CASE REPORT

Extensive peritoneal carcinomatosis secondary to renal cell carcinoma with sarcomatoid and rhabdoid differentiation

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SUMMARY

Renal cell carcinoma (RCC), the most common malignancy of kidney, originates from renal tubular epithelium. It is subclassified based on histological and molecular features. Rarely, RCC can show focal to extensive sarcomatoid or rhabdoid differentiation. RCC with extensive sarcomatoid differentiation and no identifiable epithelial component is designated as unclassified RCC with sarcomatoid differentiation. Presence of sarcomatoid or rhabdoid differentiation is associated with poor prognosis. We describe autopsy findings in a case of RCC with extensive sarcomatoid and focal rhabdoid differentiation presenting with malignant ascites secondary to peritoneal carcinomatosis and multiorgan metastasis.

INTRODUCTION

Renal cell carcinoma (RCC) is the most common renal malignancy arising from renal tubular epithelium and constitutes 90% of renal malignancies in adults. Based on histology, RCC is classified into clear cell, papillary, chromophobe and collecting duct carcinomas. The uncommon histological variants include medullary, mucinous tubular and spindle cell, tubulocystic and thyroid-like follicular carcinomas. Most RCCs are sporadic. However, 4% of RCCs are associated with autosomal dominant familial cancer syndromes, including von Hippel-Lindau disease, hereditary papillary renal cell carcinoma, hereditary leiomyomatosis and renal cell carcinoma, and Birt-Hogg-Dubé syndrome. There are also distinct RCCs characterised and defined by the presence of translocations involving microphthalmia-associated transcription factor (MiTF), transcription factor binding to immunoglobulin heavy constant mu (IGHM) enhancer 3 (TFE3), or involving transcription factor EB (TFEB) genes. Unclassified RCC includes tumours which cannot be unequivocally categorised into one of the above groups.[1–3]

We report a case of RCC demonstrating a unique combination of sarcomatoid and rhabdoid differentiation presenting with rare peritoneal carcinomatosis. RCC with sarcomatoid differentiation (sarcomatoid RCC) is recognised as a distinct histological entity by the WHO classification of renal tumours (WHO, 2004) and is defined by the presence of foci of malignant spindle cells in any epithelial histological type of RCC. RCC with extensive sarcomatoid differentiation and no identifiable epithelial component is designated as unclassified RCC with sarcomatoid differentiation.[1 2] Rhabdoid differentiation is characterised by epithelioid cells with large eccentric nuclei and prominent nucleoli, globular eosinophilic paranuclear inclusions, and eosinophilic cytoplasm, reminiscent of rhabdomyoblasts. RCC with rhabdoid differentiation (rhabdoid RCC), although distinctive, is not a separate diagnostic entity, not being acknowledged in the 2004 WHO classification of tumours of the urinary system. Nonetheless, current literature suggests that it could represent a rare histological subtype of RCC.[4] Both sarcomatoid and rhabdoid RCCs represent high-grade aggressive RCCs with poor prognosis. We describe autopsy findings in a 53-year-old African-American man, who presented with massive malignant ascites due to peritoneal carcinomatosis secondary to rare unclassified RCC with sarcomatoid and focal rhabdoid differentiation. This case reflects the aggressive behaviour of this entity.

CASE PRESENTATION

A 53-year-old African-American man with medical history of type II diabetes and hypertension presented with acute on chronic abdominal pain. The patient had intermittent generalised abdominal pain for 8 months, which increased in severity for 1 month prior to admission. The patient also complained of significant weight loss and intermittent fevers with chills. CT examination showed a diffusely enlarged left kidney with retroperitoneal lymphadenopathy. A CT-guided biopsy revealed RCC with sarcomatoid and rhabdoid differentiation. Immunohistochemistry revealed tumour cells showing strong nuclear expression of paired box gene 8 (PAX8), which confirmed renal origin. Subsequently, chest x-ray revealed moderate bilateral pleural effusions. Ultrasound of the abdomen showed moderate ascites with multiple liver hypodensities consistent with metastases. Malignant cells were present in the ascitic fluid and cultures of the fluid were positive for vancomycin-resistant *Enterococcus durans*. The patient's hospital course was complicated by renal failure and acute respiratory failure requiring dialysis and intubation. The patient's health deteriorated rapidly leading to his death, less than 2 months after diagnosis of malignancy. An autopsy was performed.

