
History of radiation	0 (0)
Thyroid state	
Euthyroid	8 (80)
Hypothyroid	1 (10)
Hyperthyroid	1 (10)
Drug history	2 (20)
Presence of anterior neck swelling	10 (100)
Mean, median duration (range), months	4.2, 2 (1-12)
Ultrasound findings	
Cystic lesion	4 (40)
Complex lesion	3 (30)
Cystic lesion with microcalcification and mural nodule	3 (30)
FNA of suspected cyst	
Negative for malignancy	1 (10)
Suspicious for malignancy	6 (60)
N/A	3 (30)
Surgery indication for cancer	10 (100)
Operation type	
Sistrunk operation	5 (50)
Sistrunk operation and total thyroidectomy	4 (40)
Sistrunk operation and lobectomy	1 (10)
Histopathological examination	
PTC in TGDC	5 (50)
PTC with PTC in TGDC	2 (20)
PTMC with PTC in TGDC	3 (30)
Cyst size, cm	
<1.5	4 (40)
≥1.5	6 (60)
Lymphovascular invasion	10 (100)
Suppressive dose of thyroxine	4 (40)
Postoperative radiation	2 (20)
Need for receiving radioactive iodine	1 (10)
Postoperative ultrasound follow-up	
No suspicious lesion	10 (100)
Suspicious lesion	0 (0)

Values are expressed as the mean, median (range) or n (%). PTC, papillary thyroid carcinoma; PTMC, papillary thyroid microcarcinoma; TGDC, thyroglossal duct cyst; N/A, not available; FNA, fine needle aspiration.

80%). Only one (10%) case had a family history of thyroid cancer. The subjects had no past exposure to radiation. A total

Table II. Demographic data and clinical characteristics of each patient.

Case no.	Age, years	Gender	Symptoms/ PEF	Radiation history	POTS	U/S findings	Cyst size, cm	FNAC findings	Surgery indication	Type of operation	HPE findings	NRRI Complications	PSDT Recurrence	
1	35	Female	Anterior neck swelling	None	Hypothyroid	Infected thyroglossal cyst	1	FNAC was not conducted for TGDC FNA for thyroid and cervical LNS was positive for PTC	Cancer	Sistrunk's operation and total thyroidectomy + Lt lateral group II, III, IV dissection	PTC with PTC of TGDC	No	Yes	No
2	48	Female	Anterior neck swelling	None	Euthyroid	Complex cyst	1.3	Content of cyst	Cancer	Sistrunk's operation + Lt lobectomy	PTC of TGDC + hyperplastic nodule	No	No	No
3	36	Female	Anterior neck swelling	None	Euthyroid	Cystic lesion with microcalcification with a mural nodule	1.7	Not conducted	Cancer	Sistrunk's operation	PTC of TGDC	No	No	No
4	38	Female	Anterior neck swelling	None	Hyperthyroid	Cystic lesion with microcalcification with a mural nodule	1.5	Suspicion of PTC + PTC for bilateral thyroid nodules	Cancer	Total thyroidectomy with Lt central and lateral neck dissection + Sistrunk's operation	PTMC with PTC of TGDC	Yes	Yes	No
5	43	Female	Anterior neck swelling	None	Euthyroid	Cystic lesion with solid mural nodule containing calcification	1.3	Suspicion of PTC	Cancer	Sistrunk's operation	PTC of TGDC	No	No	No

Table II. Continued.

Case no.	Age, years	Gender	Symptoms/ PEF	Radiation history	POTS	U/S findings	Cyst size, cm	FNAC findings	Surgery indication	Type of operation	HPE findings	NRRI	Complications	PSDT	Recurrence
6	48	Female	Anterior neck swelling	None	Euthyroid	Cystic lesion	1.3	Suspicion of PTC	Cancer	Sistrunk's operation	PTMC with PTC of TGDC	No	No	No	No
7	25	Female	Anterior neck swelling	None	Euthyroid	Complex cyst	2	Suspicion of PTC	Cancer	Sistrunk's operation	PTC of TGDC	No	No	No	No
8	42	Female	Anterior neck swelling	None	Euthyroid	Cystic lesion	1.5	Suspicion of PTC	Cancer	Sistrunk's operation	PTC of TGDC	No	No	No	No
9	43	Male	Anterior neck swelling	None	Euthyroid	Complex nodule	1.5	Right thyroid nodule was suspicious for PTC FNAC was not conducted for TGDC	Cancer	Total thyroidectomy and Sistrunk's operation	PTC with PTC of TGDC	No	No	Yes	No
10	33	Male	Anterior neck swelling	None	Euthyroid	Cystic lesion	1.9	Suspicion of PTC	Cancer	Total thyroidectomy and Sistrunk's operation	PTMC with PTC of TGDC	No	No	Yes	No

PEF, physical examination findings; POTS, preoperative thyroid state; U/S, ultrasound; FNAC, fine needle aspiration cytology; LNS, lymph nodes; Lt, left; HPE, histopathology findings; NRRI, need for receiving radioactive iodine; PSDT, postoperative suppressive dose of thyroxine; PTC, papillary thyroid carcinoma; PTMC, papillary thyroid microcarcinoma; TGDC, thyroglossal duct cyst.

