



Oncology

A Rare Case of Renal Cell Carcinoma With Leiomyomatous Stroma and Concomitant Ruptured Adrenal Aneurysm



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ARTICLE INFO

Article history:

Received 22 June 2016

Accepted 30 June 2016

Keywords:

Renal cell carcinoma

Leiomyomatous stroma

Clear cell (tubulo) papillary renal cell carcinoma

Renal angiomyoadenomatous tumor

Adrenal aneurysm

ABSTRACT

Here we report a rare case of coexisting renal cell carcinoma (RCC) with leiomyomatous stroma and a ruptured adrenal aneurysm. The patient was a 75-year-old woman with acute abdominal pain. Imaging studies showed a left peri-renal hematoma and a mass in the left kidney. Left nephrectomy and adrenalectomy were performed. Pathological examination showed a ruptured aneurysm in the left adrenal gland. The renal mass was composed of tubules and acini of epithelial cells and a prominent leiomyomatous stroma. The tumor cells were positive for carbonic anhydrase IX, cytokeratin 7, and negative for AMACR, consistent with clear cell (tubulo) papillary RCC.

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Introduction

Prominent smooth muscle bundles in the stroma, so called leiomyomatous stroma, is an unusual finding in renal cell carcinomas (RCCs). It has been reported in clear cell (tubulo) papillary RCCs, renal angiomyoadenomatous tumors (RAT), and clear cell RCCs. Aneurysms in the adrenal gland are extremely rare. There are only 8 cases reported in the literature.^{1,2} Here we report a rare case of RCC with leiomyomatous stroma and a concomitant adrenal aneurysm.

Case summary

The patient was a 75-year-old woman who presented to the emergency room with acute abdominal pain. Her past medical history was significant for obesity, hypertension, diabetes mellitus, hyperlipidemia, and stage 3 chronic kidney disease. Her blood pressure was 180/110 mm Hg. Laboratory workup showed mild anemia, normal liver function, and decreased GFR (30–40 mL/min) with BUN and creatinine in the normal range. Computed tomography showed a large retroperitoneal hematoma around the left adrenal gland and the left kidney (Fig. 1A). A solid mass with central

scar was seen in the lower pole of the left kidney (Fig. 1B). Further laboratory tests of adrenal function showed normal range adrenal cortical hormone, elevation of plasma free normetanephrine 416 pg/mL (normal 0–145 pg/mL), plasma epinephrine 123 pg/mL (normal range 0–62 pg/mL). Clinically, these abnormal results raised the concern of a pheochromocytoma. Left nephrectomy and adrenalectomy were performed.

Pathological examination revealed a large peri-renal hematoma which was continuous with a ruptured dilated vascular structure (1.2 cm in diameter) in the left adrenal gland (Fig. 2A). In the lower pole of the left kidney, there was a well-encapsulated cortically based solid mass measuring 4.5 cm (Fig. 3A). The cut surface of the mass was tan pink with a central scar.

The adrenal medulla was completely replaced by an aneurysm, which had a thick wall that was ruptured (Fig. 2B). There was no evidence of a pheochromocytoma. The adrenal cortex was thickened with focal hemorrhage. The renal mass was well-encapsulated by a thick layer of smooth muscle and fibrous tissue (Fig. 3B). Prominent bundles of smooth muscle were also seen within the tumor (Fig. 3C). These muscle bundles were positive for smooth muscle actin (not shown), confirming the cells were smooth muscle cells. The epithelial component of the tumor was composed of tubules and small acini with no prominent papillae (Fig. 3D). The cells were cuboidal with clear eosinophilic cytoplasm. The nuclei were Fuhrman grade 1–2 with inconspicuous nucleoli. Linear arrangement of the nuclei away from the basement membrane was not prominent in this tumor. Immunohistochemistry demonstrated that the epithelial tumor cells were diffusely positive for carbonic anhydrase IX (CA IX)

Sources of support and funding: None to declare.

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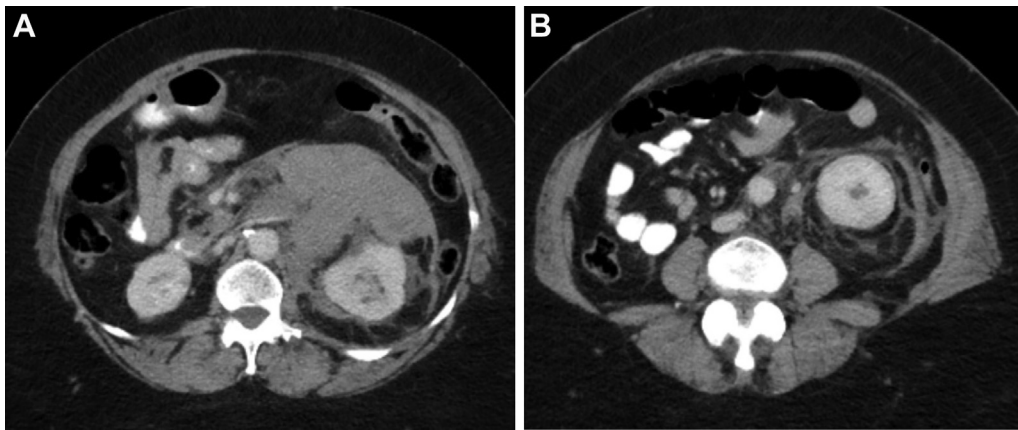


