



Metastatic Renal Cell Carcinoma to the Thyroid Gland: A Case Report and Brief Review of the Literature

Renal Hücreli Karsinomun Tiroid Bezine Metastazı: Vaka Raporu ve Literatürün Kısa Gözden Geçirilmesi

Georgios Kyriakos, Alfonso Vidal Casariego, Rocio Villar Taibo, Teresa Ribas Ariño*, Maria D. Ballesteros Pomar, Isidoro Cano Rodriguez

Complejo Asistencial Universitario de León, Department of Endocrinology and Nutrition, León, Spain
Complejo Asistencial Universitario de León, Department of Anatomic Pathology, León, Spain

Abstract

Thyroid metastases are rarely seen in clinical practice but should be considered particularly in patients with a history of non-thyroidal malignancies. Renal cell carcinoma (RCC) is the most common tumor to metastasize to the thyroid gland and may present many years after a nephrectomy. Thus, patients require a long-term follow-up and, physicians should have a high index of suspicion particularly in patients with benign disorders of the thyroid gland. Fine needle aspiration cytology (FNAC) and thyroglobulin immunohistochemical staining are considered the most effective methods for diagnosis. Surgical treatment of solitary thyroid metastases is recommended and prolongs survival. Adjuvant medical treatment may also be useful in specific situations. We present the unusual case of a relative young patient with goiter who presented with an intrathyroidal metastasis of RCC. *Turk Jem 2014; 2: 58-60*

Key words: Thyroid metastases, renal cell carcinoma, fine needle aspiration cytology

Özet

Tiroid metastazları klinik pratikte nadiren görülmekte olup görüldüğünde non-tiroidal malignite öyküsü özellikle sorgulanmalı. Renal hücreli karsinom (RHK) tiroide en fazla metastaz yapan tümör olup nefrektomiden yıllar sonra bile saptanabilir. Bu hastalarda uzun dönem izlem gerekir. Tiroid benign görünümlü lezyonları kuşku altına alınır. İnce iğne aspirasyon sitolojisi (TİİAS) ve tiroglobulinle immunohistokimyasal boyama tanıda etkin yöntemlerdir. Soliter tiroid metastazlarının cerrahi tedavisi tavsiye edilir ve bu durum sağkalımı uzatır. Adjuvan tıbbi tedavi özel durumlarda faydalı olabilir. Bu raporda genç sayılabilecek yaşta guatr ile baş vuran intratiroidal RHK metastazı olan bir hasta sunmaktayız. *Turk Jem 2014; 2: 58-60*

Key words: Tiroid metastazı, renal hücreli karsinom, ince iğne aspirasyon sitolojisi

Introduction

Although the thyroid gland has a rich blood supply, it is a rare site of clinically detectable tumor metastasis (1). It is estimated that only 1.1%-3% of all clinically detectable thyroid cancers are of metastatic origin (2,3,4). However, data from autopsies show that findings of thyroid metastasis range from 1.9% up to 25% in patients dying from disseminated malignant tumor of other primary tumors, with common sources being breast, lung and melanoma (2,3,5,6,7). Nevertheless, when metastases are clinically discovered, the most commonly reported tumor is renal cell carcinoma (RCC) (8). RCC is called the internist tumor due to its highly variable clinical presentation and course. It generally diffuses in an unpredictable manner and can metastasize to all organs (9). We present the unusual case of a relative young patient with goiter with an intrathyroidal metastasis of RCC.