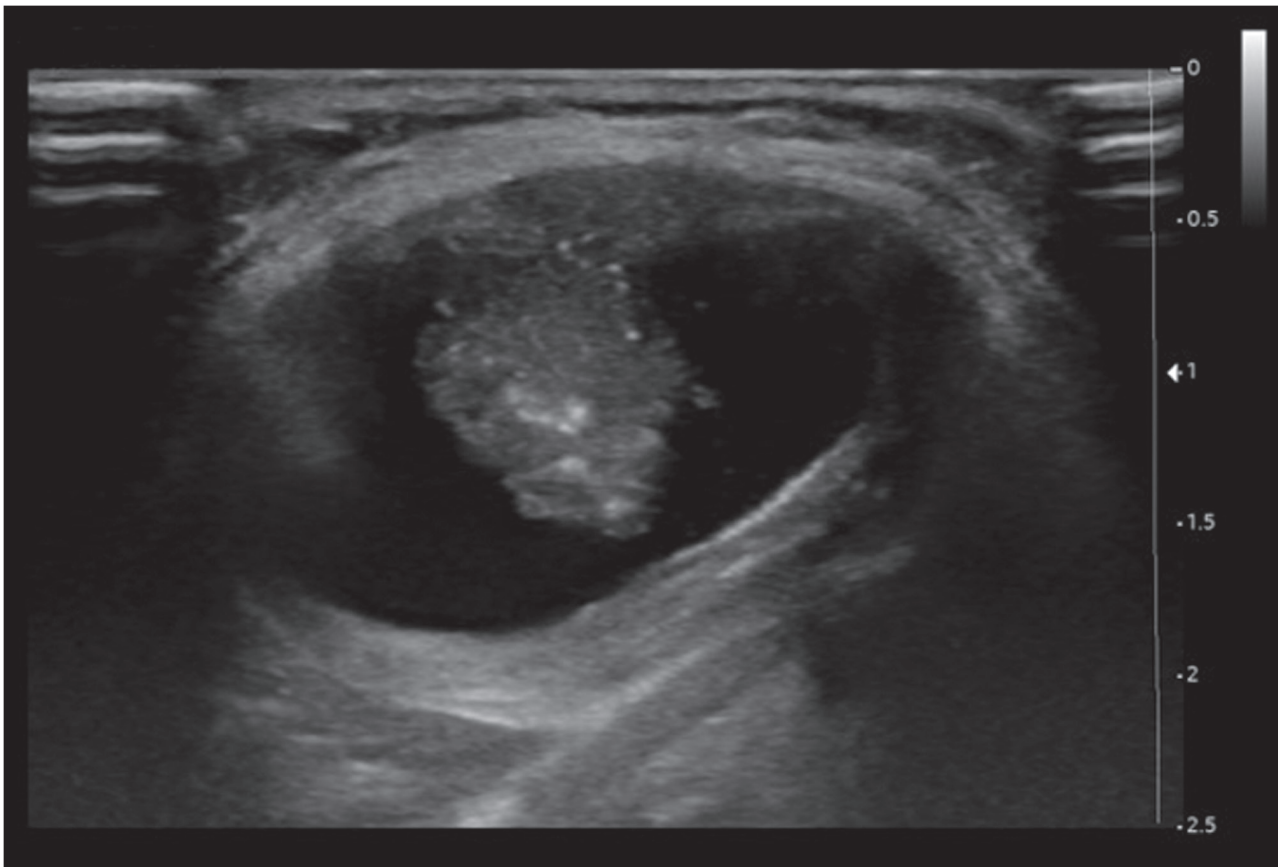


Figure 1. A well-defined 2-3 mm wall thickness complex cyst of 32x25x18 mm at the left side of the midline level of the hyoid bone to the upper part of the thyroid cartilage, containing 19x12x15 mm well-defined lobulated surface isoechoic to thyroid tissue mural nodule with microcalcification and mildly vascular on color doppler ultrasound (Case 3).

of eight cases (80%) had normal thyroid function, one (10%) had hypothyroidism and one (10%) had hyperthyroidism. Anterior neck swelling was the only clinical manifestation in all cases (100%).

Diagnostic findings and management. US studies revealed cystic lesions in four (40%) cases, complex nodules in three cases (30%) and mural nodules with cystic lesions in three cases (30%) (Figs. 1-5). FNAC of suspected nodules was positive for malignancy in six (60%) cases and negative in one (10%). Half (50%) of the cases underwent the Sistrunk operation alone; four (40%) cases underwent the Sistrunk operation plus total thyroidectomy; and one (10%) case underwent the Sistrunk operation plus lobectomy. Lymph node metastasis was only found in 2 (20%) cases. Nodes were positive only in the lateral neck compartments in one (10%) of the cases without central region metastasis. However, nodes were positive in the lateral and central neck compartments in one (10%) patient. Histopathological examination confirmed papillary thyroid carcinoma (PTC) in TGDC in all the cases (100%) (Fig. 6). In addition, in the thyroid tissue, 2 cases (20%) also had PTC and 3 cases (30%) had papillary thyroid microcarcinoma (Figs. 7 and 8).

