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Case Report

Sarcomatoid Renal Cell Carcinoma with Rhabdoid Features Presenting as Xanthogranulomatous Pyelonephritis

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ABSTRACT

Renal cell carcinoma (RCC) encompasses a diverse range of kidney malignancies, with clear cell RCC being the most common subtype. This article discusses a rare case of a 61-year-old male initially suspected of having Xanthogranulomatous pyelonephritis, ultimately diagnosed with sarcomatoid RCC featuring focal rhabdoid differentiation. The aggressive nature of this case highlights the importance of thorough diagnostic procedures. RCC, representing 90% of kidney cancers, has various histological subtypes with distinct grading systems. Sarcomatoid and rhabdoid RCC, though rare, can occur in any subtype and are associated with poorer prognosis. Genetic alterations contribute to their aggressiveness. Current guidelines recommend imaging and biopsy for RCC diagnosis, with surgical management and surveillance for high-risk features. Emerging treatments like pembrolizumab and combination therapies signify a shifting paradigm in RCC management, necessitating tailored approaches based on histology and risk factors.

Keywords: Carcinoma; Renal cell; Clear cell; Neoplasm; Sarcomatoid; Histology; Immunohistochemistry

Introduction

Renal cell carcinoma (RCC) comprises a diverse range of cancers originating from renal tubular epithelial cells[1], with more than 10 distinct histological subtypes identified[1,2]. Clear cell RCC (ccRCC) is the predominant subtype, followed by papillary and chromophobe, respectively[3]. Sarcomatoid dedifferentiation, can occur in up to 15% of RCC patients[4], It is characterized by a transformative growth pattern of the epithelial neoplasm into malignant spindle-shaped cells, exhibiting aggressive behavior[5], This tumor manifests as sheets of malignant spindle cells with immunohistochemical and ultrastructural features resembling both stromal and epithelial cells[5], Initially considered a distinct histological subtype, sarcomatoid transformation is now recognized in current classification systems as a characteristic with the potential to arise in any subtype of RCC[6,7]. Rhabdoid differentiation is also observed in RCC, most frequently in clear cell RCC[8]. Pure rhabdoid RCC is an uncommon and highly aggressive malignancy of the pediatric population. In adults, pure rhabdoid RCC is extremely rare, while RCC with rhabdoid features are more commonly found alongside clear-cell carcinoma. Very few studies report rhabdoid features alongside sarcomatoid RCC. We present one such patient in whom renal mass was found to have sarcomatoid RCC with focal rhabdoid features which mimicked Xanthogranulomatous pyelonephritis.

Case Presentation

A 61-year-old male with a history of atrial fibrillation and heart failure. Admitted to the hospital due to progressive bilateral lower limb swelling secondary to worsening acute kidney injury. On work up, Renal ultrasonography showed enlarged right kidney measuring 20*13 cm with multiple complex hypoechoic lesions largest 10 cm, with suspected etiology of Xanthogranulomatous

pyelonephritis (XGP). On history the patient wasn't complaining from any right sided abdominal/flank pain, hematuria, weight loss or any urinary symptoms.

History of anemia Hb 7.5, been evaluated previously by hematologist, with bone marrow biopsy and flow cytometry, which ruled out MDS and myeloproliferative disorder. Further imaging was done, computed tomography (CT) of the abdomen and pelvis without intravenous contrast due to the impaired renal function, showed abnormal appearing right kidney, with multiple cystic and dense appearing regions measuring 17 cm in length, with retroperitoneal, enlarged lymph nodes adjacent to the IVC up to 3 cm.

In addition, CT chest showed suspicious pulmonary nodules for metastasis, a trial of IR guided drainage of the suspected abscess vs mass was done, which was inconclusive for any malignancy. Laboratory results are shown in (**Table 1**).

Table 1. Laboratory results.

