

The Great Imposter: A Confusing Case of a Rare Renal Cell Carcinoma

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ABSTRACT

We report a 61-year-old male with sarcomatoid renal cell carcinoma (sRCC) in the context of multiple paraneoplastic syndromes, including thrombocytosis, leukemoid reaction, and paraneoplastic hepatopathy (Stauffer syndrome). The patient's clinical course was complicated by multiple medical challenges, extensive metastases, and persistent infection. This confusing presentation of a rare subtype of renal cell carcinoma (RCC) highlights the diverse and often misleading manifestations of this aggressive malignancy. Clinicians should be aware of the association between RCC, multiple paraneoplastic syndromes, and its propensity to present with systemic, non-renal symptoms.

KEYWORDS: sarcomatoid, renal cell carcinoma, paraneoplastic syndrome, leukemoid reaction

INTRODUCTION

With nearly 14,000 deaths and 63,000 new cases a year in the United States,¹ renal cell carcinoma (RCC) is a significant cause of malignancy-related morbidity and mortality. RCC is often termed the “great imposter” or the “Internist’s tumor” due to its variable presentation, which increases risk of delayed or missed diagnosis.² Sarcomatoid renal cell carcinoma (sRCC) is a rare, highly aggressive form that independently predicts poor survival³ and is often unresponsive to standard RCC treatments. Given sRCC’s potential for non-specific or misleading clinical manifestations, it is important for clinicians to recognize the protean presentations associated with sRCC. Here, we discuss a patient with sRCC presenting with multiple paraneoplastic syndromes and complicated by extensive metastases, persistent infection, and multiple medical challenges such as renal failure, hypotension, and deranged electrolyte levels.

CASE REPORT

A 61-year-old male without prior interaction with the medical system presented to the emergency department with hypotension and two months of progressively severe right lower quadrant (RLQ) abdominal pain. The pain was accompanied by anorexia, nausea, vomiting, and an unintentional

20–30-pound weight loss. At presentation, he was hypotensive (96/59, supine), tachycardic (115), and afebrile (97.6 F). Physical exam revealed temporal wasting, general weakness, evidence of dehydration, and right flank tenderness without palpable mass. There was no anterior abdominal tenderness. Laboratory values revealed acidosis (anion gap: 22; HCO₃⁻: 12 mEq/L), hyponatremia (125 mEq/L), hyperkalemia (6.5 mmol/L), thrombocytosis (1,176,000/mm³), leukocytosis (WBC 57,100/mm³), low hemoglobin (11.9 g/dL), elevated PT (14.4 sec), and elevated alkaline phosphatase (187 U/L). The patient’s elevated creatinine level of 6.68 mg/dL indicated renal failure. Urinalysis showed evidence of infection (160+ WBCs, many bacteria) and hematuria (2+ blood).

An abdominal/pelvic Computerized Tomography (CT) scan showed a large heterogeneous 10 x 10 x 19 cm obstructive right renal mass (**Figures 1 and 2**), with lytic lesions in the right femur and right iliac bones. The mass nearly obliterated the right kidney. Imaging also revealed an indeterminate 3 cm left lower pole renal lesion and indeterminate hepatic lesions. A CT Pulmonary Embolism (PE) demonstrated extensive bilateral parenchymal and pleural metastatic lesions.

The patient was stabilized and urgently treated for suspected tumor lysis syndrome and septic shock. The septic shock was potentially due to infected perinephric fluid positive for *E. coli* secondary to a bloodstream infection, pleural effusion, or pyelonephritis, or secondary infection from metastatic sites. Once stable, he required continued perinephric drainage and antibiotics.

A biopsy of the right pleural mass demonstrated malignant spindle cells, characterized by nuclear pleomorphism and numerous mitotic figures (**Figure 3**). The tumor was positive for cytokeratin; multiple additional immunohistochemical stains were performed, excluding the possibility of melanoma, solitary fibrous tumor, mesothelioma, and rhabdomyosarcoma. The presence of cytokeratin expression, multiple bilateral pulmonary nodules, and large renal mass was compatible with metastatic sarcomatoid renal cell carcinoma.

Subsequent imaging revealed numerous bilateral pulmonary nodules, suspicious for metastatic disease, that had enlarged since initial imaging 14 days prior. The patient’s course was complicated by recurrent pleural effusions which eventually required constant drainage and may have

contributed to his persistent infection. Imaging additionally demonstrated right retroperitoneal, perirenal, pelvic, right gluteal, and paraspinal rim-enhancing abscesses as well as multifocal pyelonephritis of the left kidney.

