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CASE REPORT

Renal Cell Carcinoma in Transplanted Kidney: A Case Report and Literature Review

Ana Lavratti Borga[1], André Carminati Lima[1], Juliana Carpilovsky Revoredo Alves[1,*], Luciane Mônica Deboni[1,2], Christian Evangelista Garcia[1], Jean Cristovão Pereira Guterres[1,2]

1.Hospital Municipal São José – Departamento de cirurgia – Joinville (SC), Brzsil.

2.Fundação Pró-Rim – Departamento de Urologia – Joinville (SC), Brazil.

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Correspondence author:
julianacrevoredo@gmail.com

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Nothing to declare.

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ABSTRACT

Introduction: The incidence of renal cell carcinoma in the transplanted kidney is extremely rare. **Case report:** A 42-year-old female underwent a living-related donor kidney transplant from her 60-year-old mother due to glomerulonephritis leading to end-stage renal disease. Ultrasonography, nine years after transplantation, revealed a lower pole renal tumor in the renal graft with a suspicious image of malignant neoplasm on computed tomography. The patient underwent partial nephrectomy and histological analysis revealed clear cell carcinoma. **Final considerations:** After one year of follow-up, serum creatinine levels are normal and there are no signs of metastasis or tumor recurrence.

Descriptors: Kidney Transplantation; Transplantation; Kidney Neoplasms; Carcinoma, Renal Cell; Nephrectomy.

INTRODUCTION

Renal cell carcinoma originates in the epithelial cells, mainly of the proximal tubules, corresponding to 2 to 3% of all tumors in the general population, with a higher incidence in western countries, being, among the malignant neoplasms of the kidneys, the most common type, around 90% of all these tumors.[1,2] In Brazil, it has an incidence of 7 to 10 cases per 100,000 inhabitants.[3]

According to De Paula e Ianhez,[4] In the 10-year follow-up of 1,511 patients undergoing kidney transplantation, a cumulative incidence of malignancies, including skin malignancies, of about 6.9% was reported. On the other hand, it is known that 4.6% of these malignant tumors are of renal location, 90% of which are in the primitive kidney and 10% in the graft.[5] Thus, graft renal cell carcinoma is extremely rare, affecting approximately 0.032% of patients undergoing transplantation at 10-year follow-up, or one in 3,125 patients.[4]

In this context, this paper describes a case of renal graft cell carcinoma of the renal clear cell type and reviews the literature on the topic.

CASE REPORT

A female, white, 43-year-old patient from São Francisco do Sul, Santa Catarina, Brazil, diagnosed with chronic renal disease due to glomerulonephritis, on renal replacement therapy, on hemodialysis for 1 year at the time of the transplant. She underwent kidney transplantation with her 60-year-old mother as related living donor in February 2009. Blood type O, haploidentical human leukocyte antigen, as shown in Table 1, with negative antibody reactivity panel. Preoperative abdominal imaging examinations evaluating the donor were unremarkable.

Table 1. Human leukocyte antigen (HLA) between donor and recipient.

	ABO	HLA-A	HLA-B	HLA-DR
Donor	O2, O3	27, 62	4, 6	4, -
Recipient	O2, O3	62, -	6, -	3, 4

HLA: human leucocyte antigen.

The donor underwent conventional left nephrectomy, and the graft was perfused with Custodiol preservation solution on the bench, with a cold ischemia time of 2 hours and 15 minutes. Graft with usual anatomy and with a small simple cyst in the renal parenchyma in the upper pole. Recipient induced under general anesthesia, with retroperitoneal surgical access through a right Gibson incision and end-to-side anastomosis of the renal artery to the external iliac artery and end-to-side venous anastomosis of the renal vein to the external iliac vein. Ureterovesical implantation according to the LichGregoir technique without double-J catheter. As initial immunosuppression, she received 1 g of methylprednisolone near the induction of anesthesia and then was maintained with sodium mycophenolate, tacrolimus and prednisone as basal immunosuppression. There was immediate diuresis after reperfusion of the graft and there were no other complications in the perioperative period. She was discharged from the hospital on the 17th postoperative day.

