Donor Transmission Intestinal Carcinoma After Kidney Transplantation: Case Report

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ABSTRACT

Tumor transmission is a rare complication of organ transplantation. Despite several improvements in excluding donor malignant disease, there continue to be reports of unknown tumors in the donors. The risk of having a donor with an undetected malignancy ranges between 1.3% and 2%. The cases of two kidney transplant recipients who had intestinal carcinoma transmitted from the same deceased donor are described. The clinical presentation, previous data, and management options are discussed. As a result of the increase in the overall donor pool, using extended criteria donors, donors of extreme ages, donors with prolonged intensive care admission, and donors who may potentially transmit disease to their recipients, the risk of tumor transmission and also infections should be considered.

POST-TRANSPLANTATION malignancy developing in an allograft is an uncommon complication of organ transplantation. The tumor may be due to malignant transformation of donor or recipient cells that were previously normal, metastatic malignancy of recipient origin, or malignancy transmitted from organ donor to recipient.

The risk of having a donor with an undetected malignancy ranges between 1.3% and 2% [1]. The risk of transmitting cancer by organ transplantation is even lower and is estimated to range between 0.025% [2] and 0.2% [1].

In older donors, the abdomen is frequently the only site investigated for possible malignancy. As autopsies of the donors are rarelyperformed, there is a risk of transmitting tumor cells with the transplanted organ as has been described in the literature [3–6].

In cases with evidence of metastatic disease in the donor after transplantation, the immediate transplant nephrectomy is advocated [7].

In addition, immunosuppression withdrawal will lead to resolution of transmitted malignancies in cases where the renal allograft is the origin [8].

The cases of two kidney transplant recipients who had intestinal carcinoma transmitted from the same deceased donor are described.

CASE REPORT

Both patients received the allografts from the same deceased donor, a 55-year-old man who had a subarachnoid hemorrhage, with no history of hypertension or diabetes. He had no known history of malignancy or evidence of neoplastic disease at the time of the organ procurement (his creatine level was 0.7 mg/dL). The donor had no history of screening for colon cancer and had no family history for colon cancer. The kidneys were recovered by a urologist surgeon.

The first patient was a 52-year-old woman with end-stage renal disease secondary to adult polycystic renal disease in hemodialysis for 1 year. The right kidney was transplanted at the right iliac fossa. The renal vessels were anastomosed at the external iliac recipient vessels in an end-to-side fashion after 13 hours of cold ischemia. The induction immunosuppression was performed with antithymocyte globulin. Postoperative immunosuppression included tacrolimus, mycophenolate mofetil, and prednisone as has been described elsewhere [9].

Because of delayed graft function, this patient was submitted to a percutaneous biopsy (PB) at the sixth postoperative day that yielded acute tubular necrosis with hyaline arteriosclerosis. Routine postoperative Doppler ultrasonography scans were normal. The patient did well and was discharged from the hospital 1 day after the PB (after 2 months, she had a nadir serum creatinine level of 1.54 mg/dL). Doppler imaging results 2 months after the renal transplantation were normal. Five months after transplantation the patient was readmitted because of worsened renal function. Doppler imaging showed slight thickening of the renal pelvis

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without ureteropyelic dilation. A PB at this time revealed a metastatic adenocarcinoma in the parenchyma of probable gastrointestinal primary origin. A positron-emission tomographic (PET) scan showed no evidence of metastatic disease. Upper gastrointestinal endoscopy and colonoscopy results were normal. The patient was submitted to a transplant nephrectomy. After 14 months of follow-up, a computed tomographic scan and a PET scan showed no signs of cancer. The patient will be prioritized in the waiting list after 2 years of follow-up to ensure he is cancer free and is currently in good overall condition.

The second patient was a 22-year-old woman with end-stage renal disease of an undiagnosed cause who had been on hemodialysis for 2 years. The left kidney was transplanted at the left iliac fossa using the same surgical technique after 33 hours of cold ischemia. Basiliximab was used as immunosuppression induction. Postoperative immunosuppression was the same of the previous case.

