Case Report

Can deceased donor with recurrent primary brain tumor donate kidneys for transplantation?

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ABSTRACT

Kidney transplantation from deceased donors is in its infancy in India. Cadaver organ donation was accepted legally in 1994 by the "Human Organs Transplantation Act." Marginal donors are now accepted by many centers for kidney transplantation. We report a case of procurement of both kidneys from a young deceased donor having recurrent primary brain tumor, transplanted into two adult recipients with successful outcome.

Key words: Deceased donor, recurrent primary brain tumor, renal tansplantation

INTRODUCTION

Primary central nervous system (CNS) tumors represent 3–4% of the causes of brain death among organ donors,[1] but, in one series, <0.5% of 13,000 patients dying with a glioma became organ donors.[2] Organ transplantation from deceased donor harboring recurrent primary brain tumor, to the best of our knowledge, has not been reported so far. We report a case where both kidneys from a young deceased donor having recurrent primary brain tumor were transplanted into two adult recipients with successful outcome.

MATERIALS AND METHODS

Both kidneys were procured from a brain-dead, heart-beating 28-year-old female harboring recurrent non-operable, large, low-grade astrocytoma in a city 250 km away from our center. She had no evidence of sepsis and other co-morbidity. Her hematological and biochemical investigations were within the normal range. Urinalysis revealed occasional pus cells and the serum creatinine was 0.9 mg% and serum biluribin was 0.6 mg%. Ultrasonography of the abdomen revealed that both kidney were normal in size, maintained echotexture and had preserved cortico-medullary differentiation. There was no evidence of lymphadenopathy, ascites and liver metastasis.

A standard technique of *in situ* perfusion during organ procurement was used. Briefly, midline laparotomy and thoracotomy was performed. The infra-renal and supraceliac aorta were dissected. *In situ* perfusion was performed with histidine–tryptophan–ketoglutarate solution, blood and fluid were exsanguinated in the chest. Abdominal organs were cooled by ice-slush at the time of *in situ* perfusion and then procured. Both the recipients agreed upon accepting the organ at the first instance when they were counseled regarding the availability of a deceased donor harboring brain tumor and possible risk of cancer transmission, and transplantation was carried out on 24 November 2013.

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Both recipients received induction with rabbit-anti-thymocyte globulin (r-ATG) (1.5 mg/kg) and methylprednisolone (MP) 500 mg intravenously. MP was continued for 3 days post-operatively. Maintenance of immunosuppression consisted of prednisolone (30 mg/day tapered to 10 mg/day at 3 months post-transplant and continued thereafter), mycophenolate mofetil (2 g/day) and tacrolimus (0.08 mg/kg body weight/day). Both recipients also received prophylaxis against cytomegalovirus infection (gancyclovir 1 g thrice a day × 3 months), fungal infections (fluconazole 100 mg once a day × 6 months) and *Pneumocystis carinii* pneumonia (trimethoprim/sulfamethaxazole [160/800 mg] once a day × 9 months).

RESULTS

The cold ischemia time was 9 h. The pre-op and post-op parameters of the two patients who underwent kidney transplantation is tabularized in Table 1. Graft Doppler sonography in both recipients at the 5th post-operative day and at 3 weeks showed normal color flow and spectral wave form, and there was no evidence of renal artery stenosis or renal vein thrombosis. Serum creatinine clearance of both the recipients over the 1-year period is shown in Figure 1. Both patients have completed 15 months of follow-up. During their last follow-up, biochemical investigations of both the recipients were within the normal range. Ultrasonography – whole abdomen and chest X-ray in both recipients showed no abnormality.

DISCUSSION

Despite the huge gap between the demand for and supply of organs for transplantation, it is important to ensure that the risk of transmitting disease with a transplanted organ is minimized. Use of organs from donors with primary cerebral tumors has recently been in focus because of the low risk of extraneural spread, which is reported as 0.4–2.3%.[1] It has been suggested that it is safe to use such donors, if their tumors are known to be low histological grade, but not so for high-grade lesions or where there has been a breach of the blood–brain barrier, such as with craniotomy or insertion of a cerebrospinal fluid shunt.[2-5] As a result of this, few such patients become donors.

Table 1 : Recipient and transplant characteristics

Parametrs	Recipient 1	Recipient 2
Age and sex	29 male	48 male
ABO and Rh blood group	A+	A+
Primary renal disease	Chronic glomerulonephritis	Bilateral urinary tract stone disease
Prior renal transplant	Yes (donor-mother)	none
Present site of renal transplant	Left iliac fossa	Right iliac fossa
Re-warming time	30 minutes	45 minutes
Drain tube removal	No drain kept	2nd POD
Delayed graft function	No	No
DJ stent insertion	Kept, removed after 3 weeks	No stent kept

POD=Post-operative day, DJ=Double-J

A review of the literature suggests that organs donated by deceased individuals with primary CNS tumors can be used for transplantation.[6] However, two important caveats must be kept in mind. Firstly, risk of extraneural metastasis in the presence of a shunt is likely to be <1% as majority of extraneural spread occurs without a ventriculo–systemic shunt. Therefore, absence of shunt does not provide security against possibility of spread. Although there are occasional reports of extraneural metastasis in patients who have undergone surgery, chemotherapy or radiotherapy to the tumor, there is no convincing evidence that these forms of treatment will put the recipient at significantly increased risk of tumor transfer and should not represent an absolute contraindication to transplantation. Secondly, if the lesion is a metastasis or a lymphoma, even if it is primary CNS lymphoma, these patients should not be used as organ donors.