Case Report

A 52-year-old man was referred to the Department of Urology in July 2006 for the evaluation of hematuria, flank pain and a large mass measuring 8x5 cm, arising from the right kidney. In August 2006, he underwent radical nephrectomy of the right kidney for RCC, which was staged as pT2NxM0 (Grade 3). The preoperative computed tomography (CT) revealed also an enlargement of the right thyroid lobe, and in October 2006, the patient was referred to the Division of Endocrinology for evaluation. Thirteen years earlier, he had been assessed in the Endocrinology clinic due to a long standing goiter with a large thyroid nodule in the right lobe. In this period, an ultrasound and scintigraphy were performed revealing a cold nodule of 4.4x3.4 cm. A fine needle aspiration cytology (FNAC) was programmed but the patient stopped attending the

clinic. A new FNAC was programmed in 2006 which showed clusters of epithelial cells with nuclei constant in shape and size with prominent nucleoli, some of them with clear vacuolated cytoplasm. From the cytology, it could not be determined whether the cells originated from the RCC or from the thyroid gland, as in cases of anaplastic carcinoma or an unusual clear-cell variant of follicular carcinoma. The whole-body CT scan revealed lung metastases and a nodule of 2 cm in the right adrenal gland along with the irregular growth of the right thyroid lobe. All these findings led the patient to undergo a total thyroidectomy with bilateral nodal neck dissection. The microscopic findings confirmed the presence of a clear-cell renal carcinoma in the right lobe (Figure 1). There was no metastatic disease in the lymph nodes but the histology of the left lobe revealed a sclerosing variant papillary microcarcinoma. He also received immunotherapy with interferon- α . Six years after the surgery, the patient died from metastatic RCC.

Discussion

Metastatic disease to the thyroid gland is only infrequently found (10). As early as the 1930s, Willis suggested several possible factors like the high concentration of oxygen and iodine in the thyroid gland, the local cytoregulating effect of the thyroid hormones, and the filter activity of the lungs (1). In more than 50% of the clinically recognized metastases to the thyroid, the primary cancer is RCC (7). Until now, more than 180 cases have been described in the English-language literature (4). The most frequent decade of appearance is the 7th followed by the 6th, with a female to male ratio of 1.35:1 (11). In a study of 36 cases of patients affected by thyroid metastases from RCC, the mean age was 64.9 years with a range from 53 to 80 years (10). The RCC diagnosis and thyroid metastases can be synchronous, when the RCC and metastases are detected at the same time or metachronous when metastatic disease is developed as a part of the latency of the tumor with delayed development of metastases after many years of dormancy. In the majority of the cases, thyroid metastases are metachronous appearing even more than 10 years after nephrectomy, with a case reported after 26 years (7,11). These long intervals pose a diagnostic challenge in patients with thyroid nodules and a history of RCC. Regarding our patient, the metastases to the thyroid was detected right after the diagnosis of RCC at the age of 52, in a thyroid nodule that was first seen 10 years earlier. This thyroid nodule could have been the

first sign of the RCC but FNAC was not performed at that moment, possibly delaying the diagnosis.

Nothing can clinically differentiate thyroid metastases from primary thyroid cancer. McCabe et al. suggested that when a patient has a history of cancer, a mass in the thyroid gland should be treated as a metastatic lesion until proven otherwise, even when the primary tumor has been excised completely (12). Moreover, patients with goiter, thyroid neoplasm, or thyroiditis are more vulnerable to malignant metastases due to abnormal blood supply, and a previous thyroid disease may reduce the clinical suspicion of a concurrent malignant process (4,13).

RCC metastases to the thyroid can be asymptomatic and discovered incidentally, but normally, they present with clinical complaints such as thyroid enlargement, palpable nodules, cough, hoarse, dysphagia and dyspnea (4). Differential diagnosis includes thyroid diseases where clear cells can be found, such as clear-cell carcinoma of the thyroid and some cases of benign thyroid lesions, such as goiter, Graves's disease, Hashimoto's thyroiditis, as well as metastases of non-thyroid tumors like clear-cell carcinomas of the lung, ovary, and parathyroid gland, and acinic-cell carcinoma of the salivary glands (13).

