Metastasis Of Thyroid Cancer with No Primary Focus Seen: A Case Report

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AUTHOR CONTRIBUTIONS

Author1 (First Author): Conceptualization, Writing-Original Draft.
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Author3: Visualization, Writing – Review & Editing.
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AVAILABILITY OF DATA AND MATERIALS

Not applicable.

CONSENT

Did the author obtain written informed consent from the patient for submission of this manuscript for publication?
Answer: yes.

HUMAN AND ANIMAL RIGHTS

Ethical standards follow the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5).

ABSTRACT

Objective: Differentiated thyroid carcinoma (DTC), encompassing papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC), represents the predominant histological subtype of thyroid malignancies. While distant metastases in DTC occur less frequently compared to other solid tumors, with pulmonary and osseous involvement being the most common sites of dissemination, renal metastases as the initial clinical presentation remain uncommon. Notably, synchronous metastatic involvement of multiple rare anatomical locations in DTC constitutes an exceptionally rare clinical scenario.

Subject and Methods: A 56-year-old Asian male presented with a one-month history of persistent lumbar discomfort. Computed tomography (CT) imaging revealed a hypodense mass in the right renal parenchyma, accompanied by concurrent metastatic lesions in bilateral pulmonary fields and multiple osteolytic rib lesions. Subsequent diagnostic evaluation established the provisional diagnosis of primary renal cell carcinoma with synchronous pulmonary metastases and skeletal metastases.

Results: The patient was diagnosed with metastatic differentiated thyroid carcinoma demonstrating multiorgan dissemination, presenting with synchronous renal, hepatic, cerebral, and cutaneous metastases. A multidisciplinary therapeutic regimen was implemented, comprising total thyroidectomy with bilateral recurrent laryngeal nerve monitoring, laparoscopic radical nephrectomy of the right kidney, followed by two cycles of adjuvant radioiodine therapy (131I) combined with levothyroxine-mediated thyroid-stimulating hormone (TSH) suppression therapy.

Conclusion: The management of DTC patients presenting with synchronous multiorgan metastases as initial manifestations requires a meticulously coordinated therapeutic paradigm. This clinical scenario necessitates mandatory multidisciplinary tumor board (MTB) review to formulate risk-adapted treatment algorithms, integrating systemic therapeutic modalities with metastasis-directed local interventions based on comprehensive molecular profiling and precise assessment of disease burden.

CASE REPORT

BACKGROUND

Differentiated thyroid cancer (DTC) is characterized by a gradual clinical progression and a favorable prognosis, exhibiting a 10-year survival rate of approximately 90% according to recent studies [1,2] . Notably, upon the onset of distant metastasis in patients with differentiated thyroid carcinoma (DTC), the 5-year survival rate diminishes to 50% [3]. The presence of distant metastasis significantly correlates with the mortality specific to differentiated thyroid cancer [4,5]. Instances of DTC with renal metastases presenting as the initial manifestation are uncommon, with a documented total of fewer than 30 cases in existing literature, while simultaneous metastases to multiple rare locations are exceedingly rare. The current case under examination involves secondary metastases to the lungs and bones from a tumor initially misidentified as of renal etiology. Subsequent pathological analysis revealed renal metastases originating from follicular carcinoma of the thyroid gland, with additional metastases present in various organs including the brain, lungs, liver, bones and skin post-surgery. Notably, this unique case lacks any discernible primary lesions within the thyroid gland, which is not seen in the available literature.

CASE REPORT

A 56-year-old male patient presented with lumbar discomfort as the chief complaint. Radiographic evaluation revealed a right renal mass with concomitant pulmonary parenchymal lesions and rib abnormalities. The diagnostic impression was established as primary renal carcinoma with pulmonary and osseous metastatic involvement.

CT-guided rib biopsy histopathological evaluation confirmed metastatic adenocarcinoma, demonstrating histomorphological and immunohistochemical profiles consistent with thyroid follicular carcinoma. Immunohistochemical analysis revealed: cytokeratin (CK)(+), renal cell carcinoma marker (RCC) (-), PAX-8(+), PAX-2(-), thyroid transcription factor-1 (TTF-1)(+), thyroglobulin (TG)(+), synaptophysin (Syn)(-), CD56(+), villin(-), CK8/18(+), CK7(+), CK20(-), with a Ki-67 proliferation index of 10%.