Routine postoperative Doppler ultrasonography results were normal. A PB on the 18th postoperative day to investigate a slow decrease in creatinine yielded acute tubular necrosis. The patient was discharged on the 21st postoperative day, and after 2 months the creatinine level was 2.09 mg/dL. Five months after transplantation the patient was referred to the emergency unit because of uremia and the need for hemodialysis. Doppler ultrasound showed areas of tortuosity and reduced caliber of the renal artery. Renal artery flow speed was 305 cm/s. Blood pressure was normal. An angiotomography scan revealed 85% obstruction at the anastomosis of the renal artery (Fig 1). A PB was performed during hospital stay and revealed a metastatic adenocarcinoma of gastrointestinal tract origin. A transplant nephrectomy was promptly performed. The kidney aspect is showed in Fig 2. Further staging included a PET scan that revealed no signs of neoplastic disease.

In both cases, immunohistochemistry showed positivity to CA 19.9, and cytokeratin marker KL20 and KL07. Testing for caudal type homeobox 2, prostate-specific antigen, and thyroid transcription factor 1 was negative. A metastasis from a primary malignant intestinal carcinoma was suggested by the results of the immunohistochemical staining (Fig 3).

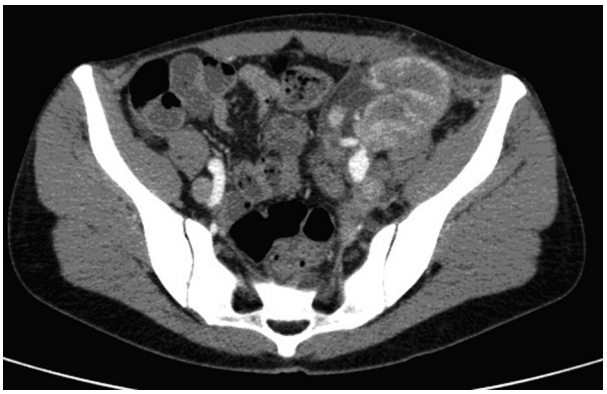

Fig 1. Computed tomography showing 85% of obstruction at the anastomosis of the renal artery.

DISCUSSION

Tumor transmission is a rare complication of organ transplantation. Because of several reports concerning the development of metastatic cancer in the recipients, the use of organs from donors with recognized malignancy was initially abandoned. Despite several improvements in excluding donor malignant disease, there continue to be reports of unknown tumors in donors [10,11].

Since 1997, 114 recipients have been reported to develop malignant disease transferred from donors with a wide variety of cancer types. They include sarcoma of Kaposi, malignant melanoma (MM), colorectum cancer, renal cancer, lung cancer, central nervous system cancer, choriocarcinoma, lymphoma, breast cancer, hypopharynx cancer, prostate, cervix, thyroid, and anaplastic cancer, and cancers of unknown origin [12–15]. It was observed that MM and choriocarcinoma presented with worse outcomes in the transplant recipient [3].

Recently, large follow-up studies showed that donors with non-skin and non–central nervous system cancers have low tumor transmission rates and their kidneys could be used with acceptable risks [2,16]. They include carcinoma in situ of organs such as the uterine cervix or the breast and tumors originating from the urogenital tract. However, some cancers have been recognized to have high transmission risk within the solid organ transplant setting of up to 43%, such as choriocarcinoma and MM [16].

A transplanted organ can transfer malignancy to the recipient in three ways. First, the transplanted kidney may have metastatic cells from a distant primary tumor that may subsequently metastasize in the organ recipient as happened to our patients. Second, the transplanted organ may present passenger leukocytes that may have already undergone malignant change to form a malignant lymphoma. Third, an unknown renal cell carcinoma in the graft may be transplanted.

Once malignancy transfer develops, the withdrawal of immunosuppression and transplant nephrectomy is the most appropriate approach to control the tumor growth, although patient and graft survival can be achieved without removal of the transplant [17].

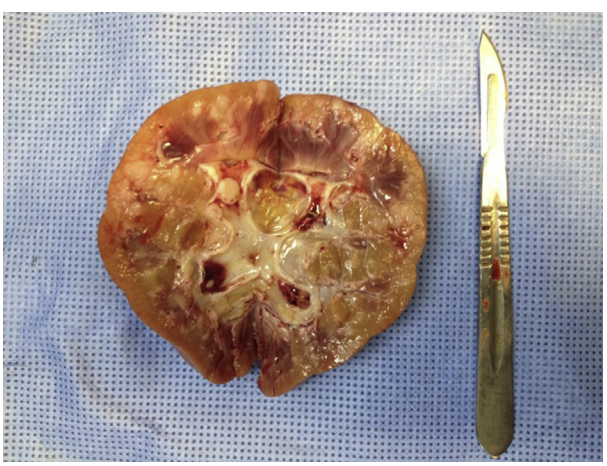

Fig 2. Multiple pearly nodules distributed in the renal parenchyma.

