Primary Tubulovillous Adenocarcinoma of Renal Pelvis: An Unusual Genitourinary Tumor

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KEYWORDS	ABSTRACT
Renal Calculi; Renal Pelvis; Pelvis Neoplasms; Tubulovillous; Adenocarcinoma	Prolonged inflammation or irritation due to renal calculi can induce glandular meta- plasia of the urothelium and even malignant neoplasm. Primary adenocarcinoma in pelvicalyceal system is a rare tumor in such patients. Here, a case of carcinoembry- onic antigen (CEA) positive primary tubulovillous adenocarcinoma in pelvicalyceal system is reported. A 57-year-old male with right abdominal pain and microscopic hematuria and the history of nephrolithotomy for recurrent renal calculi referred to our center. Radiological findings showed well-defined lobulated mass with calcifica- tion in interpolar region of right kidney extending up to pelvicalyceal system along with calculi in pelvicalyceal system and ureter with moderate hydroureteronephrosis. Laparoscopic right radical nephrectomy was performed. Histopathological examina- tion revealed tubulovillous adenocarcinoma of renal pelvicalyceal system with CEA positivity. Patient was asymptomatic and had no recurrence after one and a half years. Primary tubulovillous adenocarcinoma in renal pelvis though rare, is usually associ- ated with intestinal metaplasia of urothelium induced by prolonged chronic inflamma- tion and renal calculi.
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Introduction

Long-standing inflammation or irritation due to renal calculi can induce glandular metaplasia of the urothelium and even malignant neoplasm. Primary adenocarcinoma of pelvicalyceal system is a rare tumor in such patients. As per literature, about hundred such cases are reported and the commonest is mucinous adenocarcinoma. The current report is on a case of carcinoembryonic antigen (CEA) positive primary tubulovillous adenocarcinoma in pelvicalyceal system.

Case Report

A 57-year-old male presented with right side abdominal pain for two months. He had the history of right side pelvicaliceal calculus of 26 x 18 mm2 removed percutaneously by nephrolithotomy 10 years before the visit. He also had the history of recurrent renal calculi thereafter and managed accordingly. His laboratory investigations including complete blood counts, blood sugar, liver function tests, electrolytes, and lipid profile were within normal range. Serum creatinine (SCr) was 1.76 mg/dL. Urine examination showed proteinuria (+3) with microscopic hematuria and calcium oxalate dihydrate crystals. Ultrasonography (USG) showed 116 x 55 mm sized right kidney (RK) with multiple calculi in calyces, pelvis, and ureter along with 55 x 40 mm heterogeneous echogenic mass with internal echoes adjacent to pelvis, and moderate hydroureteronephrosis. Computed tomography (CT) urography showed 47 x 52 x 47 mm sized well-defined lobulated heterogeneously enhancing mass lesion with calcification foci in interpolar region

of RK extending up to pelvicalyceal system. Few calculi were observed in the mid and lower calyces and pelvis, the largest measured $11 \times 13 \times 16$ mm. There was moderate right hydroureteronephrosis with multiple calculi measuring $8 \times 9 \times 16$ mm in upper and $6 \times 7 \times 11$ mm in mid-ureter. He was subjected to laparoscopic right radical nephroureterectomy and specimen was sent for histopathological examination.

Gross examination revealed RK weighing 310 g and 10 x 6 x 5.5 cm in size. Outer surface was covered with perinephric fat and fascia. Capsule was adherent at places, otherwise could be stripped off easily. Outer surface was granular, bosselated, and pinkish brown. One cortical cyst was found measuring 0.6 cm in diameter at upper pole. Cut section showed ill-defined corticomedullary differentiation and dilated pelvicalyceal system filled with tumor mass measuring 4.5 x 3.5 cm in size, grey white in color, irregular and friable with areas of necrosis, and hemorrhage extending up to pelvis. Few calculi were present in mid and lower calyces (Figure 1). A cortical cyst measuring 0.6 x 0.6 cm was present at upper pole. Ureter also showed few calculi in upper and mid part. Multiple sections from the mass, renal parenchyma, and ureter were submitted for light microcopy. Sections were stained with Hematoxylin and Eosin. Immunohistochemistry for CEA and $CK_{34}\beta_{12}$ were conducted on the representative sections.