Following multidisciplinary consensus, the patient underwent combined surgical procedures including bilateral thyroid lobectomy with recurrent laryngeal nerve exploration and laparoscopic radical right nephrectomy. Histopathological evaluation demonstrated focal granulomatous changes in the left thyroid parenchyma, right lobe nodular goiter, and metastatic carcinoma in the right kidney showing immunohistochemical characteristics compatible with thyroid follicular carcinoma (AE1/AE3 (CK) (+), TG (+), TTF-1 (+), RCC (-), Ki-67 15%, CT (Calcation) (-), SYN (-), CD56 (56C04) (+), CK19 (+), HBME-1 (MC) (-), Galectin-3 (-)) (Figure 1**)**. The patient underwent three courses of adjuvant ^{131}I therapy (200 mCi per cycle) between 2018-2019, with pre-treatment stimulated thyroglobulin (sTg) levels sequentially measuring 5377→3616→1468 μg/L alongside thyroglobulin antibody (TgAb) titers of 22.37→10.76→14.97 IU/mL. Post-therapeutic ^{131}I whole-body scintigraphy demonstrated bilateral pulmonary soft tissue nodules with intense iodine avidity, accompanied by skeletal metastases manifesting as radiotracer uptake in the right glenohumeral joint, scapula, and osteolytic 8th right posterior rib. Hepatic involvement was evidenced by clustered hypodense foci with iodine accumulation in the left medial lobe. Disseminated metastatic disease was further confirmed through multiple iodine-avid lesions in cranioabdominal regions (Figure 2). Subsequent histopathological verification of cutaneous metastasis was obtained via fine-needle aspiration biopsy of a dorsal subcutaneous nodule (Figure 3).

DISCUSSION

The incidence of distant metastases in differentiated thyroid cancer (DTC) is recorded to be below 10%; however, individuals encountering such metastatic progression exhibit a grave clinical outlook, marked by a 50-60% disease-specific mortality rate over a decade [6,7]. DTC most commonly metastasizes to the lungs and bones, and the rest of the metastases are called unusual metastases (UM) [2]. The residual metastatic occurrences, often referred to as atypical metastases or unusual metastases (UM). The prevalence of UM is exceedingly rare [8]. Anabela et al. retrospectively analyzed 3982 DTC patients from 8 research centers in Argentina, and 36 cases (0.9%) metastasized to rare sites [2]. The pathologic types that frequently metastasize to rare sites are papillary thyroid carcinoma (72.2%) (PTC), follicular thyroid carcinoma (27.7%) (FTC) [2]. The reason why FTC is lower than PTC takes into account the lower incidence of FTC compared to PTC, which accounts for usually less than 5% of DTC. From the biological characterization of thyroid follicular carcinoma as more prone to hematogenous metastasis, FTC is more prone to UM, and the statistics of Anabela et al. also showed that nearly half of the pathotypes that developed solid organ metastases (liver, pancreas, adrenal glands) were FTCs. Madani et al. reported that the pathotypes in which UMs occurred, follicular carcinoma of the thyroid, accounted for 39% of the cases [9].

This case is different from the previously reported rare site metastasis cases of thyroid cancer [1]. The initial manifestation of this case was renal occupancy without clinical symptoms, accompanied by lung and bone lesions, and the initial clinical diagnosis was a renal primary tumor with lung metastasis and bone metastasis [2]. The pathology of this case confirmed that the renal and skeletal metastases originated from thyroid follicular carcinoma, and renal metastases from malignant tumors were rare [10] , renal metastases of DTC origin are even rarer, and the simultaneous occurrence of multiple rare site metastases (brain, liver, kidney, skin) originating from FTC has not been reported before [3]. The patient was male, and 80% of previous cases presenting with thyroid cancer UM were female [4,11]. The case underwent two thyroid surgeries, neither of which showed follicular thyroid cancer tissue on pathology, so the case ended up being a case of metastatic thyroid cancer without a primary site [5]. This case was definitively diagnosed by ^{131}I whole-body tomography finding of localized iodine uptake foci,

except for renal metastases and skeletal metastases, which were pathologically confirmed.

