

Metastasis of renal cell carcinoma to the thyroid gland 9 years after nephrectomy: A case report and literature review

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Summary We report a case presenting with thyroid and lung metastases of renal cell carcinoma that was treated with molecular targeted therapy followed metastasectomy. A 52-year-old female underwent radical nephrectomy of right renal cell carcinoma in 2007. The patient presented 9 years after nephrectomy at the age of 61 years with sudden loss of vision on the left side and a mass on the neck. On magnetic resonance imaging, there was a mass on the midline of the neck, extending to the left, measuring 46 x 31 mm and containing central cystic-necrotic areas. Fine-needle aspiration biopsy was performed. The histopathological examination of the biopsy specimen revealed a lesion composed of malignant epithelial cells compatible with metastasis of renal carcinoma. Computed tomography showed multiple metastases in bilateral lungs. Metastasectomy and total thyroidectomy were performed. Thyroid and lung metastasis of renal cell carcinoma were pathologically confirmed. But on the first computed tomography after metastasectomy, there was residual tumor in the thyroid. Interferon-alpha therapy was given for 8 weeks. After that, pazopanib therapy started. Three months later, on computed tomography, residual metastatic foci were regressed. The patient was followed up for 1 year after metastasectomy. The patient is currently receiving a single dose of pazopanib per day (400 mg/day) and the general condition is good. Thyroid metastasis should be considered in patients with a thyroid nodule and positive history for renal cell carcinoma. Successful results can be obtained with metastasectomy and systemic targeted therapy.

KEY WORDS: Renal cell carcinoma; Metastasis; Thyroid; Metastasectomy; Targeted therapy.

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INTRODUCTION

Renal cell carcinoma (RCC) is the most frequent renal malignancy and comprises approximately 2-3% of all adult malignancies (1). Metastases of RCC usually occur in the lungs, bones, lymph nodes, brain, liver, and skin, with other sites (such as the thyroid gland) described less frequently (2).

Thyroid metastasis is an uncommon entity despite its rich vascular supply. Metastatic thyroid nodules comprise only 2-3% of all thyroid malignancies (3). Although secondary involvement of the thyroid gland by RCC is rare (< 0.1%), RCC is one of the more common neoplasms that metastasize to the thyroid gland (2).

In this article, we presented a case with ocular emboli and metastasis of renal cell carcinoma to the thyroid gland and to the lung 9 years after nephrectomy.

CASE REPORT

The patient was 52 years old when she suffered from a 5.2 cm right renal mass with no evidence of metastasis for which right radical nephrectomy was performed. Histopathology revealed clear-cell renal cell carcinoma (cRCC), grade III, stage pT1bN0M0, with negative surgical margins. The patient was followed regularly for the first 7 years after nephrectomy, although she disrupted her follow-up in the 8th year. She presented with sudden loss of vision on the left side and a mass in the neck at the age of 61 years, 9 years after the operation.

