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Ipsilateral Renal Cell Carcinoma and Transitional Cell Carcinoma: Synchronous Dual Primary Malignancies of Kidney

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Case History

A 50-year-old male presented to the nephrology department with complaints of hematuria with passage of blood clots in urine for last two years. He was a smoker and a known case of diabetic kidney disease with baseline serum creatinine levels of 2 mg/dl. In the past, he underwent coronary artery bypass graft for ischemic heart disease. With the current complaints and previous medical history, the patient was admitted in the nephrology department. Investigations revealed that the patient was anemic (hemoglobin 6gm/dl, serum iron 19 mcg/dl, total iron binding capacity 476 mcg/dl, transferrin 456 mg/dl, ferritin 14.85, vitamin B12 195 ng/mL) and had deranged kidney function tests (serum creatinine 1.89mg/dl, blood urea nitrogen 15.44 mg/dl, spot urine protein-creatinine ratio 4.83). The serum electrolyte levels, thyroid hormone levels and liver function tests were with normal range. Routine urine analysis showed numerous RBCs along with dysmorphic ones. Few WBCs and trace sugar were seen; however, ketone bodies were not detected. Contrast enhanced KUB revealed an ill-defined lesion measuring 3.7 x 2.9 x 2.6 cm in the superior pole of right kidney with multiple filling defects in calyces suggestive of blood clots [Fig 1a and b]. Laparoscopic-guided right nephrectomy was done and sent for histopathological examination. The kidney measured 15x9x4 cm. On serial slicing, two distinct tumors were identified, one involving the pelvicalyceal system while the other involving the upper pole of kidney. The tumor in pelvicalyceal system measured 3.5x3 cm, and had a grey brown and necrotic cut surface. The tumor at upper pole measured 1.5x1 cm and had a variegated cut surface. The ureteric lumen was filled with grey brown hemorrhagic material. Microscopic examination of the pelvicalyceal tumor showed moderately pleomorphic epithelial cells present as cohesive sheets and papillae (Fig 2a). Few scattered anaplastic bizarre cells were also noted (Fig 2b). Large areas of necrosis, hemorrhage and high mitotic activity were observed. The tumor was invading the wall of pelvicalyceal system, however, renal parenchyma, sinus fat, perinephric fat, ureteric stump and hilar vessels were free of tumor. On immunohistochemistry (IHC), these cells were positive for uroplakin (Fig 3a), GATA3 and CK7 (Fig 3b); and negative for CD10 (Fig 3c) and AMACR. Hence, the tumor was typed as high grade papillary urothelial carcinoma. The tumor at the upper pole was well circumscribed and was composed of clear cells arranged in pseudo acinar and pseudopapillary pattern (Fig 4a). Tumor cells showed mild nuclear pleomorphism and had an inconspicuous nucleolus (WHO/ISUP Grade 1) (Fig 4b). On IHC, the clear cells were positive for CD10 (Fig 5a); and negative for CK7 (Fig 5b), GATA3 and uroplakin (Fig 5c). Therefore, was labelled as clear cell renal cell carcinoma (clear cell RCC). This tumor was limited to kidney. Surgical margins were negative in both tumors. A final diagnosis of synchronous high grade papillary urothelial carcinoma (pT2) and clear cell RCC (pT1a) was rendered. The patient had an uneventful post-operative course, and was doing well at his first visit after surgery. He was lost to follow-up after that and could not be contacted to assess the prognosis.

Discussion

Renal cell carcinoma (RCC) and transitional cell carcinoma (TCC) are common malignancies of urological system when taken individually. RCC is an insidious neoplasm and accounts for approximately 3.3% global cancer diagnoses [1], of which clear cell RCC represent majority (~70%) of kidney cancer cases in adults. The incidence of primary tumors of renal pelvis is around 7% of all the renal tumors [2]. However, the simultaneous occurrence of both neoplasms in a patient is exceptionally rare. Ninie et al, retrospectively reviewed twenty-seven consecutive patients of synchronous RCC and urothelial carcinoma and found the concurrence of these tumors in an ipsilateral kidney unit in only 5 of them [3]. Majority of the patients present with hematuria; other symptoms include flank pain (19%) and

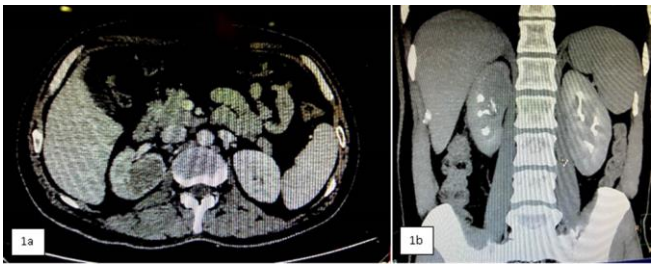

Figure 1: Axial (a) and Coronal (b) intravenous contrast enhanced CT images show an ill-defined hyperdense lesion in the superior pole of right kidney with multiple filling defects in renal calyces.

