Single-Center Case Series of Donor-Related Malignancies: Rare Cases With Tremendous Impact

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ABSTRACT

Background. Donor-related malignancy is a rare complication of organ transplantation.

Methods. In this case series, we discuss three cases of donor-related cancers in kidney transplant recipients who were registered in our center between 1979 and 2015. They account for an incidence of 0.29% of donor-related malignancies of a total of 1015 transplanted kidney grafts (deceased and living donors). The three cases that we describe presented in different ways and with different severity, although the response to the initiated treatment was comparable.

Results. All three patients not only survived their cancer episode but also had a complete oncological remission and underwent successful second kidney transplantation, accounting for a 100% survival rate in our small cohort.

Conclusions. Despite the very low incidence of this complication, transplant clinicians must be aware of the occurrence of donor-related malignancies when selecting a donor and should be able to diagnose and treat a case of donor-related cancer.

TRANSPLANT recipients are known to have a 3-fold excess risk of developing *de novo* cancer after solid-organ transplantation as a result of immunosuppression, as compared with the general population [1]. Besides, donor-related cancer may be transmitted with the graft (donor-transmitted cancer, DTC) or may develop later from the graft (donor-derived cancer, DDC) [2]. Donor-related malignancies, however, remain extremely rare [3–5]. An important study published in this field is a retrospective study of Kauffman et al [3], based on data from the Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOSS), comprising a cohort of 34,933 deceased donors and 108,062 recipients between 1994 and 2001. This retrospective analysis reports an incidence rate of 0.04% for the deceased donor-related tumor rate. Of the total of 21 tumors reported, 15 were donor-transmitted and 6 were donor-derived. The overall mortality rate was 38%, with a mortality rate among the donor-derived group of 33% [3].

In this case series, we discuss three cases of donor-related malignancies in kidney transplant recipients who were registered in our center between 1979 and 2015. They account for an incidence of 0.29% donor-related malignancies of a total of 1015 transplanted kidney grafts (deceased and living donors). The three cases we describe here presented in different ways and with different severity, although the response to the initiated treatment was comparable. Fortunately, all three patients not only survived their cancer episode but also had a complete oncological remission and underwent a successful second kidney transplantation, accounting for a 100% survival rate in our small cohort.

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Case 1: Malignant Meningioma

The first case of donor-related malignancy in our series occurred in a currently 69-year-old white man with autosomal dominant polycystic kidney disease (ADPKD) who underwent a first kidney transplantation in July 1994 at the age of 48 years. A bilateral nephrectomy was already performed 3 months before transplantation because of bilateral pyonephrosis. Polycystic kidney disease of the native kidneys was histologically confirmed without evidence of malignant degeneration of the cysts. Furthermore, there was no history of any other malignancy.

The patient received a kidney from a 35-year-old, heart-beating, male donor who remained comatose after a resection of a cerebral astrocytoma grade II, as diagnosed histologically at the donor center. In the initial surgical report, there was no evidence of meningeal invasion. The postoperative period was eventless, and the patient was soon discharged with a serum creatinine level of 1.5 mg/dL and a maintenance immunosuppressive therapy comprising steroids and cyclosporine.

Eight months after transplantation, the patient was re-admitted to our department because of a biopsy-proven, antibody-mediated, acute rejection of the kidney. He was successfully treated with a high-dose steroid regimen of methylprednisolone 1 g intravenously daily for 4 days and Muromonab-CD3 (OKT3) for 12 days. Furthermore, azathioprine was added to the maintenance therapy as well as monthly infusions with intravenous immunoglobulins.

Five months after the episode of acute rejection, the patient's kidney function deteriorated once again to a serum creatinine level of 2.25 mg/dL (estimated glomerular filtration rate [eGFR] 32 mL/min/1.73 m^2 according to the abbreviated Modification of Diet in Renal Disease [MDRD] formula) as opposed to a previous value of 1.5 mg/dL (eGFR 50 mL/min/1.73 m^2 according to the abbreviated MDRD formula). A renal ultrasound examination revealed the presence of a grade II hydronephrosis and a more convex-shaped graft with a heterogeneous aspect of the parenchyma.

Because of the unsuccessful placement of a nephrostomy and ongoing renal insufficiency, a biopsy was performed. There were no histological signs of graft rejection, but, surprisingly, a diffuse infiltration of the kidney with malignant cells was seen.

Additional imaging with abdominal computed tomography (CT) and magnetic resonance imaging (MRI) revealed the presence of a nodular lesion at the transition zone of the pancreatic tail and the spleen, bilaterally enlarged adrenal glands, a small nodular lesion in hepatic segment VII, and no lymphadenopathy. Imaging of the neck and chest was negative for additional lesions.

On the basis of the hypothesis of a metastatic tumor in an immune-compromised patient, all immunosuppressive therapies were discontinued and a radical transplantectomy was performed 20 days after presentation with acute renal failure. During the surgical procedure, tumoral invasion of the iliac vein and diffuse peritoneal metastasis were observed. Hemodialysis was restarted, and chemotherapy with doxorubicin for the presumed sarcoma was given on a weekly basis.

Further characterization of the tumor's origin was made. All biopsy and autopsy material of the donor was retrieved from the donor center and re-assessed. Immunohistochemistry testing and the homologous appearance of the tumor cells in the donor as well as in the recipient, next to a DNA analysis of the tumor showing a common HLA-DR-genotype between the tumor and the donor's HLA typing, allowed us to state the diagnosis of a donor-related tumor [6]. Hence, the initial diagnosis of astrocytoma grade II in the donor was revised to malignant meningioma with meningeal invasion.

To summarize, the final diagnosis in this patient was a donor-transmitted metastasis of a malignant meningioma in the transplanted kidney. On the basis of the donor origin of the tumoral process, the therapy with doxorubicin was stopped and no new oncological treatment was initiated. Interferon-α was given for 6 weeks to increase the immunologic alloreactivity of the patient [6].

One month after transplantectomy, the patient was discharged. He remained in complete remission, and, 1.5 years later, the patient underwent a second, uncomplicated kidney transplantation. Twenty years after the donor-transmitted malignant meningioma, our patient remained alive without any oncological relapse. Furthermore, his second graft functioned well, with a serum creatinine level of 1.13 mg/dL (eGFR, 64 mL/min/1.73 m^2 according to the abbreviated MDRD formula) and under triple immunosuppressive therapy consisting of cyclosporine, mycophenolate sodium, and a low dose of prednisolone.

Medical information of the other transplant recipients of this donor was retrieved. The liver and heart recipients did not experience any donor-related problems after transplantation, and the transplanted organs remained well-functioning. The information on the recipient of the contralateral kidney is limited to 5 years after transplantation because of allocation outside of the Eurotransplant zone. Within this time period, there were no reported complications.

Case 2: Urothelial Carcinoma

The second case of donor-related cancer in our series occurred in a white man also with ADPKD who underwent a first kidney transplantation in 1999 at the age of 47 years. One year before the transplantation, a left nephrectomy was performed to increase available infradiaphragmatic space, and, simultaneously with the transplantation, a right kidney nephrectomy took place. Polycystic kidney disease of the native kidneys was histologically confirmed, without any evidence of malignant degeneration of the cysts.

The patient received a kidney from a 50-year-old, heart-beating, female donor who had cerebral edema after a