


Case Report

Unusual Metastasis from Follicular Thyroid Carcinoma: A Case Report and Literature Review

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Abstract

Introduction

Follicular thyroid carcinoma (FTC) is a type of well-differentiated thyroid carcinoma. It has a poorer prognosis, is more metastatic, and has characteristics different from papillary thyroid carcinoma. It tends to metastasize hematogenously, usually to the bones and lungs. This study aims to present a rare case of FTC metastasis to the peritoneum and thigh of a patient with a literature review.

Case presentation

A 70-year-old patient presented with a right thigh mass. Magnetic resonance imaging of the right thigh revealed an intramedullary lesion in the femoral diaphysis. The thyroid gland was firm, with no evidence of enlargement. A computed tomography scan showed several peritoneal nodules. A core biopsy of the right upper femoral lesion and peritoneal mass was performed. Histopathologic findings and immunohistochemical analysis confirmed metastatic FTC with thyroid origin.

Literature review

Unlike widely invasive FTC, minimally invasive FTC has a better prognosis and is less metastatic. Imaging, histopathologic examination, and immunohistochemistry can help in arriving at a diagnosis of FTC. Mutations of PPAR- γ and RAS are associated with FTC. Radioiodine treatment and suppressive therapy for the thyroid-stimulating hormone have been shown to improve survival rates of FTC, with postoperative follow-ups and treatment being important.

Conclusion

Metastasis of FTC to the peritoneum is rare and could lead to a late diagnosis. Proper diagnosis with confirmatory tools such as immunohistochemistry and adequate treatment are critical.

1. Introduction

Follicular thyroid carcinoma (FTC) is an infrequent type of thyroid carcinoma that represents approximately 10% of all thyroid cancers [1]. Together with papillary thyroid carcinoma (PTC), they are classified as well-differentiated thyroid malignancies, which make up over 85% of all thyroid carcinoma cases. FTC, however, has genetic mutations, pathological characteristics, and a poorer prognosis different from PTC [2]. Follicular adenomas occur more frequently than follicular carcinomas. Follicular carcinomas are distinguished from follicular adenomas by microscopic evidence of vascular or capsular invasion [3]. Follicular thyroid cancer tends to spread through the bloodstream, which may account for its higher rate of distant metastasis compared to PTC [4]. Spreading via the lymphatic system can also occur but is rarer [3]. Distant metastasis occurs in around 6-20% of cases of FTC, with the bones and lungs being the most affected sites [4]. The tumor tends to present at a relatively older age and is associated with a higher rate of mortality compared to PTC [5]. The mortality rate of FTC is around 10–30% [6]. Metastasis is considered the most critical factor influencing survival outcomes in FTC. Sometimes, distant metastases could be the first sign of the disease, as some cases are only found after the cancer has spread to other body parts, while in others, they can appear following initial treatment [2]. Metastasis of FTC to the peritoneum is exceedingly rare. This study aims to showcase a very rare case of FTC metastasis to the peritoneum, along with the patient's thigh, combined with a literature review. The cited references in this case report have been assessed for reliability [7] and compiled with CaReL guidelines [8].

2. Case presentation

2.1. Patient information

A 70-year-old female patient presented with a right thigh mass that had been present for two weeks. She is a non-smoker with a known history of diabetes mellitus, currently managed with anti-diabetic medication. The patient underwent thyroid surgery in 2011. However, the histopathology report from the procedure was unavailable. She is presently taking levothyroxine 100 mcg once daily.

2.2. Clinical findings

The patient was vitally stable. On examination of the neck, the thyroid gland was found to be firm bilaterally upon examination, with no evidence of enlargement (Figure 1). No palpable cervical lymphadenopathy was detected. A small lymph node identified during evaluation demonstrated only reactive changes on histological examination.

