Contents lists available at ScienceDirect

Heliyon



journal homepage: www.cell.com/heliyon

Research article

5²CelPress

Ultrasonographic features and diagnostic accuracy of FNA and CNB in secondary thyroid malignancies: A retrospective study

Zhen Xia^{a, 1}, Xiaochen Huang^{b, 1}, Ting Zhang^a, Zhigang Gao^a, Xiuliang Tang^a, Wei Zhang^{a,*}, Qing Miao^{a,**}

^a Department of Ultrasound, Jiangsu Cancer Hospital & Jiangsu Institute of Cancer Research & The Affiliated Cancer Hospital of Nanjing Medical University, Nanjing, China

^b Department of Pathology, Jiangsu Cancer Hospital & Jiangsu Institute of Cancer Research & The Affiliated Cancer Hospital of Nanjing Medical University, Nanjing, China

ARTICLE INFO

Keywords: Secondary thyroid malignancy Ultrasound Fine-needle aspiration Core needle biopsy

ABSTRACT

Objective: This study aims to examine the ultrasonographic features of secondary thyroid malignancies and compare the diagnostic efficacy of fine-needle aspiration (FNA) and core needle biopsy (CNB) in this condition.

Methods: A retrospective analysis was conducted on 29 patients with secondary thyroid malignancies treated at our center between July 2011 and October 2022. Ultrasound images and clinical data were analyzed, and the lesions were classified according to the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS).

Results: Among the 29 patients studied, primary tumor sites were predominantly the esophagus, lung, and nasopharynx. Comprehensive ultrasound data was available for 28 of these patients, revealing nodular lesions in 24 cases and diffuse lesions in 4 cases. Nodular lesions were predominantly solid or nearly solid hypoechoic nodules with parallel growth and extrathyroidal extension features, with a few showing macrocalcifications. Most patients had varying degrees of metastasis to neck lymph nodes. FNA accurately diagnosed 31.6 % of the lesions as secondary thyroid malignancies, while 5.3 % were misdiagnosed as papillary thyroid carcinoma (PTC). However, CNB demonstrated 100 % reliability in diagnosing secondary thyroid malignancies.

tures identifies nodular and diffuse patterns, with the application of ACR TI-RADS proving effective for nodular types. In detecting these lesions, CNB demonstrates superior sensitivity compared to FNA. Thus, in cases of thyroid lesions suspected to be malignant, particularly with enlarged neck lymph nodes and in patients with a history of malignancy, CNB is recommended as the diagnostic method of choice.

https://doi.org/10.1016/j.heliyon.2024.e36305

Received 9 November 2023; Received in revised form 5 August 2024; Accepted 13 August 2024

Available online 14 August 2024

^{*} Corresponding author. Department of Ultrasound, Jiangsu Cancer Hospital & Jiangsu Institute of Cancer Research & The Affiliated Cancer Hospital of Nanjing Medical University, No. 42 Baiziting, Xuanwu District, Nanjing, Jiangsu, 210009, China.

^{**} Corresponding author. Department of Ultrasound, Jiangsu Cancer Hospital & Jiangsu Institute of Cancer Research & The Affiliated Cancer Hospital of Nanjing Medical University, No. 42 Baiziting, Xuanwu District, Nanjing, Jiangsu, 210009, China.

E-mail addresses: zw_jsch@njmu.edu.cn (W. Zhang), miaoqin0627@sina.com (Q. Miao).

¹ Co-first authors.

^{2405-8440/© 2024} The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC license (http://creativecommons.org/licenses/by-nc/4.0/).

1. Introduction

Thyroid secondary malignancies are relatively rare, occurring in approximately 0.5%–5.2% of patients without a history of cancer and 3.9%–8.3% of patients with a cancer history [1]. They primarily originate from organs such as the kidney, lung, and breast [2]. The optimal treatment approach for thyroid secondary malignancies remains a topic of debate. While earlier studies suggested that thyroid surgery did not provide a survival benefit [3], larger studies now demonstrate significantly higher survival rates for patients who undergo surgery compared to those who receive radiation or chemotherapy [4,5]. The location of the primary lesion is a crucial factor influencing postoperative survival [6], highlighting the importance of early and accurate diagnosis for appropriate treatment.

Ultrasound is the preferred imaging modality for assessing thyroid diseases, including endocrine disorders, inflammation, and tumors. However, there is limited research available on ultrasonographic features and diagnostic guidelines specifically for thyroid secondary malignancies due to their low incidence. Ultrasound-guided FNA and CNB are important methods for determining the nature of incidental thyroid lesions [7,8]. However, there is considerable controversy regarding the diagnostic accuracy of FNA for thyroid secondary malignancies (ranging from 11.1 % to 95.5 %), and instances where it has been misdiagnosed as primary thyroid malignancies [9–11]. In contrast, CNB demonstrates higher diagnostic accuracy, and with the aid of immunohistochemistry, it helps in identifying the primary lesion [9,12]. Additionally, the safety of thyroid CNB is now considered manageable, and there are reports suggesting that CNB should perhaps replace FNA as the preferred diagnostic method [13].

This study retrospectively analyzes ultrasound images and clinical data from patients with thyroid secondary malignancies who were treated at our center. The primary objective is to investigate the ultrasonographic features of thyroid secondary malignancies and compare the diagnostic efficacy of FNA and CNB in this disease.

