Management of papillary thyroid cancer with tracheal invasion and lung cancer: A case report

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Abstract. The present study reports the case of a 64-year-old patient with papillary thyroid cancer (PTC) and tracheal invasion, along with primary lung cancer. Firstly, the patient received tumor electrocautery under tracheoscopy to enlarge the space for tracheal intubation. Next, the patient received one-stage radical thyroidectomy, with window resection of the trachea and thoracoscopic radical resection of the lung cancer. The patient was discharged safely after several days of therapy. To the best of our knowledge, this case is the first reported case of a one-stage radical thyroidectomy with a window resection of the trachea and thoracoscopic radical resection of the lung cancer in the literature. Simultaneous surgery for PTC with tracheal invasion and lung cancer is a great challenge for the patient and the surgeon. Appropriate surgical management of the tracheal invasion is of great importance to the operation and prognosis. This case may provide reference for surgeons in similar situations.

Introduction

Thyroid cancer and lung cancer are two of the most common malignancies worldwide. The incidence rate of thyroid cancer is 3.2 cases per 100,000 individuals globally, and the mortality rate is 0.5 cases per 100,000 individuals (1). With regard to lung cancer, the incidence and mortality rates are 22.5 cases per 100,000 individuals and 18.6 cases per 100,000 individuals, respectively (2). However, the incidence of multiple primary cancers of the thyroid and lung has rarely been reported in the literature. Tumor invasion of the larynx or trachea is observed in ~6% of differentiated thyroid cancer cases (3) and increases the mortality rate. Surgery is the benchmark for treatment (4). Lung adenocarcinoma is the most dominant subtype of lung cancer (5). Surgical resection is the first step of standard treatment procedures for early stage lung cancer. However, simultaneous surgery for papillary thyroid cancer (PTC) with tracheal invasion and lung cancer is a great challenge for the patient and the surgeon. The present study reports a rare case with PTC involving the trachea and primary lung cancer that was successfully treated simultaneously by one-stage surgery on two organs.

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Case report

Patient. A 64-year-old female patient with hemoptysis that had persisted for 1 year was admitted to Ningbo No. 2 Hospital (Ningbo, China) in April 2019. The patient had no smoking history or any other underlying diseases, except for hypertension. A physical examination showed a 3-cm fixed nodule in the right thyroid lobe. Ultrasound and contrast-enhanced computed tomography (CT) of the neck indicated a suspected thyroid carcinoma in the right lobe with tracheal invasion (Fig. 1A) and right lateral cervical lymph node (LN) metastasis. Chest CT revealed a ground-glass nodule in the anterior segment of the upper lobe of the right lung, which was also highly suspected to be a malignancy (Fig. 2).

Preoperative tracheoscopy showed an endotracheal neoplasm, which occupied 90% of the lumen. The patient received tumor electrocautery under tracheoscopy and the luminal stenosis was reduced to ~15%, leaving sufficient space for tracheal intubation. Pathological examination and immunohistochemistry confirmed that the endotracheal neoplasm originated from PTC. The immunohistochemistry results were as follows: Pan-cytokeratin (CK)(+), CK7(+), CK19(+), thyroid transcription factor 1(+), NapsinA(-), mesothelial cell marker-human bone marrow endothelial cell marker [MC(HBME-1)](+), paired-box protein pax-8(+) and Ki-67(10%+).

The patient successfully received a thoracoscopic radical resection of the right upper lung cancer, a radical thyroidectomy and a window tracheal resection. The tumor had invaded 3x2.5 cm into the trachea. The bilateral thyroid gland and 3.5x3 cm of the trachea were removed simultaneously (Fig. 3A). 0# silk sutures were used to seam the tracheal gap (Fig. 3B). Next, the level II-V LNs of the right lateral neck and the bilateral level VI LNs were dissected.

The postoperative pathological examination (Fig. 4) revealed a 1.2-cm microinvasive adenocarcinoma of the right upper lung (H&E staining; magnification, x100), without lymphatic metastasis (T1bN0M0), stage Ia, according to the eighth edition of the Tumor-Node-Metastasis Classification of

