Clinical Case Report

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Papillary thyroid carcinoma with hyperthyroidism and multiple metastases

A case report

Li-li Zhang, MS[a], Bin Liu, MD[b], Fang-fang Sun, MS[a], Hong-yu Li, MD[a], Shuang Li, MS[a], Li-rong Zhao, MD[a,*]

Abstract

Rationale: Papillary thyroid carcinoma (PTC) is the most common type of primary thyroid cancer with a low incidence of distant metastases. PTC represents more than 70% to –90% of thyroid malignancies. Distant metastases have only been observed in only 1% to 15% of patients with PTC. In this article, we reported the case of a patient with PTC and hyperthyroidism as well as simultaneous multiple metastases.

Patient concerns: A 47-year-old man was admitted to our hospital on February 22, 2019, with several neck masses that had been present for 12 months, low back pain for 9 months, and lower limb paraplegia for 3 months.

Diagnoses: According to the patient physical examination, adjuvant examination (e.g., ultrasound, computed tomography, magnetic resonance imaging, blood test, and biopsy) and medical history, the clinical diagnosis was as follows: thyroid papillary carcinoma; cervical lymph node metastasis; multisite bone metastasis (6th and 7th cervical vertebrae, left clavicle proximal, right scapula bone, thoracic vertebrae, lumbar vertebrae, sacral vertebrae, bilateral ilium, and left pubic bone); muscular metastasis (the right medial femoral muscle, the vastus lateralis muscle, left thigh muscle, and the flexor superficialis of the left forearm); possible mediastinal lymph node metastasis; and paraplegia due to the soft-tissue metastasis around the 9th thoracic vertebral spine; and hyperthyroidism (free thyroxine: 36.59 pmol/L, free triiodothyronine: 9.58 pmol/L, thyroid-stimulating hormone: 0.005 μIU/mL, thyroid autoantibody: 2.53 IU/L).

Interventions and outcomes: The patient refused to undergo further intervention or follow-up.

Lessons: In summary, this is the 1st case of in which a patient with PTC and hyperthyroidism, as well as simultaneous multiple skeletal muscles and bone metastases, lymph node metastasis, and paraplegia was observed. In practice, in cases where patients have PTC and hyperthyroidism, practitioners should perform further examinations to rule out the presence of distant metastases. We believe that the use of ultrasound has a unique advantage in the diagnosis of PTC and skeletal muscle metastasis.

Abbreviations: CT = computed tomography, ^{18}F FDG PET-CT = 18-fluorodeoxyglucose PET-CT, FTC = follicular thyroid carcinoma, MRI = magnetic resonance imaging, PET-CT = positron emission tomography-computed tomography, PTC = papillary thyroid carcinoma, T1WI = T1-weighted images, T2WI = T2-weighted images, TRAb = thyroid autoantibody, TSH = thyroid-stimulating hormone.

Keywords: hyperthyroidism, metastases, papillary thyroid carcinoma, skeletal muscles, thyroid cancer

Editor: Maya Saranathan.

LZ and BL contributed equally to the work.

This study was approved by the ethics committee of The First Hospital of Jilin University. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

All data published here are under the consent for publication. Written informed consent was obtained from all individual participants included in the study.

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

[a] Department of Ultrasound, [b] Department of Hand Surgery, The First Hospital of Jilin University, Changchun, China.

[*] Correspondence: Li-rong Zhao, Department of Ultrasound, The First Hospital of Jilin University, No 3302, Jilin Road, Changchun 130021, China (e-mail: 41507209@qq.com).

How to cite this article: Zhang LI, Liu B, Sun Ff, Li Hy, Li S, Zhao Lr. Papillary thyroid carcinoma with hyperthyroidism and multiple metastases: a case report. Medicine 2020;99:30(e21346).

