



Metastasis to lymph nodes at the contralateral entrance point to the recurrent laryngeal nerve in unilateral thyroid papillary carcinoma: a case report and literature review

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Background: Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer. PTC is slow growing, and prognosis after surgery is excellent. However, PTC is associated with a high incidence of cervical lymph node metastasis, and usually metastasizes from the central lymph nodes to the ipsilateral cervical and mediastinal lymph nodes. Anatomic studies have shown that the thyroid gland and surrounding tissue have an abundant lymphatic network that facilitates tumor dissemination and lymph node metastasis, there may be many ways to connect lymph nodes on both sides of the neck of patients, which needs further research and discussion.

Case Description: We report the case of a 45-year-old female who was diagnosed with thyroid cancer of the right lobe and right lateral lymph node metastasis by fine-needle aspiration (FNA). During surgery, 0.2 mL of carbon nanoparticle (CN) suspension was injected into the right lobe of the thyroid gland, which resulted in black staining of a lymph node at the contralateral entrance point to the recurrent laryngeal nerve (LN-epRLN). The black-stained lymph node was resected, and the pathology results revealed lymph node metastasis from thyroid cancer. The left lobe of the thyroid was benign.

Conclusions: Retro-tracheal periesophageal lymph node metastasis may be a rare metastatic pathway in thyroid cancer.

Keywords: Thyroid papillary carcinoma; entrance point to recurrent laryngeal nerve; nano-charcoal; lymph node metastasis; case report

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Introduction

Globally, thyroid cancer is the most common endocrine cancer, and accounts for approximately 2.1% of all newly diagnosed cancers (1). In the United States, the incidence of thyroid cancer has been increasing by an estimated 6% per year (2). In 2020, the American Cancer Society reported that thyroid cancer was the fifth leading cause of cancer in women in the United States, accounting for 4% of all newly diagnosed cancers (3).

Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer. PTC is slow growing, and prognosis after surgery is excellent; however, PTC is associated with a

high incidence of cervical lymph node metastasis, especially central lymph node metastasis (4). The thyroid gland and surrounding tissue have an abundant lymphatic network that facilitates tumor dissemination and lymph node metastasis (5). The central lymph node is the most common site of lymphatic metastasis (5). The main methods for the diagnosis of thyroid cancer and cervical lymph nodes metastasis are ultrasound and fine-needle aspiration (FNA) biopsy, in China, guidelines for the management of patients with thyroid nodules and differentiated thyroid cancer (6) recommend ipsilateral central lymph node dissection while effectively preserving the parathyroid and the recurrent laryngeal nerve.