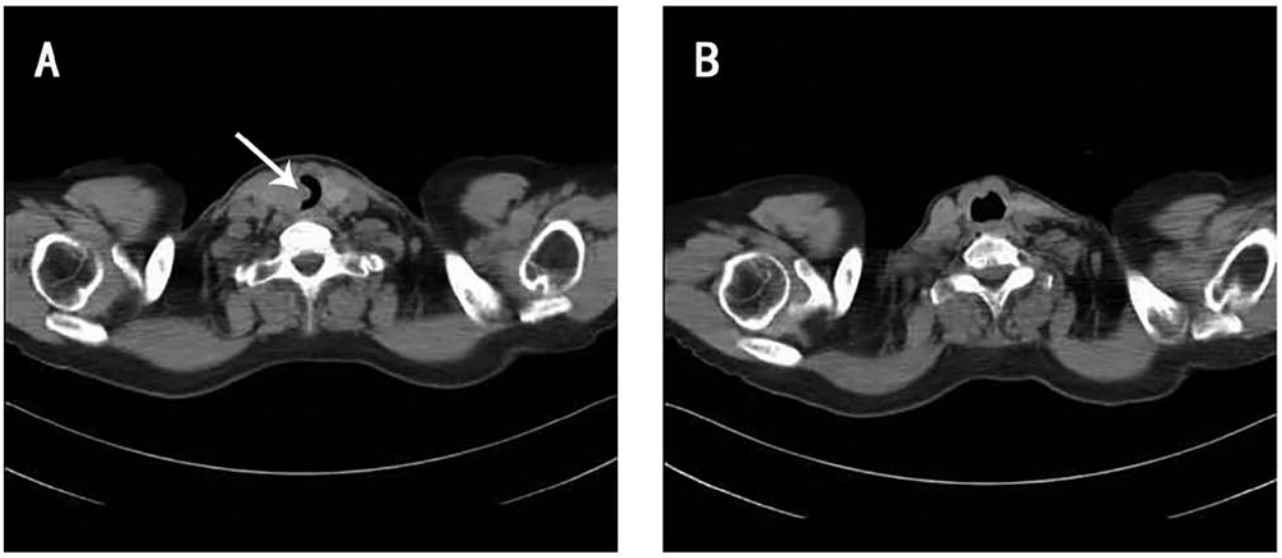

Figure 1. Neck computed tomography of the tumor and trachea. (A) Tumor invasion of the trachea 2 weeks before the surgery (white arrow). (B) The trachea was unobstructed and no recurrence was found 6 months after the surgery.

Figure 2. Chest computed tomography of a ground-glass nodule found in the anterior segment of the upper lobe of the right lung (white arrow).

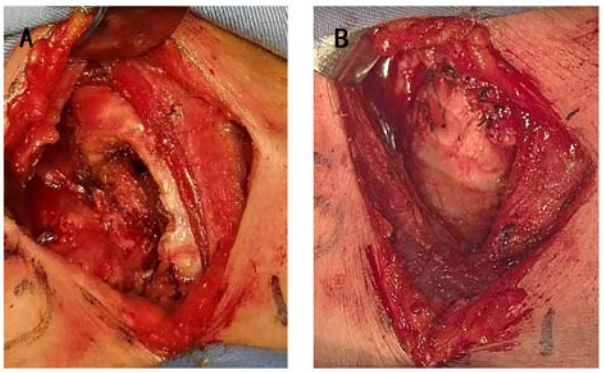

Figure 3. Surgical images. (A) Window resection of the trachea. (B) The tracheal gap was seamed closed after resection.

Lung Cancer (6). The tumor showed a predominately lepidic growth pattern, with a central focus of invasion measuring ≤5 mm that was associated with a scar. The thyroid tumor was confirmed as a right papillary thyroid carcinoma (H&E staining; magnification, x100), with tracheal invasion plus right level II-VI LN metastasis (11 positive nodes/28 total nodes) and left level VI LN metastasis (1 positive node/5 total nodes) (T4aN1bM0). The tumor showed a complex papillary architecture, intranuclear inclusions and mitotic activity. Genetic testing of the PTC was negative, without ret proto-oncogene mutation or fusion. The patient did not receive genetic testing of the lung cancer, as the postoperative pathological examination only revealed a 1.2-cm microinvasive adenocarcinoma without lymphatic metastasis; this could be classified as early stage lung cancer with a very good prognosis. Targeted therapy or immunotherapy was therefore not required.

After the surgery, the patient was sent to the intensive care unit and was extubated 7 days later. The patient received thyroid-stimulating hormone inhibitory therapy (levothyroxine sodium, 100 μg/day) and iodine-131 (^{131}I) treatment postoperatively (3.70 GBq). Bimonthly follow-up was conducted for 14 months, with no evidence of recurrence observed on CT (Fig. 1B) (Table I).

Methods

Hematoxylin and eosin of thyroid and lung specimens. Specimens were fixed with a fixation solution containing 10% formalin at room temperature for 24 h, prior to being embedded in paraffin, cut into 4-μm sections and stained for 5 min at room temperature with hematoxylin and eosin. The tissues were observed with a light microscope (Nikon Corporation) at x100 magnification.

