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CLINICAL STUDY

Solitary intrathyroid metastasis of renal cancer

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Abstract: In general, it is estimated that around 1% of all clinically detectable thyroid cancers are of metastatic origin. With regard to the origin of the metastatic thyroid lesions, the most common primary sites are tumors of kidneys, breast, lungs and gastrointestinal system, and melanomas. Patients with nodular goiter and history of malignancy should be stratified into a high risk category.
The authors present a patient with solitary thyroid metastasis from renal clear cell carcinoma 31 and 11 years after left and right nephrectomy and present a comprehensive review of the literature *(Fig. 3, Ref. 14)*. Full Text in free PDF *www.bmj.sk.*
Key words: thyroid gland, goiter, metastasis, renal cell carcinoma.

Approximately 1 % of all clinically detectable thyroid cancers are of metastatic origin (1). However, autopsy results show that 1.9 – 22.4 % of patients with generalized malignancies have metastases to the thyroid gland (2). According to some authors, the most common sites of the primary tumors with metastases into thyroid gland are the breast (21 %), kidney (12%) and lungs (11 %) (3), followed by tumors of gastrointestinal system and melanomas. By others, renal cell carcinoma is the most common source of clinically relevant metastases to the thyroid gland (4), probably because it is most often clinically manifested. Although uncommon, nearly 150 cases of clinically recognized metastatic renal cell carcinoma to the thyroid have been reported in the English-language literature up to 2008 (5).

Annually, between 250 and 300 patients are surgically treated for nodular thyroid goiter at Clinic of Otorhinolaryngology and Head and Neck Surgery, Jessenius Faculty of Medicine, Comenius University (JFM CU) and Martin Faculty Hospital (MFH) in Martin. We present a case of the only patient with solitary metastasis to the thyroid treated within last 10 years, who underwent a left nephrectomy for renal cell carcinoma 32 years and a right nephrectomy 12 years ago.

Case report

A 76-year-old woman was admitted to the Department of Otorhinolaryngology and Head and Neck Surgery JFM CU and MFH in July 2008 for goiter progression. She underwent radical nephrectomy of the left kidney in 1977 and of the right kidney in 1997, both for renal cell carcinoma. Since 2002, she was given Euthyrox 25 μg/day, later 50 μg/day. On ultrasonography both thyroid lobes were hypoechoic, more on the right site. In November 2008, differentiated thyrocytes were proved by fine needle aspiration biopsy. The final diagnosis of oligosymptomatic hyperthyreosis with retrosternal goiter was done by endocrinologist. Due to pressure of the goiter surgical treatment was indicated.

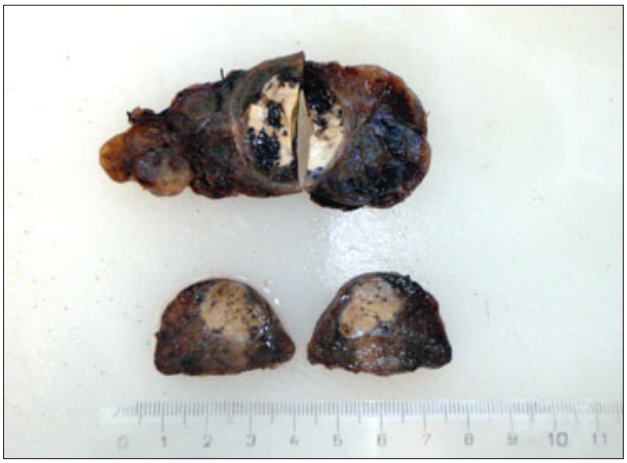

Fig. 1. Gross view of resected thyroid gland tissue with metastasis.

The patient underwent a total thyroidectomy in general anesthesia. At macroscopic examination the thyroid gland was enlarged. On cross section both lobes contained multiple solid yellowish nodules with diameter up to 25 mm (Fig. 1). Several calcifications with diameter up to 5 mm were identified. The size of the right lobe was 95 x 75 x 45 mm, of the the left lobe 85 x 65 x 40 mm. Both lobes extended approximately 2 cm retrosternally. Pyramidal lobe measuring 35 x 15 x 15 mm was made up mainly

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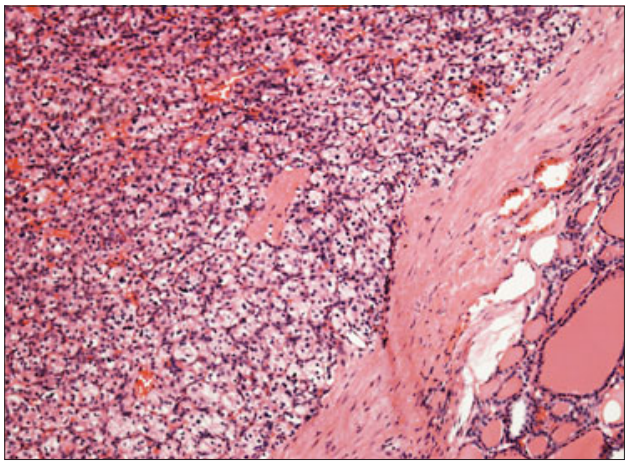

Fig. 2. Microscopic view of thyroid gland: thyroid tissue (right), thyroid capsule (middle) and metastasis (left) (Hematoxylin and eosin, 200 x).