After the occurrence of rare site metastasis in DTC patients, the median survival is 24 months [2], so how to improve the prognosis, delay the progression of the disease and prolong the survival is the focus of future research. This case suggests that [1]: when asymptomatic renal occupations are found, not only the primary renal tumor should be considered [10]. In addition, the possibility of DTC metastasis should also be considered, and a correct clinical diagnosis is necessary to formulate a reasonable treatment plan [2]; The diagnostic method of DTC rare site metastasis is not only biopsy cytology and histology, but also ^{131}I whole-body tomography is also an effective method, which is highly specific, non-invasive, economical, and can be collected from multiple sites at the same time, which is more dominant than simple CT, MR, and so on [3]. The treatment plan for DTC is surgery + ^{131}I + TSH inhibitory therapy, and about 4% of DTC patients have distant metastases as their initial presentation [12], for patients with distant metastases first detected, total thyroidectomy should still be chosen to facilitate subsequent ^{131}I treatment [4]. For renal metastases of DTC origin, depending on the patient's condition, surgical resection may be considered to improve the prognosis [5]. After experiencing ^{131}I treatment, if disease progression occurs and develops into iodine-refractory/progressive thyroid cancer, TKI treatment can be added. After the diagnosis of iodine-refractory/progressive thyroid cancer, TKI-targeted therapy was added in this case, and the current serological Tg and Tg-Ab are stable, and the imaging shows that the brain, lung, and bone foci are in a stable state, with a good quality of survival, and it is still in the follow-up stage.

In conclusion, for this kind of DTC patients with metastatic foci as the initial manifestation and multiple organ metastases at the same time, the treatment plan needs to undergo multidisciplinary consultation, combined with the patient's condition, and adopt the means of comprehensive treatment + local treatment to improve the prognosis, delay the progression of the disease, and improve the patient's quality of life. Due to the rarity of UM in DTC, relatively few studies have been conducted on this type of disease, and more clinical data and in-depth studies are yet to be accumulated.

TEACHING POINT

This case-based teaching underscores the necessity of systematically evaluating thyroid imaging characteristics (e.g., microcalcifications, spiculated margins) and serum thyroglobulin levels in patients with multifocal space-occupying lesions to differentiate rare metastatic differentiated thyroid carcinoma (DTC) from primary malignancies, revealing the critical importance of integrating radiomics-based analysis with endocrine biomarkers to mitigate diagnostic misinterpretations in clinical practice.

QUESTIONS

Questions 1: The best prognosis for thyroid cancer is?

A. medullary thyroid carcinoma.
B. Undifferentiated carcinoma.
C. Papillary adenocarcinoma. (applies)
D. ductal adenocarcinoma.
E. squamous cell carcinoma.

Explanation: The dermal malignant tumors of thyroid follicular epithelium can be divided into differentiated thyroid carcinoma (DTC) and undifferentiated thyroid carcinoma (ATC) according to histological characteristics. DTC includes papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC), and DTC accounts for more than 90% of all thyroid cancers. The prognosis of early DTC patients is good. ATC is highly invasive, has poor treatment response and prognosis .(C pair)The prognosis of early patients with papillary thyroid carcinoma (C pair) and follicular thyroid carcinoma is good. Undifferentiated thyroid carcinoma is highly aggressive (B error) and has poor treatment response and prognosis. Myeloid thyroid cancer is less effective than differentiated thyroid cancer (fault A). Ductal adenocarcinoma (D error) and squamous cell carcinoma (E error) are not common types of thyroid cancer.

Questions 2: Patient is a 47-year-old female. One month after the operation of papillary thyroid carcinoma, thyroid imaging showed residual thyroid tissue in the left lobe of the thyroid, and the rate of ^{131}I was 5%. If treated with ^{131}I after 6 Monthly reexamination, thyroid bed photography ^{131}I rate of 4%, thyroid imaging can see thyroid bed radioactive concentration, should be carried out:

A. Remove with ^{131}1 again. (applies)
B. Resect again.
C. Extra-bed thyroid irradiation.
D. Thyroid hormone suppression.
E. Chemotherapy.