Received: 4 December 2019 / Received in final form: 28 May 2020 / Accepted: 18 June 2020

http://dx.doi.org/10.1097/MD.0000000000021346

1. Introduction

Papillary thyroid carcinoma (PTC) is the most common type of primary thyroid cancer. This form of carcinoma represents more than 70% to 90% of thyroid malignancies.[1] PTC is a slowly progressive cancer with high survival rate.[2,3] Distant metastases have only been observed in only 1% to 15% of patients with PTC. Metastases are most observed in the lungs, followed by the bones.[4,5] Muscular and soft-tissue metastases of PTC are very rare.

In this article, we reported the case of a patient with PTC and hyperthyroidism as well as simultaneous multiple skeletal muscles and bone metastases, lymph node metastasis, and paraplegia. We also present a literature review, aiming to provide further evidence regarding the diagnosis, intervention, and prognosis of PTC with distant metastasis.

2. Case report

2.1. Patient information

A 47-year-old man was admitted to the First Hospital of Jilin University on February 22, 2019, with several neck masses that had been present for 12 months. The patient had also experienced low back pain for 9 months and lower limb paraplegia for 3 months. The patient had no family history of thyroid disease or any history of exposure to external or accidental radiation.

2.2. Clinical findings

Physical examination of the patient revealed the presence of multiple masses in the area of the right supraclavicular fossa and the right neck. The largest lump, of approximately 2×2 cm, was hard, mobile, and painless. Three additional lumps were identified in the left forearm, the anterior side of the right thigh, and the lateral side of the right thigh. These lumps were 3×2 cm, 3×2 cm, and 2×2 cm, respectively. All 3 lumps were hard, solid, solitary, and tender. No sensation or pain was observed below the line of the anterior superior iliac spine, and the lower extremities were paraplegic.

Blood tests for thyroid function revealed that the free thyroxine level was 36.59 pmol/L (reference value 11.50–22.70 pmol/L), the free triiodothyronine level was 9.58 pmol/L (reference value 3.50–6.50 pmol/L), the thyroid-stimulating hormone (TSH) level was 0.005 μIU/mL (reference value 0.550–4.780 μIU/mL), and the thyroid autoantibody (TRAb) level was 2.53 IU/L (reference value 0.30–1.22 IU/L). No abnormalities were observed in the expression of tumor markers.

Ultrasound examination of the thyroid and neck revealed a 4.2×2.6 cm hypoechoic nodule with blurred borders, an irregular shape, and uneven and visible internal scattered punctate hyperechoic signs on the right lobe of the thyroid gland (Fig. 1A). A rich blood flow signal was detected by Doppler ultrasound. Another similar nodule, 1.5×0.9 cm in size, was observed in the thyroid isthmus. Multiple malformed lymph nodes (levels III and IV) were observed in the right neck, in which the structure of the hilum was unclear. There were solid hyperechoic and cystic areas in the lymph nodes and multiple punctate hyperechoic signs in the solid components of the nodules. The size of the larger lymph node was 2.9×2.3 cm (Fig. 1B). Ultrasound examination of the right thigh revealed a 2.4×2.1 cm substantial hypoechoic mass in the middle of the medial femoral muscle with a blurred boundary, irregular shape, uneven internal echo, and multiple punctate hyperechoic signs

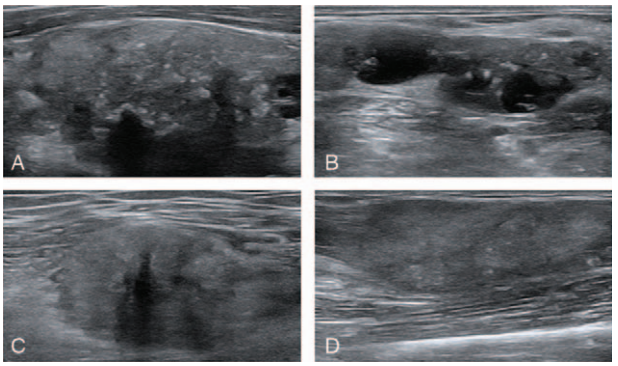

Figure 1. Ultrasound images. (A) A hypoechoic nodule with blurred borders can be seen on the upper right thyroid gland, and punctate calcification can be seen inside. (B) The right cervical lymph node has lost its hilum structure. There are solid hyperechoic and cystic areas in the lymph nodes. (C) A hypoechoic nodule can be seen in the middle part of the right thigh femoris, where punctate calcification is present. (D) A hypoechoic nodule can be seen in the middle part of the superficial flexor of the left forearm.