2.3. Diagnostic approach

Magnetic resonance imaging of the right thigh revealed a 35 × 48 mm intramedullary lesion in the femoral diaphysis. The lesion demonstrated low signal intensity on T1 and intermediate signal intensity on T2 with homogeneous post-contrast enhancement. It was associated with cortical destruction and extraosseous soft tissue extension. These imaging features are

suggestive of metastatic involvement, warranting histopathological confirmation. A computed tomography scan of the chest and abdomen revealed multiple lung nodules, with the largest measuring 27 mm. Additionally, several peritoneal nodules were identified in the right and mid-anterior abdominal regions, the largest measuring 18 mm. These findings were suggestive of metastatic disease.



Figure 1. A collar incision in the lower part of the neck was shown during the examination, with no significant palpable findings.

A core biopsy of the right upper femoral lesion was performed, confirming metastatic carcinoma. Immunohistochemical analysis suggested a thyroid origin. Laboratory investigations included thyroid function tests, which revealed that thyroid-stimulating hormone (TSH) level was 0.548 μ IU/mL (normal range: 0.8–6.0 μ IU/mL), free T4 was 21.5 pmol/L (normal range: 12.8–27 pmol/L), calcitonin (CATN) was <0.5 pg/mL (normal range: up to 9.82 pg/mL), thyroglobulin (Tg) was >500 ng/mL (normal range: 3.5–77 ng/mL), serum calcium was 9.83 mg/dL (normal range: 8.8–10.8 mg/dL), and parathyroid hormone (PTH) was 33.3 pg/mL (normal range: 15–65 pg/mL).

A neck ultrasound showed a remnant right lobe measuring 33 × 14 × 7 mm with a solid, heterogeneous echotexture. A smaller nodule measuring 12 × 7 × 4 mm of remnant tissue was detected below the lower pole of the previously noted remnant. In the midline of the neck, over the thyroid cartilage, an isoechoic, hypovascular remnant tissue measuring 15 × 6 × 4 mm was observed. The remnant left lobe measured 34 × 12 × 12 mm with a solid, heterogeneous echotexture containing a small TI-RADS 4 nodule measuring 6 × 6 × 4 mm. The isthmus was absent.

Additionally, a few small, solid, hypoechoic, hypovascular nodules were observed in the operative bed, with the largest measuring 5 × 3 mm in the left thyroid bed. Small lymph node-like structures were also noted. The patient underwent a core

biopsy of the peritoneal mass. Histopathologic examination showed cores of fibrofatty tissue infiltrated by sheets of variably sized follicles that were lined by cuboidal cells with a moderate amount of eosinophilic to clear cytoplasm and round, hyperchromatic nuclei, some of which had conspicuous nucleoli. Eosinophilic colloid material was present in the lumina of some of the follicles. There was no notable mitotic activity or necrosis. There was a mild lymphoplasmacytic infiltrate in the fibrous tissue (Figure 2). Immunohistochemistry showed positive staining of the tumor cells for CK7 (cytoplasmic staining of moderate intensity in 70% of the tumor cells), PAX-8 (nuclear staining of moderate intensity in 100% of the tumor cells), and TTF-1 (nuclear staining of strong intensity in 100% of the tumor cells). These findings confirmed the diagnosis of metastatic follicular thyroid carcinoma to the peritoneum (Figure 3).

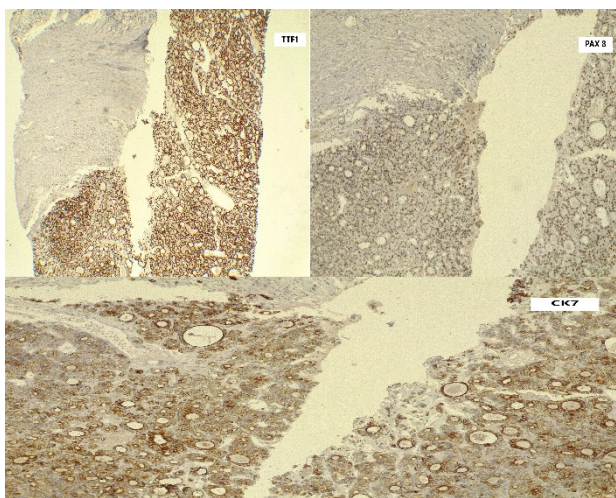


Figure 3. Immunostaining shows nuclear positivity for TTF-1 and PAX8, and cytoplasmic positivity for CK7.