Explanation: The patient has a small residual of papillary thyroid cancer after surgery, and the most reasonable treatment is to use ^{131}I de-methylation. If there is still residue after the first deratization treatment, a second deratization treatment is required.

Questions 3: Which of the following thyroid cancer is most suitable for 131I treatment after surgery?

A. medullary carcinoma.
B. Undifferentiated carcinoma.
C. Squamous epithelial carcinoma.
D. Small cell carcinoma.
E. Differentiated type A carcinoma. (applies)

Explanation: Thyroid tissue and differentiated thyroid cancer (E right, ABCD wrong) cells have the function of uptake ^{131}I, using the ionizing radiation biological effect of ^{131}I emitted beta rays can destroy residual thyroid tissue and cancer cells, so as to achieve the purpose of treatment.

Questions 4: What are the indications of treating thyroid cancer with ^{131}I?

A. Inoperable differentiated thyroid cancer (DTC).(applies)
B. Residual thyroid tissue after A cancer surgery.(applies)
C. Recurrent DTC.(applies)
D. Metastatic cervical lymph nodes and other distant organs. (applies)

Explanation: Since differentiated thyroid cancer cells (DTC, including papillary, follicular) have iodine uptake function, patients with differentiated thyroid cancer who have not been completely resected (A pair) or have metastasized can also be treated with radionuclide ^{131}I. In the treatment of DTC, the first is to remove the residual thyroid tissue (B pair) after surgery, referred to as "clearing a"; Second, the use of ^{131}I to remove unresectable DTC metastases, referred to as "cleaning". 1. For patients with obvious invasion of surrounding tissue (visible during operation), lymph node metastasis or distant metastasis (such as lung, bone, brain and other organs), ^{131}I "clear a" treatment should be performed (D pairs). 2. For patients with small tumors (≤1cm) without obvious invasion of surrounding tissues, lymph node metastasis and other invasive features, '^{131}I' nail clearing therapy can be performed for convenience of follow-up. 3. For iodine-taking DTC metastatic or recurrent lesions (C pairs), ^{131}I 'clear focus' treatment can be selectively applied.

Questions 5: Which is the common method of finding metastatic metastases of differentiated thyroid cancer?
A. ^{131}I whole-body imaging.(applies)
B. ^{99m}Tc-MIBI display.
C. ^{123}I whole body iodocholesterol imaging.
D. 99mTC-MDP whole body imaging.
E. ^{131}I-MIBG whole-body imaging.

Explanation: Cancer cells of differentiated thyroid cancers, such as papillary and follicular cancers, often express sodium-iodine isotransporters (NIS), preserving the ability of normal thyroid cells to take up iodine. Although uptake efficiency may be lower than in normal tissue, iodine uptake capacity of metastases is significantly enhanced under thyrotropin (TSH) stimulation, such as post-operative hypothyroidism or exogenous TSH stimulation, providing a physiological basis for imaging. The gamma rays emitted by ^{131}I can be detected by a full-body scan, which covers a wide range and can detect hidden metastases (e.g. lymph nodes in the neck, lungs, bones, etc.). It is especially suitable for patients after total thyroidectomy, when the serum thyroglobulin (Tg) level is elevated but other imaging tests (such as ultrasound, CT/MRI) are negative, ^{131}I imaging can provide an important supplement.(A pairs)

