Case Report

Immune Check Point Inhibition in Sarcomatoid Renal Cell Carcinoma: A New Treatment Paradigm

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Clinical Practice Points

- Sarcomatoid renal cell carcinoma is an uncommon histologic subset of renal cell carcinoma that portends a poor prognosis.
- Current treatment regimens demonstrate limited efficacy.
- PD-1 inhibition may be a promising approach in sarcomatoid renal cell carcinoma and should be considered as an option early in the management of these patients.

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Introduction

Sarcomatoid renal cell carcinoma (sRCC) accounts for approximately 5% of renal cell carcinomas (RCCs) and carries a dismal prognosis, with most case series reporting median survival of 3 to 10 months in patients with metastatic disease.[1-3] Sarcomatoid differentiation most commonly arises from RCC of the clear cell subtype, but may occur in other subtypes, such as papillary or chromophobe tumors.[4,5] Irrespective of pathologic subtype, the presence of sarcomatoid components in RCC portends a worse outcome.[6-8]

Currently, there is no standard front-line treatment for sRCC, and second-line treatment is seldom an option due to rapidly progressive disease and poor performance status. A small phase 2 trial demonstrated a median overall survival of 8.8 months with the use of a combination of doxorubicin and gemcitabine, suggesting a potential role for chemotherapy in patients with sRCC.[9] A more recent single-arm phase 2 study evaluating the combination of sunitinib and gemcitabine noted a median time to progression and overall survival of 5.5 and 10.0 months, respectively.[10] Thus, there is an urgent and unmet need to improve treatment options, especially in first- and second-line therapies.

In a series of 31 patients with sRCC, those treated with nephrectomy followed by high-dose Interleukin (IL)-2 had a median survival of 8.5 months, suggesting that sRCC is capable of eliciting immune responses.[3] Recently, immune checkpoint inhibitors, specifically those targeting the protein programmed death 1 (PD-1), or

Figure 1 Femur Biopsy. Hematoxylin-Eosin Staining of Tumor From Patient 1 Showing Renal Cell Carcinoma With Extensive Sarcomatoid Differentiation (70%) Infiltrating Between Pink-Red Bony Trabeculae

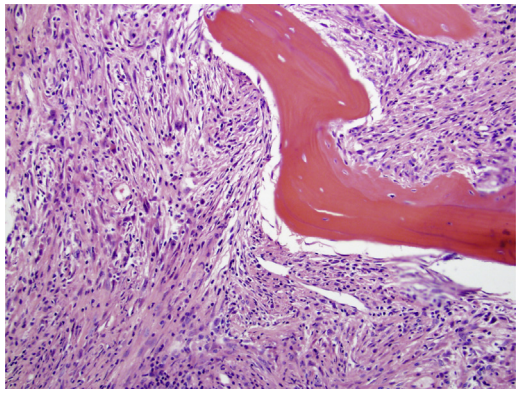

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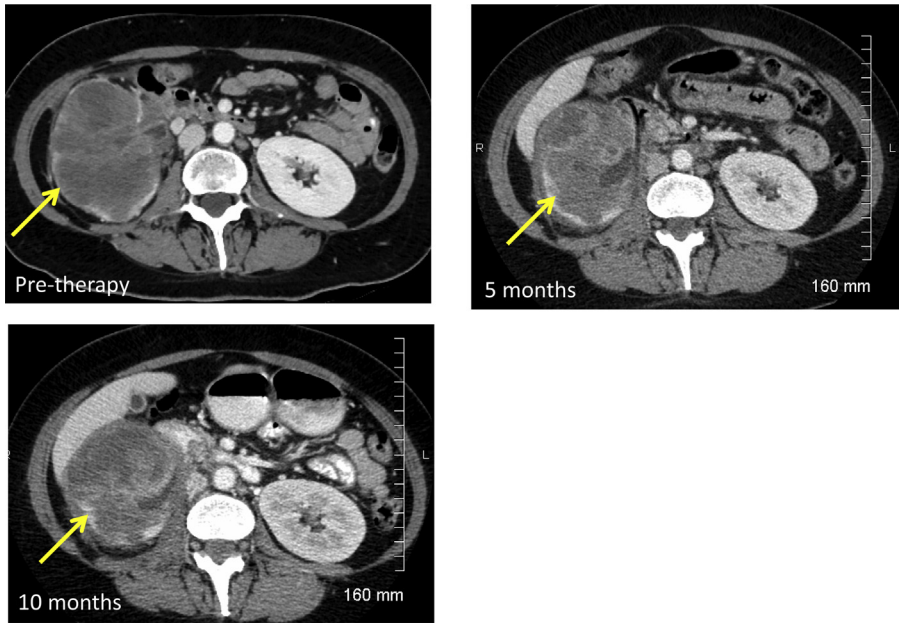
Figure 2 Primary Right Renal Mass. Axial Contrast-Enhanced Computed Tomography Images of a Large Right Renal Mass (Yellow Arrow) From Patient 1 During Initial Pre-Therapy, and 5-Month and 10-Month Follow-up Examinations. Over Time, the Size of the Primary Right Renal Tumor Was Stabilized

