Case Report

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Solitary Metachronous Drop Metastasis of a Rare Variant of Renal Cell Carcinoma to Ipsilateral Ureteric Stump - A Case Report

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Abstract

Metachronous metastasis of renal cell carcinoma (RCC) to its ureter has been scarcely reported. All such reports have involved clear cell RCC. We report the first ever case of an oncocytic variant of papillary RCC (OPRCC) - an extremely rare variant that spreads to the ipsilateral ureter. A sixty-five-year-old man, diagnosed to have non-metastatic left RCC with renal vein thrombus, underwent radical nephrectomy. Histopathology revealed large cells in papillary and tubular arrangements with abundant granular cytoplasm. On immunohistochemistry, cells strongly expressed Alpha-methylacyl-CoA racemase and were negative for CD10, C-kit, TFE3, and Melan A, hence a diagnosis of OPRCC, type 2 was given. During follow-up six months, he had a fluorodeoxyglucose avid lesion of size 2.8 cm in the proximal aspect of the left ureteric stump. Therefore, we performed robotic excision of the left ureteric stump and bladder cuff with pelvic node dissection. Pathological examination showed a ureteric mass infiltrating the muscularis propria and periureteric adipose tissue with features of OPRCC, similar to the nephrectomy specimen. It was Pax 8 positive with negativity for the urothelial markers Gata 3, uroplakin and p63, consistent with drop metastasis in a known case. Thus, clinicians must bear in mind that ureteric masses are not always of transitional cell variety and non-clear cell RCC can also metastasize to the ureter. This should be considered by pathologists while evaluating kidney specimens showing oncocytic features. This is the first case report of non-clear cell variety of drop metastasis of a rare histological variant of RCC to the ipsilateral ureter.

Keywords: Drop metastasis, papillary RCC, oncocytic, ureteric metastasis

Introduction

Ureteral metastasis is an uncommon entity. Breast and stomach are the common primary malignancies, which spread to the ureter (1). Renal cell carcinoma (RCC), mainly of the clear cell variety, spreads via hematogenous and lymphatic pathways to the lung, liver and bones. Although, few case reports of renal adenocarcinoma metastasizing to the ureteric stump have been reported, all have been of clear cell carcinoma variety (2). We present the first-ever case of drop metastasis of a rare variant of RCC to the ipsilateral ureter.

Case Report

A sixty-five-year-old diabetic and hypertensive male presented with hematuria in May 2020. On imaging, he had an eight cm left renal mid pole tumor with renal vein thrombus without distant metastasis. He underwent left robotic radical nephrectomy with para-aortic and hilar lymph node dissection. On gross examination, the tumor was unencapsulated, multinodular, solid, soft and friable with a yellowish-brown cut surface and extended into the renal sinus fat. The renal vein branch also showed a tumor thrombus and the mass did not infiltrate into perinephric fat. On histology, the tumor was composed of large cells arranged in papillary and tubular arrangements (Figure 1). The tumor cells showed a pleomorphic grade 3 nuclei and abundant granular cytoplasm. Focal cytoplasmic clearing, rhabdoid morphology, areas of necrosis and a few tumor giant cells were seen, however, sarcomatoid morphology was not seen. On immunohistochemistry, the tumor cells expressed Alpha-methylacyl-CoA racemase (AMACR) strongly and