Postoperative treatment and follow up. Overall, one patient (10%) was given radioactive iodine as well as a suppressive dosage of thyroxine and three (30%) were only given

suppressive thyroxine. The patients were followed up every three months and a three-year follow-up with US revealed no suspicious lesions in any of the cases. Patients with total thyroidectomy still receive treatment (thyroxine).

Discussion

TGDC is one of the most common congenital anomalies, with a wide range of differential diagnoses, that is rarely associated with carcinoma (1,8,9). Although it is uncertain how cancer arises at this location, it is thought to be the result of the neoplastic transformation of normal residual thyroid tissue throughout the thyroglossal cystic tube. The papillary histotype of the condition has two possible origins: Ectopic thyroid tissue formation or metastases from a primary thyroid malignancy, with the latter receiving less attention (4).

TGDC is typically seen in children, yet adults can also be affected. However, it is challenging to pinpoint an exact age distribution for TGDC due to the varied reporting time frames, which may be reported as the age at which the condition was first diagnosed when symptoms began, or some authors may reference the patient's life decade rather than their precise age. Consequently, there is no agreement in the literature concerning the age demographics of patients with TGDC. In previous studies, the age distribution of malignant TGDCs has been reported to be 41-47 years (4,10). In the current study, the

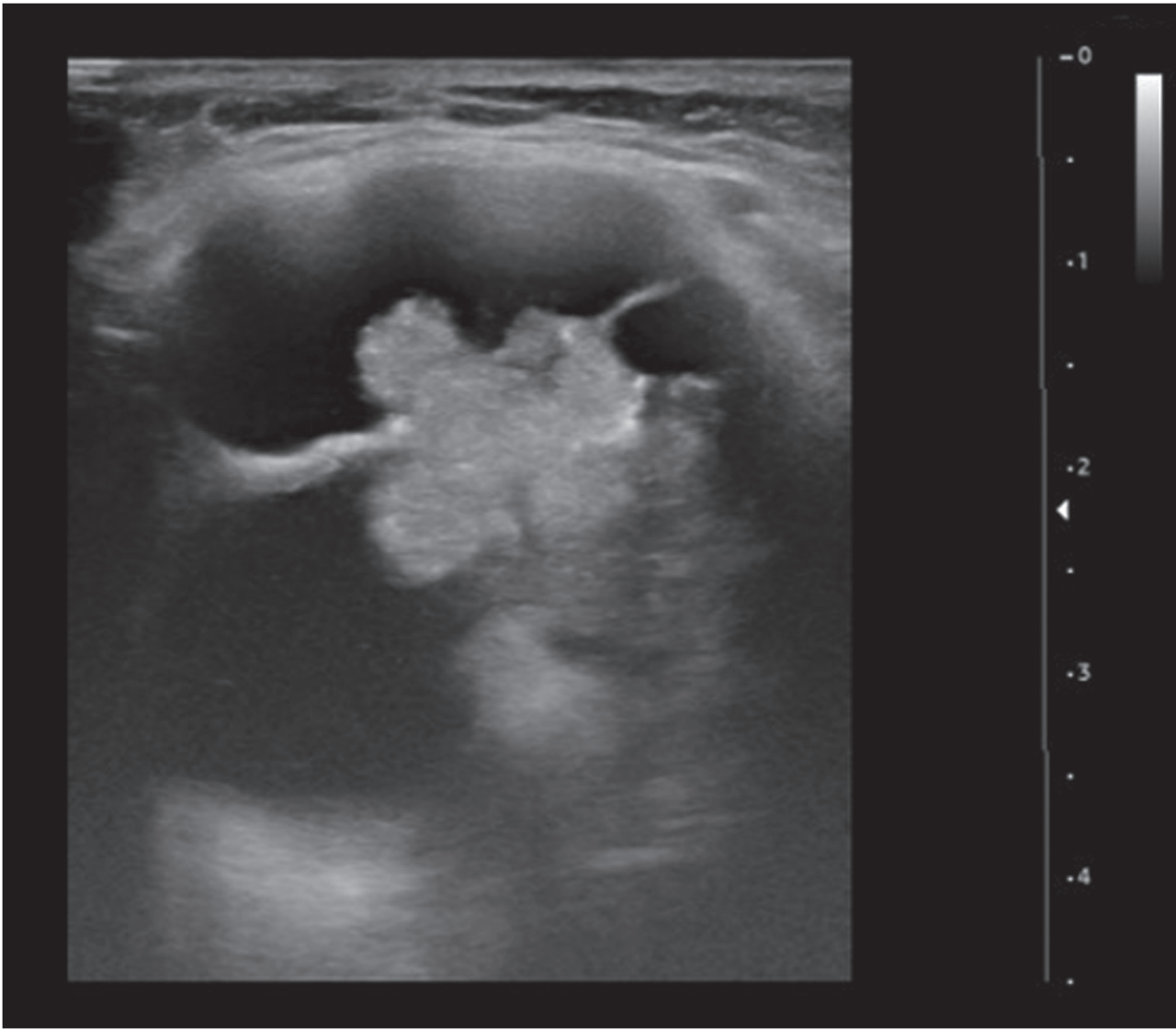


Figure 2. A large, well-defined, thin-walled cystic lesion is seen in the anterior of the neck at the level of the hyoid bone, containing a thin internal septum with a 10x7x6 mm lobulated solid mural nodule, mildly vascular and containing microcalcification, on ultrasound imaging (Case 5).

mean and median age of the patients were 39.1 and 40 years, respectively.

