

Testicular Metastasis in Renal Cell Carcinoma

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Abstract

We report on a patient, who was diagnosed with renal cell carcinoma (RCC) and presented with testicular metastasis at 5 years after the initial diagnosis, surgical interventions and systemic treatments. Although there are reports of testicular metastasis of RCC, to the best of our knowledge, our case is first who presented late recurrence in the testicular tissue despite previous tyrosine kinase inhibitor and PD1 inhibitor treatments.

Keywords: Renal cell carcinoma, testicular metastasis, case report

Introduction

Renal cell carcinoma (RCC) accounts for 2-3% of all adult malignant neoplasms and the most common sites in metastatic disease are the lungs, vertebral bones, liver and brain (1). Testis is a rare location for metastatic disease and the most common primary tumors that metastasize to the testes are reported as the prostate, lung and gastrointestinal system (2). Although RCC can metastasize to many unusual organs, testicular metastasis is an extremely rare reported issue (3).

We report on a patient, who was diagnosed with RCC and low-volume lung metastasis and presented with a testicular metastasis as the sole metastatic finding 5 years after the initial diagnosis despite tyrosine kinase inhibitor and anti PD1 inhibitor treatments.

Case Report

A 70-year-old male patient who presented with a right kidney mass was detected on ultrasonography (US) and confirmed on magnetic resonance imaging as an exophytic 58x56 mm mass with a 20x20 mm cyst (Figure 1). Staging with thorax-computed tomography showed low volume metastatic disease in bilateral lungs.

Right partial nephrectomy was performed, and the histological diagnosis of the mass was reported as RCC, clear cell type, pT1b, Fuhrman grade 2, whereas the histological diagnosis of

the cyst was also reported as RCC but multilocular cystic type. Close follow-up with periodic imaging and without adjuvant treatment was recommended by the multidisciplinary tumor council.

At 1 year after the initial diagnosis, pazopanib treatment was started due to increase in the number and size of the lung nodules. After 15 months under the pazopanib treatment, solitary metastatic lesions in both lungs were resected and histological diagnosis was reported as clear cell type metastasis of RCC. At 6 months after treatment-free period, recurrent disease in the lungs was detected and nivolumab treatment was started. After 6 courses of nivolumab treatment, progressive disease in the lungs was detected and his treatment was changed to axitinib. At 1 year under the axitinib treatment he was presented with swelling in the left testicle and a left testicular mass was detected on the patient's physical examination, which has been confirmed as 34x27 mm solid mass with scrotal Doppler US. Tumor markers for testicular carcinoma were negative and histological diagnosis of the left inguinal orchiectomy was reported as clear cell type metastasis of RCC (Figure 2). Informed consent was obtained from the patient.

Discussion

Metastatic disease in the testicular tissue is a rare finding and has been reported between 0.3-3.6% in several case reports and literature reviews (4). Back in 1972, in an autopsy series with

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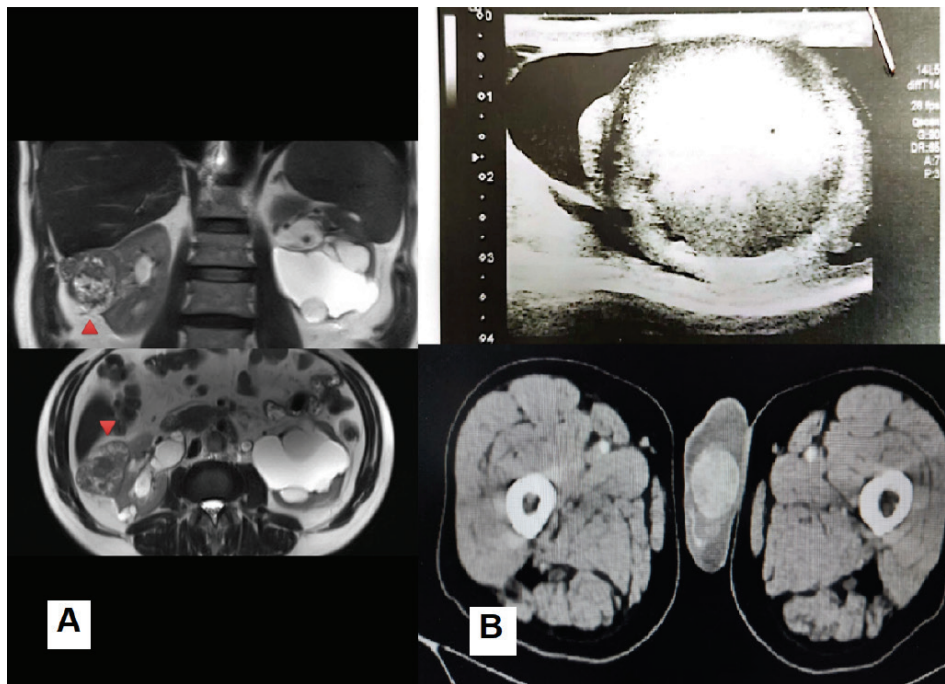


