Renal cell carcinoma (RCC) occurs more frequently in dialysis and renal transplant patients than the general population. Patients who have received a kidney transplant have been shown to have up to a 100-fold increase in risk of RCC following transplantation (1) compared with the non-dialysis general population, and the incidence of RCC in patients on dialysis has been shown to be up to 20 times higher than the general population (2). Most RCCs found in transplant patients involve the native kidney (3–7), but RCC can also occur in the donor kidney either as a de novo cancer or as a pre-existing occult neoplasm present in the donor kidney prior to transplantation. In one study, RCC was found in 0.9% of deceased donor kidneys at the time of organ recovery with none of the donors having either symptoms or a history of RCC (4). Treatment of RCC in the allograft kidney has previously consisted of total nephrectomy with a return to dialysis, but there has been recent interest in partial nephrectomy or other nephron-sparing procedures in an effort to retain function of the transplanted kidney in selected cases. The following case reports illustrate a spectrum of therapeutic options available in kidney transplant recipients diagnosed with RCC with good short-term outcomes.

Case 1
A 51-yr-old white man with end-stage renal disease (ESRD) secondary to focal segmental glomerulosclerosis received his first renal transplant in 1998 as a living donor transplant from his 44-yr-old human leukocyte antigen (HLA)-identical sister. The kidney failed in 2010 secondary to...
chronic allograft nephropathy and the patient resumed dialysis. Renal ultrasound of the transplanted kidney revealed a solid tumor in the allograft (1.5 cm × 1.3 cm) that was also visualized on computerized tomographic (CT) imaging (Fig. 1) and magnetic resonance imaging (MRI). RCC was confirmed by fine-needle aspiration biopsy and cytology under ultrasound guidance. Radical transplant nephrectomy was performed in June 2010 without complications, and the patient was discharged on post-operative day 4. The tumor (papillary type I, Fuhrman nuclear grade 3, 1.3 × 1.1 × 1.0 cm in size) was well-circumscribed and confined to the kidney. CT imaging without contrast at two, six, and 14 months post-allograft nephrectomy showed no evidence of residual or metastatic disease. The patient received his second live donor kidney transplant from a 25-yr-old donor in August 2010 as a mandatory waiting period, or disease-free interval was not deemed necessary based upon the above pathology. He had no post-operative complications and was discharged on post-operative day 4. He has had stable renal allograft function with an estimated glomerular filtration rate (GFR) > 60 mL/min, and he has not required dialysis since the second transplant. He continues to do well at two-yr-follow-up without evidence for recurrent RCC on standard maintenance immunosuppression consisting of tacrolimus, mycophenolate, and steroids.

Case 2

A 51-yr-old white man with ESRD secondary to diabetic nephropathy received a simultaneous deceased donor pancreas and kidney transplant in May 2002 from a 19-yr-old male donor and experienced excellent initial renal and pancreatic allograft function. This was the recipient’s second renal transplant following a living donor transplant from his sister in 1991 thatfunctioned well for 11 yr before failing secondary to recurrent diabetic nephropathy. On a CT scan for abdominal pain related to a ventral incisional hernia in 2011, he was found to have an incidental small renal mass on the first (failed) kidney transplant in the left lower quadrant (Fig. 2). MRI and ultrasound further characterized the mass (round, solid, and 2.3 cm in diameter), which was consistent with RCC. The patient underwent radical allograft nephrectomy of the first (failed) kidney transplant in June 2011 and was found to have RCC (type I papillary type, Fuhrman grade 2) with clear margins. He was discharged on post-operative day 3 with no complications; he subsequently underwent laparoscopic incisional hernia repair with mesh five months later without incident. The patient’s second renal (and pancreas) transplant continues to function well with an estimated GFR of >60 mL/min. CT imaging at six months post-nephrectomy showed no evidence for residual or metastatic disease, and he continues to do well more than two yr following allograft nephrectomy on tacrolimus and mycophenolate immunosuppression.

