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An Exceptional Sarcomatoid and Rhabdoid Variant of RCC - Marker of Dire Prognosis

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Abstract

Renal epithelial tumours that do not fit into any of the defined entities in the 2016 World Health Organization classification of renal cell cancer (RCC) are diagnosed as renal cell carcinoma, unclassified (RCCU). This category may include tumours with unique morphological patterns that fall outside the known categories, have overlapping features of known subtypes or are pure sarcomatoid tumours demonstrated to be of epithelial origin. We report a 65-year female who presented to us with hematuria and flank pain of 2 months duration. On evaluation, she was diagnosed with right renal tumor. On surgical exploration, the renal mass was firmly attached to lateral wall of inferior venacava (IVC), requiring local excision of lateral IVC wall with primary repair. Histopathological report was suggestive of double morphological variant of renal cell cancer consisting of sarcomatoid (75%) and rhabdoid (25%) differentiation. Patient had early massive recurrence of cancer at local site at 6 weeks follow up and succumbed during the hospital stay.

Keywords: Epithelial tumors; Sarcomatoid; Radical nephrectomy; Recurrence rhabdoid

Introduction

Renal cell cancer is the most common kidney tumour with an estimated incidence of 2.2%. RCC with sarcomatoid and rhabdoid features is an uncommon and highly aggressive malignancy. Sarcomatoid differentiation is characterized histologically by a dedifferentiated growth pattern of epithelial neoplasm into malignant spindle-shaped mesenchymal cells. Rhabdoid differentiation is characterized by sheets and clusters of variably cohesive, large epithelioid cells with vesicular nuclei, prominent nucleoli and large paranuclear intracytoplasmic inclusions. The dual variants are predictors of poor prognosis and progression free survival. We report a 65-year female diagnosed with this rare dual variant of RCC following radical nephrectomy. Patient succumbed in early post-operative period due to local recurrence and distant metastasis.

Case Presentation

A 65 year post-menopausal female presented with right flank pain and hematuria of 2-month duration. The pain was dull aching, radiating to back and relieved on taking oral analgesics. Hematuria was gross, intermittent and painless. Patient also complained of undocumented loss of weight and appetite in the past 1 month. Her past medical and family history was insignificant. On examination, patient was conscious, alert and her vitals were stable. Systemic examination showed mild fullness in the right flank region. Rest of the examination was normal. On investigation, her hemoglobin was 10.2 gm/dl, serum creatinine – 0.9 mg/dl, liver function, serum electrolytes and coagulation profile were normal. Urine analysis showed full field red blood cells. Ultrasonography of abdomen reported 6 x 7 cm hyperdense mass in the right kidney. Contrast enhanced CT abdomen revealed an 8*7 cm exophytic, heterogenous enhancing infiltrative lesion arising from mid and upper pole of right kidney with loss of fat planes with segment IV of liver and medially placed inferior venacava (Figure1 and 2). The chest X ray was normal. Patient was counselled for radical nephrectomy. Under general anesthesia, right subcostal incision was given and abdomen opened in layers. The hepatic flexure of colon was densely adherent to the upper pole of kidney. It was carefully dissected and mobilized medially. The lower pole of kidney was lifted and renal hilum dissected cautiously. A single renal artery and vein were ligated and cut. The upper pole of the kidney with tumor was densely adherent to lateral wall of inferior venacava, underlying psoas muscle and liver suggestive of local infiltration. After meticulous dissection and with assistance of surgical gastro-enterologist, upper pole of kidney was freed from the liver. The inferior venacava control was taken and side satinsky clamp was applied. The tumor with the segment of IVC wall was excised and specimen retrieved. IVC repair was done with prolene 4-0 suture. Complete hemostasis was achieved. Cut specimen of radical nephrectomy showed ill -defined grey white, firm tumor in mid pole of kidney with infiltration into adjacent renal parenchyma. The tumor was invading the renal sinus and perinephric fat. In the post-operative period, patient had severe pain at local surgical site which required opioids for pain relief. Patient was discharged on day 5 of surgery. Microscopic images of histopathology showed ill-defined tumor with extensive areas of necrosis. The tumor constituted 60% of kidney and tumor cells were arranged in nest with intervening thin branching network. In addition, there were areas of sclerosis, congestion, hemorrhage and moderate chronic inflammation. Atypical spindle cells with marked nuclear pleomorphism and abnormal mitotic figures accounted for 75% of tumor cells suggestive of Sarcomatoid variant of RCC. On immunohistochemistry, large epithelioid cells with central eosinophilic intracytoplasmic inclusions, positive for vimentin, CAIX, CK19 and CD 10 and negative for desmin and actin were also noted suggestive for rare Rhabdoid variant of renal cell cancer (Figure 3). The final report was Fuhrmann grade 4, sarcomatoid and rhabdoid variant of RCC. Patient returned at weeks' time with severe pain which was managed with intravenous analgesics. At 6 weeks follow up, patient was admitted again was significant loss of weight and appetite, unbearable surgical site pain and weakness. On evaluation, CT imaging showed large hypodense lesion in the right renal fossa with multiple metastatic deposits in the lungs (Figure 4). Ultrasound guided biopsy from the lesion showed metastatic renal cell cancer suggestive of recurrence. She succumbed during the hospital stay due to cardio-respiratory failure.