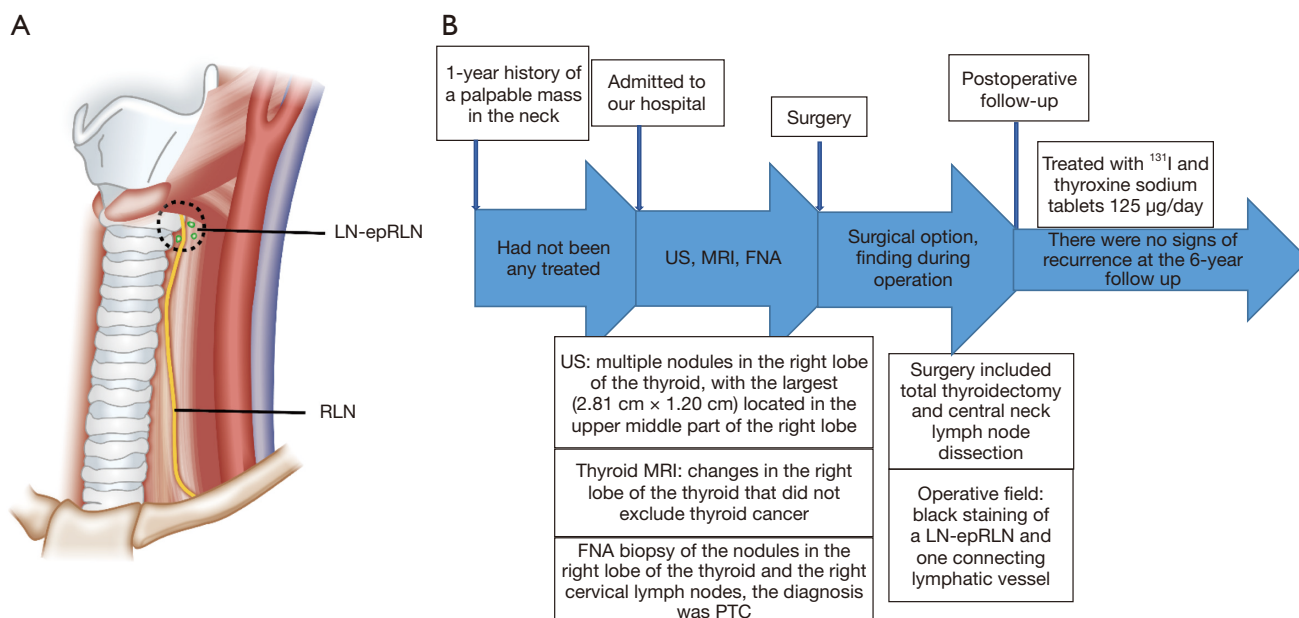


Figure 1 The schematic diagrams of LNs-epRLN and patient's treatment timeline. (A) LNs-epRLN; (B) timeline of this patient. LNs-epRLN, lymph nodes at the entrance point to the recurrent laryngeal nerve; RLN, recurrent laryngeal nerve; US, ultrasound; MRI, magnetic resonance imaging; FNA, fine-needle aspiration; PTC, papillary thyroid carcinoma.

The recurrent laryngeal nerve usually enters the larynx approximately 0.8 cm below the inferior horn of the thyroid cartilage (7). Our clinical experience revealed that the entry point of the recurrent laryngeal nerve is close to the thyroid gland; thus, the recurrent laryngeal nerve is prone to injury during thyroid surgery. Lv *et al.* identified lymph adipose tissue within 5 mm of the outer edge of the central lymph node to the recurrent laryngeal nerve entrance point as the lymph nodes at the entrance point to the recurrent laryngeal nerve (LNs-epRLN) (8) (*Figure 1*). Anatomically, the LNs-epRLN are central lymph nodes located in the tracheoesophageal groove, and thus may be overlooked during dissection. Lv *et al.* showed that the LNs-epRLN are significant in metastasis and recurrence in PTC, and LN-epRLN metastasis was found in 3.76% (33/878) of PTC patients. In this article, we report a rare case of metastasis to the contralateral LN-epRLN in a patient with unilateral thyroid carcinoma.

We present the following article in accordance with the CARE reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/gs-22-46/rc>).

Case presentation

A 45-year-old female was admitted to our hospital with

a 1-year history of a palpable mass in the neck that had not been treated. She had no family history of thyroid carcinoma. A cervical ultrasound showed multiple nodules in the right lobe of the thyroid, the largest (2.81 cm \times 1.20 cm) of which was located in the upper middle part of the right lobe, and multiple enlarged hypoechoic lymph nodes with an unclear boundary between the cortex and medulla under the inferior pole of the right lobe. Thyroid magnetic resonance imaging showed changes in the right lobe of the thyroid that did not exclude thyroid cancer, and the potential for metastasis to the right lateral lymph node in the bilateral submandibular region (*Figure 2*). Following a FNA biopsy of the nodules in the right lobe of the thyroid and the right cervical lymph nodes, the patient was diagnosed with PTC.

The surgery included a total thyroidectomy and central neck lymph node dissection. 0.2 mL of carbon nanoparticle (CN) suspension was injected into the right lobe of the thyroid. A nerve integrity monitor was used to monitor the electromyography signals of the recurrent laryngeal nerve and vagus nerve. Intraoperative observations showed 3 nodules in the right lobe of the thyroid. Among them, a node in the upper middle part of the right lobe was dorsal to the middle part of the lobe near the recurrent laryngeal nerve entrance point. After the left lobe of the thyroid was

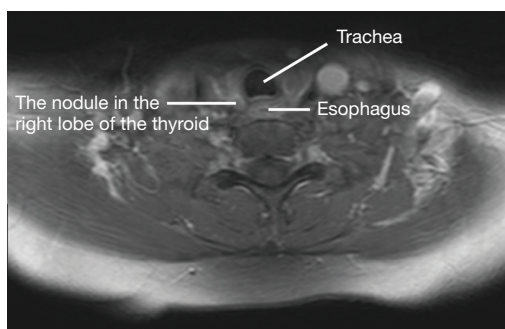


Figure 2 Thyroid magnetic resonance imaging showed changes in the right lobe of the thyroid and thus thyroid cancer could not be excluded.