Autopsy revealed massive ascites (5600 ml) and extensive peritoneal carcinomatosis with tumour deposits ranging from 0.5 to 3.5 cm, which involved the serosal surface of multiple abdominal organs (figure 1A,B). Cut sections of the diffusely

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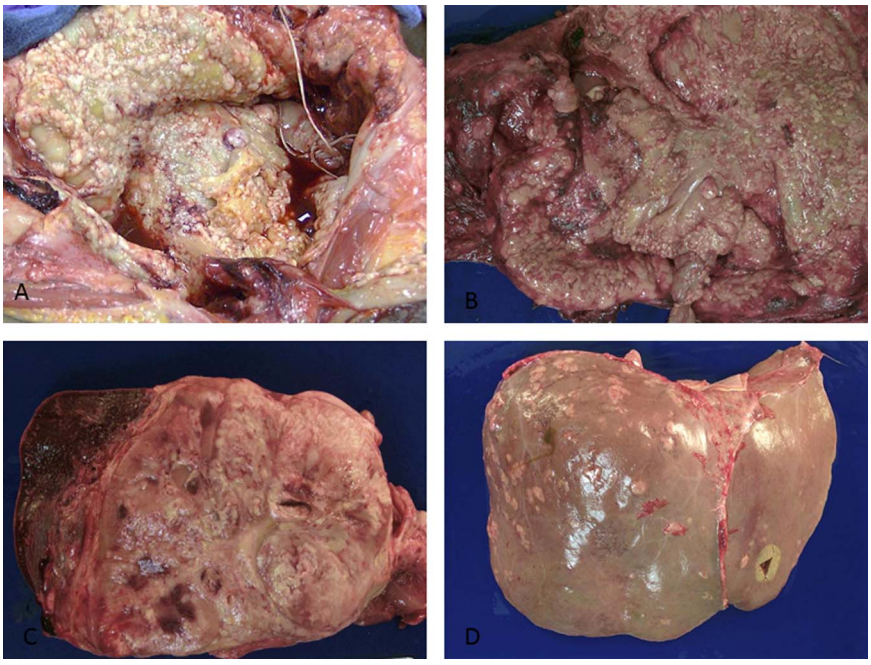

Figure 1 Extensive peritoneal carcinomatosis (A and B); cut surface of the left kidney showing tan-grey mass replacing the entire renal parenchyma and showing extensive necrosis (C); Multiple metastatic nodules in the liver (D).

enlarged left kidney revealed tan-grey tumour with extensive haemorrhage and necrosis. The tumour infiltrated into the renal pelvis, sinus fat and adjacent perirenal fat with direct invasion into the left adrenal gland and spleen (figure 1C). The renal mass did not extend into the renal vein. There was metastatic involvement of liver (figure 1D), both lungs and multiple mesenteric, retroperitoneal and pulmonary hilar lymph nodes. Microscopic examination of the renal mass and metastatic nodules revealed malignant spindle cells and occasional multinucleated tumour cells (figure 2A–C). The malignant cells showed high nuclear grade with prominent nucleoli and brisk mitotic activity. There was extensive tumour necrosis and lymphovascular invasion. The left renal mass showed focal areas of rhabdoid differentiation, characterised by large epithelioid cells having eccentric nuclei, eosinophilic paranuclear globules and dense eosinophilic cytoplasm (figure 2D). Immunohistochemical studies were performed on the renal tumour and the metastasis. Pancytokeratin was diffusely and strongly expressed in both the renal tumour and the metastasis. Vimentin and CD10 were diffusely and strongly expressed in the renal tumour only, but were not expressed in the metastasis. Epithelial membrane antigen (EMA) showed patchy expression in both the renal tumour and the metastasis. Cytokeratin 7 (CK7) was not expressed in the renal tumour or the metastasis. PAX8 nuclear expression was observed in both the renal tumour and the metastasis, confirming the renal origin of the tumour and the metastasis. No areas

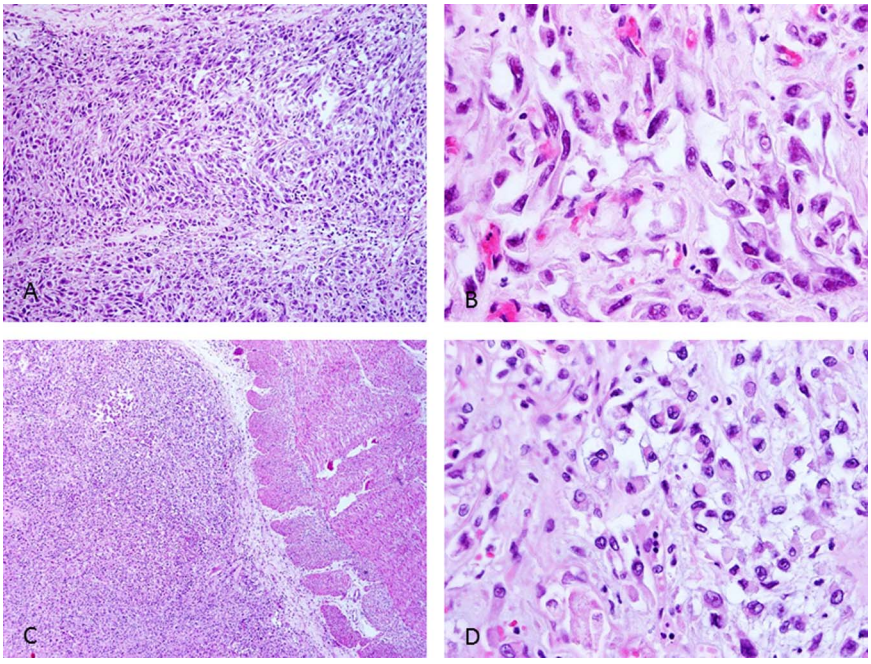

Figure 2 Malignant spindle cells consistent with sarcomatoid differentiation (A, ×100; and B, ×400); Sarcomatoid renal cell carcinoma involving the bowel wall (C, ×40); focal rhabdoid differentiation with epitheliod cells showing paranuclear eosinophilic globules (D, ×200).

of conventional RCC were identified. Therefore, diagnosis of RCC, unclassified type, with sarcomatoid and rhabdoid differentiation was made.