(Fig. 1C). A rich blood flow signal was detected by Doppler ultrasound. Two additional lumps of the same nature were observed in the middle of the vastus lateralis muscle and the flexor superficialis of the left forearm, with sizes of 3.1×1.6 cm and 4.0×1.5 cm, respectively (Fig. 1D). The ultrasound findings were as follows: hypoechoic thyroid nodules with calcification, considered to indicate thyroid cancer; cervical lymphadenopathy with calcification, considered to indicate lymph node metastasis; right thigh and left forearm muscle tissue lump with calcification without excluding to thyroid cancer metastasis.

Computed tomography (CT) scan results revealed multiple points of bone destruction in the 6th and 7th cervical vertebrae, left clavicle proximal, right scapula bone, thoracic vertebrae, lumbar vertebrae, sacral vertebrae, bilateral ilium, and left pubic bone (Fig. 2). The 9th thoracic vertebrae had obvious bone destruction, the spinal canal was destroyed, and the imaging of the spinal cord revealed a blurred structure. Pulmonary CT revealed a slight inflammation of the left lower lobe and enlarged mediastinal lymph nodes. The CT findings were as follows: multiple site bone destruction, not excluding metastatic cancer, and mediastinal lymphadenopathy, not excluding metastatic cancer.

Magnetic resonance imaging (MRI) revealed a 3.6×1.5 cm elliptical abnormal signal in the soft tissue of the left forearm ulnar with equal signal intensity on T1-weighted images (T1WI) and slightly high and low mixed signals on T2-weighted images (T2WI; Fig. 3A). Two other nodular abnormal signals were observed in the right thigh muscle group in the lower middle horizontal part and outer part separately with equal and slightly lower signals on T1WI and equal signals on fat-suppression images. A number of small mass signals were observed in the left thigh muscle group, with equal signal on the T1 image (Fig. 3B). Thoracic MRI with enhanced scanning revealed multiple thoracic vertebral bodies with multiple patchy abnormal signals, and an enhanced scan revealed mild uneven enhancement. The body of 9th Thoracic Vertebra was wedge shaped with a high patchy fat-suppression signal in the spinal cord. In some of the soft tissues around the thoracic vertebral body, strip-like abnormal signals were observed with low signal on T1WI, and high and low mixed signals on T2WI; enhanced scanning revealed mild uneven enhancement (Fig. 3C and D). The MRI findings were as follows: a muscle mass occupying lesion was observed in the left forearm

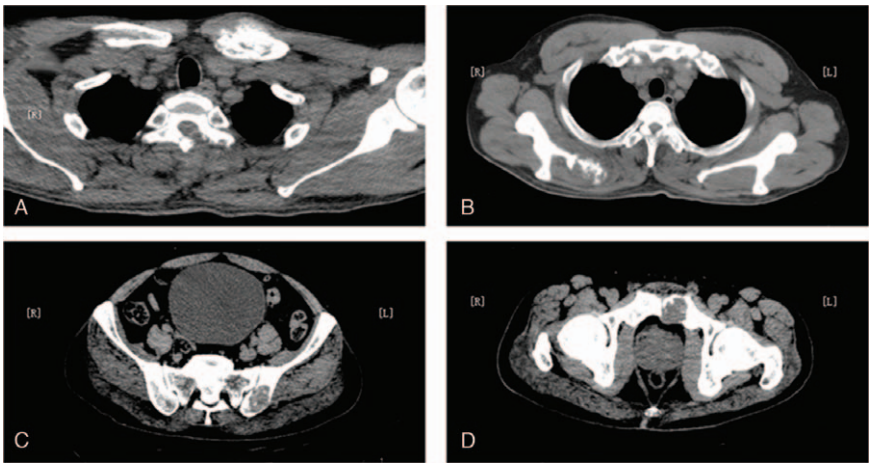

Figure 2. Computed tomography images of multisite bone destruction. (A) Left clavicle bone destruction; (B) right scapula bone destruction; (C) left iliac bone destruction; (D) left pubic bone destruction.

