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BRIEF REPORT

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Liver graft-transmitted glioblastoma multiforme. A case report and experience with 13 multiorgan donors suffering from primary cerebral neoplasia

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Abstract The transmission of donor-related malignancies by organ transplantation is a rather rare event. There has only been one report on the development of a brain tumor metastasis in liver transplantation. From September 1988 to January 1993, 342 donor hepatectomies with subsequent transplantation were performed at our center. The main donor diagnoses included subarachnoidal bleeding (n = 128; 37.4 %), isolated head injury (n = 114; 33.3 %), multiple injuries (n = 55; 16.1 %), primary cerebral neoplasia (n = 13; 3.8 %), and other (n = 32; 9.4 %). Primary cerebral neoplasia included glioblastoma (n = 4), meningioma (n = 3), astrocytoma (n = 2), angioma (n = 2), neurocytoma (n = 1), and ependymoma (n = 1). In the group of donors suffering from primary cerebral neoplasia, procured organs other than the liver included kidneys (n = 20), combined kidneys and pancreata (n = 1), pancreata (n = 2), hearts (n = 8), combined hearts and lungs (n = 1), and single lungs (n = 1). Follow-up of the respective graft recipients ranged from 28 to 68 months (median 43 months). Recurrent malignancy was observed once, in a liver graft recipient. The donor, a 48-year-old female, had undergone surgical resection of an intracerebral multiform glioblastoma and died 4 months later of a relapse in the brain stem. The 28-year-old female recipient had undergone transplantation for an autoimmune-hepatitic cirrhosis. Four months later, histopathological examination of an intraperitoneal and intrahepatic mass revealed a poorly differentiated, small-cell pleomorphic cancer, identified as a glioma metastasis by S100- and glial fibrillary acidic protein immunohistochemical staining. The patient died 6 months post-transplantation. On autopsy, no further neoplastic lesions were detected. Our review adds a second reported case of a liver graft-transmitted brain tumor to the literature and the fourth donor-related malignancy after hepatic transplantation in general.

Key words Glioblastoma, liver transplantation · Liver transplantation, glioblastoma · Malignancy, donor related, liver transplantation

Introduction

During the early years of renal transplantation, organs from donors suffering from malignancies were transplanted deliberately with the knowledge of the neoplastic disease, resulting in a 50 % recurrence rate in the recipients [2]. To comply with an increasing demand for donor organs, efforts are still aimed at extending donor pools. Therefore, exceptions to the current rule precluding organ procurement in cases of donor malignancies

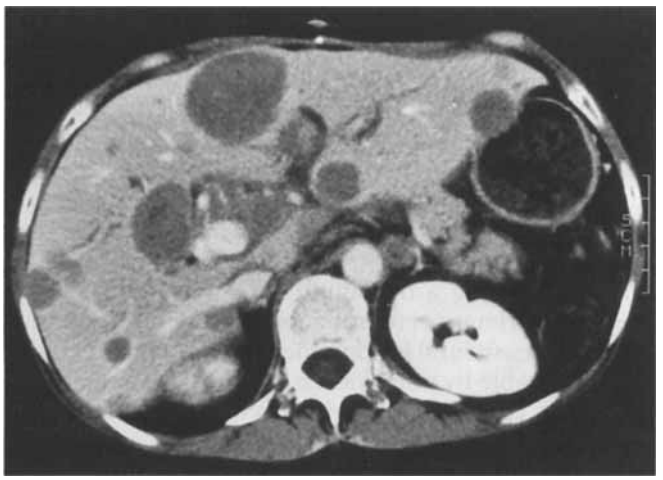

Fig. 1 CT scan 4 months after hepatic transplantation showing bilobar dissemination of glioma metastases

are made for low-grade skin cancers, carcinoma in situ of the cervix uteri, and primary brain tumors [13]. The latter group is considered suitable for organ donation since a transdural spread beyond cerebral confines is believed to be unlikely unless a potential donor had undergone irradiation therapy or ventriculosystemic shunting [3, 12]. However, three cases of donor malignomas transmitted by hepatic transplantation have already been reported: a choriocarcinoma, a lymphoma, and a malignant glial neoplasm without a donor history of cerebrospinal fluid shunting [1, 8, 15]. We describe the development of a glioblastoma multiforme metastasis in a liver allograft recipient 4 months after transplantation. Moreover, we report our experience with primary cerebral neoplasia in 13 multiorgan donors.

Case report

In June 1992, a 28-year-old female underwent orthotopic liver transplantation for chronic liver failure after a 16-year history of an autoimmune hepatitis. During the period prior to transplantation, the patient presented with ascites, encephalopathy, secondary amenorrhea, ecchymoses due to severe thrombocytopenia, and variceal bleeding requiring endoscopic intervention. A suitable liver graft was transplanted following a standardized technique in which all anastomoses were completed prior to reperfusion and both venovenous bypass and side-to-side choledocho-choledochostomy as bile duct reconstruction were performed [10].

The liver donor, a 48-year-old female, had undergone surgical resection of a right frontomedial cerebral mass, 4 cm in diameter, diagnosed histologically as a multiform glioblastoma. Four months later, suspected recurrence of the tumor required a second craniotomy, revealing an infiltrating growth of the glioblastoma into the brain stem. One week after surgical exploration, braindeath occurred. After consent was obtained, the liver, heart, and both kidneys were harvested for transplantation. Except for the craniotomy, neither ventriculosystemic shunting nor irradiation nor any other surgical intervention had been performed.