Figure 1. Pre-operative CT scan, enhanced. (A) A large hematoma near the left adrenal gland and the upper pole of the left kidney. (B) A solid well-circumscribed mass in the lower pole of the left kidney.

with cup-shaped membranous stain (Fig. 3E), strongly diffusely positive for cytokeratin 7 (CK7, Fig. 3F), and negative for AMACR (not shown). Rare tumor cells were positive for CD10 (not shown). The morphology and the expression profile of immunostaining markers were consistent with clear cell (tubulo) papillary renal cell carcinoma. The rest of the kidney showed marked arteriosclerosis, glomerulosclerosis, and tubular atrophy, likely resulting from the long term effects of diabetes mellitus and hypertension.

The patient developed pleural effusion one week after surgery, which was treated by thoracentesis. Her hypertension was controlled by medications. At one year after surgery, the patient remained tumor free.

Discussion

Coexisting adrenal aneurysms and RCCs are extremely rare and have not been reported before. Whether the coexistence of adrenal aneurysm and RCC in our current case represents a mere coincidence or a genetic syndrome remains unclear. Mutation in the VHL gene can cause Von Hippel Lindau syndrome, which is characterized by clear cell renal cell carcinoma, adrenal pheochromocytoma, and intracranial hemangioblastoma. It has been documented that pheochromocytoma can present with acute rupture and pseudoaneurysm formation. Our current patient had hypertension and

elevated plasma epinephrine and normetanephrine at the time of presentation, so pheochromocytoma was suspected. However, there was no evidence of pheochromocytoma on histology even after the adrenal specimen was extensively sampled. The medulla of the adrenal gland was replaced by the aneurysm and the cortex was thickened. In addition, the aneurysm had a thick vascular wall, which was inconsistent with a pseudoaneurysm. These findings suggest that the adrenal aneurysm was a true aneurysm. Its rupture and the hemorrhage might have destroyed the medullary tissue and also led to the abnormal test values of catecholamines.

The prominent leiomyomatous stroma in the RCC is another unique finding. The smooth muscle cells are polyclonal and represent a reactive component of the tumor.³ It can be seen in several types of renal cell carcinoma, including clear cell (tubulo) papillary RCC, RAT, and clear cell RCC. Leiomyomatous stroma is also present in other non-RCC renal tumors such as angiomyolipoma and mixed epithelial stromal tumor of kidney, but these two entities can be easily ruled out based on histology and immunohistochemistry. Clear cell (tubulo) papillary RCCs are usually well circumscribed by a thick capsule. Tumor cells are low grade, forming papillae, tubules, acini, and solid nests. On immunohistochemistry, tumor cells are strongly positive for CK7 and negative for CD10 and AMCAR. CA IX staining has a characteristic cup-shaped pattern. RATs are characterized by an intermixture of an

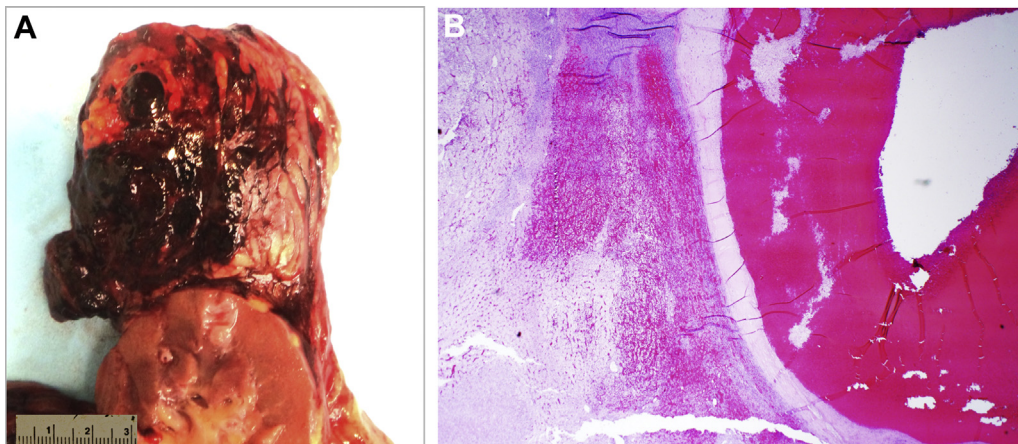


Figure 2. Ruptured aneurysm in the left adrenal gland. (A) Gross specimen. (B) Histology showing an aneurysm with thick wall.