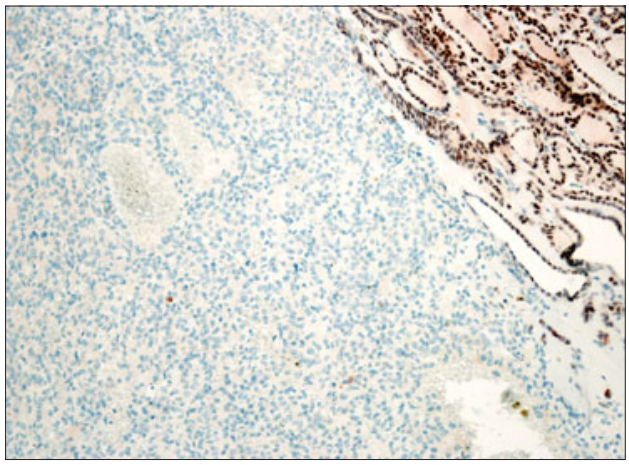

Fig. 3. Right: Thyroid transcription factor (TTF-1) positivity in residual thyroid gland tissue. Left: negative TFF-1 in renal cell carcinoma metastasis (100x).

of a node with 15 mm in diameter. At both sites, parathyroid glands and recurrent nerves were detected and they remained intact. Surgical intervention was uncomplicated and there was no need for blood loss compensation. In postoperative course, the patient suffered from temporary laboratory proven hypocalcaemia without clinical signs that was corrected by oral calcium preparations. Postoperatively at laryngoscopic investigation there was a physiological movement of vocal cords. The patient was released from the hospital in to outpatient care.

Biopsy of the removed tissue revealed morphologically as well as phenotypically metastasis of renal clear cell (RCC) carcinoma (Figs 2 and 3). The appearance of the surrounding tissue was typical for nodular goiter with regressive changes, lymphocytic infiltration and small areas of follicular epithelium activation.

Discussion

Renal clear cell (RCC) carcinoma is a tumor of adult age. It is mostly seen in adults in the sixth decade with male predominance. The behavior of RCC carcinoma is difficult to predict. Metastases usually develop in lungs, lymph nodes, bones, brain, liver and skin. The other sites are described less frequently (2). Metastatic foci from RCC carcinoma in thyroid gland are more often seen in females.

Thyroid gland is one of the most vascularized organs in the body and one would expect it to be a site of metastatic disease. By contrast, thyroid gland is protected from colonization by tumor cells by rich vascular supply. On the other hand, when thyroid gland is altered by goiter, neoplasma or inflammation, metabolic changes related to decrease in oxygen and iodine content may enhance metastatic growth (2). RCC carcinoma can metastasize to the thyroid gland bypassing the lungs through the valveless paravertebral venous plexus of Batson (6).

In biology and medicine, tumor-to-tumor metastases are a rare and interesting phenomenon. Their mechanism is not fully elucidated. Kameyama et al. (7) published autopsy case reports of two patients with metastases of sigmoid colon adenocarcinoma and primary lung adenocarcinoma into the thyroid follicular adenoma. By 2000, only five similar cases were reported in the literature. More recently, another case of primary RCC carcinoma metastasis in thyroid follicular adenoma was described (8).

Metastases into the thyroid gland may appear later than 20 years after nephrectomy, with reported maximum of 35 years (9). The mean interval from the diagnosis of the primary tumor to the development of the thyroid metastasis is 7.5 months (5). The long period between nephrectomy and development of thyroid metastases reflects the need for long-lasting clinical follow-up of patients after nephrectomy.

Thyroid gland metastases are most often clinically silent. They are usually manifested by thyroid enlargement with palpable lymph nodes, cough, dysphony and dysphagy, and according to the tumor size also by stridor. Acute respiratory failure due to metastasis of RCC carcinoma was recently reported (10).

Diagnosis and treatment

A patient with nodular thyroid disease and former history of malignant tumor belongs to high-risk group. It is necessary to exclude possible metastases, however, it might be very difficult to differentiate between primary tumor and metastases in thyroid gland. That is because imaging techniques as ultrasonography, computer tomography, or scintigraphy do not offer any specific marker enabling to distinguish the primary thyroid follicular epithelial neoplasm and metastatic RCC carcinoma to correctly manage the patient (3, 11). Both lesions will appear as "cold" nodules on radioiodine uptake studies or as hypoechoic mass on ultrasonography.

Most important diagnostic method is cytological examination after fine needle aspiration biopsy (FNAB), combined with immunohistochemical staining (3, 10). In patients with positive history of renal carcinoma surgical excision without FNAB is recommended. The final diagnosis must be proved by histopatho-

logical examination. Negative staining with anti-thyroglobulin anti-bodies would exclude the thyroid as primary origin of the neoplastic cells.

The management of patients with metastatic thyroid disease is determined by histological classification of primary tumor, presence of other metastatic sites, clinical picture and patient condition. In the case of isolated thyroid metastasis, surgical treatment is recommended (2, 12). Metastasis in thyroid gland indicates poor prognosis. However, an aggressive surgical therapy and sometimes correct conservative treatment may be sufficiently effective, also in metastases of RCC carcinoma (13). Total thyroidectomy is a method of choice. The regional application of radiotherapy in symptomatic patients may achieve sufficient improvement of the quality of life and represents an acceptable alternative approach. In patients with disseminated disease a systemic treatment is indicated. The time between the presentation of thyroid metastases and death ranged from 3 to 45 months (14).

Conclusions

Metastatic thyroid disease is relatively rare. However, it must be anticipated in every patient with nodular goiter and history of neoplasm. Isolated thyroid metastases are treated surgically. The prognosis is dubious.

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