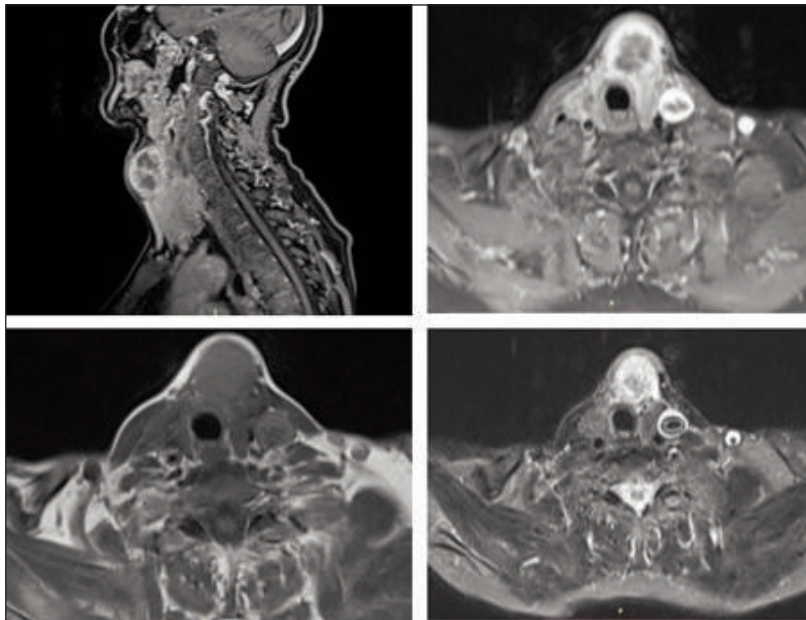
Ophthalmologic disturbances were interpreted as left ocular embolism. At magnetic resonance imaging (MRI), a mass on the midline of the neck was demonstrated, which extended to the left, measuring 46 x 31 mm and containing central cystic-necrotic areas. The mass showed diffuse restriction and peripheral heterogeneous enhancement. The plan between the mass and the posterior thyroid cartilage was not clearly visible. The mass was invasive to the isthmus of the thyroid gland inferiorly and showed diffuse restriction and peripheral heterogeneous contrast enhancement (Figure 1).

On Positron Emission Tomography/Computed Tomography (PET/CT), there was a nodular lesion with increased 18 F-fluorodeoxyglucose (FDG) uptake of approximately 2.4 x 2.2 cm located in thyroid gland isthmus (SUV max: 8,7). In the mediastinum, there were numerous lymph nodes in the right paratracheal region. The largest was 2.1 x 1.4 cm and some showed increased FDG uptake (SUV max: 7.7). In the anterior segment of the upper lobe of the left lung there was a nodular lesion of 2.2 x 1.5 cm with increased FDG uptake (SUV max: 7.0). In the superior segment of the lower lobe of the right lung, there were subpleural localized nodular lesions, which showed increased FDG uptake. In addition, there was a parenchymal nodular lesion in the lower laterobasal segment of the right lobe, 5 mm in diameter and without increased FDG uptake.

These lesions in the lung and in the thyroid gland were evaluated radiologically as RCC metastases due to the

Figure 1.

Magnetic resonance imaging showing a solid mass on the midline of the neck, extending to the left, measuring 46 x 31 mm and containing central cystic-necrotic areas.



medical history of the patient. Subsequently, a fine-needle aspiration biopsy (FNAB) of the nodule of the thyroid that was metabolically active node on PET/CT was performed. On FNAB, there were solid areas composed of cells with large, oval-round nucleus, some with nuclei, eosinophilic cytoplasm, and common coagulation necrosis. Neoplastic cells were antigenically positive with vimentin and PAX8, and showed focal positivity with pancytokeratin, EMA and CD10.

There was no immunoreactivity with thyroglobulin, thyroid transcription factor-1 (TTF-1), parathormone (PTH), calcitonin and CK7. Thus, the clinical and radiological diagnosis of mRCC was also confirmed pathologically. Hormonal status of the patient was euthyroid (T3, T4 and TSH hormone levels were normal). On color Doppler ultrasonography of the patient, there was no thrombus in the bilateral carotid arteries and jugular veins. Metastasectomy and systemic targeted therapy was planned after oncologic consultation. Two separate operations were planned for metastatic foci in the lung. First, metastasectomy was performed for the foci in the left lung. Two weeks later, the right lung foci and mediastinal lymph nodes were resected. But after thoracic lymphadenectomy, lymphatic leakage occurred due to thoracic duct injury. Percutaneous drainage was performed and it revealed milky fluid consistent with chylous leakage of 1200 mL per day. Conservative treatment including oral feeding with medium chain triglycerides or cessation of oral feeding and total parenteral nutrition was initiated in order to treat the lymphatic leak. Although the lymphatic leakage initially decreased, it gradually increased back to former levels. With the aim of stopping the leakage, percutaneous intervention was planned to embolize the leakage site. For this purpose, intranodal lymphangiogram and CT-guided percutaneous thoracic

duct embolization was performed in the Department of Radiology, Interventional Radiology Section.