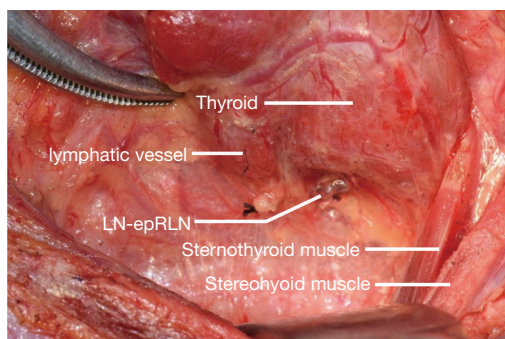


Figure 3 CN suspension was injected into the right lobe of the thyroid, and revealed black staining of a LN-epRLN, and 1 connecting lymphatic vessel on the left. CN, carbon nanoparticle; LN-epRLN, lymph node at the entrance point to the recurrent laryngeal nerve.

removed, the middle thyroid vein was severed and raised inward and upward, which exposed the black staining of a LN-epRLN and 1 connecting lymphatic vessel (*Figure 3*). The black-stained lymph node was resected, and the pathology results revealed lymph node metastasis from thyroid cancer. Subsequently, the left central lymph nodes and the right lateral lymph nodes were resected.

Postoperatively, the patient experienced no hoarseness or numbness of the extremities. The nodules in the right lobe of the thyroid were diagnosed as PTC by paraffin pathology. The nodules in the upper middle part of the right lobe had invaded the thyroid capsule. The left lobe of the thyroid was not affected. Metastasis from thyroid cancer occurred in the bilateral central lymph nodes and the right lateral lymph node. After surgery, the patient was treated with I^{131} and levothyroxine sodium tablets (125 $\mu\text{g}/\text{day}$).

No adverse or unexpected events were observed during treatment. Her prognosis was good, and there were no signs of recurrence at the 6-year follow up appointment. A timeline is shown in *Figure 1*.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

In PTC, the persistence, progression, and recurrence of cancer are usually localized to the cervical lymph nodes (9). Notably, PTC metastasizes from the central lymph nodes to the ipsilateral cervical and mediastinal lymph nodes (10). Anatomic studies have shown that lymphatic drainage around the thyroid gland is extensive, and extends to 20–30% of the lymph nodes in the body located on either side of the neck (10,11). The lymphatic drainage pathways are accompanied by blood vessels that supply the thyroid gland. Specifically, the lymphatic drainage of the upper pole of the thyroid proceeds along the superior thyroid artery, the lymphatic drainage of the lower thyroid proceeds along the inferior thyroid artery, and the lymphatic pathways drain from the central neck directly to several levels of the lateral neck (11).

FNA has been widely utilized as the sensitive and specific tool in the diagnosis of thyroid cancer and cervical lymph nodes metastasis (12). Intraoperative lymph node evaluation also plays an important role in the surgical management of patients with PTC. In 2007, the Chinese Food and Drug Administration approved the application of CN suspension for lymph node imaging. Since then, CNs have been used as a safe and efficacious lymphatic tracer in gastric cancer, colorectal cancer, breast cancer, and thyroid cancer (13–16). CN suspension is an activated carbon product processed by nanotechnology. CNs have a uniform diameter of 21 nm, and the suspending agents form a stable suspension of carbon pellets that are 150 nm in diameter. These pellets can pass through the 100–500 nm gap in the lymphatic capillary endothelial junction, but cannot pass through the endothelium of capillaries that have a gap size of 30–50 nm. After being injected into the submucosal layer around a tumor, the CNs enter the lymphatic vessels and

Table 1 Comparison of resected and metastatic lymph nodes with and without injection of CN suspension

Author	Year	Metastatic lymph nodes, n/N (%)		Average number of lymph nodes per patient, mean \pm SD	
		With CN	Without CN	With CN	Without CN
Wang (18)	2015	38/193 (19.7)	19/123 (15.4)	6.89 \pm 4.15	4.56 \pm 1.58
Wang (19)	2016	135/640 (31.2)	178/769 (23.1)	7.11 \pm 5.40	5.45 \pm 3.53
Xu (20)	2017	81/342 (23.7)	27/261 (10.3)	6.00 \pm 0.98	4.58 \pm 0.60
Zhao (21)	2017	43/131 (32.8)	56/234 (23.9)	–	–
Liu (22)	2018	57/211 (27.01)	35/166 (21.08)	4.7 \pm 3.0	3.5 \pm 2.3
Wang (23)	2018	308/770 (40.9)	342/982 (34.8)	11.2 \pm 5.7	7.7 \pm 4.0
Zhang (24)	2019	45/161 (28.0)	48/192 (25.0)	–	–
Zhang (25)	2020	330/1,059 (31.2)	213/872 (24.4)	–	–
Li (26)	2021	189/741 (25.5)	148/575 (25.7)	7.72 \pm 4.98	5.87 \pm 4.48