2.4. Therapeutic intervention

Following a comprehensive evaluation by a multidisciplinary team, the patient was scheduled for radioactive iodine ablation and subsequently underwent a total revision thyroidectomy. Both recurrent laryngeal nerves were successfully preserved. The excised tissue was submitted for histopathological examination, which revealed nodular Hashimoto's thyroiditis with adenomatoid nodules and multiple reactive lymph nodes but no malignancy. The patient's vital signs remained stable with smooth postoperative recovery. The peritoneal metastasis was managed with a plan for radioactive iodine ablation. Considering the patient's clinical stability and the iodine-avid characteristics of the lesions, she was deemed an appropriate candidate for the therapy and was subsequently scheduled to receive it.

2.5. Follow-up and outcome

The patient recovered well postoperatively without complications. She was subsequently referred for radioactive iodine ablation and to an oncologist for ongoing follow-up and management. Her condition remains clinically stable, and she continues to be monitored pending treatment.

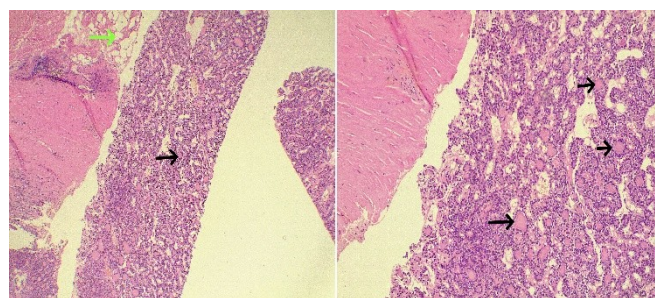


Figure 2. Section showing follicular epithelial cells arranged in microfollicles containing colloid material within their lumens (dark arrows). Low-power view is shown on the left (4×) and higher-power view on the right (10×), with peritoneal tissue visible (green arrow).

4. Discussion

Well-differentiated thyroid cancers like FTC and PTC will rarely metastasize to locations other than bones, lungs, and lymph nodes. Nonetheless, the occurrence of this small probability can lead to a late diagnosis [9]. Distant metastases to sites such as the brain, liver, breasts, muscles, kidneys, and skin are uncommon or occur infrequently. Distant metastasis is the most critical negative prognostic indicator; around 50% of affected patients survive beyond 10 years [10]. There is scant documentation of FTC metastasis to the peritoneum or abdominal area, with only a few case reports [11]. A struma ovarii containing FTC and metastasizing or spreading to the peritoneum can also occur [12, 13]. Mesentery metastasis of said carcinoma is rare as well [14]. Some cases of differentiated thyroid carcinoma metastases or spread to the peritoneum in literature have been reviewed in (Table 1) [11-15]. Iodine-sufficient and iodine-deficient regions show different ratios of papillary to follicular thyroid carcinoma, with iodine-deficient areas typically having lower ratios. Consequently, dietary iodine supplementation causes an increase in the said ratio [16].

When it comes to FTC, it can be cytologically very similar to follicular thyroid adenoma, unlike papillary carcinoma, which is typically easy to diagnose due to its distinctive nuclear features and growth pattern. In such situations, the growth pattern of the tumor (particularly the presence of capsular and/or vascular invasion) can be used to differentiate carcinoma from adenoma [17]. Follicular thyroid adenomas and FTC also have distinct microarray expression profiles, which set them apart from each other, with FTC showing more overexpression of autotaxin, EMMPRIN, GADD153, and galectin-3 mRNAs, and follicular thyroid adenomas showing increased TFF3 mRNA expression [18]. Follicular thyroid cancer can be classified into minimally invasive FTC, widely invasive FTC, and encapsulated angioinvasive FTC, with minimally invasive FTC having a better prognosis and being less metastatic. In contrast, widely invasive FTC is typically associated with a larger tumor, occurring in older individuals, more invasive growth into the thyroid, and distant metastasis [2]. Both minimally invasive FTC and widely invasive FTC show a lack of cytological atypia. Histological features required for FTC diagnosis include angioinvasion and/or invasion that penetrates the full thickness of the tumor-surrounding capsule [17]. Multiple factors affect FTC prognosis, including the presence of residual tumor after

Table 1 (Part A). A review of some cases of differentiated thyroid carcinoma metastases or spread to the peritoneum in the literature.