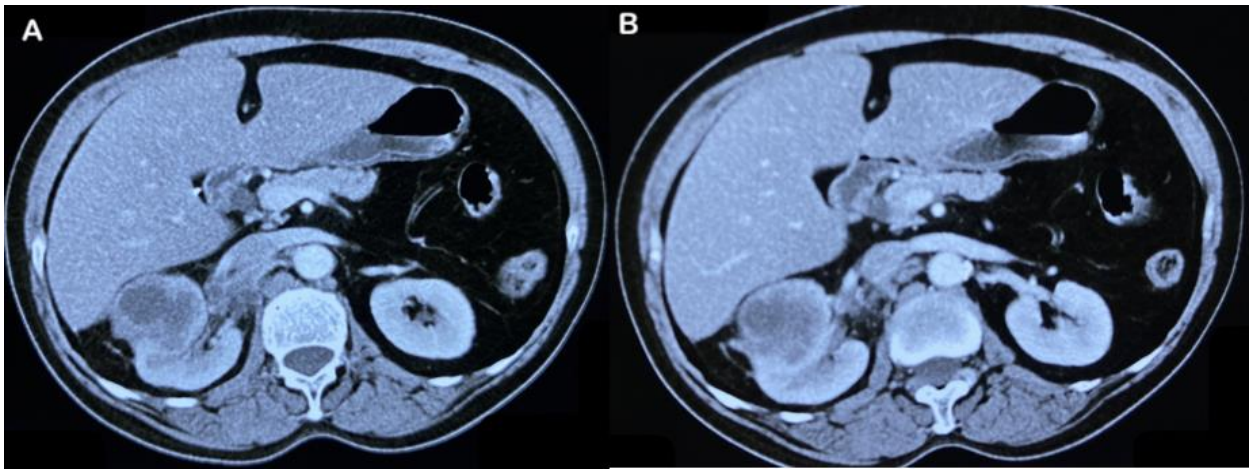

Figure 1A and B: Contrast enhanced CT abdomen axial images showing heterogenous enhancing mass in upper and mid pole of right kidney with central area of necrosis.