CN, carbon nanoparticle; SD, standard deviation.

lymph nodes, are engulfed by macrophages, and dye the lymphatic connections and lymph nodes black, allowing the pathways of the lymphatic drainage around the tumor to be visualized (17), and thus improving the efficiency of lymph node dissection (Table 1). In thyroid cancer, CNs negatively develop and protect the parathyroid glands, which remain unstained, as they have a different lymphatic system from the thyroid gland (15). CNs have few harmful effects and are widely used in cancer surgeries (13,14,16,17,27,28).

In the present case, the patient had unilateral thyroid carcinoma and metastasis to the contralateral LN-epRLN. In China, guidelines for the management of patients with thyroid nodules and differentiated thyroid cancer (6) recommend ipsilateral central lymph node dissection while effectively preserving the parathyroid and the recurrent laryngeal nerve, lateral cervical lymph nodes dissection should be performed in patients with evidence of lateral cervical lymph node metastasis according to ultrasound or FNA. However, 16–24.2% of patients with unilateral thyroid cancer have metastasis of the contralateral central cervical lymph nodes, particularly if the Delphian lymph node is involved (29–31). The lymphatic network in the neck is complex (10), and includes lymphatic drainage into the pre-tracheal and contralateral cervical (inferior jugular) lymph nodes (32).

CN suspension may not successfully locate metastatic lymph nodes if lymphatic vessels are obstructed (e.g., by a tumor thrombus or infection), which may lead to the formation of a collateral lymphatic circulation and altered lymphatic dynamics (33). Our patient had multiple

metastatic lymph nodes in the central and lateral neck that may have obstructed the surrounding lymphatic vessels, formed collateral circulation with the periesophageal lymphatic vessels, and caused metastasis to a contralateral LN-epRLN. Notably, there was no obvious lymphatic bed in the pre-tracheal region that connected to the LN-epRLN, which suggests that the lymphatic spread occurred through a different pathway. During surgery, we observed an isolated small black-stained lymphatic vessel on the dorsal side of the right lobe of the thyroid gland, which appeared to be a skip metastasis, and the pathway of lymphatic spread involved the periesophageal lymph node on the dorsal side of the trachea.

Extra-thyroid invasion is a risk factor for cervical lymph node metastasis, and results in poor prognosis in patients with PTC, reducing the recurrence-free survival rate (34–36). The invasion of the thyroid capsule allows the thyroid cancer to spread to nearby structures and lymph nodes. In the present case, the nodule in the upper middle part of the right lobe had invaded the thyroid capsule, and may have directly involved the periesophageal lymphatic vessels, resulting in metastasis to the contralateral LN-epRLN.

Previous reports suggest that the lymph node adjacent to the recurrent laryngeal nerve is among the most common metastatic sites of esophageal cancer, and can be used as the sentinel lymph node (37,38). Esophageal cancer may metastasize to the thyroid gland and the lymph nodes around the thyroid gland. When lymph node metastasis adjacent to the recurrent laryngeal nerve is found, the

presence of a primary malignant tumor other than thyroid cancer should be considered.

Conclusions

Thyroid cancer usually metastasizes from the central lymph nodes to the ipsilateral cervical and mediastinal lymph nodes. However, the lymphatic system draining the thyroid gland has not yet been fully described, and retro-tracheal periesophageal lymph node metastasis may be a rare metastatic pathway.

Thyroid cancer is associated with a risk of cervical lymph node metastasis. We recommend routine ipsilateral central lymph node dissection while considering the potential for contralateral central lymph node metastasis and skip metastasis. When lymph node metastasis is suspected, CN suspension can improve the detection rate of metastatic lymph nodes, but may not accurately identify all lymph nodes. Surgical resection extension in thyroid cancer should be informed by a combination of CN suspension, preoperative imaging, and intraoperative pathology.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <https://gs.amegroups.com/article/view/10.21037/ggs-22-46/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/ggs-22-46/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review

by the editorial office of this journal.

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