Transplant International ISSN 0934-0874

CASE REPORT

Donor transmitted anaplastic carcinoma in a kidney-transplant recipient

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Keywords
anaplastic carcinoma, kidney transplantation, tumor transmission.

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Received: 23 February 2005
Revision requested: 23 February 2005
Accepted: 25 April 2005

doi:10.1111/j.1432-2277.2005.00178.x

Summary

With the more frequent use of organs from elderly donors, the risk of transmitting tumor cells to the recipient increases. We report a case in which anaplastic carcinoma tumor cells from an organ-donor were transmitted to a kidney transplantation recipient. The donor's metastatic disease was discovered 7 days after harvest of the kidney following a brain biopsy undertaken at admission of the donor. The risk of transmitting the disease was generally estimated as so small that the excellently functioning kidney was not removed. Twelve weeks later, however, malignant cells were found in a biopsy of the transplanted kidney. The organ was removed immediately, but the intraoperative situs showed advanced disease with lymph-node-metastasis. Twelve months later no tumor progress could be detected. This case shows that there is considerable risk of transmitting formerly undetected cancer in elderly donors. Autopsies of donors who are older than 60 years of age should be routinely performed after organ donation.

Introduction

Shortage of suitable organs increasingly forces transplant surgeons to use organs from elderly donors. In donors older than 60 years of age, however, there is considerable risk of the presence of previously undetected metastatic tumor disease. Frequently only the kidneys of senior program donors are required so that only the abdomen is investigated for possible tumor disease. Autopsies of the donors are rarely performed. This leads to a notable risk of transmitting tumor cells with the transplanted organ. Although such cases are rare, several of them have been described [1–8]. We now present a new and very dramatic case of fast tumor progress in the organ recipient and a very short interval between transplantation and the first occurrence of symptoms.

Case report

A 60-year-old male with a 6-year history of end-stage renal disease secondary to glomerulonephritis was admitted to our hospital for kidney transplantation. The kidney was provided through the European senior donor program by Eurotransplant. There was an excellent match in the human leukocyte antigens (HLAs) between the donor (BG: A+, HLA: A9 A11 A24 B13 B15 DR4 DR 6 DR 13 DR52 DR53) and the recipient (BG: A+, HLA: A9 A24 A11 B15 B62 BW6 CW3 DR4 DR6 DR13 DR52 DR53). The donor was a 64-year-old male with a history of arterial hypertension which had led to intracerebral bleeding and death. A brain biopsy was performed after admission to the hospital because a cerebral angioma was suspected on CT scan. Unfortunately the patient died and both kidneys were explanted before the histologic results could be provided. Moreover nor the explant team or the transplant surgeon were informed about the brain biopsy. The left kidney was transplanted heterotopically into the right iliac fossa of our patient, the right kidney to a second patient at another hospital. After transplantation immunosupression was started with cyclosporine, MMF and prednisolone. The further postoperative clinical course was eventless and the function of the transplanted kidney was excellent during follow up. During the first 24 h diuresis was 4500 ml and creatinine decreased to 20 mg/l

within 3 days. Seven days after the transplantation we were informed that the brain biopsy of the donor revealed a malignant tumor (Fig. 1). Immunohistochemistry showed a strong positive reaction to the proliferation marker Ki 67 (over 50%), a slightly positive reaction against the cytokeratine marker KL1 and no reaction against vimentine (sarcoma), HMB45 (melanoma) or GFAP (glioma). A metastasis of a highly malignant anaplastic carcinoma (G4) of the lung was suggested by the results of the immunohistochemical stainings, but could not be proven, because an autopsy of the donor had not been performed.