		Normal range
Hb	7.5 g/dL	13.5-17 g/dL
MCV	87 fl	80-100 fl
Serum Iron	16 mcg/dL	65-175 mcg/dL
Ferritin	996 ng/ mL	24-336 ng/ mL
Iron Saturation	12.7 %	20-50%
TIBC	126 mcg/dL	250-450 mcg/dL
LDH	99 U/L	125-220 U/L
ESR	98 mm/hr	0-20 mm/hr
CRP	19.8 mg/L	<10mg/L
Creatinine clearance	30 mL/min	>90 mL/min

Renal nuclear scan (99 M MAG3 scan) showed negligible right kidney function, which supported the decision to proceed with nephrectomy. Pathological exam of the right radical nephrectomy showed poorly differentiated sarcomatoid renal cell carcinoma with focal rhabdoid features, involving the right entire kidney with extension into the renal sinus and perirenal fat with extensive necrosis, focal tumor invasion into the renal vein, but not lumen, negative extension into the adrenal gland and ureteral resection margin with staghorn calculus of the renal pelvis with abscess formation.

Positive right retroperitoneal lymph node for poorly differentiated sarcomatoid, and Rhabdoid RCC, infiltrating, fibroadipose tissue and regional blood vessels. Tumor markers with positive for, CK7, vimentin, AE1/AE3, PAX8, CD10, negative for CK20, RCC, P40, GATA-3. Pathological stage pT3a N1, MX (**Figures 1 and 2)** showing multiple cystic and solid appearing areas, dense calcifications in the inferior aspect.

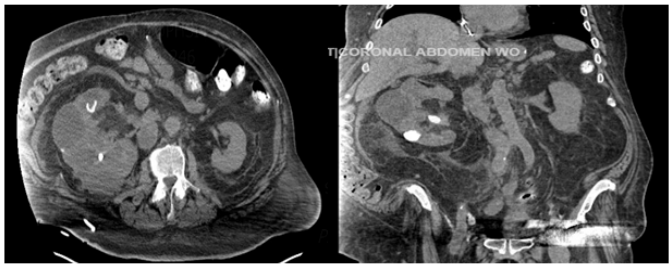

Figure 1. Computed Tomography of the abdomen and pelvis with oral contrast.

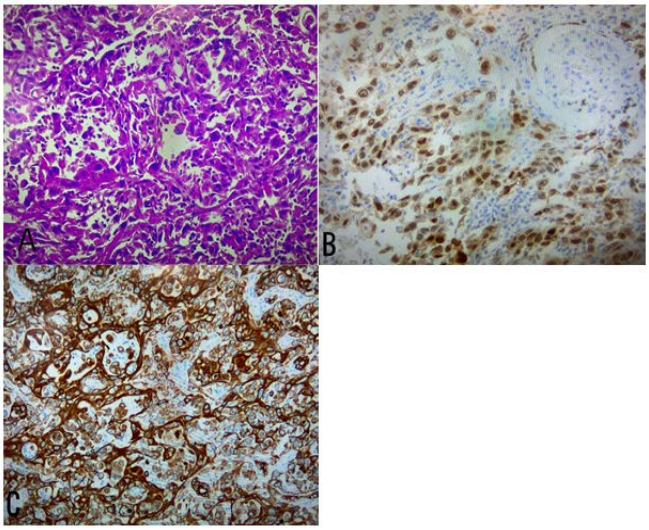

Figure 2. Histological findings

A: H/E stain, tumor shows moderate atypical spindle cells forming fascicles and rhabdoid features with no epithelial component, B: PAX8 slide, C: positive for Vimentin

he decision was made to refer the patient to a highly specialized cancer center due to the poor prognosis and requirement of an experienced center to tackle such an aggressive tumor, to our best current knowledge the patient passed away after 2 months of diagnosis and didn't receive any treatment.