2. Materials and methods

2.1. Patients

A retrospective analysis was performed on a cohort of 29 patients who were diagnosed with thyroid secondary malignancies and received treatment at our center between July 2011 and October 2022. The inclusion criteria required pathological evidence of thyroid secondary malignancies, while cases of lymphomas were excluded from the study (Fig. 1).

2.2. Imaging methods

Ultrasound images were obtained from the patients prior to FNA, CNB, or surgical procedures. The focus of the imaging was on the thyroid lesions and cervical lymph nodes. Given the extended timeframe and multiple updates to the thyroid reporting system, two



Fig. 1. Flowchart depicting the patient enrollment process. The numbers indicate the number of patients at each stage. NPC, Nasopharyngeal Cancer; MT, Malignant Tumor; AC, Adenocarcinoma; SCC, Squamous Cell Carcinoma; PDC, Poorly Differentiated Carcinoma; MC, Mucinous Carcinoma; LUAD, Lung Adenocarcinoma; BIDC, Breast Invasive Ductal Carcinoma; BLCA, Bladder Urothelial Carcinoma.

experienced radiologists with a decade of ultrasound diagnostic experience independently reviewed the images using the ACR TI-RADS published in 2017 [14]. The analysis primarily concentrated on thyroid nodules that had undergone FNA and CNB.

2.3. FNA or CNB

The procedures were executed under ultrasound guidance using the MyLab 90 ultrasound system (ESAOTE, Italy). For the FNA, a 25-gauge needle attached to a 5 mL syringe was utilized, with samples collected using the conventional smears technique. The CNB was performed employing an 18-gauge fully automatic biopsy needle. Both FNA and CNB procedures adhered to standard operating protocols [15,16].

For the selection of thyroid puncture lesions, the choice of biopsy method is based on the evaluation of the lesion's ultrasonographic features and clinical data. Typically, for nodular lesions, biopsy preference is given to the nodule exhibiting the highest degree of malignancy, as evidenced by its ultrasonographic features. If multiple nodules present similar malignant characteristics, the largest nodule is selected. For diffuse lesions, in patients highly suspected of thyroid occupancy (common features include enlarged thyroid volume, reduced echogenicity, scattered calcifications, and concurrent abnormal cervical lymph nodes), the biopsy site is chosen at areas of markedly reduced echogenicity or dense calcifications. If the lesion is uniformly distributed, multiple angle samplings of the

Table 1

Clinical Information of patients.

Patient	Gender	Age	Thyroid Primary?	Primary Site	Primary Treatment	Metastasis Time (months)	Other Metastasis	Follow-up Treatment	
1	Female	66	No	Esophagus	Unknown	Unknown Unknown		Unknown	
2	Female	50	No	Esophagus	RT, CT	4	Unknown	Unknown	
3	Female	84	Yes	Esophagus	N/A	N/A	Right Neck	Unknown	
4	Male	63	No	Esophagus	Surgery, RT, CT	21	21 Right Neck		
5	Male	74	Yes	Esophagus	N/A	N/A	N/A Right Neck		
6	Female	73	No	Esophagus	ESD	24 Esophageal Recurrence,		Immunotherapy RT, CT,	
_							Mediastinum, Bilateral Neck	Immunotherapy	
7	Male	69	No	Esophagus	Surgery	180	Internal Jugular Vein, Left Neck	Unknown	
8	Male	51	Yes	Esophagus	N/A	N/A	Left Neck	Refused Treatment	
9	Male	70	No	Esophagus	Unknown	Unknown	Unknown Right Neck		
10	Female	61	No	Lung	Surgery	35	Bilateral Neck, Mediastinum, Lung, Bones	RT	
11	Female	70	Yes	Lung	N/A	N/A	Bilateral Neck, Mediastinum,	CT	
12	Female	49	Yes	Lung	N/A	N/A	Multiple Systemic Metastases	Targeted Therapy	
13	Male	66	No	Lung	Surgery, CT	41	Not Observed	Unknown	
14	Female	55	Yes	Lung	N/A	N/A	Bilateral Neck, Lung Hilar Nodes, Mediastinum, Retroperitoneum	CT	
15	Male	64	Yes	Lung	N/A	N/A	Mediastinum, Left Adrenal Gland, Right Lumbar Region	Refused Treatment	
16	Male	66	Yes	Lung	N/A	N/A	Bilateral Neck	Refused Treatment	
17	Female	83	Yes	Lung	N/A	N/A	Mediastinum, Pleura, Lung, Liver	RT, CT, Immunotherapy	
18	Male	62	No	Nasopharvnx	Surgery, RT, CT	36	Unknown	Unknown	
19	Female	62	No	Nasopharynx	RT, CT	125	Left Neck, Left Parotid Gland	1 Unknown	
20	Female	59	No	Nasopharynx	Surgery, RT, CT	216	Left Neck	Unknown	
21	Male	50	No	Nasopharynx	RT, CT	34	Right Neck, Mediastinum	Surgery, RT, CT, Immunotherapy	
22	Female	66	No	Tongue	Surgery, RT, CT	27	Bilateral Neck, Lung, Bones	RT. CT	
23	Female	55	No	Tongue	Surgery	4	Tongue, Left Neck, Nasopharynx, Esophagus,	Targeted Therapy, CT	
24	Female	40	No	Breast	Surgery CT	67	Lung Multiple Systemic Metastases	Endocrine Therapy	
25	Female	39	No	Gallbladder	Surgery, CI	24	Bilateral Neck Left Internal	СТ	
23	remate	55	140	Gailbladder	Surgery	24	Mammary Region, Mediastinum	61	
26	Male	66	No	Bladder	TURBT	20	Bilateral Neck, Mediastinum, Lung	Surgery	
27	Male	69	No	Esophagus/ Pharynx	RT, CT, Particle Implantation	15	Bilateral Neck, Left Parotid Area	Particle Implantation	
28	Female	81	Yes	Unknown	N/A	N/A	Bilateral Neck, Mediastinum, Lung Hilar Nodes, Bones	RT	
29	Male	56	Yes	Unknown	N/A	N/A	Left Neck	RT, CT, Immunotherapy	