and bilateral thigh; there was horizontal spinal cord compression at the 9th thoracic vertebral body and edema due to the soft-tissue metastasis around the spine, and the 9th thoracic vertebral compression fracture.

The patient underwent an ultrasound-guided biopsy of the thyroid nodules, right cervical lymph nodes, and right thigh mass under local anesthesia on February 26, 2019. The postoperative pathologic report revealed: pleomorphism of the follicular epithelium, partial papillary hyperplasia, and glassy nuclei presence in the thyroid nodule sample with a diagnosis of thyroid papillary carcinoma (Fig. 4A and B); the biopsy tissue in the right cervical lymph node was consistent with thyroid papillary carcinoma metastasis with immunohistochemical results of cytokeratin 19 (CK19) (+), cytokeratin 7 (CK7) (+), thyroglobulin (TG) (weak +), TTF-1(+), cytokeratin 20 (CK20)

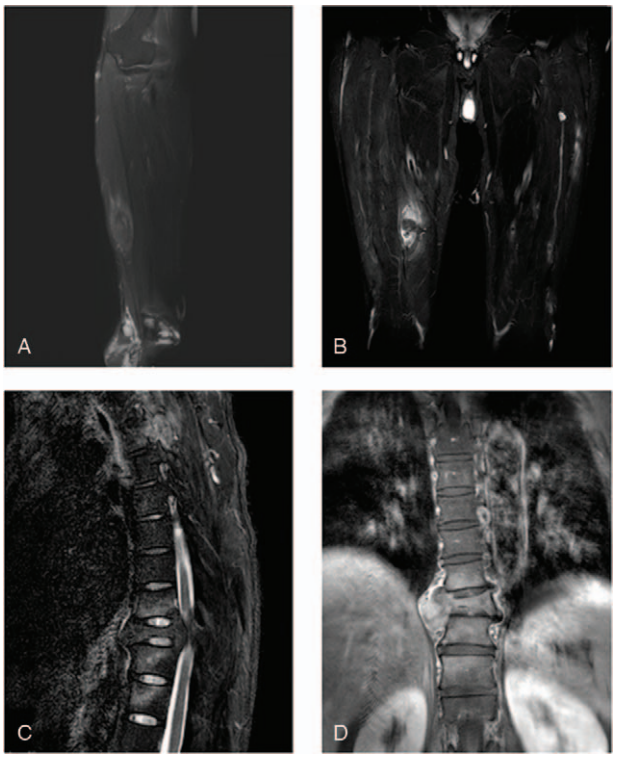

Figure 3. Magnetic resonance images. (A) A lump can be seen on the ulnar side of the left forearm muscle with a slightly higher signal in the T2-fat-suppression images. (B) A lump can be seen in the middle part of the right thigh with an equal signal in fat-suppression images, and a high signal in the peripheral muscle tissue. (C) The body of the 9th thoracic vertebrae is flattened and wedge shaped. There is a high patchy fat-suppression signal in the spinal cord. (D) A strip-like abnormal signal and mild uneven enhancement in the soft tissue around the 9th thoracic vertebrae can be observed in an enhanced scan.