After intensive discussion with leading transplant centers in Europe and within our department the overall consensus was that the calculated risk of transmitting tumor cells with the transplanted kidney was very small. The patient was immediately informed about his status and agreed to keep the kidney although experience with transplantations from donors with metastatic tumors and the potential risk of developing cancer is scanty [1–9]. The patient was discharged 20 days after transplantation in excellent condition. At an examination 12 weeks later, however, the blood-creatinine level had risen and a biopsy of the transplanted kidney was subsequently performed. The biopsy revealed no signs of graft rejection, but there was evidence of a great number of malignant cells (Fig. 1). A magnetic resonance scan the day after the biopsy revealed many nodules in the transplanted kidney highly indicative of carcinoma. Immunosuppression was discontinued immediately and a radical transplant-nephrectomy with iliac and paraaortal lymphadenectomy was performed because the tumor had already invaded the whole kidney and spread into the iliac and paraaortal lymph nodes (Fig. 2). Postoperative histology revealed the same tumor cells that had been found in the brain biopsy of the donor. The tumor marker Cyfra 21–1 was slightly elevated (9.6 ng/ml). We immediately contacted the transplantation center that had transplanted the donor's second kidney. They recalled their patient and found tumor lesions within the graft. After removal of the graft there was also evidence of tumor infiltration of the same type of tumor cells as the donor's.

After removal of our patient's graft, we started immunostimulatory therapy with interferon-γ (100 μg one time per week), followed by adjuvant chemotherapy with cis-platin and vinorelbine. Twelve months after the removal of the transplanted kidney no further tumor progress of the carcinoma could be detected and the patient is in good overall condition.

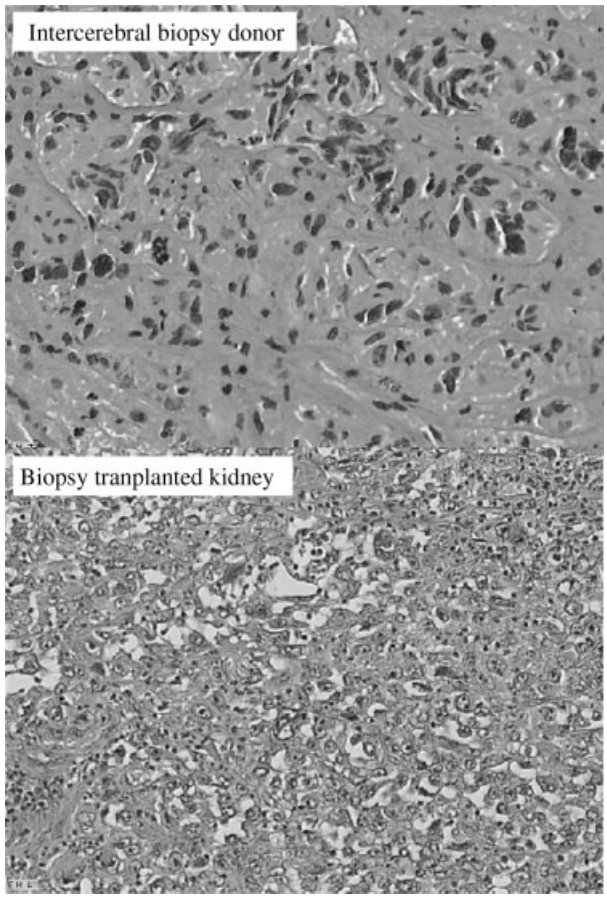

Figure 1 Histology of a brain-biopsy of the donor (up) and of the removed kidney-transplant (down). The same anaplastic tumor could be detected.

Discussion

The considerable risk of transmitting cancer cells by using organs from elderly donors was demonstrated in this case. The probability of a young organ donor having a formerly unknown malignancy is relatively low, but becomes more frequent with elderly donors [1,4,6,7]. The subgroup of organ donors over 65-years of age has risen in Germany from 53 in 1992 to 179 in 2001. In the USA the development is even more dramatic and the number of donors over 65 has risen from 176 in 1992 to 522 in 2001.

In cases with evidence of metastatic disease in the donor after transplantation has occurred, the immediate removal of the organ is indicated to prevent possible tumor-transmission.

