Casuistry

Conservative treatment of de novo renal carcinoma on kidney graft


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Abstract

Background: de novo renal carcinoma in kidney transplants is an uncommon but not an exceptional condition and is of significant importance due to the potential for recipient mortality and graft loss. The aim of our study was to determine the management and outcome of these tumors in our Kidney Transplantation Unit.

Material and methods: We analyzed cases of de novo kidney tumors among patients who underwent transplantation in the last 17 years in our Kidney Transplantation Unit. We detected 3 cases of clear cell carcinoma and 1 case of papillary carcinoma on the graft. We conducted follow-up on the tumor and renal function and analyzed patient responses to changes in immunosuppression.

Results: Tumorectomy was performed in all cases, and subsequent transplantectomy was required for patients with papillary carcinoma. None of the patients had relevant surgical complications.

We also changed the patients’ regimen to a proliferation signal inhibitor or mTOR inhibitor and completely withdrew all anticalcineurin agents.

With a mean follow-up of 43.5 months (15–61), the 3 patients with clear cell carcinoma survived with good graft function and with no evidence of tumor recurrence. The patient with papillary carcinoma underwent follow-up at another hospital center.

Conclusions: Conservative surgery along with conversion to a proliferation signal inhibitor appears to be a safe option for treating primary tumors in kidney grafts and offers good oncological and renal function results in the short and medium term.

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Keywords
Renal carcinoma; Conservative surgery; mTOR inhibitors

Palabras clave
Carcinoma renal; Cirugía conservadora; Inhibidores mTOR

Tratamiento conservador del carcinoma renal de novo sobre injerto renal

Resumen

Introducción: El carcinoma renal de novo en el trasplante renal es una situación poco frecuente pero no excepcional, de mucha trascendencia por la potencial mortalidad del receptor o pérdida del injerto. El objetivo de nuestro trabajo es conocer el manejo y evolución de estos tumores en nuestra unidad de trasplante renal.


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Material y métodos: Analizamos los casos de tumor renal de novo entre los trasplantados de los últimos 17 años en nuestra unidad de trasplante renal, detectando 3 casos de carcinoma de células claras y uno de carcinoma papilar sobre el injerto. Se realizó seguimiento desde el punto de vista oncológico y de función renal, y se analizó la respuesta a cambios en la inmunosupresión.

Resultados: En todos los casos se practicó tumorectomía, precisándose en el paciente con carcinoma papilar trasplanteó en otro centro hospitalario. El paciente con carcinoma papilar realiza seguimiento en otro centro hospitalario. Conclusiones: La cirugía conservadora, junto con la conversión a un inhibidor de señales de proliferación, parecen ser una opción segura para el tratamiento de tumores primarios en injerto renal, ofreciendo buenos resultados oncológicos y en cuanto a función renal a corto y medio plazo.

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Clinical problem

The main causes of mortality in renal transplant recipients are, in order of frequency, cardiovascular disease, infections, and de novo malignancies. Among the latter, the majority in this population are lymphoproliferative disorders and skin malignancies.1-5

Kidney transplants are 15 times more likely to develop renal cell carcinoma compared with the general population,6 most often located in the native kidneys.

The appearance of de novo renal cell carcinoma on the transplanted kidney is a rare but not exceptional situation (incidence of 0.19–0.50%),1,7 and it acquires much significance due to the potential mortality of the receptor or graft loss.

There is a trend toward nephron-sparing surgery in the management of these tumors,8,9 along with a modification of immunosuppression, with reduction or withdrawal of calcineurin inhibitors and introduction of mTOR inhibitors, reducing the likelihood of recurrence and disease progression after surgical treatment.10,11

Despite this, there is currently no standardized treatment and follow-up for this type of tumors in kidney transplants.12

The aim of this study is to present the diagnostic and therapeutic management, as well as medium-term evolution of these neoplasms in our kidney transplant unit.

In our center, 1148 renal transplants were performed to adult recipients between early April 1997 and the end of March 2013, detecting among them 3 cases of clear cell carcinoma and one case of papillary carcinoma on the graft (incidence of 0.35%), summarized in Table 1.

The average age of patients at diagnosis was 61 years, with a mean of 94 months (4–158) from the transplant to the detection of the lesion. In no case did the maximum diameter of the tumors exceed 4 cm, the stage in all being pT1a (Fig. 1).

Figure 1 Representative cut of computed axial tomography in one of the patients diagnosed with clear cell carcinoma. Injury to the anterior aspect and middle-lower third of the graft of about 2.8 cm × 3.2 cm × 3.5 cm in diameter is observed.
All patients underwent a lumpectomy, subsequently carrying out in the patient with papillary carcinoma a transplactectomy due to tumor involvement of surgical margins of the piece and there being a greater likelihood of multicentrality. In no case were there significant surgical complications (all Clavien I-II).

