Neoadjuvant Tyrosine Kinase Downstaging of T2 Renal Cell Carcinoma in Solitary Kidney Before Robotic Partial Nephrectomy

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Abstract
We highlight the use of a tyrosine kinase inhibitor, pazopanib, for neoadjuvant downstaging a 7.4 cm right biopsy-proven clear cell renal-cell carcinoma in a solitary kidney before surgical intervention of robotic partial nephrectomy with retrograde cooling to induce cold ischemia in a 79-year-old male.

Clinical History
This case describes a 79-year-old male with history of recurrent renal-cell carcinoma with initial presentation in 2005. He underwent a left laparoscopic radical nephrectomy with intracorporeal morcellation at an outside hospital that demonstrated clear cell renal-cell carcinoma. He was lost to follow-up, and on subsequent surveillance imaging 9 years later, he was found to have a 7.4 cm right upper pole renal mass on CT scan. The tumor abutted the collecting system and extended caudally below the renal hilum, but no renal vein thrombus was noted.

He underwent two percutaneous biopsies, the first being negative for malignancy. His second biopsy confirmed clear cell renal-cell carcinoma. The patient denied any history of gross hematuria, flank pain, or weight loss. In addition, the patient has a history of coronary artery disease, stroke, and two myocardial infarctions, for which he has been maintained on Plavix.

Physical Examination
On physical examination, his abdomen was remarkable for laparoscopic scars caused by his previous left laparoscopic radical nephrectomy as well as left inguinal incision, which the patient was unsure of the etiology of this scar. His right renal mass was not palpable despite his body mass index of 20.3. He did not have any signs of venous thrombus, including lower extremity edema or a pathologic varicocele. His preoperative creatinine was 1.2 mg/dL with glomerular filtration rate (GFR) of 69 and his remaining laboratories were unremarkable.

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patient reported some loss of taste in his taste buds and sensed bitter taste in certain foods, but he remained relatively asymptomatic during his treatment course. After 4 months of medical therapy, repeat axial imaging was obtained. There was a 25% reduction in his tumor size down to 3.7 × 5.5 cm and it had regressed away from the renal hilum (Fig. 2). The patient held his pazopanib therapy for 2 weeks before operation, as it can complicate wound healing. He underwent effective right robotic partial nephrectomy with retrograde renal cooling with a total renal clamp time of 28 minutes and estimated blood loss of 600 mL. At the termination of the case, a ureteral stent was placed. It was noted during renorrhaphy that the TKI produced a sponge-like edematous change in the characteristic of the tissue.

Follow-Up

Postoperatively the patient received two units of packed red blood cells. His serum creatinine peaked at 2.4 in the immediate postprocedural period. He convalesced in the hospital and was discharged on postoperative day 3. Pathology report demonstrated clear cell renal-cell carcinoma, 3.8 cm, Fuhrman grade 3, negative margins but renal sinus vein involvement, Stage T3aN0M0. Interestingly, there was a 50% reduction in size of the tumor on final pathology analysis.

Five days after operation, he returned to the emergency room with gross hematuria and clot retention. He underwent bedside irrigation and was placed on continuous bladder irrigation. Before angiography, Mucomyst was administered, IV hydration performed, and CO2 used for renal angiography to minimize contrast load by interventional radiology, which demonstrated a right lower pole pseudoaneurysm, which was effectively coiled. His serum creatinine peaked at 3.8 after coil embolization. His hematuria resolved and he was discharged.

Now the patient is 1 year after operation and he remains off of hemodialysis with a latest creatinine of 2.8. He followed for both nephrology for chronic disease and urology for surveillance for his history of renal-cell carcinoma, and currently has no evidence of recurrence.

Outcomes

Neoadjuvant TKI therapy before surgical intervention has been described, particularly for use in tumor downstaging; however, there have been no reports of application in a solitary kidney before robotic partial nephrectomy. Studies demonstrate that sunitinib therapy can reduce renal cell tumor sizes from 21% to 55%.

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demonstrated by multiple studies is thought to be secondary to delayed wound healing associated with inhibition of vascular endothelial growth factor (VEGF) receptors, which is the main mechanism of TKI. Wound strength, re-epithelialization, and revascularization inhibition of VEGF signaling can all lead to impaired wound healing. Floseal hemostatic matrix was used intraoperatively during renorrhaphy to prompt the coagulation cascade and facilitate fibrin formation. Other risk factors associated with TKI use include hypertension, proteinuria, gastrointestinal perforation, thrombosis, cardiac impairment, or hypothyroidism. Further studies demonstrated comparable results with only 1 of 10 patients experiencing disease recurrence and that the patient effectively underwent tumor thrombectomy at 8 months postoperatively. Our patient is experiencing similar results with no evidence of tumor recurrence at 1 year. The use of tyrosine kinase therapy for neoadjuvant surgical downstaging of high-risk renal-cell carcinoma before robotic partial nephrectomy presents a viable option in these challenging cases.

Disclosure Statement

No competing financial interests exist.

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Abbreviations Used
CT = computed tomography
GFR = glomerular filtration rate
TKI = tyrosine kinase inhibitor
VEGF = vascular endothelial growth factor

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