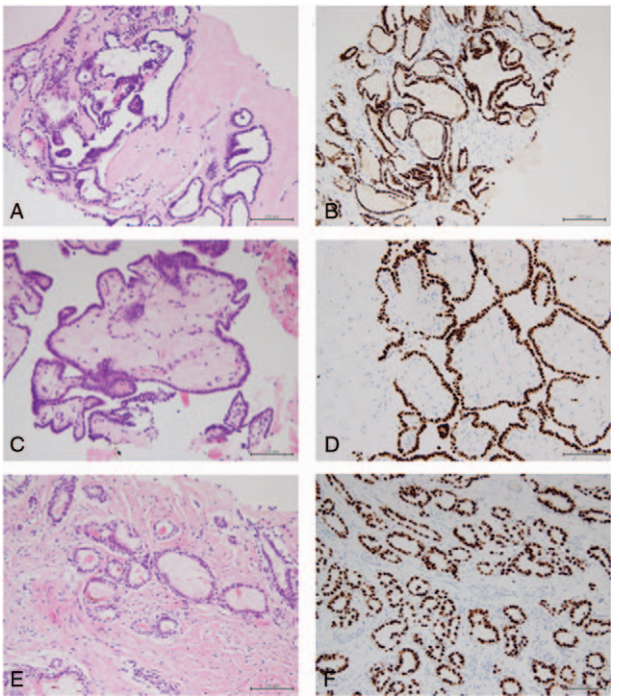

Figure 4. Pathologic slide (hematoxylin and eosin staining) images. (A, B) Thyroid follicular epithelium cells can be seen with atypical, partial papillary hyperplasia, immunohistochemistry TTF-1(+) (×200). (C, D) Papillary carcinoma metastasis can be seen in lymph nodes, immunohistochemistry TTF-1(+) (×200). (E, F) Papillary carcinoma metastasis can be seen in the right thigh lump, immunohistochemistry TTF-1(+) (×200).

(−), napsin A (−), and villin (−) (Fig. 4C and D); the biopsy tissue in the right thigh mass was consistent with thyroid papillary carcinoma metastasis with immunohistochemical results of CK19(+), CK7(+), TG(+), TTF-1(+), CK20(−), napsin A(−), and villin(−) (Fig. 4E and F). The patient refused to undergo further examination, such as positron emission tomography-CT (PET-CT), to determine whether additional lymph node or distant metastases were present.

2.3. Diagnostic assessment

According to the physical examination, adjuvant examination, and medical history of the patient, the clinical diagnosis was as follows: thyroid papillary carcinoma; cervical lymph node metastasis; multisite bone metastasis (6th and 7th cervical vertebrae, left clavicle proximal, right scapula bone, thoracic vertebrae, lumbar vertebrae, sacral vertebrae, bilateral ilium, and left pubic bone); muscular metastasis (the right medial femoral muscle, the vastus lateralis muscle and the flexor superficialis of the left forearm); possible mediastinal lymph node metastasis; and paraplegia due to soft-tissue metastasis around the 9th thoracic vertebral spine; hyperthyroidism.

2.4. Treatment and follow-up

The patient refused to undergo further intervention and asked to be discharged from the hospital on March 20, 2019. He did not consent to take part in any follow-up observations.

3. Discussion

The PTC is mainly transferred to the local lymph nodes through lymphatic drainage, and distant metastasis is very rare. However, in addition to the observation of metastasis in the lung and bone, there have been reports of metastasis in very rare sites such as the skeletal muscle (see details in Table 1), brain,[33] breasts,[34] parotid gland,[35] liver,[36] adrenal gland,[37] kidney,[37] ovary,[38] and the nasal cavity.[39] The presence of distant metastasis indicates a poor prognosis. In such cases, the 10-year survival rate is only around 50%.[40]

Cervical lymph nodes are the most prone to metastasis in PTC, and 23% to 56% of patients with PTC have clinically significant lymph node metastasis; while in cervical lymph node prophylactic dissection, in up to 90% of cases the histologic results reveal lymph nodes metastasis.[41] Lymph node metastasis is also a risk factor for high recurrence of the disease.[42,43] In the present case, right cervical lymph node metastasis was observed.