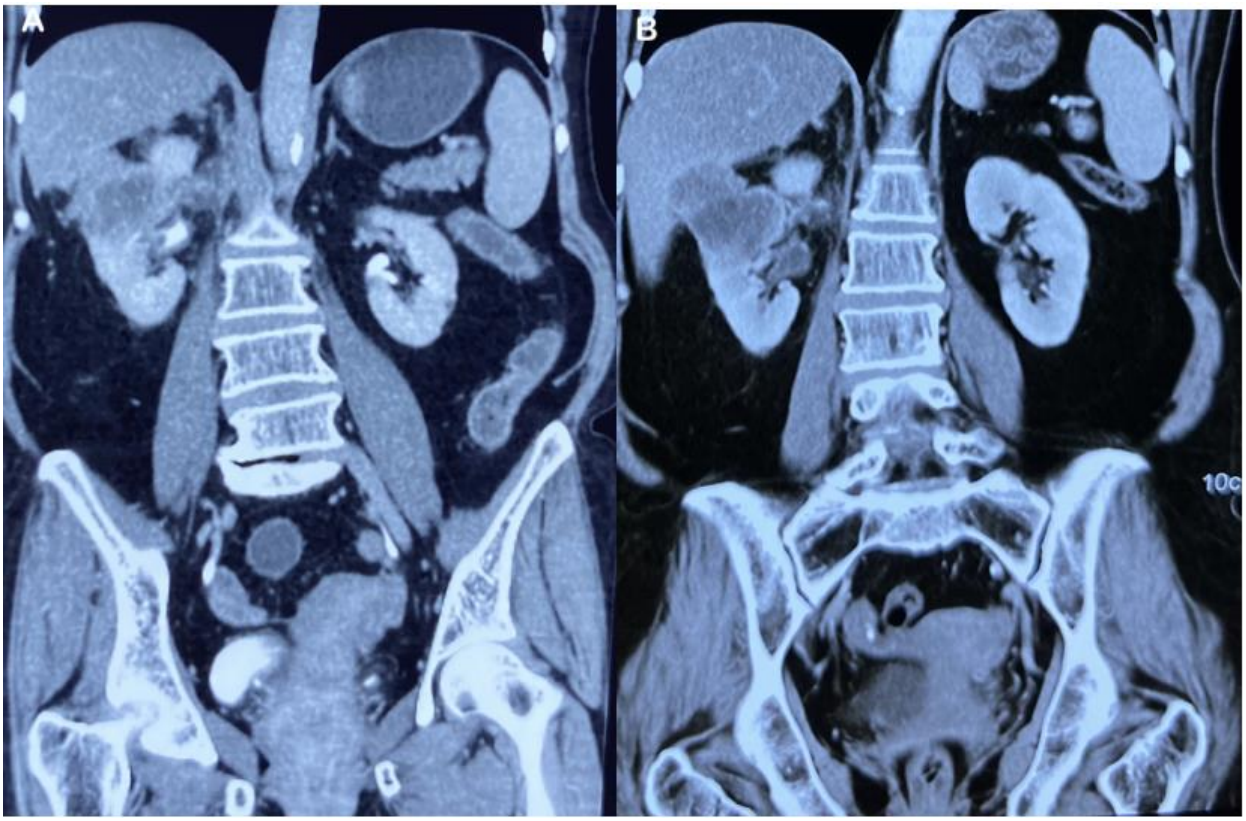

Figure 2A and B: Contrast enhanced CT abdomen coronal images with delayed cuts showing renal mass with central necrosis and loss of fat planes with liver.

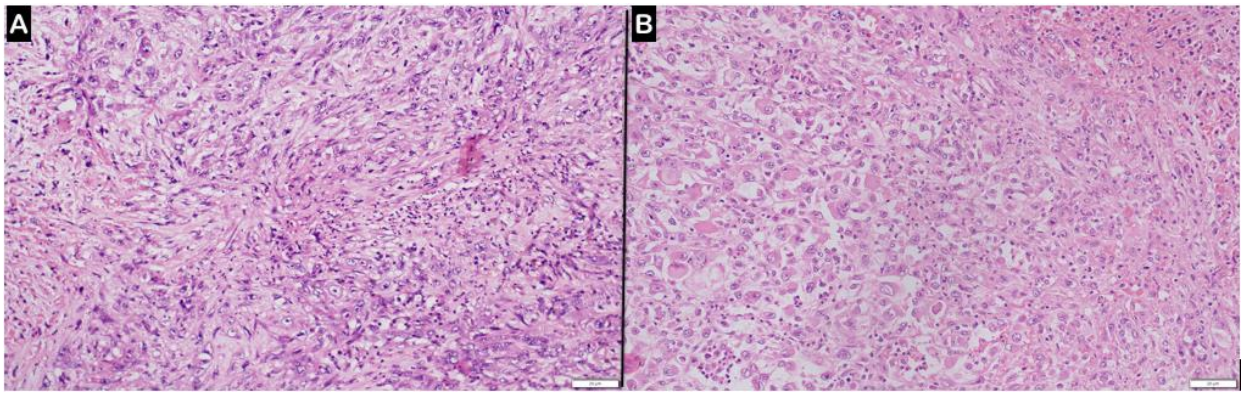

Figure 3: Panel of microphotographs showing; **(A):** Atypical spindle cells with marked nuclear pleomorphism and abnormal mitotic figures suggestive of Sarcomatoid differentiation of RCC; **(B):** Tumour arranged as solid clusters and sheets of variably cohesive large epithelioid cells with central eosinophilic intracytoplasmic inclusions suggestive of Rhabdoid differentiation of RCC.