All patients received post-transplant immunosuppression with calcineurin inhibitors, which were replaced by a proliferation signal inhibitor (PSI) or mTOR inhibitor (rapamycin in this case) after surgical treatment. After conversion to PSI, in one case significant proteinuria occurred, which required reintroducing calcineurin inhibitors, with complete resolution of the symptoms.

With a mean follow-up of 43.5 months (15–61), the 3 patients with clear cell carcinoma survive today with good graft function and no evidence of tumor recurrence. The patient with papillary carcinoma undergoes follow-up at another hospital, with no data in the last relapse check-ups of cancer process.

**Commentary**

Urological neoplasms may be up to 15% of de novo tumors in renal transplant patients, these being able to be up to 15 times more likely to develop renal cell carcinoma (RCC) compared to the general population. These RCCs appear more frequently in native kidneys, also appearing on the graft (incidence of 0.19–0.50%, that of our series being 0.35%).

There is not only the possibility of developing de novo tumors on the graft after the transplant, but also of transplanting a kidney with millimeter malignant or not visible lesions. This possibility is strengthened especially when these tumors occur shortly after the transplant (less than 2 years), like the patient with papillary carcinoma, diagnosed only 4 months after the transplant. A genetic study of this patient’s tumor was performed (as recommended by some authors), ruling out that it was a transmitted malignancy, being genetically different from the sex of the donor.

It is therefore essential to conduct an early detection of these tumors by periodic ultrasound screening of native kidneys and the graft. This routine check-up is the one by which most patients are diagnosed, as very few have symptoms associated. In our case, the 4 patients were asymptomatic and with good graft function at the time of diagnosis.

The median time to onset of the tumor from the kidney transplant is, according to the literature, over 90 months (with wide variability, 12–144 months) our average being 94 months.

Currently, there is controversy about the appropriateness of performing percutaneous biopsy of the mass before choosing a treatment. Some groups perform it systematically, as it can really determine the malignancy of the tumor and help the therapeutic approach, discouraging in some cases conservative management. We, like other teams, do not systematically perform biopsy given its uncertain therapeutic benefit and the risk of complications.
Despite what has been said, there is currently no standardized treatment and standardized follow-up for the management of these tumors in kidney transplant patients.

Nowadays, treatments that preserve kidney function whenever possible are prioritized.1 Given the extensive experience in nephron-sparing surgery for RCC, it is reasonable to extend the indications for this surgery to transplant patients with RCC in the graft.13,18 These interventions are of high technical complexity since they are performed on a manipulated field and with generally perirenal fibrosis.12,18 In our case, it all patients underwent open lumpectomy, without major complications. The patient with papillary tumor had to subsequently undergo nephrectomy for reasons discussed above.

When opting for partial surgery with graft preservation, it is necessary to maintain the immunosuppressive regimen to prevent rejection. Several authors recommend its modification, with reduction or removal of calcineurin inhibitors (potentially promoters of carcinogenesis and angiogenesis),11,16 and introduction of double effect drugs (such as mTOR inhibitors or ISP), which simultaneously provide protection against rejection and have a tumor antiproliferative effect.18,10–12,15,19 Following these recommendations, we proceeded to suspend calcineurin inhibitors and include rapamycin after lumpectomy.

Currently, the 3 patients with clear cell carcinoma survive with good graft function and no evidence of tumor recurrence. The patient with papillary carcinoma is followed-up at another center after restarting the program of peritoneal dialysis.

Conclusions

The appearance of de novo renal cells on the renal graft is a rare situation and usually incidental in kidney transplant patients.

Despite the absence of a standardized follow-up and treatment for these tumors, many authors recommend the use of nephron-sparing techniques along with changes in immunosuppressive regimens, with suspension of calcineurin inhibitors and introduction of mTOR inhibitors.

Our unit achieved good oncological results, and in terms of renal function after nephron-sparing surgery (lumpectomy) and replacement of tacrolimus by rapamycin in the 4 patients diagnosed with de novo malignancy on the graft. All patients currently survive without evidence of cancer recurrence.

In light of these results, and comparing them with the existing literature, we believe that nephron-sparing surgery along with conversion to an mTOR inhibitor can be a safe option for the treatment of primary tumors of the renal graft. Through these 2 procedures, transplantectomy and subsequent return to renal replacement therapy are avoided, with a low probability of short- or medium-term cancer progression or recurrence.

Conflict of interest

The authors declare that they have no conflict of interest.

References