Outpatient follow-up periods without significant intercurrences, with ultrasound examinations without significant changes. Abdominal ultrasound in 2015 visualized 1.9 cm nodule in the lower pole of the transplanted kidney, to be clarified, questioning the possibility of angiomyolipoma, which was complemented with abdominal computed tomography that did not visualize nodules. The patient was kept on follow-up.

During 2016 and 2017, she underwent treatment for recurrent urinary tract infections, with several hospitalizations over the course of those years. She performed a new ultrasound in 2018, which again showed an isoechoic nodular image with permeating cystic content and peripheral flow on color Doppler, located in the lower third of the transplanted kidney parenchyma measuring 2.9 × 2.5 × 2.5 cm, complemented with non-contrast abdominal computed tomography scan, which showed heterogeneous solid nodular image measuring 32 mm in diameter in the lower pole.

She was then submitted to ultrasound-guided percutaneous biopsy of the transplanted organ, with three fragments of 0.8 cm, and sent for histopathological and immunohistochemical analysis demonstrating the presence of three glomeruli in the sample, identifying interstitial fibrosis, tubular atrophy, and the presence of renal clear cell carcinoma in two fragments of the sample.

Given the size and location of the nodule and histopathological findings, surgical treatment with partial nephrectomy of the graft was proposed.

Having located the nodule with the aid of intraoperative ultrasound and with isolation of the right external iliac artery and vein, clamping of the vessels was performed followed by temperature reduction with sterile ice and sectioning of the lesion delineated with ultrasound, followed by hemostasis with nephrorrhaphy, without injury to the excretory duct. She was discharged on the 15th postoperative day without further complications. Pathological analysis showed a 3.9 cm diameter nodule of renal clear cell carcinoma, unifocal, with free surgical margins (product of partial nephrectomy measuring 6.3 × 5.0 × 4.0 cm), with tumor limited to the kidney, without angiolymphatic invasion, determining a pT1aNx staging.

After the partial nephrectomy, the patient evolved with a urinary fistula, requiring reintervention, with suture and double-J stent. After her fistula was healed, immunosuppression was switched to sirolimus, considering the antiangiogenic potential of mTor inhibitors, associated with tacrolimus and prednisone.

In September 2019, she had a double-J catheter removed via cystoscopy and is still being followed up as an outpatient, with good evolution since then, maintaining good graft function, on deflazacort 6 mg.

DISCUSSION

The kidney transplant service at Hospital Municipal São José/Fundação Pró-Rim has performed 1,747 transplants since 1978.

The development of malignant tumors in transplant patients is considered high and significant, and is a topic addressed in papers, studies, and reviews because of the concern during long-term follow-up.[4]

The incidence of neoplasms in post-kidney transplant patients is 3 to 5 times higher than in the general population, and up to 72% higher. Also, in another comparison, neoplasms occur at earlier ages in post-transplant patients.[6]

According to data collected from the Cincinnati Transplant Tumor Registry (CTTR), a retrospective database, renal cell carcinoma is the most common malignant neoplasm after skin disorders, lymphoproliferative disorders, and Kaposi's sarcoma in renal transplant recipients. The incidence increases with post-transplant survival time, with the average period of lesion diagnosis ranging from 63 to 85 months post-transplant.[4–7]

An interaction of risk factors, such as blood component transfusions and antigens from the transplanted organ, leads to chronic antigenic stimulation of a depressed immune system with loss of regulatory systems. Age, sex, and donor type showed no significant relationship with the incidence of neoplasms.