Rubinstein has reported that distant dissemination may occasionally occur with histologically benign astrocytoma of the cerebellum, third ventricle and hypothalamus.[7] Dissemination within neuraxis in histologically benign intracranial astrocytoma has been described. Metastasis from the astrocytomas through the cerebrospinal fluid pathway is rare. It is more likely to arise once growth has breached through the ventricular ependyma and, in most cases, it is accompanied by anaplastic change. The available literature suggests that deceased donor harboring low-grade astrocytoma (as in our case) carries a very low risk of tumor transmission (0.1–1%) to the recipient.[8] Occasional case reports of metastasis to the kidney graft from high-grade lesions (glioblastoma multiforme) has been documented in the literature.[9] However, one of our recipients (who underwent repeat kidney transplant) may be at slightly higher risk for skin

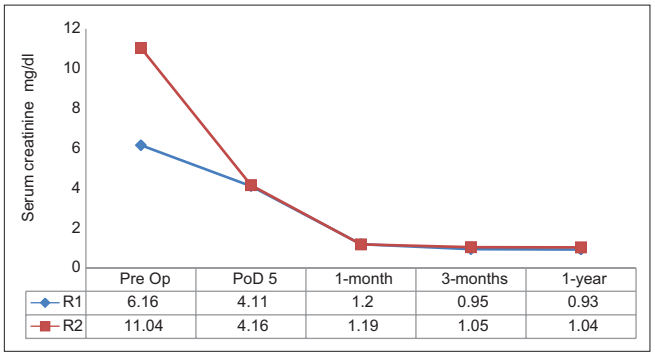

Figure 1: Serum creatinine clearance of both recipients over a period of 1 year

Table 2: Risk of cancer transmission from donors with CNS tumors

Absolute contra-indications	Intermediate risk of transmission (2.2% with an upper 95% CI of 6.4%)	Low risk of transmission (<2%)
Primary cerebral lymphoma	WHO grade 4 tumors and equivalents	WHO grade 3 tumors and equivalents
All secondary intracranial tumors	Glioblastoma including giant cell glioblastoma	Anaplastic astrocytoma/oligoastrocytoma
	Gliosarcoma	Anaplastic oligodendroglioma
	Pineoblastoma	Ependymoma
	Medulloblastoma	Choroid plexus carcinoma
	CNS PNET	Anaplastic ganglioneuroma
	Medulloepithelioma	Pineal parenchymal tumor of intermediate differentiation
	Ependymoblastoma	Pineal papillary tumor
	Atypical teratoid/rhabdoid tumor	Anaplastic/papillary/rhabdoid meningioma
	Malignant peripheral nerve sheath tumor	Hemangiopericytoma
	Germinoma	
	Teratoma: Immature or with malignant transformation	
	Yolk sac tumor	
	Embryonal carcinoma	
	Choriocarcinoma	

CI=Confidence interval, PNET=Primitive neuroectodermal tumor, CNS=Central nervous system

malignancy and lympho-proliferative disorders because of immunological risk factors: Sensitization from prior transplant and cumulative immune-suppression. This small risk of tumor transmission should be balanced against the likely mortality for potential recipients who remain on the transplant waiting list.

Warren *et al.* published recommendations for use of organs from potential donors with CNS tumors [Table 2] based on a UK review of 448 recipients of organs from 177 donors with primary CNS tumors.[6]

Our cadaveric donor had convulsions and recurrent attacks of altered sensorium for the last 1 year before the primary diagnosis of brain tumor in the left temporal region measuring 6.8 cm × 4.5 cm × 5.5 cm on magnetic resonance imaging of the brain. She underwent surgery for the same. Histopathology turned out to be low-grade (grade 2) astrocytoma. She had been advised chemo–radiation but she did not follow-up on the advice. She remained asymptomatic for 3 years. Again, she developed recurrence of brain tumor in the left fronto–temporal region extending to the left cerebello–pontine angle; biopsy revealed low-grade astrocytoma. The tumor was inoperable. As a consequence of this, she succumbed to her condition.

Several important factors should be considered while accepting such a donor. These include cell types, grade of the tumor, prior history of craniotomy, ventriculo–systemic shunt and duration of patient's disease. In view of organ shortage, potentially no organ should be wasted. However, the potential inherent risks of the organs from a deceased donor need to be clearly documented and the patient needs to be counseled before implanting the organ and intensive follow-up with a high index of suspicion should be maintained.

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Conflicts of interest
There are no conflicts of interest.

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