Case Report

Chromophobe renal cell carcinoma of the kidney with neuroendocrine differentiation: A case report with review of literature

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Abstract

Chromophobe renal cell carcinoma (chRCC) is a distinctive type of malignant kidney tumor characterized by large cells with defined cell membrane. Primary renal neuroendocrine tumors (NET) are rare with morphology similar to NET at other sites. There are few case reports describing the coexistence of these 2 neoplasms within the same tumor mass. We describe a case of chRCC with neuroendocrine features in a 70-year-old male patient who presented with hematuria and right flank pain. The histological and immunohistochemical features of both components were characteristic with no overlapping features. The neuroendocrine element was associated with nodal metastasis.

Key Words: Chromophobe, neuroendocrine carcinoma, RCC

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INTRODUCTION

Chromophobe renal cell carcinoma (chRCC) is a malignant tumor of the kidney that constitutes 4-5% of all renal tumors.[1] Renal neuroendocrine tumors (NET) are rare but considered to be a distinct entity in the 2004 World Health Organization classification scheme.[2] Composite tumors of the kidney are even rarer; however, various combinations have been reported including renal cell carcinoma (RCC) with angiomyolipoma[3] and clear cell RCC with NET.[4] chRCC has been described in association with other renal tumors like collecting duct carcinoma, conventional and sarcomatoid RCC.[4-7] Three case reports have been reported showing the co-existence of chRCC and renal NET.[5-7] Here, we describe an interesting renal cell neoplasm composed of both chRCC and neuroendocrine carcinoma.

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CASE REPORT

The present case report is about a 70-year-old hypertensive male patient with a long history of hematuria and left flank discomfort. Laboratory investigation showed normal hemoglobin count and liver function test. Creatinine was slightly elevated (126 Umol/l) normal range is (53-115 Umol/l); urine analysis showed 8 red blood cell/HPF and urine culture was normal.

Contrast-enhanced axial computed tomography (CT) images obtained during the nephrographic phase show a 14 cm heterogeneously enhancing mass in the left kidney with perinephric stranding.

He was admitted for left radical nephrectomy which passed uneventfully and the patient started on the postoperative analgesia and resumed oral diet 24 h postoperatively.

The day after, he developed chest pain and drop in his blood pressure (BP) to 80/50, electrocardiogram shows acute ischemic changes in the left ventricle with elevated cardiac enzymes and troponin T.

He was connected to the cardiac monitor and resuscitated until the BP elevated to 97/57 temporarily.

During the preparation for cardiac catheterization, the BP dropped again and the patient was coded. After 3 failed resuscitation, the patient was announced dead.

PATHOLOGICAL FINDINGS

Gross features

Gross examination of the left nephrectomy specimen showed a well-demarcated and encapsulated tumor occupying most of the kidney and measuring 14 cm × 13.5 cm. Cut section of the tumor is heterogeneous with foci of brown and yellow-white cut surface along with foci of hemorrhage [Figure 1]. The tumor grossly infiltrates the renal sinus and perinephric fat.

A single 2 cm × 1.5 cm perihilar lymph node was also submitted separately.

Microscopic examination

The mass is composed of two different components with a different histological appearance. The main component consisted of solid nests and sinusoidal pattern of cuboidal to polygonal cells with well-defined cell border, pale to deeply eosinophilic cytoplasm and hypechromatic pleomorphic nuclei with focal rasinoid appearance and perinuclear haloes [Figure 2a]. Binucleated and multinucleated cells were present. These nests were separated by delicate fibrovascular septae. The second component is composed of mainly of descohesive sheets of cells with plasmacytoid appearance [Figure 2b] and focal trabecular and insular pattern of smaller round tumor cells with abundant eosinophilic granular cytoplasm and finely granular chromatin. [Figure 2c]. Foci of hemorrhage and necrosis were noted. The tumor infiltrates the perinephric fat and the renal sinus with foci of vascular invasion. The surrounding renal parenchyma shows glomerulosclerosis, tubular atrophy and congested blood vessels.