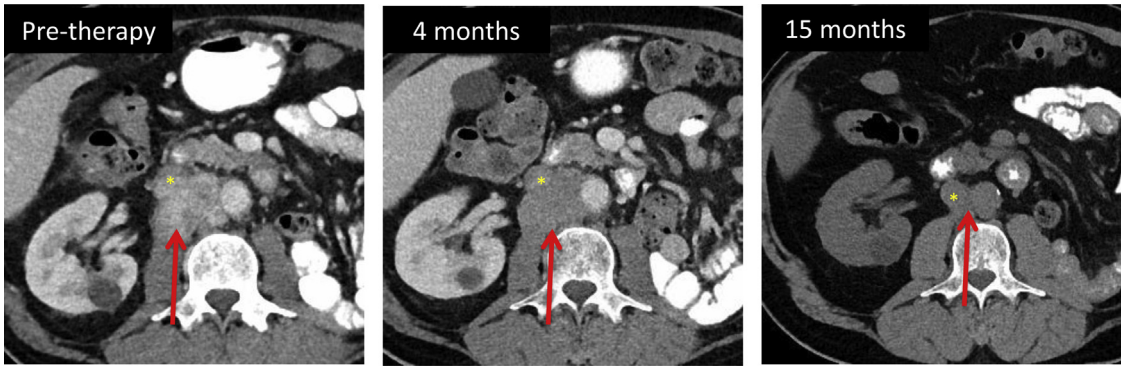


its ligand, PD-L1, have demonstrated a survival benefit in patients with a variety of malignancies.[11] In clear cell RCC, nivolumab, an antibody targeting PD-1, demonstrated improved survival compared with everolimus in patients who had previously been treated with a vascular endothelial growth factor (VEGF) inhibitor.[12] Several other trials evaluating other checkpoint inhibitors both in front- and second-line settings in RCC are ongoing.[13] In these trials, inclusion criteria generally exclude patients with non–clear cell histology or require the presence of clear cell disease. The efficacy of targeting PD-1 or PD-L1 in sRCC, to date, has not been described. Herein, we report 2 cases of sRCC with significant clinical responses to nivolumab.

Patient 1

A 36-year-old woman with no significant medical history presented with gradually worsening low back pain, left buttock pain radiating to the thigh, a 20% decline in weight from baseline, and a palpable right flank mass. Imaging revealed an 8.6-cm right renal

Figure 3 Right Para-aortic Retroperitoneal Metastatic Nodes. Axial Computed Tomography Images (Enhanced and Nonenhanced) of Patient 2. Postoperatively, Metastatic Para-aortic Adenopathy (Red Arrows) Was Identified. Initial Baseline Pretherapy, and 4-Month and 15-Month Follow-Up Examinations Demonstrate Essentially Complete Response to Therapy Over Time. The Displaced Inferior Vena Cava (Asterisks) Has Normalized in Anatomic Position and Diameter on the Most Recent Examination. Contrast Was Withheld on the Most Recent Examination Due to Decreased Renal Function



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