RT, Radiotherapy; CT, Chemotherapy; TURBT, Transurethral Resection of Bladder Tumor.

Z. Xia et al.

same thyroid lobe are performed as safely as possible.

The cytological analysis of FNA utilizes The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) [17]. If the FNA results were inconclusive or further examination was required, a CNB was performed on the same nodule. In cases where patients had a history of cancer and the ultrasound sonogram indicated larger thyroid lesions, infiltration beyond the thyroid capsule, or multiple lymph node metastases in the neck, a direct CNB was chosen for diagnosis, with a focus on ensuring safety [18]. Thyroid lesion CNB samples are diagnosed using the standards of 'Pathology Reporting of Thyroid Core Needle Biopsy' proposed by the Korean Endocrine Pathology Thyroid Core Needle Biopsy Study Group [19]. The diagnosis involves initially ruling out primary thyroid malignancies (such as papillary carcinoma, follicular carcinoma, medullary carcinoma, etc.) through hematoxylin and eosin staining, and then determining the source by combining immunohistochemical markers with the patient's medical history.

2.4. Statistical analysis

Statistical analysis was conducted using SPSS 26.0. Results are presented as percentage for nominal variables and as the mean and standard deviation for continuous variables. Group comparisons were performed using the chi-square test or Fisher's exact test, as appropriate. A *p*-value of less than 0.05 was considered statistically significant.

3. Results

3.1. Demographic and clinical data

Out of the 29 patients included in the study, there were 13 male and 16 female participants, with an average age of 62.7 ± 11.3 years (range: 39–84 years) at the time of secondary thyroid malignancy diagnosis. The primary tumor sites were distributed as follows: esophagus (9 cases), lung (8 cases), nasopharynx (4 cases), tongue (2 cases), bladder (1 case), gallbladder (1 case), breast (1 case), esophagus or hypopharynx (1 case), and unknown (2 cases). Among these patients, 11 initially presented with symptoms related to the thyroid, while 18 had a documented history of primary malignancies. Excluding 2 cases with unknown medical history, the time interval between the primary lesion and thyroid metastasis ranged from 4 to 216 months, with an average duration of 54.6 ± 63.2 months (Table 1).

3.2. Ultrasonographic features

Out of the 29 patients, complete ultrasound images and reports were available for 28 patients, while data for 1 patient was missing. Based on the ultrasonographic features, the patients were divided into two groups: 1) The Diffuse Type (n = 4), characterized by bilateral thyroid gland involvement without nodules [20,21], and 2) Nodular type (n = 24), identified by the presence of nodules. In the nodular type, patients exhibited nodules with sizes ranging from 13 to 70 mm (mean size 34.6 ± 12.6 mm). Among these cases, 5 (20.8 %) had multiple bilateral nodules, 1 (4.2 %) had multiple nodules in the left lobe, and 18 (75.0 %) had a single nodule, with 7 cases (29.2 %) in the left lobe, 10 cases (41.7 %) in the right lobe, and 1 case (4.2 %) in the isthmus. Further ultrasonic characteristics of the 24 nodular lesions are detailed in Table 2. The diffuse lesions caused noticeable enlargement of the thyroid gland, characterized by

Characters	Total (n = 24)
ACR TI-RADS	
4	4 (16.7 %)
5	20 (83.3 %)
Composition	
Solid	22 (91.7 %)
Mixed	1 (4.2 %)
Nearly Solid	1 (4.2 %)
Echogenicity	
Hypoechoic	24 (100.0 %)
Hyperechoic or isoechoic	0 (0.0 %)
Taller than Wide	
<1	22 (91.7 %)
>1	2 (8.3 %)
Margin	
ETE	20 (83.3 %)
Irregular	1 (4.2 %)
Vague	2 (8.3 %)
Smooth	1 (4.2 %)
Echogenic Foci	
None	18 (75.0 %)
PEF	6 (25.0 %)

 Table 2

 Ultrasonographic features of 24 nodular lesions.

ETE, Extra-thyroidal extension; PEF, Punctate echogenic foci.

irregular solid hypoechoic patterns. 1 case (25 %) exhibited scattered punctate echogenic foci, while another case (25 %) showed prominent calcifications. The remaining two cases did not exhibit any calcifications (Table 3).

3.3. Metastasis in other sites

In this study, among 26 patients (excluding 3 patients with incomplete clinical data), only 1 patient (3.8 %) showed no apparent metastatic lesions outside the thyroid; while 2 patients (7.7 %) did not exhibit metastatic lesions in the cervical lymph nodes, but had lesions in other sites. The remaining 23 patients (88.5 %) showed varying degrees of cervical lymph node metastasis.