Imaging modalities such as ultrasound, CT, magnetic resonance imaging (MRI), and scintigraphy cannot help differentiate primary from secondary lesions. RCC has some cytological, histological and immunohistochemical features that allow it to be distinguished from a primary thyroid neoplasm. Clusters of cells with sharp borders, abundant clear cytoplasm, and large, oval, moderately hyperchromatic nuclei with visible nucleoli should raise the suspicion of metastatic RCC (10,13). However, FNAC did not yield the correct diagnosis in 28.7% of patients with RCC (4). Moreover, Mijovic et al. reported a high false-negative rate of 13% of the FNAC due to inadequate sampling in the majority of the cases (14). Thus, surgical excision may be the most appropriate management in patients with a history of malignancy when FNAC is equivocal or indeterminate (4). Most times, the diagnosis is made with pathologic assessment and immunohistochemistry. The use of negative TTF-1 staining or positive periodic acid-Schiff staining in conjunction with negative Tg staining can lead to the diagnosis of metastatic disease. The majority of RCCs are immunoreactive to keratin and epithelial membrane antigen (EMA), often stain positive for CD10, and some may also stain positive for vimentin (15).

Surgical resection is regarded as the best treatment for solitary thyroid metastases, especially when the primary tumor is controlled and is associated with good prognosis (10,16). There is no clear consensus about the extent of operation in thyroid surgery because of the complications after total thyroidectomy. Some previous studies recommended a thyroid lobectomy and/or isthectomy in case of solitary thyroid metastases and a total thyroidectomy in case of bilateral metastases (17). On the other hand, in patients with disseminated disease and poor prognosis, surgical treatment is indicated as a life-saving measure or for the palliation of significant compressive symptoms (18). In these group of patients, adjuvant medical therapy, such as interferon- α , an immunomodulator, may affect survival and should be considered (5). Survival time after

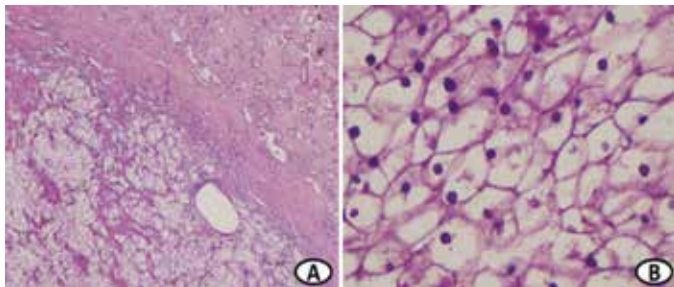


Figure 1. Microscopic findings of renal cell carcinoma metastasis in the thyroid. Capsulated intrathyroidal nodule (A) composed of large clear cells with optically empty cytoplasm, surrounded by a distinct cell membrane and containing round and uniform nuclei (B)

diagnosis of the thyroid metastases is determined by the biology of the primary disease (19). Factors that may be associated with a favorable prognosis include a long interval between the primary tumor resection and the development of metastatic focus (short survival for synchronous thyroid metastasis with a mean of 8 month versus a mean of 10 years in patients with metachronous thyroid disease), evidence of a solitary isolated lesion in the thyroid gland without evidence of widespread metastases, spontaneous regression of metastatic lesions, demonstration of extensive necrosis in the resected specimen and slow evolution or growth of the tumor, and a lack of clinical symptoms (10). In general, the longer is the interval between the diagnosis of renal cancer and the appearance of thyroid metastases, the better is the prognosis (20). In conclusion, patients who present with thyroid nodules and have a history of a previous malignancy must be considered for metastatic disease. RCC is the most common tumor to metastasize to the thyroid gland, and a careful histopathological and immunohistochemical examination can allow differentiating primary thyroid neoplasm from metastases from RCC. Surgical treatment of solitary thyroid metastases is recommended and prolongs survival. Adjuvant medical treatment may also be useful in specific situations.

Conflicts of Interest

There are no conflicts of interest.