Immunohistochemical staining of the thyroid tumor. The tissue was fixed with 10% formalin at room temperature for 24 h, cut into 2- to 3-mm sections and embedded in paraffin.

Table I. Basic information on the papillary thyroid cancer and lung cancer.

Parameter	Thyroid cancer	Lung cancer
Diameter, cm	3.0	1.2
Pathological type	Papillary thyroid carcinoma	Microinvasive adenocarcinoma
Local invasion	Tracheal invasion	No
Lymphatic metastasis	Yes	No
Distant metastasis	No	No
TNM stage	T4aN1bM0	T1bN0M0
Genetic testing	Negative	Not available
Recurrence	No	No

TNM, Tumor-Node-Metastasis.

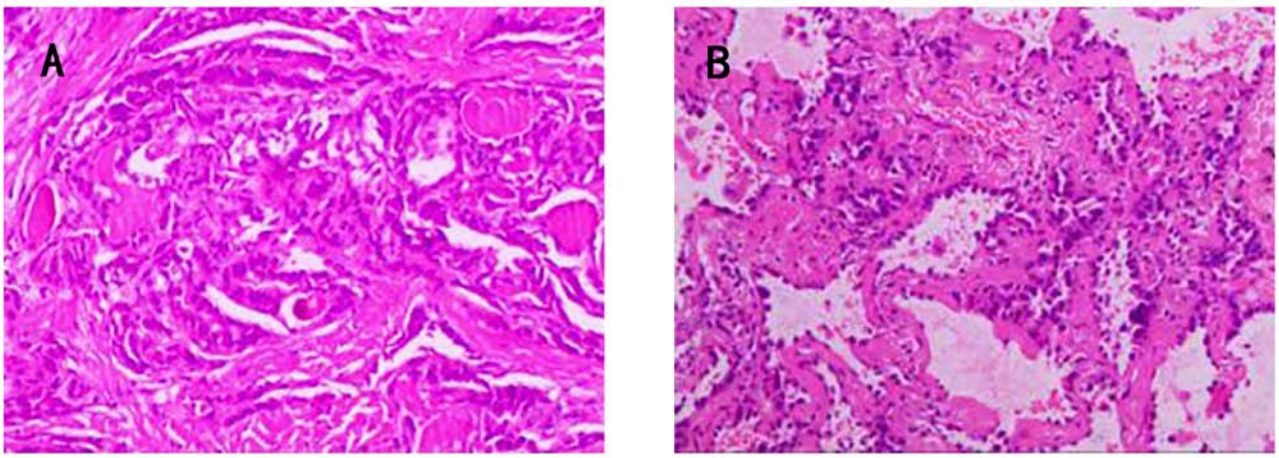

Figure 4. Pathological images. (A) Pathological images (H&E staining; magnification, x100) of the papillary thyroid cancer. The tumor showed a complex papillary architecture, intranuclear inclusions and mitotic activity. (B) Pathological images (H&E staining; magnification, x100) of the lung cancer. The tumor showed a predominately lepidic growth pattern, with a central focus of invasion measuring ≤5 mm that was associated with a scar.

Paraffin-embedded tissues were cut into 4-μm sections and sealed with 3% hydrogen peroxide at room temperature for 10 min. Antigen retrieval was performed with EDTA at 100˚C for 2.5 min, followed by washing with PBS. Primary antibody incubation was performed at 37˚C for 60 min and secondary antibody incubation at 37˚C for 20 min. The primary antibodies were purchased ready to use from OriGene Technologies, Inc. The following primary antibodies were used: Pan-CK (1:1,000; cat. no. ZM-0069), CK7 (1:1,000; cat. no. ZA-0573), CK19 (1:1,000; cat. no. ZA-0670), thyroid transcription factor 1 (1:1,000; cat. no. ZM-0270), NapsinA (1:1,000; cat. no. ZM-0473), MC(HBME1) (1:1,000; cat. no. ZM-0386), paired-box protein pax-8 (1:1,000; cat. no. ZA-0666) and Ki-67 (1:1,000; cat. no. ZM-0166). Secondary antibodies were obtained from Fuzhou Maixin Biotech. Co., Ltd. Goat anti-mouse IgG polymer III (1:200; cat. no. 220426S935c) was used as the secondary antibody. The results were observed using a light microscope (Nikon Corporation) at x100 magnification.