3.4. FNA and CNB

In the study involving twenty-nine patients, nineteen initially underwent FNA, with all cases (100 %) showing abnormalities. Of these, 7 (36.8 %) displayed atypical cells (TBSRTC Category III), 5 (26.3 %) were diagnosed with malignant tumors (TBSRTC Category V), and 1 (5.3 %) was erroneously diagnosed as having PTC (TBSRTC Category VIa). Furthermore, 6 cases (31.6 %) suggested the presence of secondary malignancies in the thyroid(TBSRTC Category VIe): 3 (15.8 %) with adenocarcinoma, 2 (10.5 %) with squamous cell carcinoma, and 1 (5.3 %) with nasopharyngeal carcinoma. It should be noted that in 2 cases (Patient 8 and Patient 29), FNA cytology suggests atypical cells with a consideration for metastasis, excluding primary malignancy. After correlating with the medical history and confirmed metastatic sources in the lymph nodes on the same side of the neck, these were considered to be thyroid secondary malignancies.

Of the remaining patients, 9 initially had CNB, and an additional 7 underwent CNB following FNA. In all these 16 CNB cases, the findings were indicative of secondary malignancies in the thyroid gland (100 %).

3.5. Thyroid surgery

Among the 4 patients who underwent thyroidectomy, 1 was operated on due to an erroneous diagnosis of PTC following FNA. Another patient, suspected of having a primary thyroid malignancy, proceeded to surgery without preoperative FNA or CNB. The remaining 2 patients underwent surgical intervention for confirmed thyroid secondary malignancies.

4. Discussion

Nodular thyroid secondary malignancies often exhibit similar characteristics to primary thyroid lesions, particularly PTC, with predominant solid hypoechoic features. However, there are notable differences between the two. In this study, we observed that the typical malignant ultrasonographic features associated with PTC, such as a Taller-Than-Wide shape and microcalcifications [22,23], were not prominent in the 24 nodules analyzed. Only 2 cases (8.3 %) showed a Taller-Than-Wide shape, with one nodule measuring 36 mm wide and 38 mm tall, demonstrating a tall height nearly equal to its width. The other case presented as a large cystic-solid mass, with the cystic portion primarily located deep within the thyroid, resulting in a Taller-Than-Wide appearance. The relatively larger size of these two nodules with a Taller-Than-Wide shape may be influenced by surrounding tissues and blood vessels during growth, causing inward growth towards the posterior thyroid space. It is also worth noting that the Taller-Than-Wide feature is considered more applicable for small nodules and is not commonly used when the nodule size exceeds 10 mm [24], the average maximum diameter of the nodules in this study was notably larger, reaching 34.6 mm. Regarding microcalcifications, only 1 case (4.2 %) of the nodular type exhibited them, while 5 patients (20.8 %) had macrocalcifications, indicating significant differences from PTC.

Previous reports have indicated that diffuse lesions account for approximately 33.3 %–34.6 % of thyroid secondary malignancies [3,25], often accompanied by lymph node metastasis in the neck or supraclavicular region (78.8%–100.0 %). In our study, a lower proportion (13.8 %) of diffuse lesions was observed, all of which showed associated neck lymph node metastasis, suggesting a potentially higher invasiveness [26,27]. Diffuse punctate echogenic foci is another ultrasonographic features observed. In one case, we observed diffuse heterogeneous echogenicity combined with diffuse punctate echogenic foci (Fig. 2A). This case was initially misdiagnosed as PTC during FNA (Fig. 2B) but was later confirmed to be secondary to lung adenocarcinoma following surgical evaluation (Fig. 2C). It remains unclear whether this misdiagnosis is related to the presence of these punctate echogenic foci. Differentiating between secondary malignancies of diffuse thyroid lesions and various diffuse thyroid pathologies, including the Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma (DSV-PTC) and thyroid lymphoma, based on similar ultrasonographic features such as diffuse calcifications and lymph node metastasis, poses a significant challenge [25,28–30]. Therefore, when such ultrasonographic features are observed, it is crucial to exercise heightened vigilance and conduct thorough investigations to facilitate accurate diagnosis, and, if necessary, perform a CNB to facilitate an accurate diagnosis.

The ACR TI-RADS provides standardized guidelines for classifying thyroid nodules and determining the need for FNA or follow-up ultrasound. In this study, all nodules were classified as either category 4 or 5, indicating a high suspicion of malignancy. According to the ACR TI-RADS, FNA is recommended for category 4 nodules larger than 15 mm and category 5 nodules larger than 10 mm. Only 1 case, classified as category 4 with a diameter of 13 mm, did not meet the FNA criteria. This finding confirms the applicability of ACR TI-RADS for risk assessment in thyroid secondary malignancies.

In this study, 88.5 % of cases diagnosed with thyroid secondary malignancies showed a significantly higher incidence of cervical lymph node metastasis compared to PTC [31]. In this study, all nine cases of secondary malignancies originating from the esophagus presented as solitary nodules, with 5 on the left and 4 on the right side. Contrastingly, among the 18 cases with non-esophageal or

Table 3
Ultrasonographic features and pathological diagnostic of thyroid lesions.