Author and year of publication	Age	Sex	Diagnosis	Clinical findings	Imaging
Hamdy et al. 2024 [12]	22	F	left ovarian highly differentiated FTC from struma ovarii with peritoneal and omental spread.	Iliac fossa pain, hypomenorrhea, & palpable lower abdominal mass.	US: multicystic pelviabdominal lesion. Post-contrast MRI: midline multi-locular pelviabdominal left ovarian cystic mass.
Porntharukcha reon et al. 2023 [11]	44	F	FTC metastasis to peritoneum.	Multiple peritoneal nodules, low FT4 & normal TSH levels.	CT of the peritoneum negative. US: small left thyroid nodule.
Chwa et al. 2023 [14]	62	M	Metastatic FTC on mesentery.	Mesentery mass during check-up.	PET/CT: mesentery mass. Chest CT: enhancing nodule in the left lower lobe.
Miles et al. 2016 [15]	68	F	Primary pelvic PTC metastasis to peritoneal surface.	Urinary retention.	US: heterogeneous pelvic mass. MRI: deep central pelvic mass like a uterus solid leiomyoma with extensive central necrosis.
Choi et al. 2012 [13]	33	F	Peritoneal dissemination of follicular carcinoma arising from struma ovarii.	Enlarged uterus.	MRI: bilateral par-ovarian solid tumors & unusual metastatic lesions manifestation in the pelvic cavity.

Table 1 (Part B). A review of some cases of differentiated thyroid carcinoma metastases or spread to the peritoneum in the literature.

Immunohistochemical tests	Treatment	Postoperative care	Outcome
IHC: +ve TTF1, & Tg.	Left salpingo-oophorectomy, omental & peritoneal biopsies, & thyroidectomy.	Radioactive iodine treatment, & levothyroxine.	Is in stable condition.
IHC: +ve CK-7, Tg, & TTF-1.	Total thyroidectomy.	Radioactive iodine treatment.	Is in stable condition.
IHC: < 3% Ki-67.	Lung lower lobe wedge resection, mesentery mass, & small bowel segment removed.	Radioactive iodine treatment.	Is in stable condition.
IHC supported the diagnosis of thyroid carcinoma.	Surgically resected retroperitoneal mass, total hysterectomy, resected superficial peritoneum tumor implants, & elective total thyroidectomy after 3 months.	Radioactive iodine treatment.	Is in stable condition.
Peritoneal mass HPE: thyroid gland enveloped in a fibrous capsule.	Exploratory laparotomy under the impression of bilateral ovarian malignancy, total thyroidectomy.	Radioactive iodine treatment.	Is in stable condition.

M = Male, F = Female, IHC = Immunohistochemistry, PET = Positron emission tomography, CT = Computed tomography, US = Ultrasound, MRI = Magnetic resonance imaging, Tg = Thyroglobulin, +ve = Positive, FT4 = Free T4, TSH = Thyroid stimulating hormone, FTC = Follicular thyroid carcinoma, PTC = Papillary thyroid carcinoma.

surgery, the patient's age, whether there is local or distant metastasis, the size of the tumor, and the tumor's pathological classification [1]. On ultrasonography, the presence of microcalcifications, which may indicate the presence of psammoma bodies, is rare in FTC and common in PTC. At the same time, both PTC and FTC could have rim and coarse calcifications [16].