The duration and intensity of immunosuppression are important risk factors associated with the development of neoplasms.[8] Individual susceptibility, such as that related to human leukocyte antigen, which plays an important role in the host's defense against certain malignancies, can contribute to the development of some types of skin tumors. In addition, one must also consider the geographical factor, such as sun exposure, to these types of tumors. The activation of oncogenic viruses, such as papillomavirus, herpes virus, and Epstein–Baar virus, is higher in immunosuppressed patients, which makes them related to an increased incidence of post-transplant neoplasms.[6,8]

The investigation can be done with ultrasound, computed tomography, or magnetic resonance imaging, which initially shows a nodule in the graft. It can be complemented with biopsy, for histopathological evaluation preoperatively.[5] This diagnosis has become increasingly common and is directly related to the waiting time on the pre-transplant list. Hidden malignant neoplasms in both recipients and donors with the presence of micrometastases are not uncommon and account for the majority of post-transplant diagnoses. The incidence of these neoplasms is also due to pre-existing underlying disease. Multicystic kidneys, tuberous sclerosis, Von Hippel–Lindau disease, and previously dialysis patients have a higher incidence of post-transplant tumors, and may occur in this up to 90%.[8]

According to the CTTR, 24% of neoplasms are renal tumors, the majority being renal cell carcinoma. These comprise several histological subtypes, as classified by the 2016 World Health Organization. There are three main subtypes: clear cell carcinoma, papillary carcinoma, and chromophobe carcinoma, the former being the most common type, accounting for 80% of cases. The incidence of renal cell carcinoma is estimated to be 4.6% in transplant patients, with only 10% of these in the graft.[6]

As preventive measures for the development of these neoplasms, the maintenance of adequate levels of immunosuppressants, minimally necessary for the good functioning of the graft, must be considered. Vaccines against oncogenic viruses seem to have a positive effect on the prophylaxis of many of these lesions, as well as the use of oral antiviral agents.

Treatment of these lesions may involve radical nephrectomy, with the patient returning for renal replacement therapy, or conservative treatments such as partial nephrectomy or ablative therapies (cryoablation or radiofrequency ablation).[5]

Drugs such as mTor inhibitors (rapamycin) have antiproliferative activity, with antiangiogenic action, and are the preferred alternative for immunosuppression in cases of post renal transplant neoplasia in which it is possible to maintain immunosuppression.

In this patient's case, classic risk factors for renal tumor such as smoking, obesity, family history, and polyomavirus infection were not present, except for hypertension.

Periodic imaging exams are an important tool for the follow-up of transplanted patients, even with preserved renal function and without intercurrences, aiming at an early detection of potential neoplastic lesions and enabling curative treatment.

CONCLUSION

We present the case of a 60-year-old post-operative living donor kidney transplant patient who, during post-transplant follow-up, developed a nodule in the renal graft, detected on routine ultrasound at post-transplant follow-up, with a diagnosis of renal clear cell carcinoma after biopsy of the transplanted kidney, treated with partial nephrectomy of the graft and conversion of immunosuppression to rapamycin. She is being followed up as an outpatient, with good evolution since then, maintaining good graft function, and taking deflazacort 6 mg. He is being followed up as an outpatient, with good evolution since then, maintaining good graft function, and taking deflazacort 6 mg.

PROTECTION OF PEOPLE AND ANIMALS

The authors declare that the procedures followed were in accordance with the regulations established by the heads of the Clinical Research and Ethics Committee and in accordance with the World Medical Association Helsinki Declaration.

INFORMED CONSENT

Obtained.

AUTHORS' CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Borga AL, Lima AC, Revoredo JC, Garcia CE, Deboni LM and Guterres JCP; **Conception and design:** Borga AL, Lima AC, Revoredo JC and Garcia CE; **Data analysis and interpretation:** Borga

AL and RevoredoJC; **Article writing:** Borga AL and Revoredo JC; **Critical review:** Borga AL, Lima AC, Revoredo JC and Garcia CE; **Final approval:** Borga AL, Lima AC and Revoredo JC.

DATA AVAILABILITY STATEMENT

All dataset were generated or analyzed in the current study.

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