Case 3

A 66-yr-old white man with ESRD secondary to hypertension and type 2 diabetes mellitus received a deceased donor kidney in June 2011 from a 65-yr-old man who died in a motorcycle accident. This was the recipient’s first kidney transplant after having been on hemodialysis for 28 months. Following reperfusion, the allograft kidney was found to have a tumor with an appearance not characteristic of RCC (a small, whitish, fatty tumor in the mid-portion of the renal parenchyma on the antihilar side that was approximately 0.5 cm in diameter). This lesion had been noted during the back bench preparation of the kidney but was more apparent after reperfusion. An excisional wedge biopsy of the tumor (0.7 × 0.6 × 0.5 cm in size) later revealed RCC on permanent section (Fuhrman nuclear grade 3 conventional/clear cell type) extending to the margin of resection. Additionally, the patient had delayed graft function requiring hemodialysis once on post-operative day 3. The patient (as well as the recipient of the mate kidney) were given the options of nephrectomy, partial nephrectomy, or observation with imaging. The recipient of the mate kidney chose observation with imaging, whereas this patient chose partial nephrectomy prior to retransplantation.
nephrectomy, which was performed on post-operative day 5 without incident as the patient did not receive blood transfusions or dialysis following the open wedge resection of the previous biopsy site. The follow-up excisional wedge biopsy (2.8 × 1.8 × 0.9 cm in size) revealed no residual neoplasia. His estimated GFR was 14 mL/min immediately prior to the partial nephrectomy and 15 mL/min immediately post-operatively; his estimated GFR rose to 49 mL/min two wk post-operatively. He was discharged in good condition after a nine-d length of stay on post-operative day 4 following his partial nephrectomy. A one-month post-transplant surveillance kidney biopsy showed no evidence for RCC, and serial renal transplant ultrasonography at one, four, and six months following transplant revealed no masses in the transplanted kidney. CT imaging without contrast at five, seven, 10, and 13 months post-transplant showed no evidence of a renal mass, adenopathy, or metastatic disease. He received low-dose maintenance immunosuppression with tacrolimus and mycophenolate until August 2012, when he returned to dialysis secondary to allograft failure after multiple hospital admissions secondary to pneumonia and urinary tract infections. His immunosuppression is currently being tapered, and a renal transplant USN performed in August 2012 (14 months post-transplant) was negative for any masses in the allograft.

Case 4

A 66-yr-old white woman underwent pre-emptive living-related donor kidney transplantation from her daughter in August 2000 for chronic kidney disease secondary to membranoproliferative glomerulonephritis. Her post-transplant course was largely uneventful except for mild post-transplant diabetes and recurrent squamous cell skin cancers. Serial ultrasound imaging studies of her native and transplant kidneys revealed cystic changes but no solid or suspicious lesions. She underwent a urological evaluation in January 2012 for microscopic hematuria that included negative cystoscopy and a CT scan that showed incidental 7 mm-solid and 15 mm-complex hemorrhagic cystic lesions in the periphery of the transplanted kidney (Fig. 3). Subsequent MRI (Fig. 4) suggested that the smaller lesion was suspicious for RCC and the patient subsequently underwent image-guided aspiration biopsy and radiofrequency ablation (RFA) for six min in the smaller (Fig. 5) and 10 min in the larger lesions with a core temperature exceeding 60°C in the ablation zones. She experienced no post-ablation complications or need for transfusion and was discharged home the day of the procedure. Fine-needle aspiration cytology of the solid lesion demonstrated RCC with clear cell features. Estimated GFR decreased from 42 mL/min pre-ablation to 34 mL/min post-ablation with a range of 21–34 over the next eight months. MRI with contrast three months after radiofrequency ablation showed no evidence of malignancy. In addition, she was switched from cyclosporine to everolimus-based immunosuppression and is currently undergoing active MRI surveillance of the transplanted kidney. She is currently doing well with stable albeit suboptimal renal allograft function.