The usual presentation of TGDC is a moveable, painless midline or, less commonly, a lateral neck mass (11), while malignant TGDC should be suspected in any cysts that are irregular, hard, rapidly increasing in size, fixed to surrounding tissues or present in cervical lymph nodes (12,13). Most of the time, it is impossible to clinically differentiate between a TGC and a benign TGDC. Usually, the diagnosis is made by histopathological examination after excision of the resected tissue (14,15). A study by Kennedy *et al* (16) showed only three cases of PTC and a single case of squamous cell carcinoma (SCC) in a large review of 115 cases of TGDC, whose presentations were the same as that of benign TGDC. Khalaf *et al* (17) reported a case of a 44-year-old female with coexisting hyperthyroidism and TGDC. In the current study, all of the cases had anterior neck swelling for a mean and median of 4.2 and 2 months, respectively. Only one case had hypothyroidism, one had hyperthyroidism and the others were euthyroid.

Imaging diagnostic tools for neck masses include US, scintigraphy and computerized tomography (CT), which are less likely to diagnose malignant diseases preoperatively (18,19). The US of TGDC frequently shows a well-defined cystic area with anechoic fluid. Their walls are thin without internal vascularity. On the other hand, the presence of microcalcification and a solid component within the cyst can predict malignancy (7). Branstetter *et al* (20) reported that carcinoma should be suspected in TGDC when a mural nodule or calcification is seen on CT. Acultae *et al* (7) reported a case of a 21-year-old female diagnosed with TGC in whom the neck US revealed a predominantly cystic lesion with a central solid component lying between the hyoid bone and thyroid cartilage. In this study, the US revealed a cystic lesion in four cases (50%), a complex nodule in three cases (30%), a cystic lesion with microcalcification and a mural nodule in three cases (30%) (cases 3, 4 and 5).

The role of FNAC in detecting TGC has been well investigated (21). In particular, US-guided FNAC is the main diagnostic investigation of TGC, with a positive accuracy rate

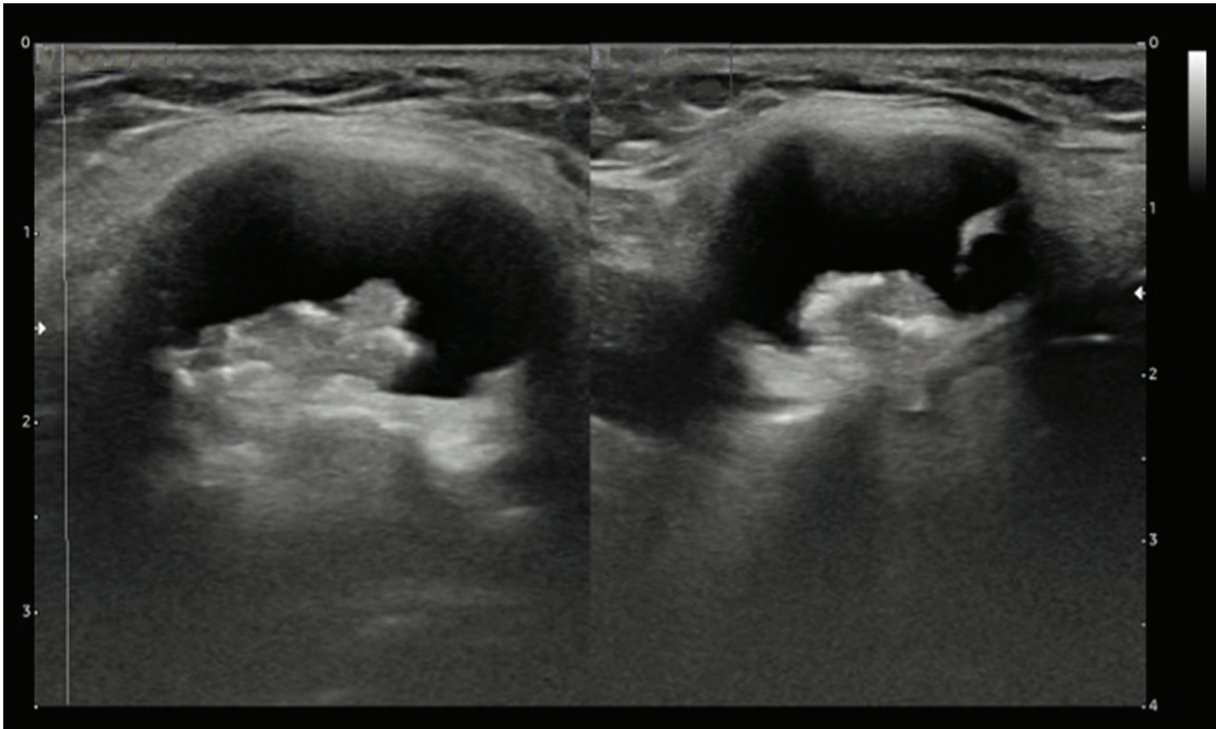


Figure 3. A well-defined, thin-walled complex cystic nodule of 24x21x16 mm on the left side of the midline level of the hyoid bone and extending inferiorly to the upper part of the thyroid cartilage, containing a 13x10x6 mm lobulated surface isoechoic to thyroid tissue mural nodule with microcalcification and mildly vascular on color doppler ultrasound in a 38-year-old female (Case 4).