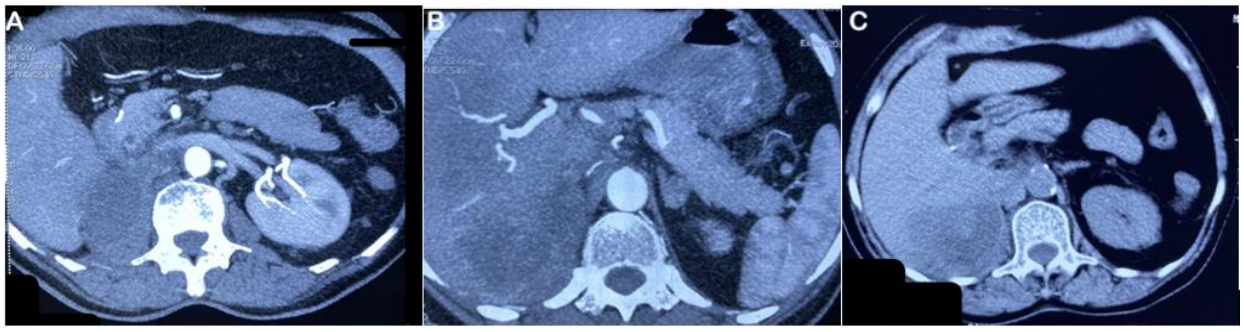

Figure 4A, B and C: Contrast CT imaging showing hypodense lesion in the right renal fossa with local infiltration.

Discussion

Renal cell carcinoma unclassified, is a diagnosis that is recommended for 'tumours that do not readily fit into any of the recognized subtypes' of RCC according to the 2016 World Health Organization Classification [1,2]. The growing awareness of emerging RCC sub-types and increasing utilization of immunohistochemical stains and ancillary studies may contribute to an increasing use of this category in practice [3,4]. Renal cell carcinoma (RCC) with sarcomatoid differentiation belongs to the most aggressive clinicopathologic phenotypes of RCC [5]. It is characterized by a high propensity for primary metastasis and limited therapeutic options due to its relative resistance to established systemic targeted therapy. Most studies report a poor median overall survival of 5 to 12 months [6]. Sarcomatoid features are found in 5-8% of clear-cell RCC (ccRCC), 8-9% of chromophobe RCC and 2-3% of papillary RCC [7]. About 75% of patients with sarcomatoid RCC generally present with metastatic disease and outcomes are modest. Xiang et al. reported a case of sarcomatoid RCC in a 45-year male with severe, aggressive and rapid disease progression following radical nephrectomy. The patient succumbed in 6 weeks following surgery [8]. Wang et al. reported that worse survival rate if >50% sarcomatoid elements are present in RCC with median survival time of 14 months [9].

RCC with rhabdoid morphology (RCC-RM) is a recently described variant of RCC, which has an aggressive biologic behavior and poor prognosis, akin to sarcomatoid RCC [10]. Renal cell carcinoma with rhabdoid morphology may represent a dedifferentiation of a classifiable-type RCC, similar to that of sarcomatoid differentiation. The recognition of RCC-RM is important as it allows for the inclusion of these high-grade malignancies into a category associated with poor prognosis despite lacking the spindle cell component classically identified as sarcomatoid change [11]. Zhang et al. reported that RCC with rhabdoid differentiation were significantly more likely to die than high grade clear cell RCC suggestive of its highly aggressive nature with risk of early recurrence and metastasis [12].

Yang et al. reported their experience of 125 patients of RCC and concluded that sarcomatoid differentiation and rhabdoid differentiation are both independent predictors of poor prognosis in RCC treated surgically [13].

Conclusion

Sarcomatoid and Rhabdoid variants of RCC are extremely rare. They are predictors of poor recurrence free survival and overall survival. In dept genetic analysis and molecular biology studies are needed to understand these variants and design new chemotherapeutic agents.

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