Discussion

RCC in an allograft kidney identified at the time of transplantation is rare. However, with older donor age and increasing utilization of kidneys from expanded criteria donors, the risk of transmission of a number of different malignancies is higher. The first step in addressing this problem is prevention. Many patients with RCC are asymptomatic, so organ recovery should be done with the knowledge that any donor could have RCC. Careful dissection and examination of the kidneys as well as accessible intrathoracic and intra-abdominal organs during organ retrieval has been suggested as one mechanism of prevention (5) as well as complete removal of perinephric fat for better visualization and inspection of the renal parenchyma prior to transplantation (8). In one study, four of the five renal tumors found in donor kidneys were noted during inspection/palpation of the kidney at
the time of abdominal exploration, and the fifth was discovered during preparation of the kidney after recovery but before transplantation (9). Extra attention at this stage would help to avoid the accidental transplantation of pre-existing RCC into a recipient. Case 3 of our series is unique in that it highlights the importance of careful inspection of the kidney following reperfusion, which may also identify suspicious lesions missed during either organ recovery or bench preparation. Intraoperative ultrasonography has also been suggested as a method to detect hidden neoplasms in transplanted kidneys not visible to the surgeon (6). Careful review of pre-donation truncal imaging studies (when available) may also identify potential lesions in explanted organs. If a suspicious nodule or cyst is found, it should be excised with a margin of normal tissue and a prompt frozen section examination should be obtained to determine adequate margins (9, 10). If the biopsy reveals cancer, the kidney can be transplanted subsequently with informed consent depending on cell type, size of the primary tumor, and margins of resection (11). Patients should also be informed that frozen

---

**Fig. 3.** Non-contrast-enhanced CT scan demonstrating: (A) a 15-mm lesion (arrow), and (B) a 7-mm lesion (arrow) along the anterior aspect of a functioning living donor renal allograft (case 4).

---

**Fig. 4.** Contrast-enhanced axial LAVA MRI demonstrating the 7-mm solid lesion (arrow) in Fig. 3B (A) and delayed contrast-enhanced axial LAVA MRI demonstrating the same lesion (B), found to be suspicious for RCC in the renal allograft.

---

**Fig. 5.** Non-contrast-enhanced CT scan during (A) and immediately after ablation (B) of the 7 mm-solid enhancing lesion (arrow) in case 4.
section examination may not always accurately identify a malignancy. Consequently, permanent section examination (as in case 3 of our series) may subsequently determine whether or not further treatment is indicated. In this circumstance, the recipient of the mate kidney (as well as recipients of any other organs from the donor) must be counseled regarding the potential transmission of a donor-derived malignancy.

After transplantation, RCC in the allograft kidney can be treated with radical nephrectomy, partial nephrectomy, RFA, or close observation in selected cases. Radical nephrectomy has been shown to be curative for tumors in native kidneys that are confined to the kidney (4). Given that transplantation usually improves life expectancy and quality of life compared to dialysis in ESRD, preservation of the transplanted kidney may be an important consideration (12). Nephron-sparing surgery may be an appropriate alternative to radical nephrectomy with small tumors because they have a relatively low risk of recurrence in the remaining parenchyma. Partial nephrectomy and RFA in native kidneys have been shown to be safe and effective treatments with minimal potential for recurrent or metastatic disease in the non-transplant population (13), but there is concern that circulating tumoral cells are not recognized and can spread despite adequate resection margins in the transplant population, particularly in the setting of ongoing immunosuppression (8). In addition, primary thermal ablation, whether it is with RFA or cryoablation, may preclude or complicate attempts at future partial nephrectomy (14).

Partial nephrectomy allows for an acceptable quality of life and avoids immediate dialysis (6, 15). In the short term, it has been shown to result in good outcomes (16), but graft survival after kidney resection depends on the quality of the remaining parenchyma. One must balance the benefit of preserving the graft and keeping a transplanted patient off dialysis with the risk of developing metastatic disease from RCC (17, 18). One patient with RCC of the donor kidney initially refused total nephrectomy due to her improved quality of life following the transplant (19). However, three months after partial nephrectomy and discontinuation of immunosuppressive medications, the patient experienced a recurrence of RCC and underwent total nephrectomy; fortunately, she had no evidence of disease at six-month follow-up. In case 3 of our series, the patient experienced good recovery of allograft function with an improved GFR after partial nephrectomy with no recurrence of RCC at 16-month follow-up. This case is a unique example of successful treatment of a donor-derived RCC immediately after transplantation with preservation of allograft function. Unfortunately, this patient resumed dialysis at 14 months after reduction in immunosuppression for multiple infectious complications. He will continue to require surveillance imaging of his failed allograft, and consideration may be given to allograft nephrectomy if his operative risk improves or the failing kidney becomes symptomatic.