Patient	Lesion Type	Location	Unifocal/ Multifocal	Maximum Diameter (mm)	ACR TI- RADS	Composition	Echogenicity	Taller than Wide	Margin	Echogenic Foci	FNA	CNB	Surgery
1	Nodular	Left	Unifocal	28	5	Solid	Hypoechoic	<1	ETE	MCF		SCC	
2	Nodular	Left	Unifocal	31	5	Solid	Hypoechoic	<1	ETE	None	SCC		
3	Nodular	Right	Unifocal	43	5	Solid	Hypoechoic	<1	ETE	None		SCC	
4	Nodular	Right	Unifocal	31	5	Solid	Hypoechoic	<1	ETE	None		SCC	
5	Nodular	Left	Unifocal	38	5	Solid	Hypoechoic	>1	ETE	None	Atypical Cells	SCC	
6	Nodular	Right	Unifocal	32	4	Solid	Hypoechoic	<1	Irregular	None		SCC	
7	Nodular	Left	Unifocal	26	5	Solid	Hypoechoic	<1	ETE	None		SCC	
8	Nodular	Left	Unifocal	35	4	Solid	Hypoechoic	<1	Ill- defined	None	Atypical Cells		
9	Nodular	Right	Unifocal	32	5	Solid	Hypoechoic	<1	ETE	MCF	Atypical Cells	PDC	
10	Nodular	Bilateral	Multifocal	51	5	Solid	Hypoechoic	<1	ETE	MCF		MC	
11	Nodular	Right	Unifocal	36	5	Solid	Hypoechoic	<1	ETE	None		SCC	
12	Nodular	Bilateral	Multifocal	20	4	Solid	Hypoechoic	<1	Smooth	None	AC		
13	Nodular	Right	Unifocal	38	5	Solid	Hypoechoic	<1	ETE	MCF	MT	AC	
14	Diffuse	Bilateral	-	-	Unclassfied	-	-	-	-	PEF	PTC		LUAD
15	Nodular	Left	Unifocal	_	Unclassfied	-	-	-	-	-	AC		
16	Nodular	Bilateral	Multifocal	70	5	Mixed	Hypoechoic	>1	ETE	None	MT		
17	Nodular	Left	Unifocal	56	5	Solid	Hypoechoic	<1	ETE	None	MT		
18	Nodular	Right	Unifocal	41	5	Solid	Hypoechoic	<1	ETE	PEF	SCC		
19	Nodular	Bilateral	Multifocal	41	5	Solid	Hypoechoic	<1	ETE	None	NPC		
20	Diffuse	Bilateral	-	_	Unclassfied	-	-	-	-	None		NPC	
21	Nodular	Right	Unifocal	22	5	Solid	Hypoechoic	<1	ETE	None			NPC
22	Nodular	Left	Unifocal	34	5	Nearly Solid	Hypoechoic	<1	ETE	None	Atypical Cells	SCC	
23	Diffuse	Bilateral	-	-	Unclassfied	-	-	-	-	MCF	Atypical Cells	SCC	
24	Nodular	Right	Unifocal	21	5	Solid	Hypoechoic	<1	ETE	None	MT		BIDC
25	Diffuse	Bilateral	_	_	Unclassfied	_	_	_	_	None	AC		
26	Nodular	Bilateral	Multifocal	38	5	Solid	Hypoechoic	<1	ETE	MCF		PDC	BLCA
27	Nodular	Left	Multifocal	36	5	Solid	Hypoechoic	<1	ETE	None	Atypical Cells	SCC	
28	Nodular	Right	Unifocal	18	5	Solid	Hypoechoic	<1	ETE	None	MT	SCC	
29	Nodular	Isthmus	Unifocal	13	4	Solid	Hypoechoic	<1	Ill- defined	None	Atypical Cells		

ETE, Extra-thyroidal extension; PEF, Punctate echogenic foci; MCF, Macrocalcifications.

6



Fig. 2. Patient No.14 was misdiagnosed as PTC based on FNA and underwent surgery. A: Bilateral diffuse thyroid lesions with punctate echogenic foci; B: FNA cytology: loosely arranged tumor cells, enlarged nuclei, light staining, visible nucleoli, and nuclear furrows; C: Poorly differentiated carcinoma with vascular invasion (Hematoxylin and eosin staining x10).

unidentified origins, 9 cases (50 %) exhibited bilateral thyroid involvement. This observation suggests that direct invasion by esophageal malignancies could be a contributing factor, despite some patients having undergone treatments like surgery or radio-therapy before their diagnosis. At the same time, metastasis originating from distant sites appears more prone to affecting both thyroid lobes.

FNA has been widely adopted in clinical practice due to its simplicity, cost-effectiveness, and accuracy, making it advantageous for diagnosing thyroid diseases, particularly PTC. However, with the growing recognition of non-PTC thyroid malignancies, there is an ongoing debate about the preference for CNB over other methods in diagnosing thyroid nodules, particularly for larger nodules[18, 32–34]. For thyroid secondary malignancies, the success rate of identifying them through FNA has been reported to range from 46 % to 94 % [35], and the accuracy of FNA diagnosis has been suggested to depend on the type of primary malignancy [36]. In our study, only 31.6 % of the lesions were directly diagnosed as thyroid secondary malignancies through FNA, while 5.3 % were misdiagnosed as PTC. To minimize the influence of confounding factors, we conducted statistical analysis on factors such as medical history, thyroid ultrasonographic features, and nodule size, and found that these factors did not significantly affect the diagnostic performance of FNA (Table 4). In contrast, CNB in our study provided 100 % reliable results.