Immunohistochemistry can be handy in confirming the thyroid origin of a metastatic tumor [19]. In this case, each of CK7, PAX-8, and TTF-1 were utilized to diagnose and confirm metastatic origin. TTF-1 and PAX-8 can be produced in the lung

and kidney, respectively. However, they are co-expressed with one another in thyroid follicular cells, highlighting the importance of this specific combination for establishing the thyroid of the tumor [20]. CK7 is a type of cytokeratin with a low molecular weight, an intermediate filament protein specific to epithelial cells, and it is typically found in glandular epithelium. It is more commonly used in diagnosing tumors outside the thyroid, where it helps determine the tumor's origin, rather than in tumors within the thyroid gland itself. It may also be used with CK20 to help with the diagnosis, with CK7 positivity accompanied by CK20 negativity being found in a few

organs including the thyroid [19]. The thyroid-specific enhancer-binding protein TTF-1 can also help confirm a tumor's thyroid origin, but not in differentiating among different thyroid lesions, with positive results found in around three-quarters of thyroid carcinoma metastases [19]. Li et al. utilized TTF-1 and CK7 positivity, along with thyroglobulin and partial CD56 positivity, in their immunohistochemical analyses to help confirm metastatic FTC in a chest wall lymph node [21].

Thyroglobulin is close to TTF-1 when it comes to sensitivity in identifying primary and secondary thyroid follicular lesions, but with these antibodies together, their diagnostic sensitivity may increase [19]. Serum thyroglobulin can be a dependable marker for detecting metastasis or recurrence since it has a 30-hour half-life following a total thyroidectomy [14]. Olejarski et al. report a 73-year-old with a right thigh soft tissue mass, surrounding a right proximal-mid femoral prosthesis on a computed tomography scan. A core biopsy of the mass revealed a follicular lesion showing positive results for TTF-1 and thyroglobulin, indicating a metastatic tumor of thyroid origin. The patient showed an elevated serum thyroglobulin indicative of a significant volume disease [22]. Genetic mutations associated with FTC include mutations of PPAR- γ and the mitogen-activated protein kinase activator and PI3K-AKT pathways known as RAS, which is frequently found in follicular adenomas, indicating a role in its early tumorigenesis. Other mutations are required to transform the adenoma into a carcinoma, such as PIK3CA mutations and PTEN, a tumor suppressor gene [16].

When the cytological or ultrasound findings indicate a higher risk of cancer, or if malignancy is present and to allow for radioiodine treatment postoperatively, total thyroidectomy may be considered [23]. Grani et al. found several studies showcasing that patients with FTC who were given radioiodine treatment had better chances of survival than those patients who did not. Another one showed that patients with distant metastases had improved chances of survival with radioiodine treatment, and in those without distant metastases, it increased local control. They also found several studies that showed better results with suppressive therapy for the thyroid-stimulating hormone after the initial treatment. External beam radiotherapy is also linked to better relapse-free survival for FTC when treating local or distant areas [16]. Post-therapy ¹³¹I whole-body scintigraphy and ¹³¹I single photon emission computed tomography/computed tomography are essential for patient management in differentiated thyroid carcinomas due to their high sensitivity and specificity [10]. Miles et al., for example, made use of whole-body radioactive iodine scanning for their patient with primary pelvic PTC metastasis to the peritoneal surface after the surgeries to follow up on the patient's condition. In it, two faint areas of activity were seen on the right side of the thyroid region, likely indicating small remnants of thyroid tissue, along with a small but clearly defined area of activity in the pelvic region, helping in the patient's management as they got better [15].

5. Conclusion

The rarity of FTC metastasis to locations like the peritoneum could lead to a late diagnosis and complications. Thus, it is

critical to consider this probability, make proper diagnoses with tools such as immunohistochemistry, and treat accordingly.

Declarations

Conflicts of interest: The authors have no conflicts of interest to disclose.

Ethical approval: Not applicable.

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Use of AI: ChatGPT version 5.2 (OpenAI) was used solely for language editing, paraphrasing, and improvement of clarity and grammar in this manuscript. The artificial intelligence tool did not contribute to the study design, data collection, data analysis, data interpretation, or the generation of scientific content. All outputs produced with the assistance of ChatGPT were carefully reviewed, verified, and approved by the authors. The authors take full responsibility for the accuracy, integrity, and originality of the entire manuscript.

Data availability statement: The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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