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LETTER TO THE EDITOR

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Malignancy transplantation with graft: do patients with primary central nervous system tumors have to be excluded from the donor pool?

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Sir: We read with great interest the paper by Jonas et al. [3] published in the July issue of *Transplant International*. This paper emphasized once again the risk of neoplasm transplantation with grafts. In our transplantation department, we have been very aware of this problem since we have had to face some cases of undetected donor neoplasm, as we reported in 1993 in *Transplant International* [2]. In this paper, we addressed the implications of misdiagnosed malignancy in transplanted organs. As the best prevention for this dreadful complication of transplantation is detection of the malignancy in the donor, we recommended careful observation of the donor during procurement, an immediate frozen section of any suspect lesion, and peroperative echography of the liver and kidney transplants. Following this policy, we have detected two other cases of unknown malignancy before graft transplantation. During multiorgan harvesting in a 47-year-old female donor who died from spontaneous cerebral hemorrhage, a suspect nodule, 5 cm in diameter, was detected in the superior pole of the right kidney. An immediate frozen section demonstrated a clear cell carcinoma. The liver and left kidney were not transplanted; however, the heart had already been transplanted when the results of the pathological analysis became known. The graft was not removed, and the patient was free of recurrent malignancy after a follow-up of 6 months. The second case involved a kidney harvested by another transplantation team, in which a small nodule, 4 mm in diameter, was detected. The immediate frozen section of this nodule revealed a small, well-differentiated renal adenocarcinoma, and so the kidney was not transplanted. However, the contralateral kidney, heart, and liver were transplanted in the transplantion center that did the harvesting, and no recurrence was reported in the 1 year follow-up of these recipients.

In their paper, Jonas et al. reported an interesting case of transmitted glioblastoma in a liver recipient [3]. They compared this case to three other cases of donor-related malignancy after liver transplantation that had been reported in the literature: a choriocarcinoma, a glioblastoma, and a lymphoma. In our opinion, this case of lymphoma of donor origin arising in a liver graft was not a case of transplanted malignancy but rather a de novo malignant tumor that developed in the graft a few months post-transplantation and that was exacerbated by the immunosuppression [8]. This lymphoma presumably arose from lymphoid tissue present in the graft and may have been quite similar to classical lymphoma complicating the post-transplant period. To our knowledge, the third reported case of a malignancy being transplanted with a liver graft was the choriocarcinoma transplantation in a hepatic recipient that we reported in 1993 in *Transplant International* [2].

In their paper, Jonas et al. accurately addressed what is still an unsolved problem: should patients with primary central nervous system (CNS) tumors be considered suitable multiorgan donors? The authors reported one isolated case of glioblastoma transplantation in a liver recipient. Some other sporadic cases of transmission of CNS malignancies to recipients have been reported in the literature [1, 4, 5, 7]. Obviously, the risk of CNS tumor transmission with a graft is very low; however, it is not equal to zero [6]. Jonas et al. concluded from this isolated case that the use of these donors should be avoided. However, in their experience including this disastrous case, organs were harvested from 13 donors suffering from primary CNS neoplasia, resulting in the procurement of 20 kidneys, 13 livers, 8 hearts, 2 pancreases, 1 kidney-pancreas, 1 heart-lung, and 1 single lung graft ($n = 46$). Among these recipients, there was no other case of recurrent donor malignancy after a median follow-up of 43 months. Should the 45 other patients who were successfully transplanted with organs from donors with CNS tumors be refused transplantation because one developed tumor recurrence?

Up to now, there has been no clear answer to this question, and following guidelines from one isolated case is dangerous. For instance, in our department we recently accepted a liver graft harvested from a donor who died from an operated grade II astrocytoma. There was no recurrence at the 6-month follow-up. In order to draw scientific guidelines, it is necessary to analyze larger series of donors who have died from primary CNS tumors, as in the Eurotransplant database, and to study the outcome of the recipients of these organs with special regard to the type of tumor and the neurosurgical procedure. Obviously, several factors may be associated with an increased risk of CNS tumor transplantation, among them: cell type of the CNS tumor, grade of the malignancy, duration of the disease, previous radiation therapy, use of ventriculosystemic shunts, and pre-

vious large craniotomy [4]. Glioblastoma and medulloblastoma seem to be among the more aggressive CNS tumors and, to our knowledge, all of the reported cases of CNS tumor transplantation involved glioblastoma and medulloblastoma [4].

Ideally, any patient with a history of malignant CNS tumors should be rejected for organ donation because a low risk of transmission of malignancy exists. Moreover, ideally, there should be no waiting list for organ transplantation, no shortage of donors, and no deaths among patients on the waiting list. Unfortunately, we are not living or working in an ideal world. Excluding donors with CNS tumors may, in fact, cost more in terms of patients dying while on the waiting list than including them and running the risk of encountering a few cases of tumor transferral.

In conclusion, we presently feel, as others do [1], that patients who die from CNS tumors other than medulloblastoma or gliobastoma should be considered suitable organ donors. There has been no reported case of tumor transplantation with these types of unoperated CNS tumors, despite some cases of spontaneous metastases in nontransplanted patients that have been reported in the neurosurgical literature. Patients with medulloblastoma or glioblastoma, especially if they have undergone surgery, should be rejected as donors since the risk of tumor transferral, although low, does exist. Malignant (grade IV) astrocytoma are aggressive tumors that must be considered as glioblastoma. However, because of the lack of statistical studies, the precise risk is unknown. Yet, what transplant surgeon would refuse a liver graft harvested from a patient with CNS medulloblastoma or glioblastoma for a young patient dying from fulminant hepatitis and awaiting emergent liver transplantation? We believe that these donors should be considered "marginal donors" and that the risk of tumor transplantation should be individually balanced against the natural risk of the recipient's disease. In these donors, peroperative echography would be particularly useful.

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