This study has certain limitations, including its retrospective design as a single-center study and the notable difference in the primary types of thyroid secondary malignancies compared to other epidemiological reports. Notably, while renal cancer is often reported as one of the primary sources of thyroid secondary malignancies in international studies, our research found no cases originating from renal cancer. Instead, esophageal and lung cancers were more prevalent among our cases. This variation might be related to the specific patient population at our center, where lung and esophageal cancer patients are more common compared to those with renal cancer. This disparity in primary disease sources reported in various studies underscores the need for broader epidemiological surveys to better understand these differences [12,37].

Moreover, as a retrospective analysis, the ultrasound images used in this study were static images, potentially introducing bias into the results. Although the ultrasound and clinical data in our study were relatively comprehensive and could reflect the ultrasonographic features of some thyroid secondary malignancies, the number of cases was comparable to previous publications. Considering

Table 4	
---------	--

Clinical and ultrasonographic features of the metastasis and malignant by FNA.

01	6 1		
	Metastasis by FNA	Malignant by FNA	Р
Malignancy History ($n = 19$)			>0.05
yes	4	6	
no	2	7	
Lesion Type $(n = 18)$			>0.05
Diffuse	1	2	
Nodular	4	11	
Echogenic Foci (n = 18)			>0.05
None	4	9	
MCF	0	3	
PEF	1	1	
Unifocal or Multifocal $(n = 15)$			>0.05
Unifocal	2	9	
Multifocal	2	2	
Maximum Nodule Diameter (n = 15)			>0.05
< 3 cm	1	3	
\geq 3 cm	3	8	
ACR TI-RADS ($n = 15$)			>0.05
4	1	2	
5	3	9	

19 patients underwent FNA, with complete ultrasound data available for 18 of them. Among these, 15 cases were of the nodular type and were subjected to statistical analysis of ultrasonic features.

Z. Xia et al.

the low incidence of thyroid secondary malignancies, a more scientifically and systematically designed analysis would require a larger sample size from multiple centers.

In conclusion, this study categorizes the ultrasonographic features of thyroid secondary malignancies into nodular and diffuse types, with ACR TI-RADS being particularly suited for nodular types. CNB exhibits greater sensitivity than FNA in detecting thyroid secondary malignancies. Therefore, when a thyroid lesion is suspected of being malignant, particularly when accompanied by enlarged neck lymph nodes and a history of malignancy, CNB is the recommended diagnostic method.

Ethics approval

This study was approved by the Jiangsu Cancer Hospital Ethics Committee (Approval No. 2023-074; date of approval October 27, 2023).

CRediT authorship contribution statement

Zhen Xia: Writing – review & editing, Writing – original draft. **Xiaochen Huang:** Investigation, Resources, Supervision, Visualization, Funding acquisition. **Ting Zhang:** Investigation, Supervision. **Zhigang Gao:** Supervision, Validation. **Xiuliang Tang:** Investigation. **Wei Zhang:** Writing – review & editing, Project administration, Conceptualization, Funding acquisition, Visualization. **Qing Miao:** Resources, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This work was supported by grants from Research Project of Jiangsu Cancer Hospital (No. ZL202217, ZJ202208).

