Oncology

PD-L1 pathway as a novel target in carcinosarcoma of the kidney and renal pelvis

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ABSTRACT

Carcinosarcoma of the kidney and renal pelvis (CSKP) is a rare and highly-aggressive malignancy characterized by rapid progression and widespread metastases. To date, few studies describe the natural history of the disease. We present a patient placed on pembrolizumab therapy for suspected metastatic colon cancer. The patient was found to have a right renal mass with caval extension on surveillance and ultimately underwent radical surgery revealing carcinosarcoma with positive PD-L1 expression with no evidence of recurrence to date. To our knowledge, this is the first case describing PD-L1 expression in CSKP and presents a novel pathway for future treatment algorithms.

Introduction

Carcinosarcoma of the kidney and renal pelvis (CSKP) is a rare and highly-aggressive malignancy of both epithelial and mesenchymal origin. It is characterized by both rapid progression and widespread metastases portending a poor prognosis. To date, there have been few studies in the literature describing the disease, its natural history, and optimal treatment guidelines, with most cancers poorly responsive to chemoradiation. Pembrolizumab, a PD-1 inhibitor has shown promise in preliminary trials involving intermediate-poor risk metastatic renal cell carcinoma as well as carcinosarcoma of other tissues. We present a patient with previously colonic adenocarcinoma placed on pembrolizumab therapy following local recurrence after surgical therapy. The patient was found to have a right renal mass on surveillance imaging and interval development of renal vein and IVC involvement. The patient ultimately underwent radical nephrectomy with caval thrombectomy almost 1.5 years following initial discovery and histologic examination revealed high-grade undifferentiated carcinosarcoma with chondromyxoid sarcomatoid elements consistent with carcinosarcoma. Tumor was found to be positive for PD-L1 expression. To our knowledge, this is the first case describing PD-L1 expression in CSKP with evidence of survival benefit and presents as a novel pathway for future treatment algorithms.

Case presentation

Our patient is a 66-year-old Caucasian male who was found to have a right renal mass on positron emission topography (PET-CT) for surveillance of known stage III colonic adenocarcinoma. Patient had previously undergone left hemicolectomy with development of local recurrence at the right pelvic sidewall and an additional pelvic mass, thought to be an enlarged lymph node. This encasing mass was found to be causing right ureteral obstruction. Patient underwent resection of this mass in conjunction with a Hartmann’s procedure with end-colostomy. Histopathology showed evidence of moderately differentiated adenocarcinoma consistent with local recurrence of primary colonic malignancy, however the right pelvic mass/node was found to be a high-grade sarcomatoid lesion. At the time, this was thought to be a dedifferentiated component of patient’s primary colon cancer. The patient underwent seven total cycles of targeted chemotherapy as well as palliative radiation therapy. Follow-up at completion of the patient’s chemoradiation regimen showed enlarging retroperitoneal lymph nodes, however further treatment was deferred due to stable carcinoembryonic antigen (CEA) levels used to monitor disease progression. Subsequent PET-CT imaging showed interval growth in these retroperitoneal nodes with worsening right-sided hydronephrosis and discovery of an enlarging right renal mass.

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The patient was seen by urology and underwent biopsy of the renal mass, having been previously started on pembrolizumab therapy due to concern for metastatic colon cancer. Renal biopsy showed poorly differentiated neoplasm favoring sarcomatoid renal cell carcinoma. A decision was made to pursue a right radical nephrectomy. The patient underwent preoperative staging with magnetic resonance (MR) angiogram showing malignant replacement of a majority of the right renal parenchyma with tumor thrombus extending to the renal vein ostia (Fig. 1). There was no definitive inferior vena cava (IVC) extension noted.

The patient underwent a right radical nephrectomy with caval thrombectomy. Tumor thrombus was found to be limited to the confluence of the renal vein and IVC. Histologic examination revealed high-grade undifferentiated carcinoma with chondromyxoid sarcomatoid elements (Fig. 2) diffusely positive for GATA 3 on immunohistochemistry (IHC) indicative of urothelial origin (Fig. 3). Specimen was subsequently sent for PD-L1 expression testing which was 30% positive on tissue analysis. Final tumor stage was pT3cN0M0. The patient underwent an otherwise unremarkable postoperative course and as of a year postoperatively has been disease free while maintained on pembrolizumab therapy.

Discussion

Carcinosarcoma of the kidney and renal pelvis (CSKP) is an extremely rare biphasic malignancy consisting of both epithelial and mesenchymal components. It has been sparsely described in the literature with fewer than 30 documented studies, mostly case reports and pathologic analyses. Within these studies, even fewer describe localized carcinosarcoma of the kidney and no study to our knowledge describes tumor thrombus extension to the renal vein or IVC. This malignancy tends to present as high-grade advanced disease and portends a poor prognosis. In a cohort of 43 patients selected from a SEER database with CSKP, there was a median cancer-specific survival (CSS) of 6 months and 1-year CSS of 30.2%. Nephrectomy and chemoradiation have been used independently or in conjunction with limited results – surgical resection traditionally has offered the longest survival benefit.

The definitive histopathologic etiology of this disease remains to be fully characterized and is somewhat controversial. There are, however, two leading theories. The monoclonal theory (divergence hypothesis) describes a common pluripotent progenitor that differentiates into separate epithelial and mesenchymal cell lines. Conversely, the multi-clonal theory (convergence hypothesis) postulates separate stem cell lines that coalesce as part of a “collision event”, giving rise to individual sarcomatous and carcinomatous elements within a single tumor.

Based on our patient’s overall clinical course, there is evidence to suggest CSKP may be an immunogenic malignancy and respond to checkpoint inhibition targeting the programmed cell death 1 (PD-1) protein, which has been demonstrated in advanced renal cell carcinoma. Pembrolizumab and nivolumab in combination therapy have shown improvements in overall and progression-free survival over traditional tyrosine kinase inhibitors (e.g., Sunitinib) in phase III studies involving intermediate-poor risk metastatic renal cell carcinoma and are now recommended as preferred regimens in the most recent National Comprehensive Cancer Network (NCCN) guidelines. Additionally, there is evidence that pembrolizumab monotherapy shows benefit in intermediate-poor risk disease with overall objective response rate of 38% with median progression-free survival of 8.7 months in a cohort of 110 patients in a recent KEYNOTE-427 phase III trial. Pembrolizumab and nivolumab have also shown short-term tumor control of multi-focal metastatic ovarian carcinosarcoma, another rare and aggressive malignancy with similar histopathologic etiology, indicating a further need for studies evaluating their efficacy in management of this disease process.

Conclusion

Carcinosarcoma of the kidney and renal pelvis is a rare, highly-aggressive malignancy that usually presents as late-stage disease with no optimal treatment regimen. PD-1 inhibitors present as a potentially novel treatment option for these malignancies. Future research is needed to characterize response to immunotherapy and optimal treatment regimens.

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Declaration of competing interest

The authors declare no conflict of interest.
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