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LETTER TO THE EDITORS

Extended Criteria Donors: The Case for Liver Procurement in Donors with a Central Nervous System Malignancy

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TO THE EDITORS:

In the December issue of *Liver Transplantation*, Durand et al.[1] extensively reviewed the issue of extended criteria donors in liver transplantation. They mentioned the problem of donors with a history of malignancy and recommended in Table 2 that donors with grade III/IV central nervous system (CNS) malignant tumors be rejected as the risk of malignancy transmission is estimated at 40%. This estimation is in fact very controversial.

The risk of CNS cancer transmission should be evaluated with the ratio of the number of patients who have experienced transmission to the entire population of patients who have received an organ from donors with CNS cancer.[2] For decades, donors with CNS cancer have been accepted as potential donors as CNS cancer very rarely spreads outside the CNS.[3] With increasing experience in transplantation, a few cases of CNS cancer transmission have been reported,[4] and caution has been advised. It was progressively learned that the risk of transmission is higher if the donor had a history of craniotomy, radiotherapy, or ventriculoperitoneal shunt.[5]

The Cincinnati Transplant Tumor Registry, established by Israel Penn, has collected cases of cancer transmission in organ transplant recipients for decades. This registry, now called the Israel Penn International Transplant Tumor Registry (IPITTR), is based on voluntary reports of cancer cases in organ recipients. In this database, the calculated risk of donor cancer transmission with grade III/IV CNS cancer is 40%,[6] and this estimation was reproduced in Durand et al.'s review of marginal liver donors.[1] However, this estimation is biased. First, the IPITTR has collected cases since the 1970s and may not reflect the actual practice of organ transplantation. Moreover, the denominator of the ratio is certainly underestimated in the IPITTR, as it receives cases of cancer in recipients on a voluntary basis and is not designed to scientifically register and analyze malignancies in donors, which have to be prospectively recorded to achieve a good estimation of the total ratio. The underestimation of the denominator of this ratio is the cause of the high calculated risk of CNS cancer transmission in the IPITTR.

More scientifically, the United Network for Organ Sharing (UNOS) collected data from donors with a history of malignancy.[7,8] Between 2000 and 2005, they registered 1069 donors with a history of malignancy, including 642 donors with CNS malignancy. There were 175 glioblastomas, 152 astrocytomas, 31 pituitary tumors, 8 ependymomas, 31 oligodendrogliomas, and 165 other malignancies. These 642 donors allowed the procurement and transplantation of 179 liver grafts. From this large consecutive series, only 1 donor with glioblastoma multiforme transmitted cancer to 3 separate recipients of his kidney, liver, and lung.[8] The overall transmission of CNS cancer with liver transplantation was 0.55% (1/179), and it was 1.8% (1/55) for the highest risk group (glioblastoma multiforme). The only donor who transmitted cancer to his recipients had particular risk factors, including the presence of enlarged thoracic lymph nodes whose later pathology revealed cancerous involvement.[9]

In a perfect world without organ donor shortage, all extended criteria donors would be avoided as they carry an increased risk of graft failure and recipient death. However, in real life, we, the members of the transplant community, face the problems of long waiting lists and waiting list mortality. We try to limit this mortality by the extension of donation criteria to marginal donors, such as donation after cardiac death donors (up to 10% primary nonfunction) and living donors (0.2%-0.5% mortality for healthy donors). The issue of organ donation for patients with grade III/IV CNS malignant tumors should be evaluated according to the balance between the risk of cancer transmission and the chances of being transplanted with a non–extended criteria donor. The risk of transmission of donor grade III/IV CNS malignancy has not been determined yet; it is certainly lower than the unacceptable value of 40% reported by the IPITTR and much closer to the value of 1% to 2%

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estimated by the UNOS database, a more acceptable figure. Recommending the avoidance of liver procurement from donors with a grade III/IV CNS malignancy on the basis of the IPITTR may lead to a much higher number of deaths on the waiting list versus potential transmissions of cancer to the recipients, and it also may put at legal risk those transplant physicians who would accept such extended criteria donors.

The real transmission risk should be evaluated with further prospective studies using, for example, the UNOS or Eurotransplant database. Meanwhile, we think that liver grafts from donors with a grade III/IV CNS malignancy should be used with caution by center-based allocation in fully informed patients who have a high risk of death on the waiting lists or as a replacement for living donor liver transplantation.

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