References

- [1] P.H. Montero, T. Ibrahimpasic, I.J. Nixon, A.R. Shaha, Thyroid metastasectomy, J. Surg. Oncol. 109 (2014) 36-41, https://doi.org/10.1002/jso.23452.
- [2] C.A. Ghossein, A. Khimraj, S. Dogan, B. Xu, Metastasis to the thyroid gland: a single-institution 16-year experience, Histopathology 78 (2021) 508–519, https:// doi.org/10.1111/his.14246.
- [3] Y. Saito, I. Sugitani, K. Toda, K. Yamada, Y. Fujimoto, Metastatic thyroid tumors: ultrasonographic features, prognostic factors and outcomes in 29 cases, Surg. Today 44 (2014) 55–61, https://doi.org/10.1007/s00595-013-0492-x.
- [4] S. Stergianos, C.C. Juhlin, J. Zedenius, J. Calissendorff, H. Falhammar, Metastasis to the thyroid gland: characterization and survival of an institutional series spanning 28 years, Eur. J. Surg. Oncol. 47 (2021) 1364–1369, https://doi.org/10.1016/j.ejso.2021.02.018.
- [5] P. Straccia, C. Mosseri, C. Brunelli, E.D. Rossi, C.P. Lombardi, A. Pontecorvi, G. Fadda, Diagnosis and treatment of metastases to the thyroid gland: a metaanalysis, Endocr. Pathol. 28 (2017) 112–120, https://doi.org/10.1007/s12022-017-9475-6.
- [6] J.O. Russell, K. Yan, B. Burkey, J. Scharpf, Nonthyroid metastasis to the thyroid gland, Otolaryngology-Head Neck Surg. (Tokyo) 155 (2016) 961–968, https:// doi.org/10.1177/0194599816655783.
- [7] M.C. Zatelli, G. Trasforini, S. Leoni, G. Frigato, M. Buratto, F. Tagliati, R. Rossi, L. Cavazzini, E. Roti, E.C. degli Uberti, BRAF V600E mutation analysis increases diagnostic accuracy for papillary thyroid carcinoma in fine-needle aspiration biopsies, Eur. J. Endocrinol. 161 (2009) 467–473, https://doi.org/10.1530/EJE-09-0353.
- [8] H.S. Ahn, I. Youn, D.G. Na, S.J. Kim, M.Y. Lee, Diagnostic performance of core needle biopsy as a first-line diagnostic tool for thyroid nodules according to ultrasound patterns: comparison with fine needle aspiration using propensity score matching analysis, Clin. Endocrinol. 94 (2021) 494–503, https://doi.org/ 10.1111/cen.14321.
- [9] O.K. Song, J.S. Koo, J.Y. Kwak, H.J. Moon, J.H. Yoon, E.-K. Kim, Metastatic renal cell carcinoma in the thyroid gland: ultrasonographic features and the diagnostic role of core needle biopsy, Ultrasonography 36 (2017) 252–259, https://doi.org/10.14366/usg.16037.
- [10] J.H. Yoon, E.-K. Kim, J.Y. Kwak, H.J. Moon, G.R. Kim, Sonographic features and ultrasonography-guided fine-needle aspiration of metastases to the thyroid gland, Ultrasonography 33 (n.d.) 40–48. https://doi.org/10.14366/usg.13014.
- [11] Z. Tang, L. Gao, X. Wang, J. Zhang, W. Zhan, W. Zhou, Metastases to the thyroid gland: ultrasonographic findings and diagnostic value of fine-needle aspiration cytology, Front. Oncol. 12 (2022) 939965, https://doi.org/10.3389/fonc.2022.939965.
- [12] S.H. Choi, J.H. Baek, E.J. Ha, Y.J. Choi, D.E. Song, J.K. Kim, K. Chung, T.Y. Kim, J.H. Lee, Diagnosis of metastasis to the thyroid gland, Otolaryngology-Head Neck Surg. (Tokyo) 154 (2016) 618–625, https://doi.org/10.1177/0194599816629632.
- [13] S.R. Chung, C.H. Suh, J.H. Baek, Y.J. Choi, J.H. Lee, The role of core needle biopsy in the diagnosis of initially detected thyroid nodules: a systematic review and meta-analysis, Eur. Radiol. 28 (2018) 4909–4918, https://doi.org/10.1007/s00330-018-5494-z.
- [14] F.N. Tessler, W.D. Middleton, E.G. Grant, J.K. Hoang, L.L. Berland, S.A. Teefey, J.J. Cronan, M.D. Beland, T.S. Desser, M.C. Frates, L.W. Hammers, U.M. Hamper, J.E. Langer, C.C. Reading, L.M. Scoutt, A.T. Stavros, ACR thyroid imaging, reporting and data system (TI-RADS): white paper of the ACR TI-RADS committee, J. Am. Coll. Radiol. 14 (2017) 587–595, https://doi.org/10.1016/j.jacr.2017.01.046.
- [15] J.S. Yeon, J.H. Baek, H.K. Lim, E.J. Ha, J.K. Kim, D.E. Song, T.Y. Kim, J.H. Lee, Thyroid nodules with initially nondiagnostic cytologic results: the role of coreneedle biopsy, Radiology 268 (2013) 274–280, https://doi.org/10.1148/radiol.13122247.
- [16] B. Degirmenci, A. Haktanir, R. Albayrak, M. Acar, D.A. Sahin, O. Sahin, A. Yucel, G. Caliskan, Sonographically guided fine-needle biopsy of thyroid nodules: the effects of nodule characteristics, sampling technique, and needle size on the adequacy of cytological material, Clin. Radiol. 62 (2007) 798–803, https://doi.org/ 10.1016/j.crad.2007.01.024.
- [17] E.S. Cibas, S.Z. Ali, The 2017 bethesda system for reporting thyroid cytopathology, Thyroid 27 (2017) 1341–1346, https://doi.org/10.1089/thy.2017.0500.
- [18] E.J. Ha, J.H. Baek, J.H. Lee, J.K. Kim, D.E. Song, W.B. Kim, S.J. Hong, Core needle biopsy could reduce diagnostic surgery in patients with anaplastic thyroid cancer or thyroid lymphoma, Eur. Radiol. 26 (2016) 1031–1036, https://doi.org/10.1007/s00330-015-3921-y.
- [19] C.K. Jung, H.S. Min, H.J. Park, D.E. Song, J.H. Kim, S.Y. Park, H. Yoo, M.K. Shin, Pathology reporting of thyroid core needle biopsy: a proposal of the Korean endocrine pathology thyroid core needle biopsy study group, J Pathol Transl Med 49 (2015) 288–299, https://doi.org/10.4132/jptm.2015.06.04.