References

- Willis RA. Metastatic Tumours in the Thyroid Gland. *Am J Pathol* 1931;7:187-208.3.
- Shimaoka K, Sokal JE, Pickren JW. Metastatic neoplasms in the thyroid gland. Pathological and clinical findings. *Cancer* 1962;15:557-565.
- Papi G, Fadda G, Corsello SM, Corrado S, Rossi ED, Radighieri E, Miraglia A, Carani C, Pontecorvi A. Metastases to the thyroid gland: prevalence, clinicopathological aspects and prognosis: a 10-year experience. *Clin Endocrinol (Oxf)* 2007;66:565-571.
- Chung AY, Tran TB, Brumund KT, Weisman RA, Bouvet M. Metastases to the thyroid: a review of the literature from the last decade. *Thyroid* 2012;22:258-268.
- Wood K, Vini L, Harmer C. Metastases to the thyroid gland: the Royal Marsden experience. *Eur J Surg Oncol* 2004;30:583-588.
- Berge T, Lundberg S. Cancer in Malmo 1958-1969. An autopsy study. *Acta Pathol Microbiol Scand Suppl* 1977;260:1-235.
- Nakhjavani MK, Gharib H, Goellner JR, van Heerden JA. Metastasis to the thyroid gland. A report of 43 cases. *Cancer* 1997;79:574-578.
- Chen H, Nicol TL, Udelsman R. Clinically significant, isolated metastatic disease to the thyroid gland. *World J Surg* 1999;23:177-180; discussion 181.
- Motzer RJ, Bander NH, Nanus DM. Renal-cell carcinoma. *N Engl J Med* 1996;335:865-875.
- Heffess CS, Wenig BM, Thompson LD. Metastatic renal cell carcinoma to the thyroid gland. *Cancer* 2002;95:1869-1878.
- Sindoni A, Rizzo M, Tuccari G, Ieni A, Barresi V, Calbo L, Cucinotta E, Trimarchi F, Benvenega S. Thyroid metastases from renal cell carcinoma: review of the literature. *ScientificWorldJournal* 2010;10:590-602.
- McCabe DP, Farrar WB, Petkov TM, Finkelmeier W, O'Dwyer P, James A. Clinical and pathologic correlations in disease metastatic to the thyroid gland. *Am J Surg* 1985;150:519-523.
- Pang PY, Koh AJ, Tan NC, Agrawal R. A case of late metastasis of a renal cell carcinoma to a multinodular goitre. *Ann Acad Med Singapore* 2011;40:298-299.
- Mijovic T, Rochon L, Gologan O, Hier MP, Black MJ, Young J, Payne RJ. Fine-needle aspiration biopsies in the management of indeterminate follicular and Hurthle cell thyroid lesions. *Otolaryngol Head Neck Surg* 2009;140:715-719.
- Lee J-G, Yang Y, Kim KS, Hyun CL, Lee JS, Koh G, Lee D. A Case of Metastatic Renal Cell Carcinoma to Thyroid Gland. *Chonnam Medical Journal* 2011;47:130-133.
- Turino-Luque JD, Jorge-Cerrudo J, Munoz-Perez N, Villar-Del Moral JM, Ferrón-Orihuela JA. [Thyroid metastasis from clear cell renal carcinoma]. *Endocrinol Nutr.* 2011;58:145-147.
- Vardar E, Erkan N, Bayol U, Yilmaz C, Dogan M. Metastatic tumours to the thyroid gland: report of 3 cases and brief review of the literature. *Radiol Oncol* 2011;45:53-58.
- De Stefano R, Carluccio R, Zanni E, Marchiori D, Cicchetti G, Bertaccini A, Sensi L, Pedrini L, Martorana G, Marlia E. Management of thyroid nodules as secondary involvement of renal cell carcinoma: case report and literature review. *Anticancer Res* 2009;29:473-476.
- Dionigi G, Uccella S, Gandolfo M, Lai A, Bertocchi V, Rovera F, Tanda ML. Solitary intrathyroidal metastasis of renal clear cell carcinoma in a toxic substernal multinodular goiter. *Thyroid Res* 2008;1:6.
- May M, Marusch F, Kaufmann O, Seehafer M, Helke C, Hoschke B, Gastinger I. Solitary renal cell carcinoma metastasis to the thyroid gland--a paradigm of metastasectomy?. *Chirurg* 2003;74:768-774.