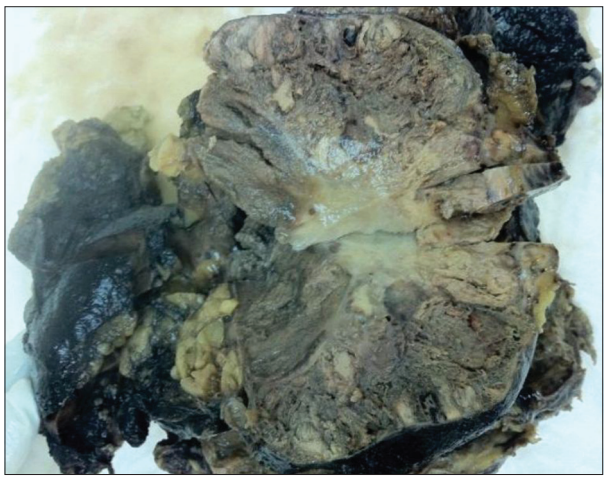

Figure 1: Gross morphology. Cut section of the right kidney showing a well-demarcated large tumor with a heterogeneous cut-surface, brown in color with yellow and hemorrhagic foci

The lymph node showed evidence of metastasis, consisted exclusively of the second component with neuroendocrine features.

Immunohistochemical findings

Immunohistochemical examination confirmed the presence of two different populations of tumor cells. The first component with typical histological features of chRCC was positive for cytokeratin (CK) AE1/AE3 (AE1/AE3, Dako, 1:50) and CK7 (OVTL-L-CE, Novocastra, 1:50) [Figure 3a], while negative for vimentin (V9, Dako, 1:100). The second component showed strong expression of vimentin [Figure 3b], CK AE1/AE3, Synaptophysin (polyclonal, cell marque, 1:200) [Figure 3c] and CD56 (1B6, 1:50; Novocastra) while negative for CK and CD38 (Novocastra, 1:100).

DISCUSSION

chRCC is a distinctive type of renal neoplasm that was 1st described by in 1986.[6,8] It comprises approximately 4-5% of renal tumors.[8] Histologically, these tumors are characterized by compact architecture, prominent cell borders and variable cell size. Two variant has been described, the classical and eosinophilic variant.[6]

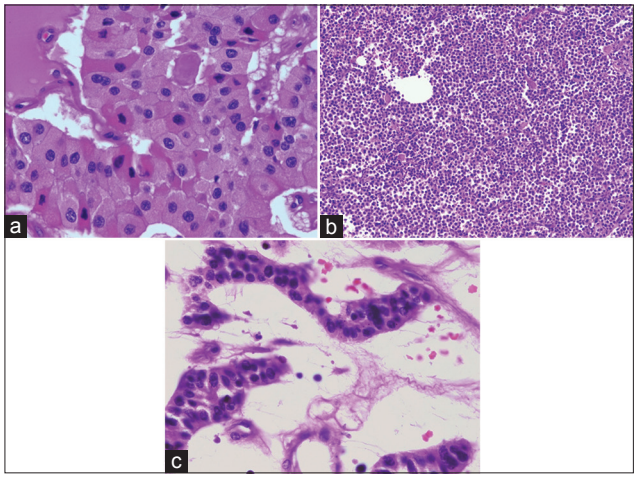

Figure 2: Microscopic features. (a) The first component of the tumor consists of solid nests and sinusoidal pattern of polygonal tumor cells with abundant eosinophilic cytoplasm, rasinoid hyperchromartic nuclei and well-defined cell borders (H and E, ×400), (b) The second component composed of dyscohesive sheets of smaller cells with plasmacytoid appearance (H and E, ×100), (c) Focal insular pattern of cells with abundant cytoplasm and finely granular chromatin (H and E, ×400)

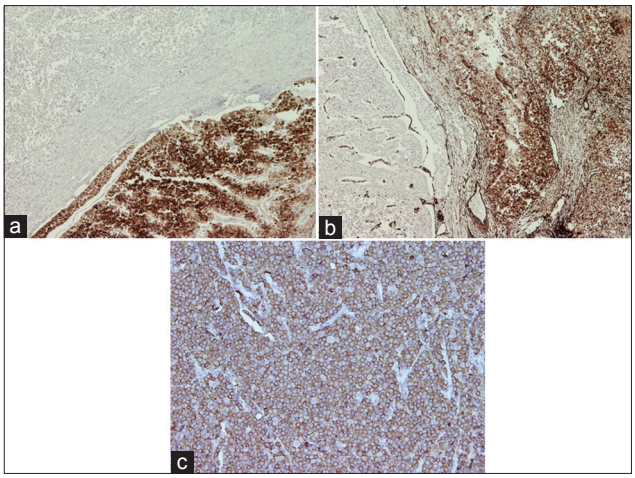

Figure 3: Immunohistochemistry study. (a) The chromophobe renal cell carcinoma (chRCC) component was strongly positive for cytokeratin 7 (DAB, ×40). (b) The nuclear envelope component was positive for vimentin while the chRCC was negative (DAB, ×40). (c) Strong positivity for synaptophysin in the second component of the tumor (DAB, ×100)