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diffusely. They were negative for Ca 9, CD10, cytokeratin-7 (CK-7), C-kit, TFE3 and Melan A (Figure 2). A diagnosis of oncocytic variant of papillary RCC (OPRCC), type 2 with focal rhabdoid features, International Society of Urological Pathology nuclear grade 3 and pathological stage pT3aN0 was given. Ureteric and vascular margins were free. At six months, follow-up ultrasonography showed a three cm hypoechoic lesion in the left iliac fossa. In view of a raised creatinine level of 2.41 mg/dL, fluorodeoxyglucose, positron emission tomography (PET) computerized tomography (CT) scan without contrast was performed. It showed an avid soft tissue lesion of size 2.8 cm in the proximal aspect of the left ureteric stump abutting the left psoas muscle (Figure 3). Urine cytology was negative for malignant cells. In view of increased avidity for PET scan, it was decided to excise the mass. The patient underwent robotic excision of the left ureteric stump with bladder cuff excision and left pelvic lymph node dissection. Pathological examination revealed a tumor in the left ureteric wall filling up the lumen similar in appearance to the previously excised left renal tumor (Figure 4). The immunohistochemistry profile was similar to the renal tumor and it was Pax 8 positive with negativity for the urothelial markers Gata 3, uroplakin and p63. A diagnosis of an OPRCC type 2 infiltrating muscularis propria of the ureter and periureteric adipose tissue was given, consistent with drop metastasis in a known case. The pelvic nodes were negative for metastasis. His post-operative recovery was uneventful. Currently, he is doing well on a one-year follow-up. Written valid informed consent has been obtained from the patient for the publication of this manuscript.

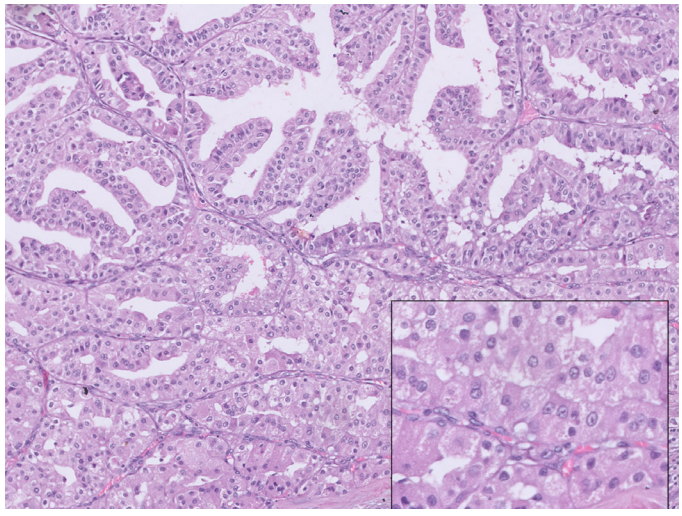

Figure 1. Left renal tumor 10x - Composed of cells arranged in papillary and acinar formations

Inset - 40x: The tumor cells show abundant eosinophilic granular cytoplasm. The nuclei showed conspicuous nucleoli (grade 3)

Discussion

The unpredictable nature of RCC with regard to its presentation, spread and metastasis is well known. Although the majority of the metastases are widespread, up to 10% can be solitary as well (3). RCC metastasizing to the ureter is an uncommon entity. There have been 57 cases of RCC metastasizing to ureter in the literature (4). Several mechanisms responsible for cancer spread are the hematogenous route, retrograde spread through