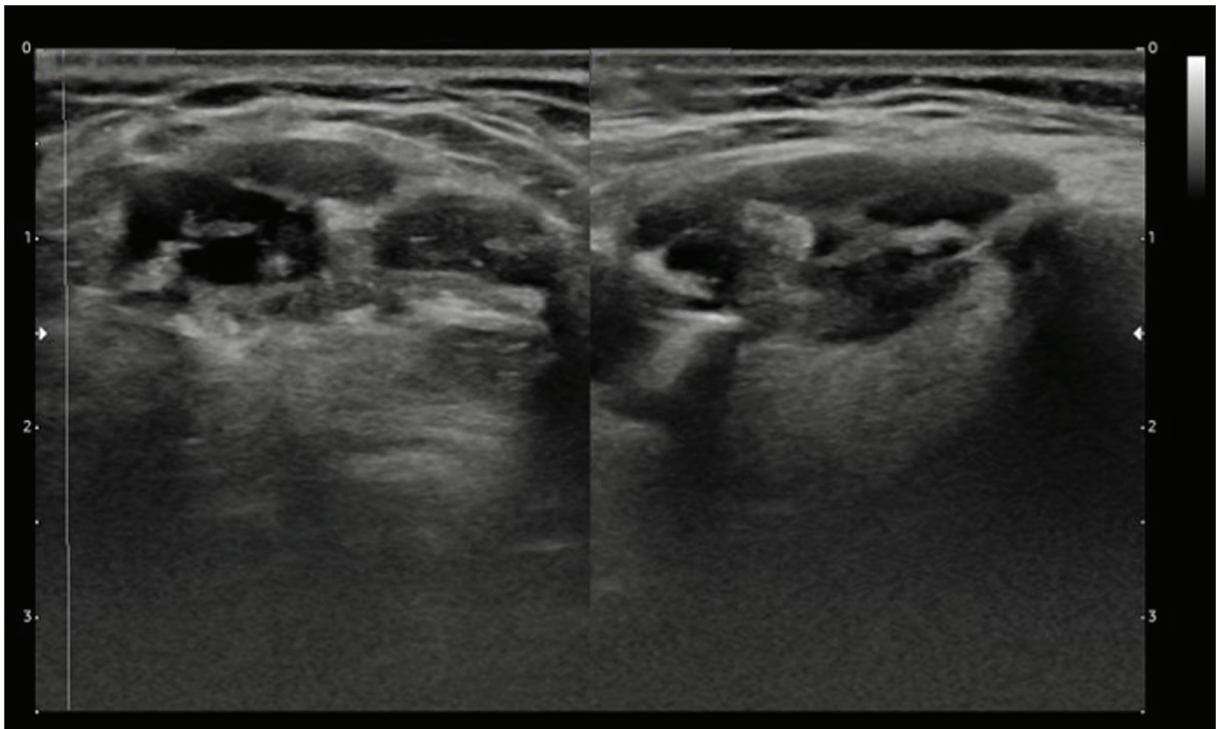


Figure 4. A well-defined complex nodule of 22x15x10 mm is seen in the midline of the neck at the level of the hyoid bone in a 48-year-old female, via ultrasound imaging (Case 2).

of 53% and a false negative rate of 47%. Peripheral locations of swelling in some of the patients, low cellularity of aspirated cytology due to dilution of the cystic region after aspiration and small tumor size make TGC diagnosis by FNAC

challenging (6,21). Repeating the FNAC under US guidance and taking a sample from the solid part of the cystic area or soft tissue mass may improve diagnostic accuracy (13). In the current study, only seven of the cases had a preoperative