Microscopic examination from kidney tumor showed a malignant tumor comprising of cells arranged in glandular fashion. Individual cells were polygonal, moderately large, and had fine granular eosinophilic cytoplasm with well-defined borders, round vesicular nuclei, moderate to marked anisonucleosis with prominent nucleoli and coarse nuclear chromatin. Atypical mitotic figures were observed frequently. There was focal hemorrhage and necrosis in the tumor. The adjacent parenchyma showed focal calcification, tumor infiltration, and changes of acute tubular necrosis. No tumor infiltration was noted in ureter and vessels. Surgical margins were free from tumor infiltration (Figure 2a, 2b). The cyst showed features of simple epithelial cyst lined by flattened epithelial cells. CEA was positive and CK34\beta12 was negative (Figure 3). Final diagnosis was adenocarcinoma of renal pelvicalyceal system (tubulovillous pattern).

On the last follow-up of one and a half years postsurgery, the patient was asymptomatic with normal renal function and had no recurrence.



Figure 1. Gross photograph of cut section of kidney showing tumor occupying the dilated pelvicalyceal area, with changes of hydronephrosis

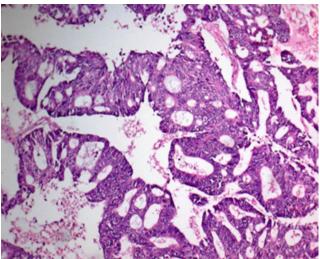


Figure 2a. Microphotograph of section of tumor mass showing tubulovillous pattern of adenocarcinoma; H & E stain, X50

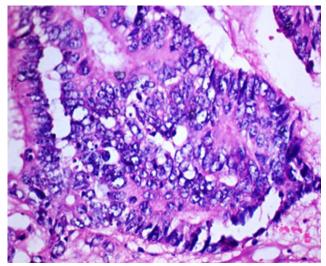


Figure 2b. Tumor cells are polygonal and moderately large, with fine granular eosinophilic cytoplasm and well-defined borders, round vesicular nuclei, moderate to marked anisonucleosis with prominent nucleoli, and coarse nuclear chromatin; H & E stain, X200

Discussion

Urothelial carcinomas (UC) are the most common tumors of renal pelvis and ure-ter comprising around 7% of all renal tumors. Squamous cell carcinomas (SCC) (metaplastic) are less common and primary adeno-carcinomas are the rarest (1). Various subcategories of adenocarcinoma are described such as tubulovillous, mucinous, and papillary non-intestinal. Tubulovillous and mucinous groups representing intestinal adenocarcinoma constitute 93% of cases (2, 3). Review of the literature showed very few cases of mucinous adenocarcinoma in kidney and ureter, but report of tubulovillous pattern in adenocarcinoma was not known to the authors. Five years of authors' institutional study revealed 67.9% UC, 25% SCC, and 7.1% adenocarcinoma in renal pelvic tumors. It showed that incidence of adenocarcinoma and SCC increased (4). It is usually preceded by glandular metaplasia of the urothelium induced by longstanding chronic inflammation or secondary to renal stones and the hypothesis of its pathogenesis was also shown stepwise in case reported by Sagnotta et al. (5, 6). Therefore, renal stone chemical analysis along with metabolic work up help in further management and definitely minimize recurrence of calculi. Early diagnosis and management can avoid chronic inflammation and thus prevent the progression to metaplasia

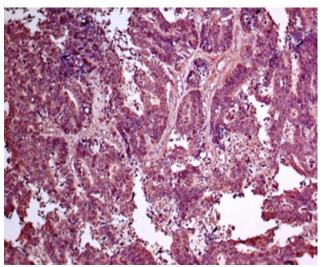


Figure 3. Immunohistochemistry showing CEA positive tumor cells; CEA, X50

and malignant neoplasm. The radiological investigations such as USG, intravenous (IVU), retrograde urography, and CT are helpful to plan management. Radical nephrectomy and urethrectomy including the bladder cuff is the treatment of choice for such tumors. Histopathological examination of the specimen biopsy is conclusive for the diagnosis. Differential diagnoses such as collecting duct carcinoma, high-grade urothelial carcinoma, papillary renal cell carcinoma, and neuroendocrine tumor should be considered. Immunohistochemistry (IHC) studies with CK7, CK20, CK₃₄β₁₂, PAX8, mucin, AE1/AE3, P63, vimentin, S100, AFP, and CEA help to differentiate and diagnose such tumors. In the current case, urothelial carcinoma and collecting duct carcinoma were ruled out as CK34β12 was absent and CEA positivity favored adenocarcinoma. Prognosis depends on the grade and stage of the tumor. One series reported that adenocarcinoma and sq¬uamous cell carcinoma were high-grade tumors (7).

Conclusion

The current case is addition of rarely reported cases of primary tubulovillous adenocarcinoma in renal pelvis usually associated with intestinal metaplasia of urothelium induced by long-standing chronic inflammation and renal calculi. 371. Tubulovillous Adenocarcinoma of Renal Pelvis

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providing the case details.

Conflict of interest

The authors had no conflict of interest.

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