DISCUSSION

Previously, renal sarcoma or carcinosarcoma was the term used by pathologists to describe sarcomatoid RCC. In 1968, it was proposed that the sarcoma-like histology represented transformation of malignant epithelial cells.[5] Later chromosomal and genetic studies confirmed epithelial and sarcomatoid components are clonal but with extensive genetic diversity.[6 7] The sarcomatoid differentiation has been observed in association with all subtypes of RCC and thus is considered to represent the final common dedifferentiation of various renal epithelial malignancies. The factors leading to sarcomatoid transformation are unknown. Studies have shown that the sarcomatoid component has a high proliferation rate, as indicated by high Ki-67 expression,[8 9] reduced expression of cell–cell adhesion molecules,[9] and p53 overexpression[10] when compared to the epithelial component. It also demonstrates increased expression of hypoxia signalling pathway molecules including hypoxia-inducible factor-1 α, carbonic anhydrase IX, glucose transporter 1 and vascular endothelial growth factor,[11] all of which play a major role in tumour neovascularisation. Cases with a sarcomatoid component show increased expression of tyrosine kinase receptors KIT and platelet-derived growth factor receptor α (PDGFRA); although specific mutations have not yet been identified, these receptors might play a role in aggressiveness of sarcomatoid RCC.[12]

Clinically, abdominal pain and haematuria are common complaints of patients with sarcomatoid RCC. The average age at diagnosis is 60 years; and is approximately two times more common in men than women. Sarcomatoid differentiation is seen in approximately 5% of all RCCs. Approximately 80% of these cases are associated with clear cell RCC; but, when adjusted for the incidence rates, its frequency is higher in chromophobe RCC. The percentage of sarcomatoid component can be variable. However, a higher percentage (>50%) of sarcomatoid component is associated with poor prognosis. Approximately half of these patients present with distant metastasis and more than 80% of the patients die of disease; the median survival is less than 2 years.[13 14]

RCC with rhabdoid differentiation or rhabdoid RCC is rare with approximately 50 cases having been reported. Rhabdoid RCC resembles malignant rhabdoid tumour of kidney, a paediatric malignancy, but does not show mutations of hSNF5/INI1 gene with loss of expression of INI1 protein. Rhabdoid RCCs are biologically aggressive. They show higher proliferation rate[15] and overexpression of p53.[16]

Clinically, the average age at diagnosis in rhabdoid RCC is 62 years; and it is approximately two times more common in men than women. Abdominal/flank pain and haematuria are common presenting symptoms. Rhabdoid RCCs are associated with all RCC subtypes and are frequently associated with renal medullary carcinoma. The percentage of rhabdoid component is variable.

Three cases of concomitant sarcomatoid and rhabdoid differentiation in RCC have been previously reported, with only one case being categorised as unclassified RCC showing sarcomatoid and rhabdoid differentiation, similar to our case. Distant metastasis is seen in 70% of cases of rhabdoid RCC; the median survival is less than 1 year.[4 16–18]

RCC rarely present with peritoneal carcinomatosis, which is commonly associated with carcinomas of the gastrointestinal and female reproductive tracts, especially ovarian high-grade serous carcinoma. Including our case, only nine cases of RCC associated with peritoneal carcinomatosis have been reported.[19–23] This is the first reported case of unclassified RCC with sarcomatoid and rhabdoid features showing peritoneal carcinomatosis, which is not curable. The main goal of surgical and medical treatments in cases with peritoneal carcinomatosis is palliation.[24]

For pathologists, identification of sarcomatoid and rhabdoid differentiation is very important. It is currently recommended that any component of sarcomatoid and rhabdoid differentiation should be included in the pathology report.[4]

Learning points

- Sarcomatoid and rhabdoid components in renal cell carcinoma (RCC) represent dedifferentiation of conventional type of RCC.
- RCCs with sarcomatoid and rhabdoid differentiation are aggressive and associated with poor prognosis.
- Identification and reporting of sarcomatoid and rhabdoid differentiation in RCC is very important because of reduced survival and limited treatment options.

Contributors All the authors were involved in the care of the patient. Dr Esnakula collected the clinical information and prepared the draft. TJN, WG and BS provided the additional pertinent clinical information and reviewed and added critical information regarding the topic based on their expertise and current level of information.

Competing interests None.

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