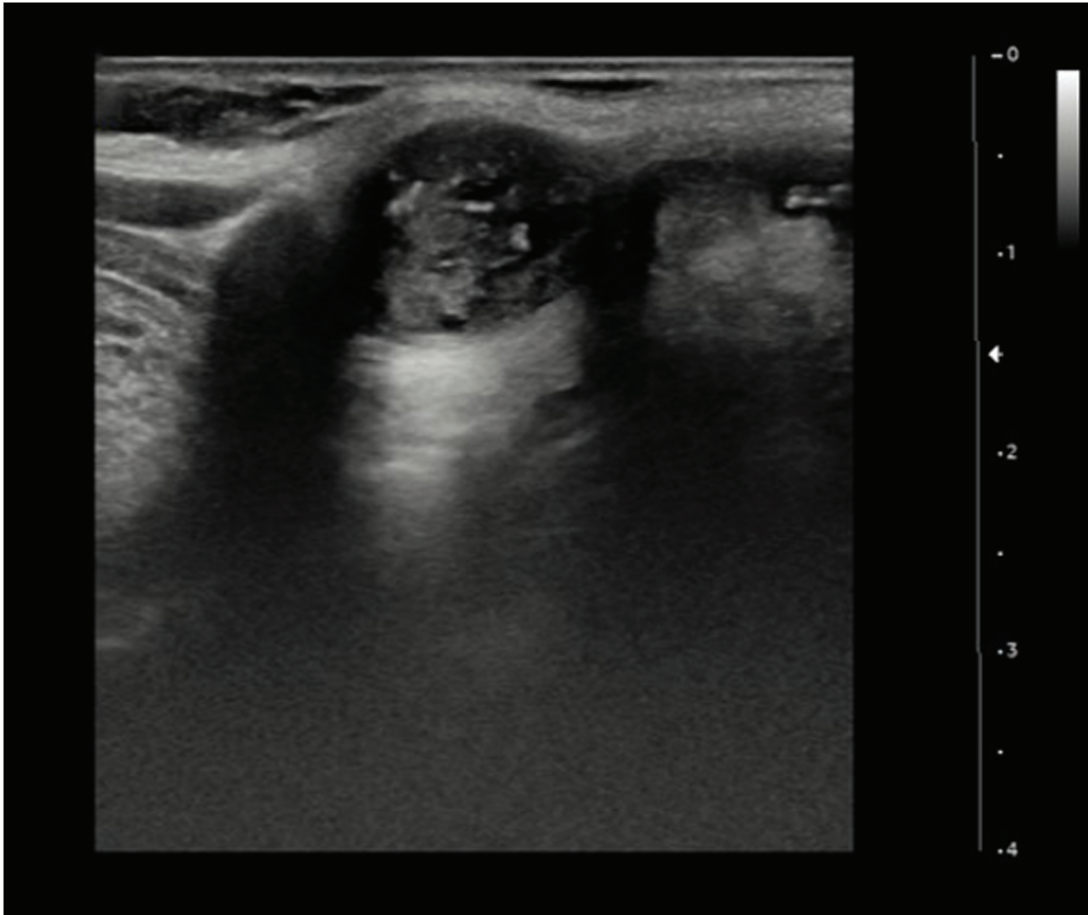


Figure 5. A well-defined, complex, mildly vascular nodule of 15x11x9 mm is seen in the midline of the neck on the inferior surface of the hyoid bone in a 43-year-old male, ultrasound imaging (Case 9).

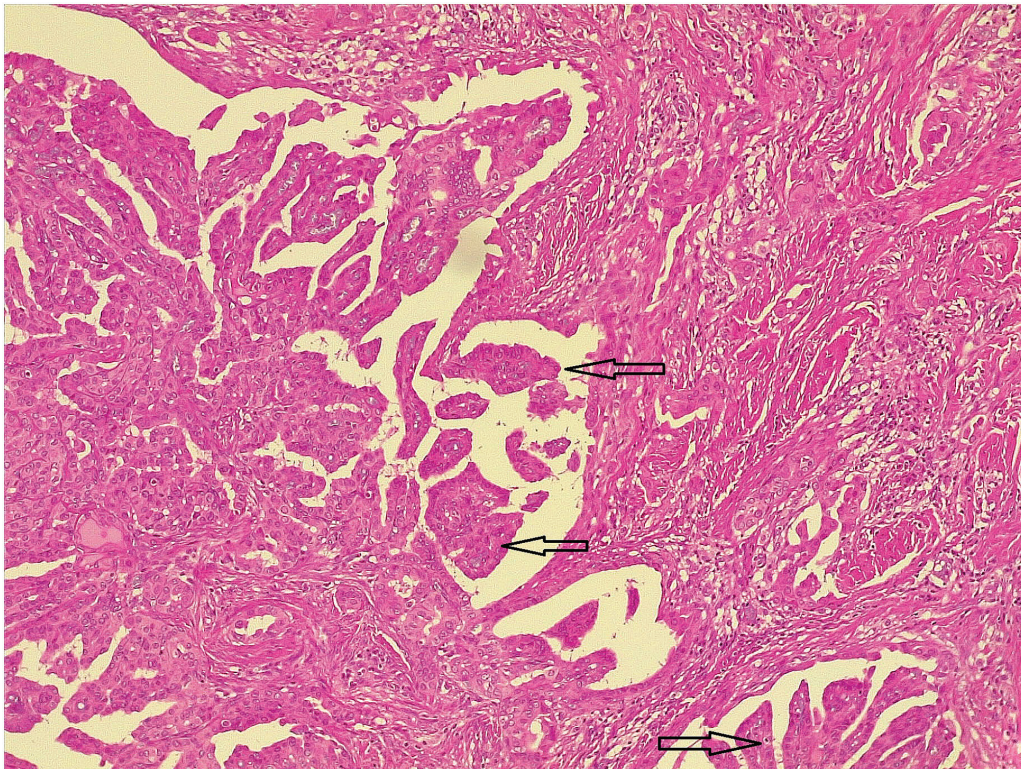


Figure 6. Papillary structures (black arrows) with nuclear features of papillary thyroid carcinoma are visible on histology (surgical specimen; hematoxylin and eosin stain; magnification, x100) (Case 3).