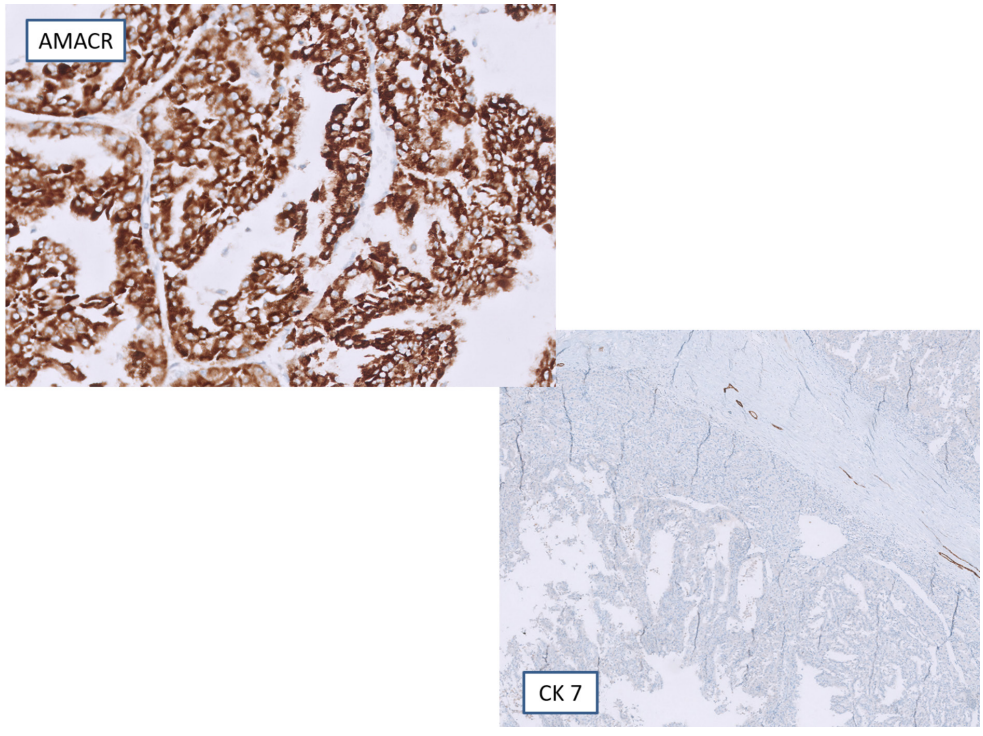

Figure 2. The tumor cells show strong and diffuse AMACR expression and are negative for CK-7

AMACR: Alpha-methylacyl-CoA racemase

veins and lymphatic channels and direct spread by seeding of urothelium (2). Any mechanism could be responsible for the solitary ureteral metastasis in the current case.

Our patient was incidentally found to have a ureteric mass on a routine follow-up after radical nephrectomy. Since PET CT showed uptake, the differential diagnoses were metastatic RCC or transitional cell carcinoma of the ureter. Generally, a surgical approach is preferred for solitary renal cancer metastasis due to high resistance to chemotherapy and radiotherapy and metastasectomy provides the best shot at cure (5). Thus, we performed robotic excision of the ureteric stump and bladder cuff along with left pelvic lymph node dissection much like Bhoopathy et al. (6) who performed a similar case robotically in a metastatic clear cell carcinoma. The histopathology reports of both, the radical nephrectomy specimen and ureteric stump were similar with regards to histological subtype (OPRCC), presence of necrosis and immunohistochemical features.

Although clear cell carcinoma is a common renal malignancy, papillary subtypes can be found in 10 to 15% cases (7). Papillary RCC (PRCC) has traditionally been divided into types 1 and 2 based on the nuclear features (8). The new 2016 edition of the World Health Organization Classification of Tumors of the Urinary and Male Genital Organs has mentioned an oncocytic variant (9). It was reported for the first time in 2005 in a series of 10 cases. The tumor is uncommon and there is a lack of understanding of its immunohistochemical features

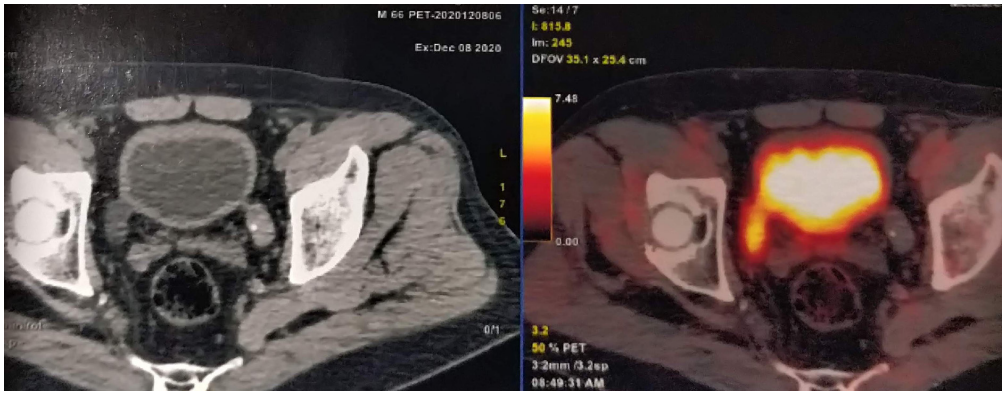

Figure 3. Avidity seen in the right ureteric stump on fluorodeoxyglucose positron emission tomography computerized tomography scan