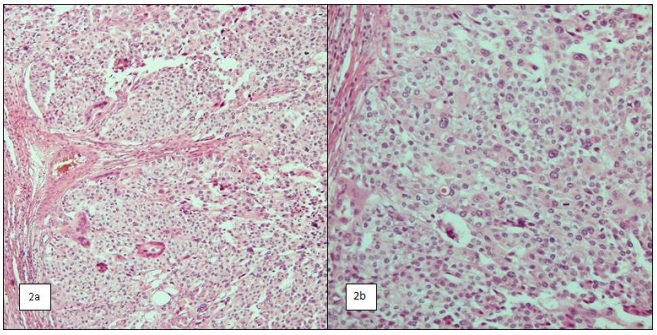

Figure 2: 2a: Urothelial carcinoma arranged in cohesive sheets and papillae (H and E 100x), 2b: Moderately pleomorphic tumor cells with few scattered anaplastic bizarre cells (H and E 200x)

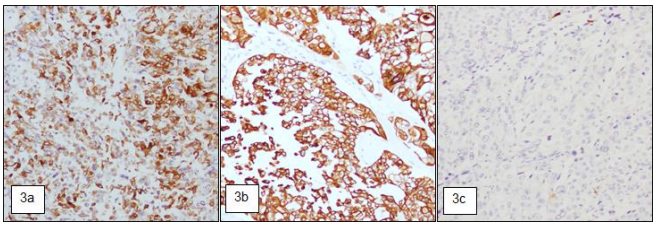

Figure 3: IHC staining (a) Uroplakin positive (200x); (b) CK7 positive (200x); (c) CD 10 negative (200x)

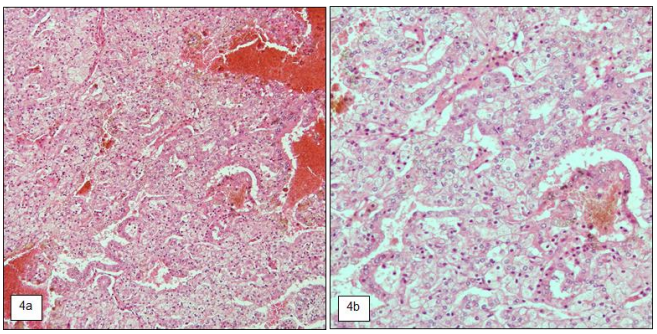

Figure 4: 4a: Renal cell carcinoma arranged in pseudoacinar and pseudopapillary pattern (H and E 100x) 4b: Tumor composed of clear cells with mildly pleomorphic nuclei and inconspicuous nucleoli (H and E 200x)

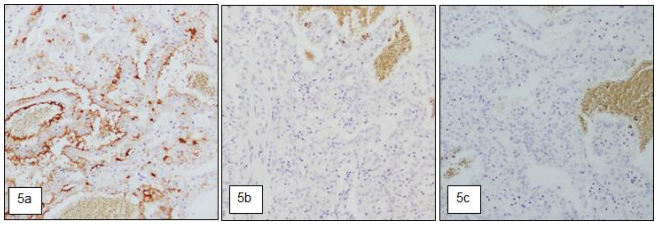

Figure 5: IHC staining (a) CD 10 positive (200x); (b) CK7 negative (200x); (c) Uroplakin negative (200x)

palpable flank mass (14%) [4]. There are several predisposing factors for multiple malignancies in a patient and may have a common carcinogen exposure, such as tobacco/ alcohol or a genetic predilection. In the present case, smoking was the only common causal factor for both the tumors. No other predisposing factor or a positive family history were noted which might have contributed to this rare disease.

It is important to keep in mind, that both the tumors should have distinct morphological features of respective malignancy. Possibility of a multifocal tumor should be categorically excluded before making a diagnosis of synchronous tumors. Pre/ intraoperative diagnosis of this synchronous presentation of dual tumors of kidney is important so that ureteral resection is performed to avoid chances of recurrence. The gold standard surgical management of such tumors is radical nephroureterectomy [5]. The prognosis and survival outcome of a patient with dual malignancies is most likely influenced by the more aggressive one of the two; like in our case, it was the urothelial carcinoma of the pelvis. Park et al, in their analysis of 86 patients with upper urinary tract TCC, concluded that the survival outcome of a ureteral primary was poorer as compared to a primary of renal pelvis [6]. The patient should be kept on regular follow up; and periodic cystoscopy for TCC and chest X-ray and abdominal CT scan for RCC metastasis should be done.

Conclusion

This coexistence of two histologically dissimilar malignant neoplasms in the same organ is a rare phenomenon; hence, knowledge of the possibility of synchronous primary genitourinary tumors is required for correct diagnosis and surgical intervention. The patients should be on strict follow-up to avoid chances of metastasis or recurrence.

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