The postoperative course of the liver graft recipient was uneventful. Immunosuppression consisted of quadruple-drug, sequential induction therapy comprising cyclosporin, steroids, azathioprine, and a monoclonal interleukin-2-receptor antibody [9]. The patient was discharged from the hospital 35 days post-transplantation. Four months later, routine ultrasound examination of the upper abdomen disclosed multiple hepatic masses, and this was confirmed by computed tomography (Fig. 1). Exploratory laparotomy demonstrated an extensive extrahepatic spread of the neoplasia. Histopathological examination of a subdiaphragmatic tumorous nodule revealed a poorly differentiated, small-cell pleomorphic cancer, identified as a glioma metastasis by S100- and glial fibrillary acidic protein immunohistochemical staining [5, 14]. Immunosuppression was continued with low-dose cyclosporin monotherapy. The patient died 6 months post-transplantation. At autopsy, no further neoplastic lesions were detected. The other centers that had transplanted the kidneys and the heart of the same donor were informed. However, the decision was made to dispense with organ removal or retransplantation. After a follow-up of 34 months, no signs of recurrent malignancy or other graft-related complications were evident in the renal or cardiac grafts.

Results

From September 1988 to January 1993, 342 donor hepatectomies were followed by transplantation in our center, and these included a total of 13 (3.8 %) multiorgan donors suffering from primary cerebral neoplasia. The other donor diagnoses were subarachnoidal bleeding ($n = 128$; 37.4 %), isolated head injury ($n = 114$; 33.3 %), multiple injuries ($n = 55$; 16.1 %), and other ($n = 32$; 9.4 %). Primary cerebral neoplasia included glioblastoma ($n = 4$), meningioma ($n = 3$), astrocytoma ($n = 2$), angioma ($n = 2$), neurocytoma ($n = 1$), and ependymoma ($n = 1$). In two of the donors in the glioblastoma group and in one from each of the other groups (except ependymoma), the intracerebral mass had been resected prior to brain death. In another case of glioblastoma, trepanation had been performed, whereas none of the donors had undergone ventriculosystemic shunting. In the group of donors suffering from primary cerebral neoplasia, procured organs other than the liver ($n = 13$) included kidneys ($n = 20$), combined kidneys and pancreata ($n = 1$), pancreata ($n = 2$), hearts ($n = 8$), combined hearts and lungs ($n = 1$), and single lungs ($n = 1$). Follow-up of the respective graft recipients ranged from 28 to 68 months (median 43 months).

Post-transplant graft-related complications resulting in a loss of the graft were mainly associated with donor-independent causes, most frequently rejection (kidneys $n = 3$; hearts $n = 2$), initial nonfunction (liver $n = 1$; kidneys $n = 2$), and thrombosis (kidneys $n = 2$; pancreata $n = 1$). No further case of recurrent donor malignancy was observed.

Discussion

Our report adds to the literature the second case of a liver graft-transmitted brain tumor metastasis and the fourth donor-related malignancy after hepatic transplantation in general [1, 8, 15]. Ventriculosystemic shunts and radiation therapy are well recognized as risk factors for extraneural seeding of brain tumors [12]. Moreover, major craniotomies are reported as an additional factor favoring the spread of brain tumors and may have been operative in our patient as well [3]. However, it is less well known that more than 10 % of all cases reported have shown remote metastases in the absence of any previous surgical manipulation [11]. Glial tumor cells, having access to the systemic circulation, are known to implant and grow in lung, liver, and other tissues [16]. The liver has a tenfold risk of becoming a prime target for metastatic growth of neural cancers compared to the kidneys [11]. Hence, in our series, a recurrent intracerebral donor malignancy was observed only once in a liver graft, while the heart and kidneys of the same donor remained free of tumor recurrence. Although the heart seems to be affected by metastatic seeding of glioma twice as often as the kidney, to our knowledge only one case of transplantation-associated transmission (a medulloblastoma of a donor who had a ventriculoatrial shunt) has been reported [6]. The organs most likely to be involved in metastatic growth of cerebral tumors are the lungs and pleura. This route of transplant-associated transmission has not occurred in our experience or been reported in the literature.

While astrocytoma and glioblastoma are the brain tumors most likely to be associated with extraneural metastases, the cancerous potential of other primary cerebral neoplasia is less explicit. Medulloblastoma are reported to be the type of lesion most likely to metastasize via ventricular shunts [7]. Metastatic growth of meningiomas is also well recognized, and approximately 15 % of those forming metastases display an angioblastic pattern [4].

For several reasons, we would not recommend the use of donors suffering from primary cerebral neoplasia for liver transplantation. First, brain tumors seem to have a more pronounced metastasizing potential than is generally assumed, possibly due to longer survival times, permitting a transdural spread. Second, though the term "primary cerebral neoplasia" describes a variety of diverse neural lesions, these may frequently be indistinguishable by noninvasive diagnostic examinations. Moreover, community hospitals in which organ retrieval is done frequently do not provide the appropriate equipment for extensive intracranial diagnostic procedures, especially when the procurement is done at night. Autopsies performed after organ procurement have demonstrated that even cerebral metastases of occult primary neoplasms are able to mimic brain cancers [12]. Third, although organ donors suffering from primary cerebral neoplasia represented only a small portion of our donor pool, about 70 % of them had undergone surgical interventions prior to brain death or were suffering from either glioblastoma or astrocytoma. Therefore, this subgroup should certainly not be considered for organ donation in the future. The risk of organ retrieval from the remaining pool cannot be assessed reliably either.

While there are certainly no statistical grounds for discarding potentially usable organs, it is unacceptable to transplant organs into patients when the possibility of tumor transmission exists. On the contrary, it is our obligation to each individual patient to dispose of all potentially hazardous organs.

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