One day after embolization, the catheter drainage reduced from 1200 mL to 500 mL daily and stopped on day 7.

The pathological diagnosis of lung and mediastinal lesions was confirmed as RCC metastasis. But, because of the complication of lymphatic leakage, total thyroidectomy could be performed 10 weeks after thoracic lymphadenectomy. In the pathological examination of thyroidectomy material, there were solid and diffuse necrotic-neoplastic proliferations and neoplastic cells had a large and oval-round nucleus, distinct nucleolus and clear cytoplasm, and occasionally glandular growth pattern (Figures 2, 3). On immunohistochemical examination, neoplastic cells were positive with CD10 and showed focal positivity with EMA and PAX-8, but were negative with CK7, CK20, TTF-1, thyroglobulin, calcitonin and PTH. Tumor involved the surgical margin. PET/CT at 6 weeks after thyroidectomy showed significant

findings for postoperative residual tumor in thyroidectomy area. Two new nodules were also demonstrated, one of which retained FDG in the upper lobe of the right lung and the other of which did not retain FDG in the right lung apex. The 4 mm nodule in the right lower lobe of the lung observed in the previous PET/CT also enlarged to 5 mm, although no FDG uptake of this nodule was still observed.

The patient started interferon-alpha (INF- α) for 8 weeks as first-line adjuvant systemic therapy for mRCC. After 8

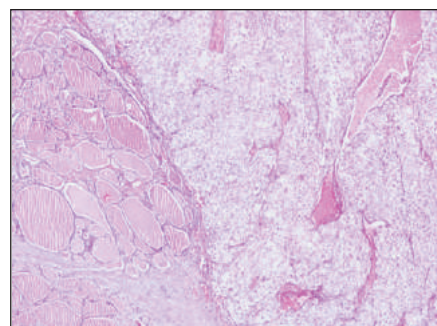


Figure 2. Renal cell carcinoma metastasis with clear cytoplasm in the vicinity of normal thyroid tissue (HEx40).

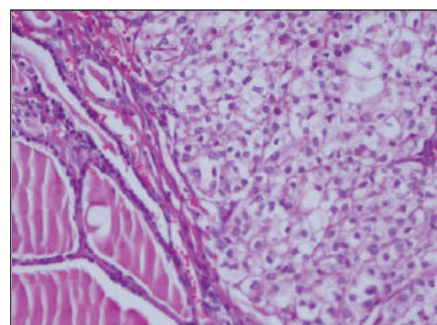


Figure 3. Renal cell carcinoma with clear cytoplasm showing nest growth in normal thyroid tissue (HEx200).

weeks, INF- α was stopped and pazopanib was started as second-line adjuvant systemic therapy for mRCC (2 x 400 mg/day). Three weeks after the start of *pazopanib* therapy, on PET/CT, there were nodular densities in the right upper lobe of the lung and in the lower lobe of the left lung that were millimeter in size, faintly confined, and without significant FDG uptake. At the mediastinum there were two hypermetabolic lymphadenopathies with suspected subcarinal and retrotracheal metastases. The patient is currently receiving one dose of pazopanib per day (400 mg/day) after 12 months of thyroidectomy and the general condition is very good.

CONCLUSIONS

RCC can metastasize to the thyroid gland even years after nephrectomy. In patients with a history of RCC, both past and present, a thyroid mass, especially co-existing with adenomatous goiter, should prompt a work-up for thyroid metastasis. If thyroid metastasis is present, metastasectomy and systemic targeted therapy may prolong the patient's survival. This is also true for lung and other organ metastases of

RCC. Because despite multiple morbidities and treatment-related side effects, long-term survival can be reached in cases of mRCC with metastasectomies and systemic targeted therapies.

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