Discussion

RCC is the most common kidney cancer, accounts for ~ 90% of all kidney cancer cases. In 2023, the estimated incidence of RCC is 81,800, resulting in nearly 14,890 of annual deaths[9] According to the classical histopathological classification, RCC can be classified into three main groups: clear cell carcinoma (ccRCC) which accounting for 75% of cases, papillary renal cell carcinoma (pRCC) making up 15–20% of cases, and chromophobe cell renal carcinoma (chRCC) representing 5% of cases[10]. Multiple grading systems have been used to stratify RCC [11] The WHO/ISUP grading system, introduced as a replacement for the Fuhrman grading system for RCC, relies on nucleolar prominence alone to identify grade 1 to 3 tumors. Conversely, extreme nuclear pleomorphism, sarcomatoid morphology, rhabdoid morphology are utilized to identify grade 4 tumors[12,13]. Tumor grade has been considered an independent prognostic factor for RCC, where higher grades carry worse prognosis[14].

Both sarcomatoid and rhabdoid RCC can arise in any type of RCC, more commonly in ccRCC, sarcomatoid dedifferentiation accounts up to 15% of RCC cases and the incidence of rhabdoid transformation within RCC is 4%[15,13] with a mean age of early 60[15]

Multiple genetic alterations that are alterations independent of those fundamental to original RCC tumor formation have been identified in sarcomatoid and rhabdoid differentiation these genetic alterations include chromosomal rearrangements such as loss of chromosomes 9q, 15q, 18p/q and 22q[16], Gains of 1q and 8q have been associated with metastatic disease[17,18] in sarcomatoid case, in rhabdoid tumors loss of *BAP1* or *PBRM1 on* chromosome 3p has been also noticed[19-21] and loss of chromosome 9, loss of chromosome 11q and loss of chromosome 17p[22]. These genetic alterations have been associated with poor outcome in renal cell carcinoma with

rhabdoid and sarcomatoid features[22-24], it tends to have an aggressive behavior with high tendency for early metastasis, causing a rapidly fatal outcome with a median survival rate of 8 in rhabdoid RCC[25] and 4-12 months in sarcomatoid RCC.

Management of Stage I disease is primarily surgical with either partial or radical nephrectomy, more frequent surveillance imaging studies are recommended post-surgery in sRCC patients[26]. Radical nephrectomy is preferred in locoregional RCC with sarcomatoid features, though even with early surgical management in localized sRCC; patients faced a 72% recurrence rate at a median time of recurrence of 26.2 months[27], For Patients with advanced disease; cytoreductive nephrectomy is recommended, as it showed improved survival with a median of 10.2 months in comparison to 5.5 months in patients who did not undergo surgery[28]. No benefit of radiotherapy on overall survival was demonstrated in comparison to surgical management alone[29]. Systemic cytotoxic chemotherapy failed to demonstrate improved survival for patients with sRCCs, while targeted therapy with VEGF inhibitors (i.e sunitinib, sorafenib, axitinib, pazopanib, tivozanib or bevacizumab) only showed limited overall response rates of 11-19%, even with combination of cytotoxic and targeted therapy response rates remained modest at best[30]. This resulted in increasing interest in studying the role of immune checkpoint inhibitors. Expression of PD1/PDL1 was shown to be higher in sRCCs (54%) in comparison to non-sarcomatoid RCC (17%), moreover retrospective subgroup analysis from CheckMate 214,KEYNOTE-426 studies demonstrated higher rates of PDL1 positivity 51%, 74.5–79.6% respectively[30,31]; therefore multiple trials have been done showing promising results for immune checkpoint inhibitors as a treatment modality for advanced sRCC, with 44% mortality risk reduction, and overall response rate of (52.6%) over sunitinib's (20.7%) which was considered the standard of care then[32], systemic therapy with Axitinib + pembrolizumab or Ipilimumab + Nivolumab or Axitinib + Avelumab or Atezolizumab+Bevacizumab was studied in the KEYNOTE-426[33] CheckMate 214[34] ,JAVELIN Renal 101[35] IMmotion151[36] Trials respectively, those therapies persistently showed improved outcomes as demonstrated in subsequent meta analyses[30,32].

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