Figure 1. A. MRI of the right kidney mass, B. US and CT images of testicular mass 663x475mm (47x47 DPI)

MRI: Magnetic resonance imaging, US: Ultrasonography, CT: Computed tomography

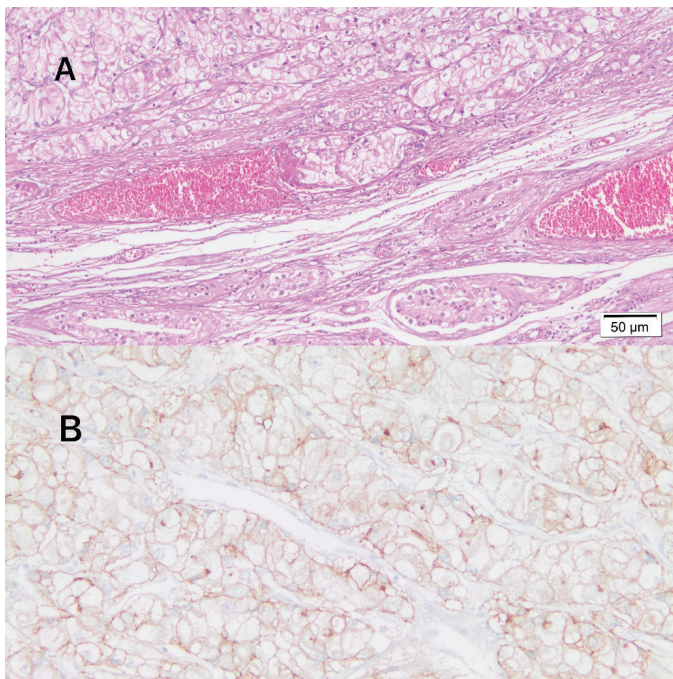


Figure 2. Histologic images of the testicular mass A. Tumor cells with clear cytoplasm adjacent to the seminiferous tubules (H&E, x100) B. Diffuse membranous staining of tumor cells with CAIX (IHC, x200) Macroscopically the tumor was a well circumscribed mass. The microscopic examination identified cells with clear cytoplasm arranged in a nested pattern with intervening delicate fibrous tissue and blood vessels (A). On immunohistochemical staining, Carbonic anhydrase IX (CAIX), was found to be positive (B) in addition to CD10, and vimentin. Histological diagnosis of the left inguinal orchiectomy was reported as clear cell RCC. 1106x1106mm (47x47 DPI)

H&E: Hematoxylin and eosin stain, IHC: Immunohistochemistry

24,000 people, metastatic disease in the testis was reported as 0.06% and the most common primary diagnosis was reported as prostate adenocarcinoma (5).

Testicles can be called a tumor sanctuary because tumor cells cannot grow easily in the testicular environment (6,7). There are some opinions explaining the rarity of testicular metastases. One of the potential reasons is that the temperature of the scrotum is lower than the normal body temperature (8). Another potential explanation might be the physiological blood testicular barrier, which is formed by Sertoli cells and protects spermatozoa's cells and prevents testicular metastasis (7).

Clinical and autopsy studies have reported that RCC can metastasize to many unusual organs (9). Testicular metastasis of RCC was reported for the first time when a patient who underwent right orchiectomy in 1943 with a pre-diagnosis of orchitis and the pathological diagnosis was not clearly understood and the patient presented with hematuria in 1945, when nephrectomy was performed in the right kidney mass and a kidney tumor was detected (10).