Figure 1. A CT abdomen pelvis with IV contrast (coronal) demonstrates a large heterogeneous 10 x 10 x 19 cm right renal mass (red arrow), largely replacing the right renal parenchyma.

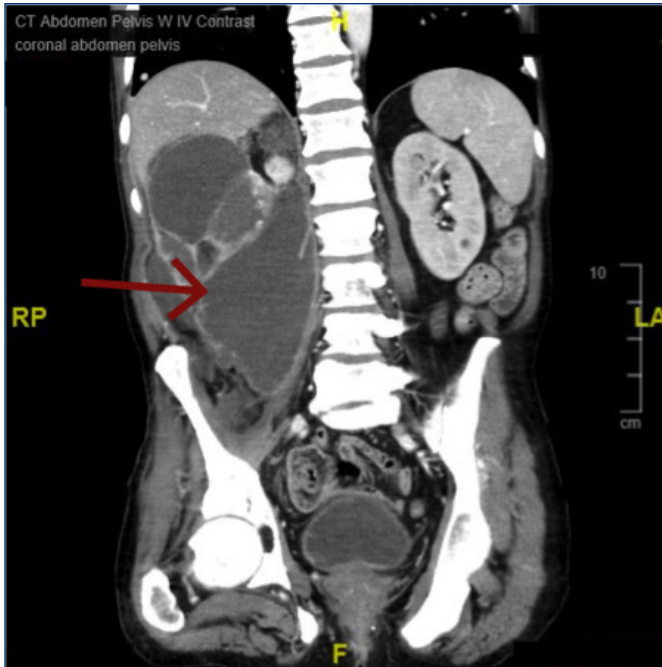
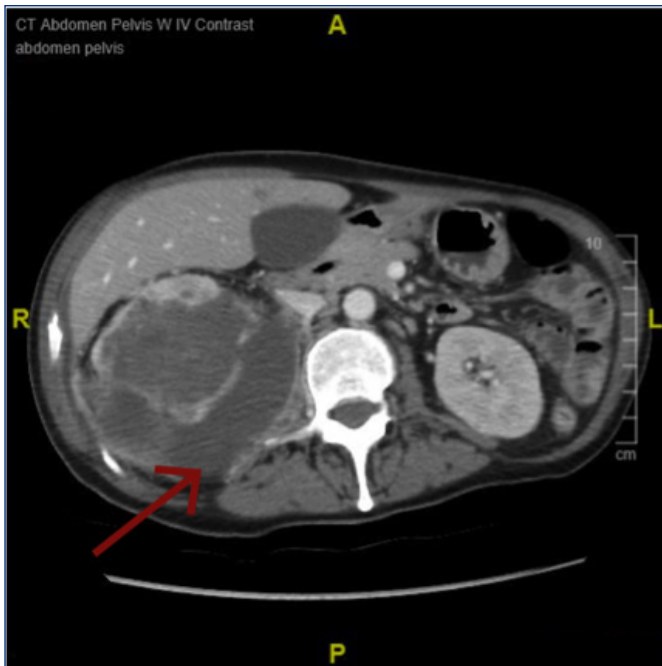
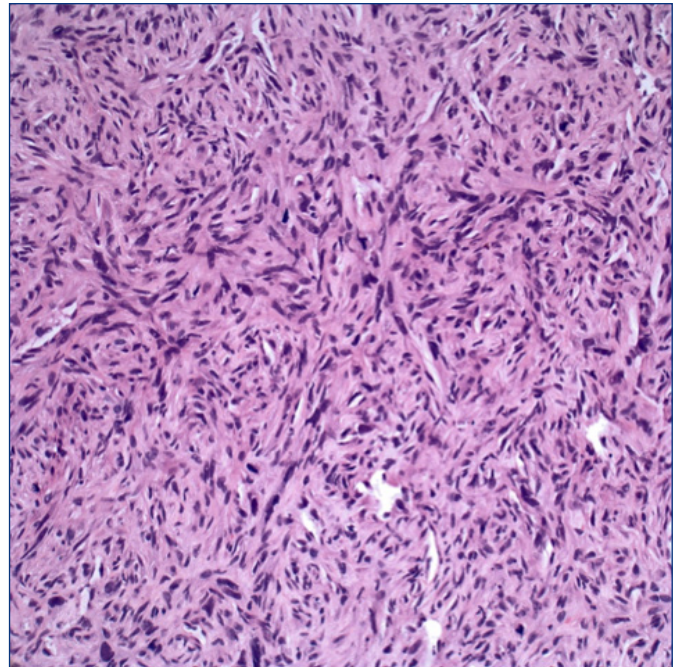


Figure 2. CT abdomen pelvis with IV contrast (transverse) again demonstrates a 10 x 10 x 19 cm right renal mass (red arrow).