Z. Xia et al.

- [20] H.J. Baek, D.W. Kim, K.H. Ryu, G.W. Shin, J.Y. Park, Y.J. Lee, H.J. Choo, H.K. Park, T.K. Ha, D.H. Kim, S.J. Jung, J.S. Park, S.H. Moon, K.J. Ahn, Thyroid imaging reporting and data system for detecting diffuse thyroid disease on ultrasonography: a single-center study, Front. Endocrinol. 10 (2019), https://doi.org/ 10.3389/fendo.2019.00776.
- [21] H.J. Baek, K.H. Ryu, H.J. An, J.P. Kim, E.J. Jung, D.W. Kim, Validation of diagnostic performance and interobserver agreement of DTD-TIRADS for diffuse thyroid disease on ultrasound: a single-center study, Am. J. Roentgenol. 216 (2021) 1329–1334, https://doi.org/10.2214/AJR.20.23231.
- [22] H.J. Moon, J.Y. Kwak, E.-K. Kim, M.J. Kim, A taller-than-wide shape in thyroid nodules in transverse and longitudinal ultrasonographic planes and the prediction of malignancy, Thyroid 21 (2011) 1249–1253, https://doi.org/10.1089/thy.2010.0372.
- [23] J.K. Hoang, W.K. Lee, M. Lee, D. Johnson, S. Farrell, US features of thyroid malignancy: pearls and pitfalls, Radiographics 27 (2007) 847–860, https://doi.org/ 10.1148/rg.273065038.
- [24] J. Ren, B. Liu, L.-L. Zhang, H.-Y. Li, F. Zhang, S. Li, L.-R. Zhao, A taller-than-wide shape is a good predictor of papillary thyroid carcinoma in small solid nodules, J. Ultrasound Med. 34 (2015) 19–26, https://doi.org/10.7863/ultra.34.1.19.
- [25] J.M. Debnam, M. Kwon, B.D. Fornage, S. Krishnamurthy, G.L. Clayman, B.S. Edeiken-Monroe, Sonographic evaluation of intrathyroid metastases, J. Ultrasound Med. 36 (2017) 69–76, https://doi.org/10.7863/ultra.16.02033.
- [26] P. Malandrino, M. Russo, C. Regalbuto, G. Pellegriti, M. Moleti, A. Caff, S. Squatrito, R. Vigneri, Outcome of the diffuse sclerosing variant of papillary thyroid cancer: a meta-analysis, Thyroid 26 (2016) 1285–1292, https://doi.org/10.1089/thy.2016.0168.
- [27] Q. Wang, Q. Chang, R. Zhang, C. Sun, L. Li, S. Wang, Q. Wang, Z. Li, L. Niu, Diffuse sclerosing variant of papillary thyroid carcinoma: ultrasonographic and clinicopathological features in children/adolescents and adults, Clin. Radiol. 77 (2022) e356–e362, https://doi.org/10.1016/j.crad.2022.01.051.
- [28] Y. Zhang, D. Xia, P. Lin, L. Gao, G. Li, W. Zhang, Sonographic findings of the diffuse sclerosing variant of papillary carcinoma of the thyroid, J. Ultrasound Med. 29 (2010) 1223–1226, https://doi.org/10.7863/jum.2010.29.8.1223.
- [29] H. Ota, Y. Ito, F. Matsuzuka, S. Kuma, S. Fukata, S. Morita, K. Kobayashi, Y. Nakamura, K. Kakudo, N. Amino, A. Miyauchi, Usefulness of ultrasonography for diagnosis of malignant lymphoma of the thyroid 16 (2006) 983–987, https://doi.org/10.1089/thy.2006.16.983.
- [30] L.-S. Gu, N.-Y. Cui, Y. Wang, S.-N. Che, S.-M. Zou, W. He, J.-Y. Liu, X.-T. Gong, Comparison of sonographic characteristics of primary thyroid lymphoma and anaplastic thyroid carcinoma, J. Thorac. Dis. 9 (2017) 4774–4784, https://doi.org/10.21037/jtd.2017.09.48.
- [31] M.J. Jeon, W.G. Kim, Y.M. Choi, H. Kwon, D.E. Song, Y.-M. Lee, T.-Y. Sung, J.H. Yoon, S.J. Hong, J.H. Baek, J.H. Lee, J.-S. Ryu, T.Y. Kim, Y.K. Shong, K.-W. Chung, W.B. Kim, Recent changes in the clinical outcome of papillary thyroid carcinoma with cervical lymph node metastasis, J. Clin. Endocrinol. Metabol. 100 (2015) 3470–3477, https://doi.org/10.1210/JC.2015-2084.
- [32] M.J. Hong, D.G. Na, H. Lee, Diagnostic efficacy and safety of core needle biopsy as a first-line diagnostic method for thyroid nodules: a prospective cohort study, Thyroid 30 (2020) 1141–1149, https://doi.org/10.1089/thy.2019.0444.
- [33] A. Matrone, L. De Napoli, L. Torregrossa, A. Aghababyan, P. Papini, C.E. Ambrosini, R. Cervelli, C. Ugolini, F. Basolo, E. Molinaro, R. Elisei, G. Materazzi, Core Needle Biopsy Can Early and Precisely Identify Large Thyroid Masses, Front. Oncol. 12 (n.d.). https://doi.org/10.3389/fonc.2022.854755.
- [34] Z. Chen, J. Wang, D. Guo, Y. Zhai, Z. Dai, H. Su, Combined fine-needle aspiration with core needle biopsy for assessing thyroid nodules: a more valuable diagnostic method? Ultrasonography 42 (2023) 314–322, https://doi.org/10.14366/usg.22112.
- [35] M. Nguyen, G. He, A.K.-Y. Lam, Clinicopathological and molecular features of secondary cancer (metastasis) to the thyroid and advances in management, Int. J. Mol. Sci. 23 (2021) 3242, https://doi.org/10.3390/ijms23063242.
- [36] A.Y. Chung, T.B. Tran, K.T. Brumund, R.A. Weisman, M. Bouvet, Metastases to the thyroid: a review of the literature from the last decade, Thyroid 22 (2012) 258–268, https://doi.org/10.1089/thy.2010.0154.
- [37] M. Garneau, E. Alyzadneh, G. Lal, A. Rajan Kd, Metastatic disease to a concurrent thyroid neoplasm: a case series and review of the literature, Consult. Pathol. (2023), https://doi.org/10.1007/s12105-022-01509-7.