Theoretically, metastatic cells can come to the testicle with retrograde venous flow, arterial embolism, lymphatic pathway, and intracanalicular spread (8). Testicular metastasis of RCC is usually ipsilateral (6,11) and left testicular metastasis has been reported more common (11). It is thought that this situation may be due to tumor cells escaping retrograde to the testicle through the left spermatic venous plexus, which is directly opening to the left renal vein. However, for the right side, it is thought

that cancer cells might migrate to the right testicle through the arterial system (7). Contralateral testicular metastasis of RCC has also been reported in the literature, and it is thought that contralateral metastases also come to the testicle through the bloodstream (11,12).

In this study, left testicular metastasis was detected 5 years after the initial diagnosis and surgical intervention. Although there are reports of testicular metastasis of RCC, to the best of our knowledge, our case is first who presented with sole metastatic lesion in the testicular tissue after previous tyrosine kinase inhibitor and PD1 inhibitor treatments for recurrent disease. The effect of testicular metastases on prognosis in RCC is not fully known due to the small number of cases.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: G.Ö., T.T., D.F., İ.T., Concept: M.Ç., İ.T., Design: G.Ö., İ.T., Data Collection or Processing: G.Ö., M.Ç., T.T., D.F., Analysis or Interpretation: M.Ç., Literature Search: G.Ö., D.F., Writing: G.Ö., D.F., İ.T.

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References

1. Bianchi M, Sun M, Jeldres C, Shariat SF, Trinh OD, Briganti A, Tian Z, Schmitges J, Graefen M, Perrotte P, Menon M, Montorsi F, Karakiewicz PI. Distribution of metastatic sites in renal cell carcinoma: a population-based analysis. *Ann Oncol* 2012;23:973-980.
2. Dutt N, Bates AW, Baithun SI. Secondary neoplasms of the male genital tract with different patterns of involvement in adults and children. *Histopathology* 2000;37:323-331.
3. Villarreal-Garza C, Perez-Alvarez SI, Gonzalez-Espinoza IR, Leon-Rodriguez E. Unusual Metastases in Renal Cell Carcinoma: A Single Institution Experience and Review of Literature. *World J Oncol* 2010;1:149-157.
4. Dieckmann KP, Düe W, Loy V. Intrascrotal metastasis of renal cell carcinoma. Case reports and review of the literature. *Eur Urol* 1988;15:297-301.
5. Pienkos EJ, Jablolkow VR. Secondary testicular tumors. *Cancer* 1972;30:481-485.
6. Moriyama S, Takeshita H, Adachi A, Arai Y, Higuchi S, Tokairin T, Chiba K, Nakagawa K, Noro A. Simultaneous bilateral testicular metastases from renal clear cell carcinoma: A case report and review of the literature. *Oncol Lett* 2014;7:1273-1275.
7. Camerini A, Tartarelli G, Martini L, Donati S, Puccinelli P, Amoroso D. Ipsilateral right testicular metastasis from renal cell carcinoma in a responder patient to interleukine-2 treatment. *Int J Urol* 2007;14:259-260.
8. Blefari F, Risi O, Pino P. Secondary tumors of testis: two rare cases and review of the literature. *Urol Int* 1992;48:469-470.
9. Pagano S, Franzoso F, Ruggeri P. Renal cell carcinoma metastases. Review of unusual clinical metastases, metastatic modes and patterns and comparison between clinical and autopsy metastatic series. *Scand J Urol Nephrol* 1996;30:165-172.
10. Bandler CG, Roen PR. Solitary testicular metastasis simulating primary tumor and antedating clinical hypernephroma of the kidney; report of a case. *J Urol* 1946;55:663-669.
11. Steiner G, Heimbach D, Pakos E, Müller S. Simultaneous contralateral testicular metastasis from a renal clear cell carcinoma. *Scand J Urol Nephrol* 1999;33:136-137.
12. Kolukcu E, Kilic S, Parlaktas BS, Deresoy FA, Atilgan D, Gumusay O, Uluocak N. Contralateral Testicular Metastasis of Renal Cell Carcinoma: A Case Report. *Eurasian J Med* 2019;51:310-312.