The patient's deteriorating condition and persistent infection limited chemotherapeutic or surgical options; care was transitioned to comfort measures. He died 39 days after admission.

Figure 3. A high power view of the tumor demonstrates a malignant spindle cell tumor with nuclear pleomorphism and numerous mitotic figures (H&E, 200X)



DISCUSSION

Renal cell carcinoma classically presents as gross hematuria, flank mass, and flank pain, though the entire triad is present in less than 15% of patients.^{4,5} Up to 10–40% of patients develop paraneoplastic syndromes.⁴ Our patient's initial, non-specific symptoms of hypotension, nausea, and weight loss, in addition to the absence of gross hematuria or palpable flank mass, mimicked symptoms of more common infectious, inflammatory, or neoplastic disorders.

Our patient notably presented with multiple paraneoplastic syndromes associated with RCC, including thrombocytosis and leukemoid reaction. The mechanism underlying thrombocytosis in solid tumors is poorly understood, but may be associated with platelet release of angiogenic growth factors such as Vascular Endothelial Growth Factor (VEGF).⁶ Thrombocytosis in RCC is an independent predictor of poor prognosis, with higher platelet levels correlated to advanced stage.⁶ The patient's markedly elevated WBC count of $57.1 \times 10^9/L$ indicated a leukemoid reaction, defined by a peripheral WBC count of greater than $50 \times 10^9/L$ and persistent neutrophilia. Commonly associated with solid tumors of the lung, bladder, and ovary, leukemoid reaction has rarely been reported in RCC.⁷ Furthermore, malignancy is a common underlying cause of unintentional weight loss. Our patient's weight loss, anorexia, and nausea may have resulted from

renal failure, leading to cachexia and wasting; or from cancer cachexia, a muscle-wasting syndrome common in metastatic malignancies.⁸

In diagnosing renal cell carcinoma, it is important for clinicians to consider paraneoplastic hepatopathy (Stauffer's syndrome), a rare manifestation of renal cell carcinoma characterized by cholestasis with elevated alkaline phosphatase, erythrocyte sedimentation rate, alpha-2-globulin, and gamma-glutamyl transferase in combination with prolonged prothrombin and thrombin times and hepatosplenomegaly, without hepatic lesions.⁹ Stauffer's syndrome is a clinical diagnosis, reported rarely in other solid tumors. Each component noted is variably present, sometimes absent. The pathophysiology behind Stauffer's syndrome is poorly understood, but associations with elevated IL-6 are frequently reported.⁹ Our patient's liver dysfunction in the context of RCC is suggestive of Stauffer's syndrome.

Further complicating management, our patient presented with a rare, highly aggressive variant of renal cell carcinoma, sarcomatoid RCC (sRCC). sRCC accounts for a disproportionate fraction – around 15–20% – of stage IV RCC cases.¹⁰ Incidence of metastatic disease upon presentation is approximately 20–30%,¹¹ most commonly to the lungs, bone, lymph nodes, liver, and brain.¹⁰ Sarcomatoid differentiation can occur in any histologic subtype of RCC. The presence of sarcomatoid features is associated with a less favorable prognosis¹² and poor survival.¹³

Treatment options for sRCC are limited. While cytoreductive nephrectomy is the standard treatment, 5-year survival rates are as low as 14.8%.¹⁴ Trials of systemic therapies such as anti-VEGF therapy and IL-2 based immunotherapies have failed to improve outcomes.¹³ Early diagnosis and detection are important in establishing early intervention and may improve outcomes.¹³ Consequently, it is important for clinicians to understand the diverse, often non-specific, and confusing non-renal manifestations of RCC, particularly as paraneoplastic features may be the only presenting clues.

CONCLUSION

Sarcomatoid renal cell carcinoma is a rare, aggressive cancer with extremely poor outcomes. We present a patient with sRCC in the context of numerous challenging medical problems and multiple paraneoplastic syndromes. Our patient's non-specific presentation exemplifies the potentially misleading features of sRCC. Clinicians should consider renal cell cancer in selected patients with multiple, confusing paraneoplastic associations of thrombocytosis, leukemoid reaction, and unintentional weight loss.

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