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FIGURES

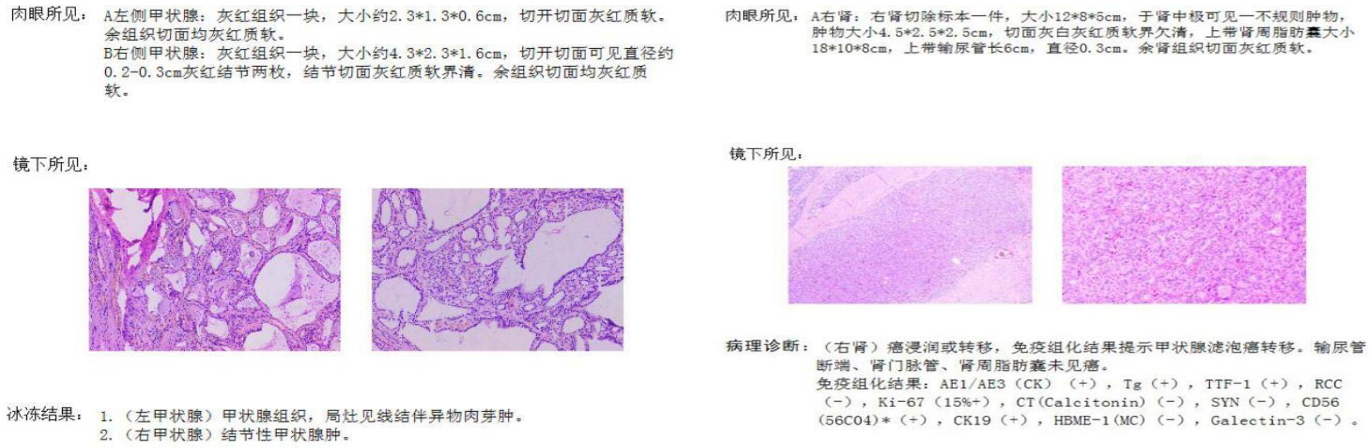
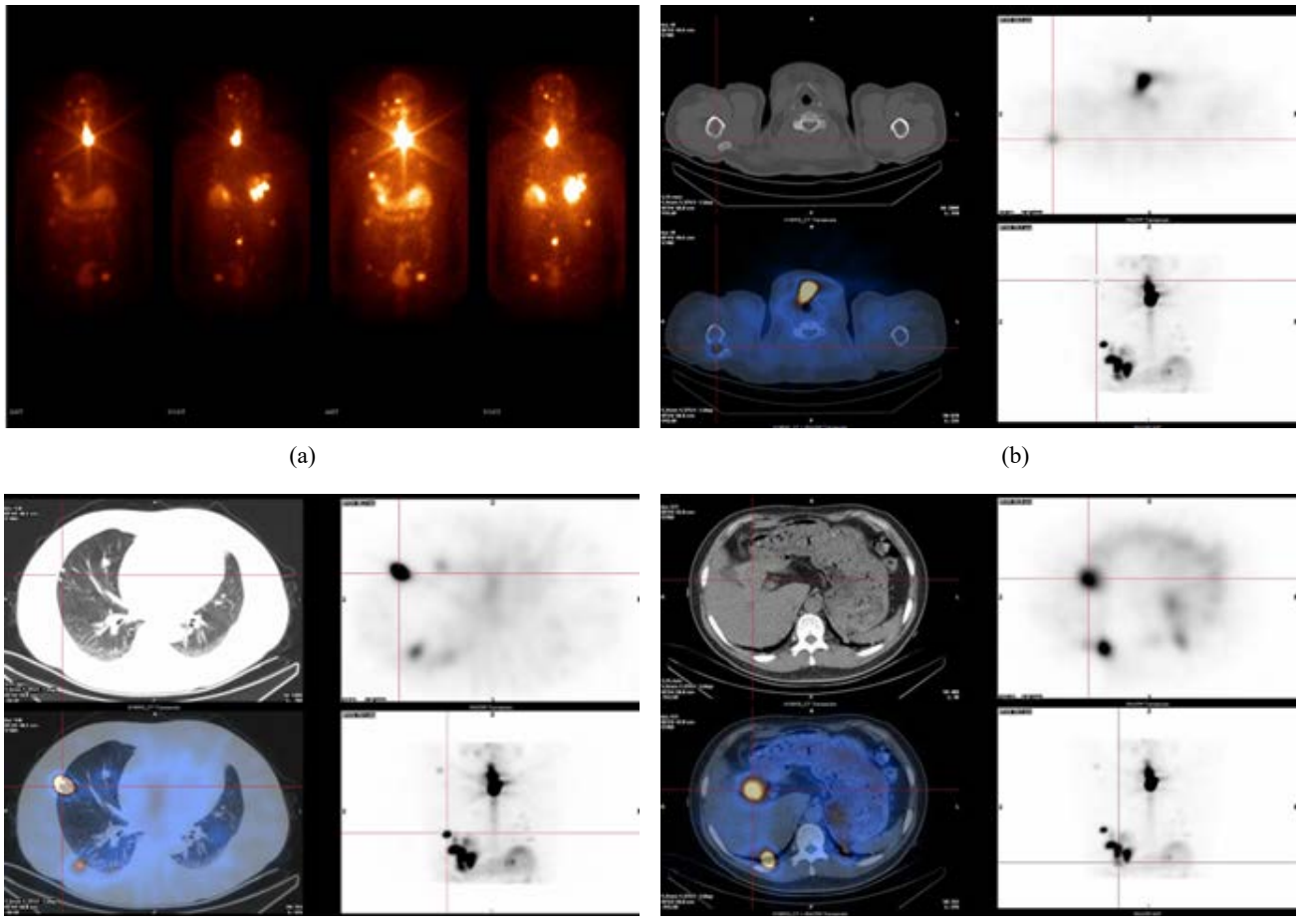


