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Metachronous contralateral testicular and bilateral adrenal metastasis of chromophobe renal cell carcinoma: a case report and review of the literature

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Abstract: Chromophobe renal cell carcinoma (ChRCC) metastatic to the testis has not, to the best of our knowledge, been reported in the literature. Nor have there been reports of delayed bilateral adrenal metastasis of ChRCC. Here we report a case of metachronous contralateral testicular and bilateral adrenal metastasis of ChRCC in a 70-year-old man who underwent right radical nephrectomy for RCC six years ago. He was admitted to the hospital because of left intrascrotal enlargement of two-month duration. Ultrasonography revealed a mass in the upper pole of the left testis. Computed tomography (CT) showed irregular masses in the bilateral adrenal area. Left radical orchiectomy and laparoscopic bilateral adrenalectomy were performed. The pathologic examination showed metastatic ChRCC in the left testis and bilateral adrenal gland. Postoperative follow-up showed that the patient had survived for at least 56 months without recurrence. The case highlights the unique behavior of RCC with an unusual site of metastasis and favorable survival after multiple metastasectomy.

Key words: Renal cell carcinoma (RCC), Testicular metastasis, Adrenal metastasis, Metastasectomy
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1 Introduction

It has been reported that testicular metastasis from renal cell carcinoma (RCC) is predominantly ipsilateral and invariably on the left side. It usually presents simultaneously with the renal primary tumors or precedes the diagnosis of renal tumors (Nabi *et al*., 2001). The histological subtype of RCC metastatic to the testis almost always shows clear cell carcinoma (Datta *et al*., 2001; Steiner *et al*., 1999). Only one case of metachronous contralateral testicular metastasis from RCC has been reported (Nabi *et al*., 2001), and no case of chromophobe RCC (ChRCC) metastatic to the testis was reported, to the best of our knowledge. Delayed bilateral adrenal metastasis of RCC is also very rare (Antonelli *et al*., 2006; Bonnet *et al*., 2008). To date, there have been no reports on delayed bilateral adrenal metastasis of ChRCC. Here we report a case of metachronous contralateral testicular and bilateral adrenal metastasis of ChRCC and review the literature.

2 Case report

A 70-year-old male patient was admitted to the hospital because of left intrascrotal enlargement of two-month duration. He underwent right radical nephrectomy for right RCC in a local hospital six years ago. Physical examination revealed a palpable mass of the left testis with 4 cm×3 cm×2 cm in size. Superficial lymph nodes were not palpable. Serum

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alpha fetoprotein (AFP) and β-human chorionic gonadotropin (β-HCG) were within normal limits. B-ultrasound showed a 3.9 cm×2.8 cm mass in the left testis. A positive computed tomography (CT) (Fig. 1) scan of the abdomen revealed that total right nephrectomy had been done, and irregular masses were seen in bilateral adrenal areas. The right adrenal mass was 7.7 cm×5.5 cm in size and the left one 5.6 cm×6.0 cm. Single photon emission computed tomography (SPECT) of bone showed no bony metastasis.

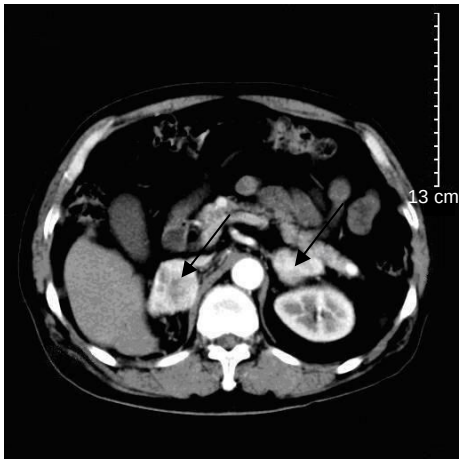

Fig. 1 CT showed irregular masses of bilateral adrenal areas (black arrows)

The patient underwent left radical orchiectomy. The pathologic examination showed ChRCC of the left testis (Fig. 2). Immunohistochemistry of the left testicular tumor was positive for intra-cellular cytokeratin and vimentin. The patient accepted laparoscopic bilateral adrenalectomy seven days after left radical orchiectomy. The pathological findings indicated metastatic ChRCC of the bilateral adrenal glands. His postoperative course was uneventful. Postoperative follow-up showed that the patient had survived for at least 56 months without recurrence (Fig. 3).

3 Discussion

The incidence rate of secondary testicular tumors ranges from 0.3% to 3.6% (Dieckmann *et al*., 1988). The most frequent origin of them is the prostate (Dutt *et al*., 2000; Llarena Ibarguren *et al*., 2008). Very rarely, intrascrotal metastasis from RCC has been reported (Schmorl *et al*., 2008). The pathologic diagnosis of RCC metastatic to the testis almost always reveals a clear cell tumor (Datta *et al*., 2001; Steiner *et al*., 1999).