The incidence of bone metastasis in PTC has been reported to be around 6.9%.[44] The size of PTC nodules is closely related to the occurrence of bone metastasis, and the risk of bone metastasis for nodules larger than 4 cm is 1.54 times that for nodules smaller than 1 cm.[45] The spine is the most vulnerable site of PTC bone metastasis, and 28% of patients with spinal metastasis will 1st show pain at the corresponding metastatic site.[46,47] In the present case, the patient developed back pain 9 months before admission to hospital. Spinal metastasis often leads to neuronal motor paralysis of the lower extremities, various sensory impairments, defecation

Table 1

Reported muscle metastases from PTC previously in the literature.

Author	Publication date	Patient's age	Patient's gender	Subtype	Nodular size, cm	Muscle metastases
Baloch et al[6]	2000	43	F	Follicular variant	1.1	The left psoas muscle
Karwowski et al[7]	2002	59	F	NA	2.1 × 1.9 × 1.8	The sternocleidomastoid muscle
Colella et al[8]	2003	50	F	NA	NA	The pterygoid muscle
Pucci et al[9]	2006	77	M	Follicular variant	3.5	The right bycipites muscle
Tamiolakis et al[10]	2006	45	F	NA	2.5 × 1.5 × 2	Sternocleidomastoid muscle
Panoussopoulos et al[11]	2007	69	F	Tall cell type	4.5	The trapezoid muscle
Kim et al[12]	2008	25	F	NA	3.1	The sternocleidomastoid muscle, the strap muscle
Luo et al[13]	2008	29	M	NA	NA	The erector spinae muscle
Qiu et al[14]	2009	82	F	NA	NA	The erector spinae muscle
Qiu et al[14]	2009	63	M	Follicular variant	NA	The left lower erector muscle
Bruglia et al[15]	2009	44	M	NA	1.1	The thigh muscle
Zhao et al[16]	2010	53	M	NA	NA	The left rectus abdominis muscle
Krajewska et al[17]	2010	55	M	NA	NA	The pterygoid muscle
Caobelli et al[18]	2011	68	F	NA	NA	The adductor longus, iliopsoas muscles
Bae et al[19]	2011	31	F	NA	1.5 × 0.9	The vastus medialis muscle
Li et al[20]	2012	39	F	Columnar cell type	2.9 × 2.0	The sternocleidomastoid muscle
Mohapatra et al[21]	2012	42	M	NA	NA	The luteus and paraspinal muscle
Morita et al[22]	2012	74	M	NA	NA	The muscles around the infratemporal fossa
Ceriani et al[23]	2013	50	F	NA	NA	The trapeziusan and subscapularis muscles
Califano et al[24]	2013	26	M	NA	NA	The cervical muscles
Califano et al[24]	2013	64	F	Follicular variant	NA	The gluteal muscle
Yun et al[25]	2014	43	M	NA	NA	The gluteus muscle
Yang et al[26]	2015	31	M	NA	3.0	The gastrocnemius muscle
Portela et al[27]	2015	44	F	NA	NA	The sternocleidomastoid muscle, the strap muscle
Cassidy et al[28]	2015	89	F	NA	NA	The latissimus dorsi
Sarma et al[29]	2015	66	M	Micro PTC	0.1 × 0.1	The deltoid muscle
Li et al[30]	2016	84	M	NA	2 × 3.3 × 4	The not specified
Kuscic et al[31]	2016	68	M	Follicular variant	NA	The thigh
Virmani and Dabholkar[32]	2017	45	F	NA	NA	The sternocleidomastoid muscle

NA = not available, PTC = papillary thyroid carcinoma.

disorders, and nerve root pain at the corresponding metastatic site due to compression of the spinal cord.[48] In this case, the mass transfer in the para-thoracic soft tissue of the 9th thoracic vertebra invaded the spinal canal and compressed the spinal cord, which likely resulted in the symptoms of lower back pain, paraplegia of both lower limbs, sensory disorder, and defecation disorders.