Renal NET are extremely rare and have been reported in the literature as case reports.[9] Only 62 cases of renal carcinoid tumor have been reported in the English literature and primary small cell carcinoma of the kidney is even rarer with only 18 cases reported.[9] Only one case of large cell neuroendocrine of the kidney that has been described.[9] The origin of primary renal NETs is still controversial since neuroendocrine cells are not found in the normal renal parenchyma. However, different theories suggest that NETs in the kidney may arise from primitive totipotential stem cells that subsequently differentiate in a neuroendocrine direction.[9]

NET of the kidney has been reported in association with clear cell RCC,[4] mucinous tubular and spindle cell carcinoma[10] and chRCC.[5-7] The association between chRCC and neuroendocrine carcinoma was 1st reported in 2008 by Parada and Pena.[6] They described a case of RCC in a 56-year-old male who presented with right flank pain and hematuria. The tumor showed a mixture of classical and eosinophilic pattern of chRCC, in addition there were foci that showed insular, glandular and rosette formations. These foci were positive for CK and neuroendocrine markers chromogranin A, neuron-specific enolase and CD56. Thereafter, Kuroda *et al.* reported another case in a 79-year-old Japanese man who presented with significant weight loss and found to have a huge right renal mass.[5] The histology of the mass showed mainly mixed classical and eosinophilic pattern of chRCC. In addition, there was a component of smaller neoplastic cells arranged in ribbon-like cords with rosette formation and a third component of malignant spindle-shaped cells. The chRCC showed typical immunoprofile pattern of chRCc with positivity for CK7, CD82, CD117 and E-cadherin. The second component was in addition positive for CD56 and focally positive for synaptophysin. The spindle cell component was positive for CK7, CD82 and vimentin. The case was diagnosed a chRCC with neuroendocrine differentiation and sarcomatoid changes.

Roy *et al.* in their study have reported a composite tumor of the kidney in a 34-year-old male.[7] There were two distinct masses in the left kidney. One mass showed the histological and the immunohistochemical characteristic of chRCC while the other separate mass was a carcinoid tumor. The carcinoid tumor presented at a higher stage with nodal metastasis.

Up to our knowledge our case will be the 4th case in the English literature describing a hybrid tumor showing chRCC admixed with foci of neuroendocrine differentiation. The clinical presentation of our case was similar to the one reported by Prada which is flank pain and hematuria. The CT scan finding was also similar with the non-homogeneous appearance. Grossly the tumor in both cases was large, well-circumscribed pale yellow to brown with heterogeneous cut surface.

The histology of our case was also very similar to that described by Parada and by Kourda showing foci of classical and eosinophilic variant of chRCC intermixed of foci displaying neuroendocrine features with smaller cells arranged mainly in solid sheets and displaying focal insular and ribbon-like pattern. Interestingly the second population of cells had a predominant plasmacytoid appearance with peripherally placed nuclei and abundant cytoplasm raising the differential diagnosis of plasmacytoma.

In the two previously reported cases,[5,6] the neuroendocrine foci showed immunohistochemical reactivity similar to the foci of chRCC and in addition they were positive to the neuroendocrine markers. However, in our case the second populations of cells were negative for CK7, which was positive only in the foci of chRCC but were positive for neuroendocrine markers synaptophysin and CD56.

Since most of the literature on renal NET is based on case reports and small series, their prognosis and management are unclear.[4] Although renal carcinoid tumors are considered to be low-grade NET, they can behave aggressively with lymph node and distant metastasis.[4,9] In the case reported by Roy *et al.*, the patient had metastasis to the para-aortic lymph nodes and the metastatic component was the carcinoid tumor element.[7] Similarly, in the case reported by Bressenot *et al.*, of composite clear cell carcinoma and carcinoid tumor, the patient presented with metastatic liver lesion and multiple osteoblastic vertebral lesion.[4] Our patient had an enlarged perihilar lymph node which shows metastatic deposits composed exclusively of the neuroendocrine component of the tumor. This confirms the clinical observation of the aggressive behavior of renal endocrine tumors.

In summary, we describe an interesting case of chRCC with foci of neuroendocrine differentiation. Finding of a neuroendocrine tumoral element in association with RCC is important because the endocrine element is the most aggressive component and should suggest the use of a modified adjuvant therapy.

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