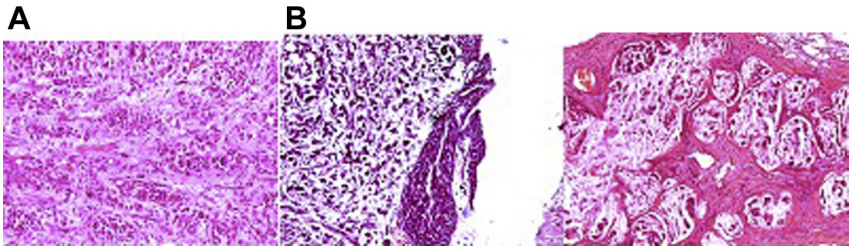

Fig 3. **(A)** Pathology study shows metastasis of mucinous adenocarcinoma that is poorly differentiated. **(B)** Signet-ring cells with vascular and lymphatic invasion.

However, there are few data in the literature regarding the outcome of patients who receive a transplanted malignancy. Penn et al have reported the development of malignancy in 78 (45%) of 142 patients who received a cadaveric graft from a donor who was subsequently found to have a malignancy. The tumor was confined to the graft in 28 cases and became metastatic in 36 cases [16].

Moreover, a recent systematic review studied all published data regarding donor cancer transmission in the kidney transplantation. This review reported 91 cases of donor-transmitted (16 living and 75 deceased) malignancy through donation. The mean ages of these donors varied by cancer types, ranging from 33 years among donors who transmitted choriocarcinoma, to 54 years among those who transmitted lung cancer [18].

The mean time between transplantation and cancer diagnosis varied by cancer type: 1.4 months (1 to 90 days) for choriocarcinoma and 40.2 months (0.3 months to 18.8 years) for renal cancer. A total of 104 confirmed cases of transmitted cancers comprised 20 (19%) renal cancers, 18 melanomas (17%), 15 lymphomas (14%), 9 lung cancers (9%), 7 sarcomas (7%), 6 glioblastoma multiforme tumors (6%), 5 choriocarcinomas (5%) and 24 other cancer types (23%) [18].

A total of 70 (67%) patients with transmitted cancer had graft nephrectomy after immunosuppression withdrawal. Regarding the outcomes, 19 (27%) patients returned to dialysis, 18 (26%) died within a mean of 17.7 months, and 8 (11%) recipients received another transplant within an average of 18.1 months [18]. To our knowledge, we describe the first case of donor transmission intestinal adenocarcinoma at the transplanted kidney. Both of the cases had early diagnoses and satisfactory outcomes.

Considering that the recipient might have to wait for many years for a second kidney transplantation, it is questionable whether a 2-year waiting time is required to reduce the risk of tumor growth under immunosuppression after re-transplantation, once the initial graft has been removed.

To reduce the risk of tumor transmission, some investigators question whether autopsies of all organ donors older than 60 years should be performed within 6 h of organ procurement. The exploration of the abdomen was routinely performed in our case, including the colon inspection. Despite our careful organ retrieval process, minor lesions may not be perceptible.

A high degree of vigilance of the surgeons during the organ retrieval process for possible malignancy of the donor should always be considered.

CONCLUSION

Post-transplantation malignancy developing in an allograft is an uncommon complication of organ transplantation and may represent an unfavorable prognosis.

As a result of the increase in the overall donor pool, the use of extended criteria donors, donors of extreme ages, donors with prolonged intensive care admission, and donors who may potentially transmit disease to their recipients, the risk of tumor transmission and also infections should be considered.

This fact reinforces the importance of a donor selection criteria screening for possible cancer transmission for living and deceased donor transplantation although routine cancer screening among deceased donors is not always possible.

Transplantation clinicians should strictly assess the donors' medical history and refuse organs from donors with any history of high-risk cancers. Therefore, any suspected and confirmed case of donor tumor transmission should be monitored and reported. This systematic register should be advocated in transplanting centers worldwide.

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