Discussion

In general, patients with PTC have a good prognosis and the 10-year survival rate can reach 90% (7). Extrathyroidal spread is an important determinant of outcome, and deep tracheal invasion and infiltration are correlated with a poorer prognosis (8,9). Surgical resection is the first step of standard treatment procedures for early stage lung cancer. A one-stage operation for lung cancer and thyroid cancer with tracheal invasion and lateral cervical lymph node metastasis is a great challenge that needs rigorous preoperative evaluation, multi-disciplinary collaboration and good postoperative care. These points mean that the patient should not have severe disease, which would affect the surgery and anesthesia. The thyroid surgeon and the thoracic surgeon should make efforts in the two procedures to shorten the operation time. After the operation, care is needed in case of difficult decannulation, anastomotic infection, pulmonary infection or phlebothrombosis, among others.

Most patients with superficial invasion of the trachea are asymptomatic. Symptoms will appear when they experience intraluminal invasion. Common symptoms include hemoptysis, stridor, dyspnea and airway hemorrhage (10). When the tumor involves the recurrent laryngeal nerve, hoarseness is also inevitable.

The tracheoscopic examination should be performed in patients with PTC and tracheal invasion. It is of great

importance to measure the extent of tracheal invasion. Meanwhile, the anesthetist should evaluate whether the tumor will affect tracheal intubation. In the present case, the tumor occupied 90% of the tracheal lumen with no space for intubation. Tracheoscopic tumor electrocautery was a prerequisite for the subsequent treatment.

Survival rate will be increased in patients with thyroid cancer who undergo airway-resection (11,12). Shave excision of the affected tissue, window tracheal resection and sleeve tracheal resection are the main surgical management techniques for tracheal invasion. Shave excision is only applied in patients with superficial tracheal invasion. Once the tracheal cartilage is transgressed, patients require window tracheal resection and sleeve tracheal resection. It has been reported in the literature that for patients with involvement of less than four tracheal rings and endotracheal involvement of <50% of the tracheal rings, a window resection of the trachea can be adopted. Sleeve tracheal resection is used in cases that have significant cricotracheal infiltration, for those cases with thyroid carcinoma invading >50% of the tracheal rings and for those with tracheal involvement of 4-6 cartilage rings (13). In the present case, although the tumor occupied 90% of the lumen, endotracheal involvement was <50% of the tracheal rings. Thus, a window tracheal resection was adopted. Considering that the incision into the trachea was limited, the tracheal gap was seamed closed with 0# silk sutures. However, for larger defects, closure should be performed using a myofascial flap or by forming a temporary tracheotomy through the defect with a delayed closure time (14).

The role of ^{131}I treatment has not been separately investigated in tracheal invasion. One study indicated that it may have limited effectiveness, as tumors invading the airway are less differentiated and may take up less of the radioactive iodine, therefore making them resistant to the therapy (15). However, adjuvant ^{131}I therapy is commonly applied in advanced differentiated thyroid carcinoma for the reason that postoperative ^{131}I therapy can reduce the risk of recurrence and improve the survival rate (16).

Surgical resection is the most effective therapy for stages I to II and selected cases of stage IIIA non-small-cell lung cancer (NSCLC) (17). The benefit of adjuvant cytotoxic therapy with a cisplatin-based doublet has been shown in patients with completely resected stage II and IIIA NSCLC (18). Targeted agents, such as erlotinib, gefitinib, afatinib and crizotinib, have been demonstrated to decrease the tumor burden and symptoms, and markedly improve the quality of life for patients with specific genetic alterations (19). The introduction of immune-checkpoint blockers such as monoclonal antibodies that target cytotoxic T-lymphocyte antigen-4 (CTLA-4) and antibodies against programmed cell death protein 1 (PD-1) or programmed cell death ligand 1 (PD-L1) has signaled a new direction for lung cancer care (20). The case discussed in the present study was stage Ia, so the prognosis is good and no treatment is needed temporarily.

In conclusion, simultaneous surgery of PTC with tracheal invasion and lung cancer is a great challenge for both the patient and surgeon. Appropriate surgical management of tracheal invasion is of great importance to the operation and prognosis.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

WZ, LD, KY, YW and QL made substantial contributions to the study conception and design, the acquisition/analysis of data and the writing of the manuscript. XW performed the operation, revised the manuscript and provided general supervision. WZ, LD, KY, YW, QL and XW confirm the authenticity of all the raw data. All authors contributed to the review of the manuscript and have read and approved the final manuscript.

Ethics approval and consent to participate

The research was conducted ethically in conformity with the World Medical Association Declaration of Helsinki. Ethical approval for this case report was waived as the patient provided consent and the report contains nothing that may be considered a risk to patient privacy and integrity.

Patient consent for publication

The patient provided written informed consent for the publication of this report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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