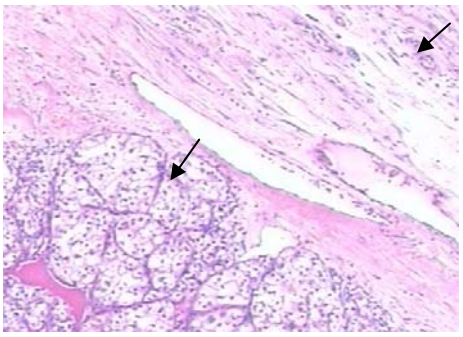

Fig. 2 Hematoxylin and eosin-stained sections of left testicular tumor
Left down arrow showed renal chromophobe cell carcinoma. Right upper arrow showed testicular convoluted seminiferous tubule (×100)

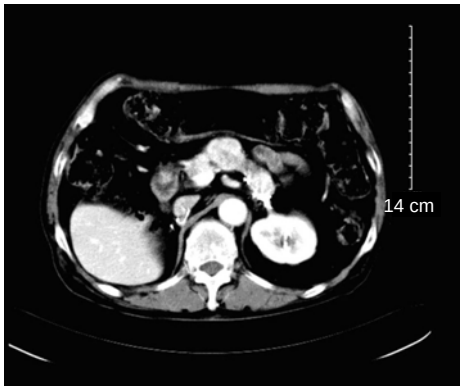

Fig. 3 CT showed no recurrent mass of bilateral adrenal area at 56 months after operation

After radical nephrectomy, approximately 25% of RCC patients developed metachronous metastasis (Bonnet *et al*., 2008), among whom less than 2% presented with metastasis confined to the adrenal glands (Antonelli *et al*., 2006; Siemer *et al*., 2004). In a recent study, a series of 1179 patients were treated for RCC, and it was found that the global incidence of adrenal metastasis among those patients was 3.7%, of which 1.9% were ipsilateral, 1.5% contralateral, 0.3% bilateral, 2.7% synchronous with the renal tumor, and only 1% metachronous (Antonelli *et al*., 2006). The incidence rate of metachronous bilateral adrenal metastasis from RCC is even more rare. There have only been three cases reported (Antonelli *et al*., 2006; Bonnet *et al*., 2008). And there are no reports concerning delayed bilateral adrenal metastasis of ChRCC.

ChRCC is biologically a tumor of low malignant potential with a 5-year survival rate of 78% to 100% and a 10-year survival rate of 80% to 90% (Amin *et al*., 2008). Metastasis of ChRCC constitutes less than 5% of all ChRCC cases and less than 1% of all metastatic RCC (Choueiri *et al*., 2008). Patients with ChRCC are more likely to experience liver metastasis (Hoffmann *et al*., 2008). Treatment modalities for metastatic RCC are limited. Chemotherapy and radiotherapy have proven to have low response rates. Immunotherapeutic combination regimens are currently being examined in clinical trials, including cytokine therapy combined with interleukin-2 (IL-2) and interferon-α (IFN-α), or targeted agents such as multitargeted tyrosine kinase inhibitors (TKIs), mammalian target of rapamycin (mTOR) inhibitors, and the monoclonal antiangiogenic antibodies. Most of the studies were focused on clear cell RCC and only a few on the ChRCC (Choueiri *et al*., 2008; Guevremont *et al*., 2009; Motzer *et al*., 2008). Although these agents show a consistent efficacy in clinical trials, surgery remains the only known curative therapy for RCC. Several studies described surgical intervention for metastatic RCC and showed that metastasectomy promoted long-term survival in the patients with a solitary metastasis (Bonnet *et al*., 2008; Daliani *et al*., 2009; Eggener *et al*., 2008; Swanson, 2004). Median survival for metastatic RCC varied from 23 months (Kierney *et al*., 1994) to 41 months in patients with resected solitary metastatic lesions (Wroński *et al*., 1996). It remains a topic of debate whether metastasectomy is feasible for the patients who have nonsolitary lesions of RCC metastasis. A study showed that, compared to resection of nonsolitary lesions, resection of solitary metastasis did not necessarily lead to longer survival. However, an interval shorter than two years between primary tumor and metastases was correlated with a shorter disease-specific survival (van der Poel *et al*., 1999).

The laparoscopic approach to adrenal malignancy still remains controversial. More recently, some authors considered laparoscopic adrenalectomy (LA) to be safe for metastatic adrenal lesions, with equivalent long-term oncological outcomes to the open surgery and an additional benefit of being less invasive. LA has been recommended as a feasible initial approach for isolated adrenal metastasis (Bonnet *et al*., 2008; Porpiglia *et al*., 2004; Moinzadeh and Gill, 2005). Moinzadeh and Gill (2005) reported that 31 patients underwent a total of 33 LAs for adrenal carcinoma and no operative mortality was reported. One case was electively converted to open surgery. Mean tumor size was 5 cm (ranging from 1.8 to 9 cm). There were metastatic cancers in 26 cases and primary adrenal malignancy in 7 cases according to the pathological findings. Cancer specific survival at a median follow-up of 42 months was 53% and a 5-year actuarial survival was 40%. Seven patients had local recurrence (23%). There was no port site metastasis. We have accomplished LA for five patients with adrenal metastatic tumors. The mean follow-up was 18 months (from 3 to 56 months). Among the five patients, there was no endoperitoneal or trocar port-site seeding found, though one case died of systemic dissemination of the disease 14 months after the operation. We consider LA a feasible option following the principles of oncological surgery. Adrenalectomy for metastasis, with intent of prolonging survival, should be offered to patients with favourable tumor biology. Nevertheless, further investigations are required to evaluate the appropriateness of this operation.

In conclusion, we present a very rare case that highlights the unique behavior of RCC with an unusual metastatic site and favorable survival after multiple metastasectomy. We consider that, when the metastatic RCC is resectable, it should be surgically treated. The patients with chromophobe histological subtype or a long interval between primary tumor and metastases may live longer with no recurrence after metastasectomy.

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