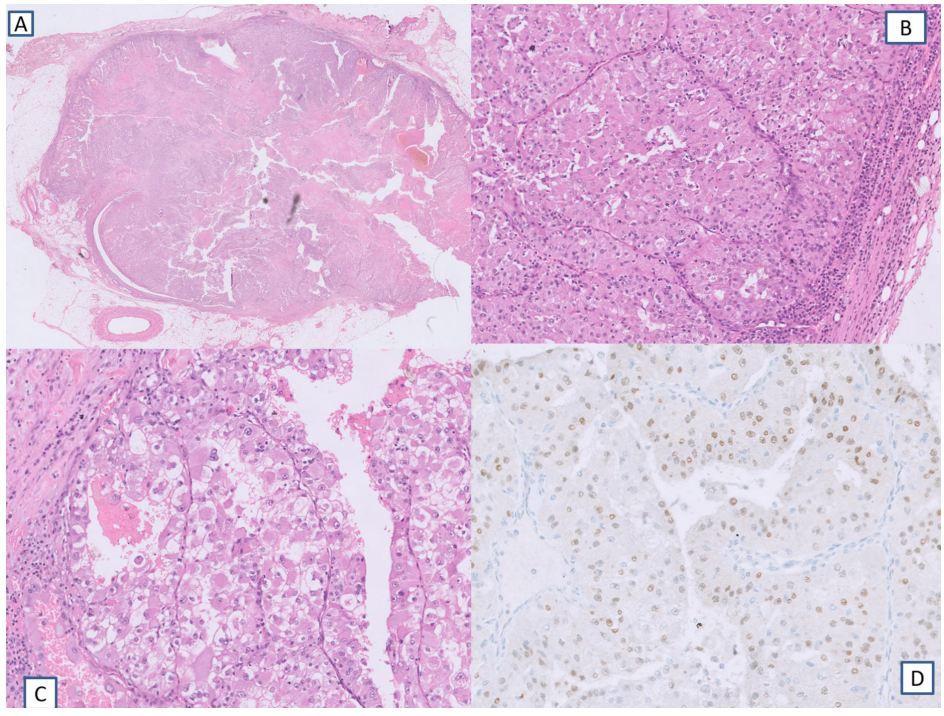

Figure 4. Left ureteric tumor

A- 4x tumor completely fills up the lumen

B&C- 20X and 40X -Eosinophilic tumor cells are similar in appearance to the renal tumor

D- The tumor cells express Pax 8

that makes the classification controversial (10). In 2016, Han et al. (11) characterized ORPCC as having a papillary structure with a single layer of cells with round or polygonal nuclei and eosinophilic granular cytoplasm. On immunohistochemistry, above 90% of the cells were positive for AMACR, whereas a few showed positivity for CD10 and vimentin (11). In this study, these pathological findings were mirrored, although CD10 was negative and vimentin immunostaining was not performed. The presence of rhabdoid features and areas of necrosis are associated with a poor prognosis. Until now, only 3 cases of metastatic OPRCC have been reported, none of them to the ureter (11). The current case, despite not having sarcomatoid features, metastasized to the ipsilateral ureter metachronously within six months of nephrectomy, highlighting the rarity of the case. The presence of renal vein thrombus, large areas of necrosis and partial rhabdoid morphology in the radical nephrectomy specimen were indicators of aggressive pathology and likely contributed to early metastasis. All of the previously reported cases of RCC metastasis to the ureteric stump have been of the clear cell type, which have occurred in a time interval ranging from four months to 12 years from nephrectomy (2).

Conclusion

The new oncocytic variant of PRCC is not well studied and can have serious metastatic implications. Clinicians must bear in mind that non-clear cell RCC can also metastasize to the ureter and ureteric masses are not always of transitional cell variety. This should be considered by pathologists while evaluating any kidney-related specimen showing oncocytic features. This is the first case report of non-clear cell variety of drop metastasis of a rare histological variant of RCC to the ipsilateral ureter. Further studies should help characterize and predict this uncommon variant.

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Ethics

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