The benefits of nephron-sparing procedures over radical nephrectomy are contingent upon a functioning transplanted kidney. Consequently, our first and second cases are examples of when radical nephrectomy remains the standard of care. Radical nephrectomy may offer these patients a cure given the small size and localization of these tumors because it has been shown to be curative in RCC of the native kidney (4). Nephron-sparing procedures would not be suitable in these cases given the lack of quality of life and mortality benefits in these cases as well as increased concerns for possible un-resected cancer in patients who remain on immunosuppression following second transplants. In this situation, non-surgical treatment options such as RFA or allograft embolization may be considered only if multiple co-morbidities and excessive medical and surgical risks prohibit more definitive therapy.

RFA is an alternative to surgical treatments of RCC in an allograft kidney. CT-guided RFA and ultrasound-guided percutaneous RFA have been shown to be safe and effective options in treating small RCC in allografts (20–23). RFA may be appropriate for patients with high surgical or anesthetic risks for which surgical therapy is not a good option. RFA may also be preferable to nephron-sparing surgery in patients with declining allograft function because of preservation of remaining renal parenchyma, low risk for blood loss or transfusion, absence of ischemic insult, and target selectivity (20). In addition to treating primary tumors, RFA has also been shown to be an effective treatment for recurrent tumors in renal allografts after initial treatment with partial nephrectomy (22). Advantages of RFA over surgical treatment include minimal invasiveness, less surrounding tissue damage, preservation of surrounding renal parenchyma, and a reduced complication rate leading to shorter hospitalization (22). However, surgery is still considered the first therapeutic option given the lack of long-term evidence for RFA compared with surgical treatments in allograft RCC. The fourth case in our series illustrates the dilemma of how to manage an incidentally discovered RCC in the allograft of a patient who is otherwise doing well with stable and excellent renal
allograft function. In this scenario, patients are often reluctant to consider allograft nephrectomy and may opt for nephron-sparing procedures or expectant management although outcome data in the transplant population is extremely limited. In this particular case, because the patient also had a history of recurrent skin cancers, a switch to mTOR-inhibitor-based immunosuppression appeared logical because of its purported antitumor effects (24, 25). Given the impetus to preserve allograft function in this patient, RFA was chosen over nephron-sparing surgery because of better localization and less overall morbidity.

The role of immunosuppressive reduction or conversion in the treatment of allograft RCC remains uncertain, particularly in patients with small tumors in which ablative therapy is thought to be sufficient. In patients undergoing nephron-sparing procedures or those with other functioning allografts, immunosuppressive manipulations could result in the development of a subsequent rejection episode. In some cases, rejection of the tumor has been reported (26). With the availability of mTOR inhibitors such as sirolimus and everolimus, it has been suggested that reduction or elimination of anti-metabolites and calcineurin inhibitors may be indicated provided that mTOR conversion can be accomplished safely (27).

Regardless of the method of treatment, close surveillance monitoring with imaging studies must be performed for an indeterminate amount of time after surgery for RCC in an allograft kidney. Different methods of monitoring that have been described include ultrasonography every 3–6 months (6), abdominal CT scans (12, 17), and MRI (15). Patients with native kidney RCC treated with RFA should be monitored at intervals of 6–12 months with MRI or CT (28). However, no studies have been performed examining the comparative effectiveness of one imaging modality over another for allograft RCC regardless of the method of treatment. Our patients have been monitored by serial ultrasonography and/or CT scans, with no evidence of RCC in short-term follow-up. The above case series illustrates the complexity of decision-making and a spectrum of management options available to patients who develop RCC in a renal allograft; treatment must be individualized and tailored to the specific case and may involve medical, surgical, and radiological alternatives.

References


22. Goeman L, Joniau S, Oyen R, Van Poppel H. Percutaneous ultrasound-guided radiofrequency ablation of