Figure 1: (a) Postoperative pathology; (b) Immunohistochemistry



(a) (b)

(c) (d)

Figure 2: Administration of therapeutic dose ^{131}I 48h imaging: multiple foci of abnormal iodine uptake in the right shoulder joint, both lungs and abdomen.

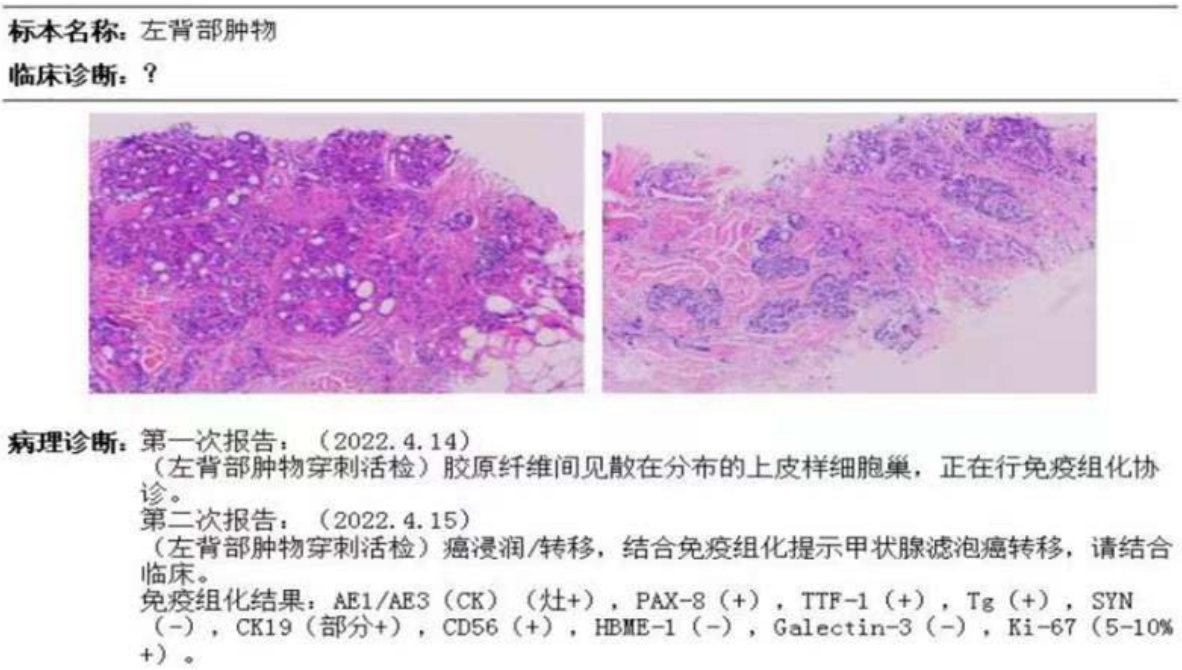


Figure 3: Pathological findings of the tumor on the left dorsal aspect.

KEYWORDS

Thyroid cancer; Differentiated thyroid cancer; Renal metastasis; Hepatic metastasis; Brain metastasis; Skin metastasis