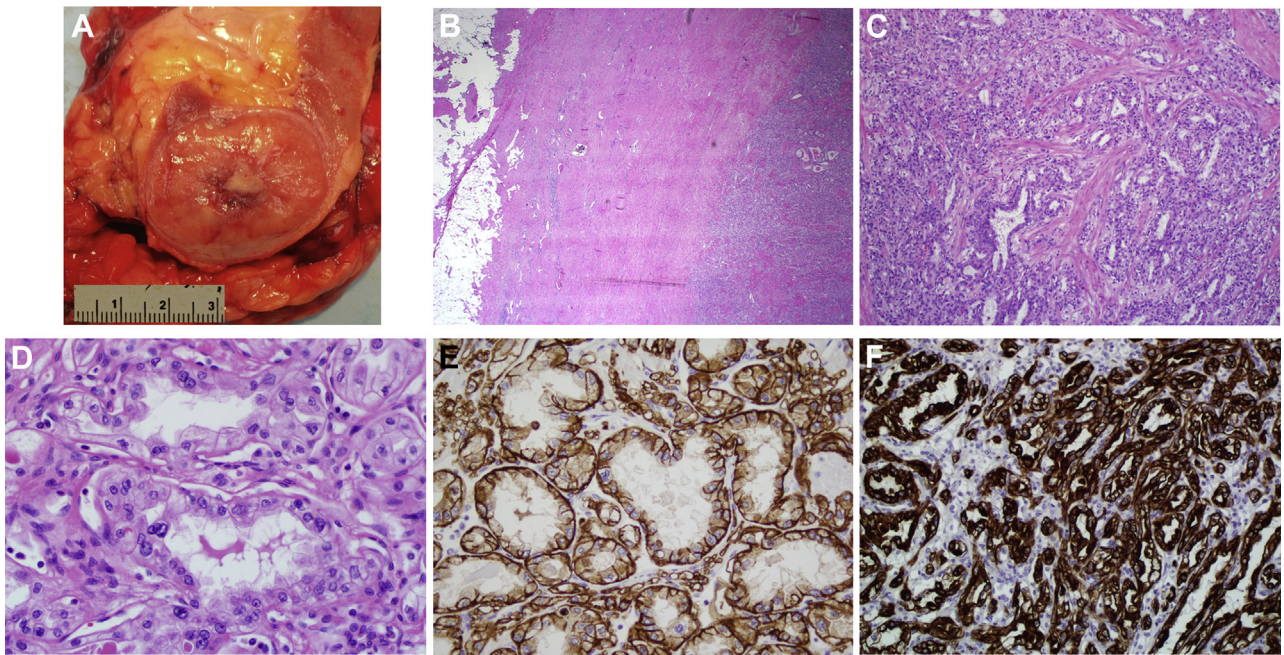


Figure 3. Renal cell carcinoma with leiomyomatous stroma. (A) Gross specimen. (B) Thick capsule of the tumor. (C) Tumor epithelial component with prominent smooth muscle bundles in the stroma. (D) The epithelial component of the renal mass showing tubule formation and low grade cytology. (E) Tumor epithelial cells are strongly positive for CA IX (box-shaped stain) and (F) CK7.

epithelial component with a leiomyomatous stroma and epithelial tubules lined by delicate capillary network. Tumor cells are positive for CK7, CK20, CAM5.2, AE1/AE3, and CD10. Clear cell RCCs usually have distinct morphological, immunohistochemical, and molecular features. The morphology and immunostain marker profile of our current case is most consistent with clear cell (tubulo) papillary RCC.

It remains controversial whether RAT should be considered as a variant of clear cell (tubulo) papillary RCC. There is evidence that clear cell (tubulo) papillary RCCs associated with or not associated with ESRD and RATs are in the spectrum of the same category of tumors.⁴ For example, Deml et al studied 27 clear cell (tubulo) papillary RCC and 7 RAT cases using histology, immunohistochemistry, and molecular assays.⁵ They found that clear cell (tubulo) papillary RCC and RAT were indistinguishable on the grounds of morphology, immunostain markers, and molecular changes. These findings were confirmed by Aron et al whose group studied 57 cases of clear cell (tubulo) papillary RCC and 7 cases of RAT.⁴ However, the current 2016 WHO classification did not fully address this controversy and classified RAT in the emerging entities category. Clinically, both clear cell (tubulo) papillary RCC and RAT

are low grade tumors and have indolent behavior, so their distinction may not have clinical significance.

Conflict of interest

There is no conflict of interest.

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