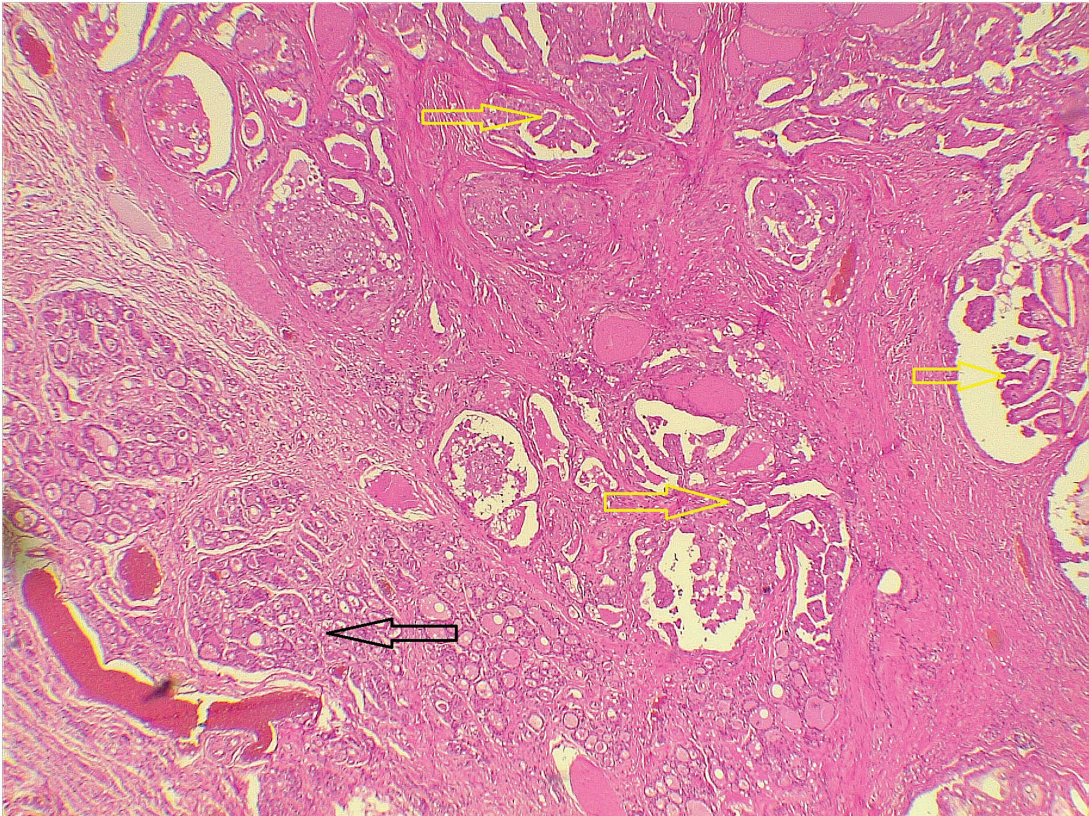


Figure 7. Benign heterotopic thyroid follicles (black arrow) with papillary thyroid carcinoma (yellow arrows) developed from a thyroglossal duct cyst (surgical specimen; hematoxylin and eosin stain; magnification, x40) (Case 7).