Skeletal muscle metastasis of PTC is very rare. Herbowski reviewed the literature and calculated the incidence of skeletal muscle metastases in PTC and follicular thyroid carcinoma (FTC) to be around 4/10.[36,49] There is a hypothesis that skeletal muscle can tolerate lactic acid produced by tumor cells, thereby inhibiting the neovascularization of tumors; in addition, the pH environment in skeletal muscle and the movement of skeletal muscle can inhibit the proliferation of tumor cells.[50] We reviewed the literature from 1999 to 2018 and found that only 29 cases of PTC skeletal muscle metastases were diagnosed, affecting 18 parts of the skeletal muscle (Table 1). Among these 29 cases, we found the most common site of metastases was the sternocleidomastoid muscle (6 cases in total), which included 4 cases of needle biopsy or implant transfer after laparoscopic treatment, and the 2nd common metastatic site was the thigh and buttock muscle (3 cases in total). For the pathologic category, only 5 cases were reported as being of follicular subtypes, and 2 cases were reported as columnar epithelial subtypes. The maximum diameter of PTC nodules with skeletal muscle metastases ranged from 1.1 to 4.5 cm. In the present case, the patient had multisite muscle metastases, including the forearm and thigh muscles. This is the first report of such a case. Another interesting case of skeletal muscle metastasis of PTC was reported by Sarma et al[29] in which the patient had both FTC ($3.3 \times 2.5 \times 2$ cm) and micro PTC (0.1×0.1 cm). The left deltoid muscle metastasis from micro PTC was found 6 months after total thyroidectomy. It was believed that the FTC was more likely to be the cause of the distant metastasis.[9,29] However, in the case reported by Sarma and colleagues, the metastatic carcinoma of the skeletal muscle came from a small positive micro PTC.[29]

In the present case, the blood test results (free thyroxine: 36.59 pmol/L, free triiodothyronine: 9.58 pmol/L, TSH: 0.005 μIU/mL, and TRAb: 2.53 IU/L) indicated that the patient had hyperthyroidism with no systemic treatment. This may have been a factor in the development of multiple bones and skeletal muscle metastases in this patient, as the high blood flow state that occurs during hyperthyroidism may have promoted the spread of tumor cells, making thyroid cancer more prone to distant metastasis. This hypothesis is consistent with the idea of Ito et al.[43]

Doppler ultrasound is the 1st choice for the examination of the thyroid and soft-tissue masses due to its economic and convenient advantages. Although the transfer of PTC to skeletal muscle is very rare, it is necessary to consider the possibility of PTC metastasis when encountering a substantial mass of microcalcification in the skeletal muscle. For the overall assessment of PTC distant metastasis, 18-fluorodeoxyglucose PET-CT (^{18}F FDG PET-CT) imaging can accurately assess the disease by detecting the local lymph node involvement and distant metastasis.[24] Unfortunately, in this case, the patient refused to undergo PET-CT examination.

In summary, this is the 1st case in which a patient with PTC and hyperthyroidism was shown to have simultaneous multiple skeletal muscle and bone metastases, lymph node metastasis, and paraplegia. The point of interest in the present case is that the high blood flow state of hyperthyroidism may be one of the factors that contributed to the occurrence of multiple distant metastases.

Therefore, in practice, for patients with PTC and hyperthyroidism, practitioners should perform further examinations to rule out the presence of distant metastases. We believe that the use of ultrasound has a unique advantage in the diagnosis of PTC with skeletal muscle metastasis.

Author contributions

Lili Zhang, Bin Liu, and Lirong Zhao designed the study, conducted all searches, appraised all potential studies and wrote and revised the draft manuscript and subsequent manuscripts. Fangfang Sun and Hongyu Li revised the draft manuscript and subsequent manuscripts. Shuang Li assisted with the presentation of findings and assisted with drafting and revising the manuscript. All authors read and approved the final manuscript.

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