In our case tumor progress was promoted and accelerated under immunosuppression [2]. As previously described, however, discontinuation of immunosuppression was not sufficient to prevent the spread of tumor cells. After removal of the transplanted kidney and the affected lymph nodes additional immunostimulatory therapy and chemotherapy were indicated to prevent tumor-progress [7]. Because of the dramatic course of the case described

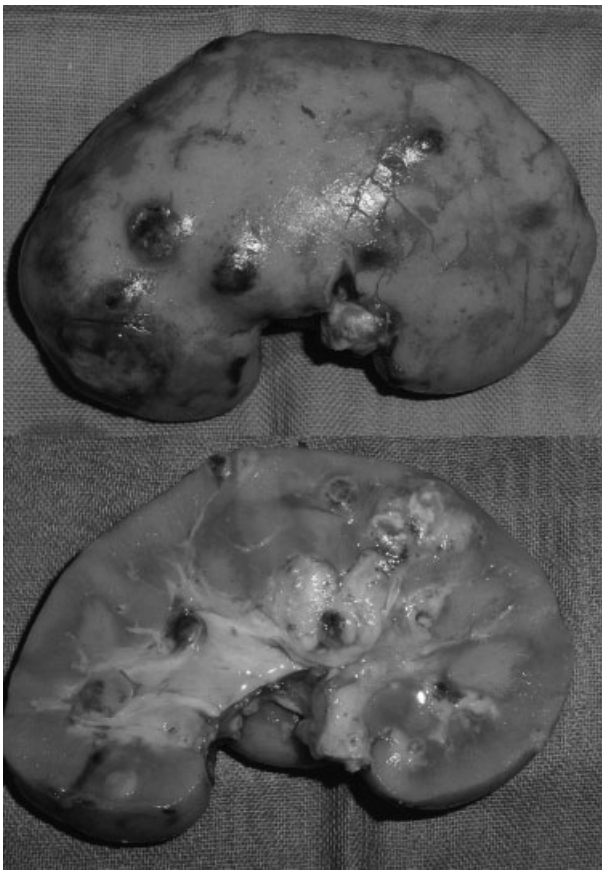

Figure 2 Explanted kidney from the recipient with multiple noduli (1–2 cm diameter) of the anaplastic carcinoma (G4) of the donor.

the question must also be raised whether autopsies on all organ donors older than 60 years of age should be routinely performed within 6 h of organ-procurement. Although this would be the safest way, we think that this would not be possible because of the high expenditure of costs, logistic, personal involvement and the lack of time. Alternatively we need a high level of vigilance of the surgeons during the organ retrieval. Possible tumor disease of the donor should always kept in mind.

Despite previously reported data on brain, melanoma, choriocarcinoma and renal donor malignancies, little data have been presented on solid malignancies. Donors with intracranial bleeding or with undiagnosed brain masses should either undergo biopsy before organ procurement or postprocurement autopsy. Organ recovery must be carried out carefully and if suspicious lesions are found within the donor, an immediate biopsy is mandatory. During the organ harvesting process all the cavities in the donors body should be opened and investigated for tumors, enlarged lymph nodes or other abnormalities. This is especially necessary in older donors when the kidneys are explanted and only a laparotomy is performed. In this case the thorax must be additionally investigated by thoracotomy. Special care should be taken in the investigation of those organs in which the most common cancers have their origin such as the lungs, colon, mamma and prostate gland. The liver should be palpated accurately for suspicious nodules. If possible any suspicious tissue should be examined by frozen section by a pathologist. If this service is not available e.g. at night no organs should be used for transplantation.

If there is evidence that kidneys have been transplanted from diseased donors with no previously known history of malignant carcinoma, immunosuppession should be discontinued and the urgent removal of the kidney is indicated. Further organ transplantation should be delayed until the patient has completed a 2-year disease-free interval. When organ removal is not possible in the case of the heart, the lung or the liver, the administration of immunosuppressives with anti-neoplastic [10] activity such as rapamycin is advocated [11]. Because of the high demand for organs for transplantation, the use of marginal donors or donors with malignancies has been discussed. Malignant tumors are a contraindication against donation except for low-grade skin tumors, *in situ* carcinomas of the cervix uteri and low grade primary central nervous system tumors that have not been subjected to any surgical manipulation. The risk of having a donor with a formerly undetected malignancy is estimated to lie between 1.3% and 2% [1]. The risk of transmitting cancer by organ transplantation is estimated yet lower and lies between 0.025% [3] and 0.2% [1]. The time interval until a tumor which was transmitted by organ transplantation becomes evident can range up to 36–42 months [6,7].

Nevertheless the risk of transmitting tumor cells by organ transplantation is low and should not be exaggerated.

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