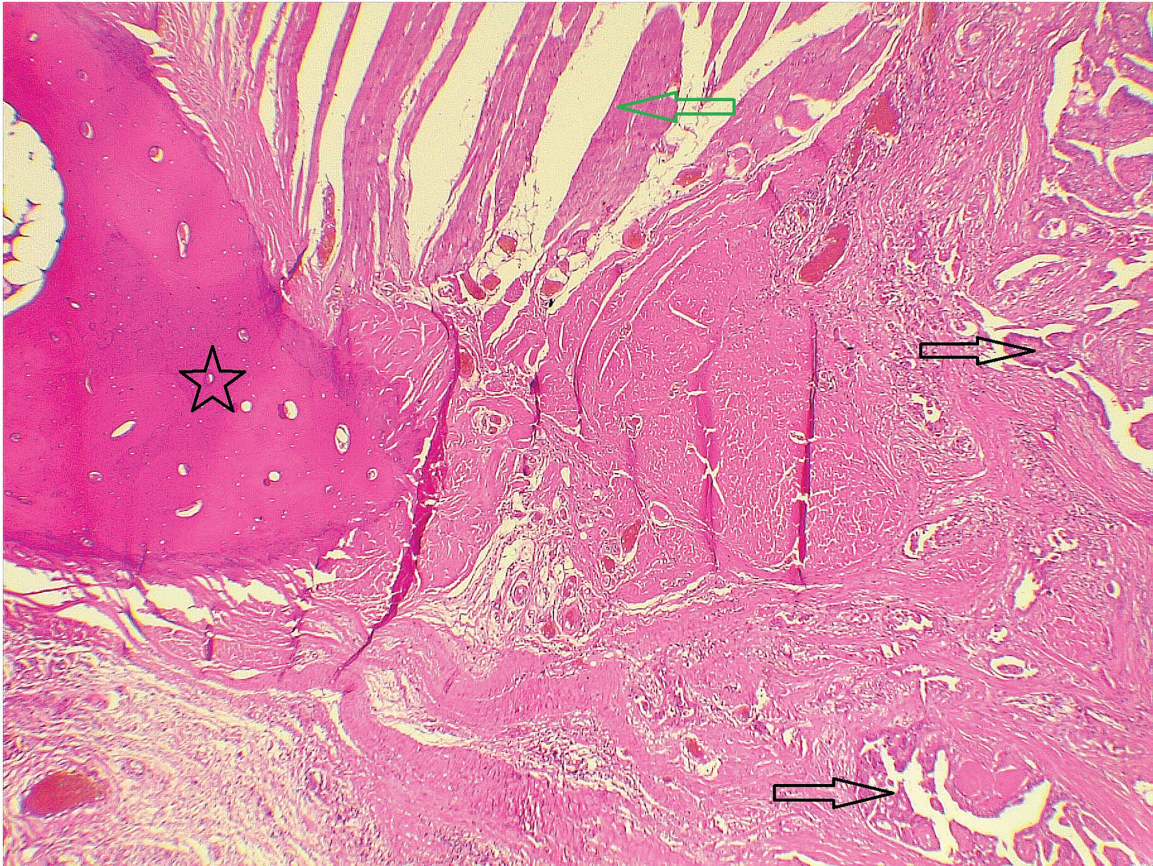


Figure 8. Benign hyoid bone (black star), with adjacent skeletal muscle (green arrow) and well-formed papillary structures with nuclear features of papillary thyroid carcinoma (black arrows) (surgical specimen; hematoxylin and eosin stain; magnification, x40) (Case 8).

FNAC of TGDC. Of the cases, six were suspected to have PTC and there was just cystic content in the sample of one of the cases.

The first case of PTC in a TGDC was reported by Owen and coworkers in 1927 (5). The majority of these malignancies come from the thyroid gland, with 75-85% being PTC, 7% being mixed papillary and follicular carcinoma and ~5% being SCC, which has the poorest prognosis (7). In a previous study, 4% of TGDC cases were found to be carcinomas and all of these were PTC (1). This aligns with prior research that also identified PTC as the most common type of carcinoma associated with TGDC (22). All of the TGCs in this study were PTC.

A common treatment for TGDC is Sistrunk's operation, which consists of the surgical removal of the TGDC and the hyoid bone central segment, along with a portion of tissue surrounding the thyroglossal tract extending towards the oral cavity at the foramen cecum (12). More aggressive management, such as the Sistrunk operation combined with a complete thyroidectomy and neck dissection, followed by treatment with radioactive iodine and thyroxine suppressive dose is beneficial for high-risk patients (older than 45 years, presence of invasion or metastatic lymph nodes in the neck, history of head and neck radiation and patients who present with a malignant thyroid nodule) (13). On the other hand, some authors recommend having a total thyroidectomy when the size of the carcinoma is >10 mm. When the size is <10 mm, a total thyroidectomy should be considered when there is a presence of cyst wall invasion, enlarged cervical lymph nodes clinically or radiologically, or a prior history of radiation (7). Furthermore, total thyroidectomy combined with Sistrunk's procedure for TGC allows for more accurate staging and therapy, as well as long-term follow-up with thyroglobulin level monitoring and a whole-body scan (13). Sistrunk surgery was performed on five patients in this study alone. A total of four of the individuals had malignant thyroid nodules, necessitating both a Sistrunk surgery and a total thyroidectomy. Due to abnormal lymph nodes in the neck, two of them underwent lateral neck dissection. Furthermore, one patient was given radioactive iodine as well as a suppressive dosage of thyroxine. The cited resources in this study have been checked for eligibility (23). The limitations of this study include the availability of only a small number of histopathological images. As some examinations were conducted in external histopathology centers, not all images could be retrieved and the mutation profiles of the patients could not be obtained due to the high cost of the examinations.

In conclusion, carcinomas arising from TGDC remnants are uncommon and may solely present as anterior neck swelling. The use of FNAC in the preoperative assessment of cystic lesions in the neck can be beneficial. If TGC is suspected, both the thyroid gland and different lymph node compartments should be evaluated for malignancy. The Sistrunk operation serves as the gold treatment approach with good outcomes. However, additional management for high-risk TGCs should be considered, such as total or partial thyroidectomy, ablation using radioactive iodine, lateral neck dissection and suppressive therapy with thyroid hormones.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

YAS, ASM and HMD: Data collection, follow-up of the patients and final approval of the manuscript. AMS: Supervision of the manuscript, major contribution to the conception of the study, as well as in the literature search for related studies. AJQ: Radiologist who assessed the subjects' thyroid. AMA: Pathologist who examined the specimens. SHH and FHK: Confirmation of the authenticity of all the raw data, critical revision of the manuscript and contribution to the conception of the study. BOH, BAA and MBAA: Literature review, final approval of the manuscript and processing of the tables. SFA and HMR: Involved in the literature review, the writing of the manuscript and data analysis and interpretation. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Ethical approval for the study was granted by the Ethics Committee of Sulaimani University (Sulaimani, Iraq; approval no. 090). Written informed consent was obtained from all individual participants included in the study.

Patient consent for publication

The patients provided written informed consent for the publication of any data and/or accompanying images.

Competing interests

The authors declare that they have no competing interests.

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