CASE REPORT

Successful Transplant of Two Kidneys Harvested from a Young Brain-Dead Liver Transplant Recipient

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Abstract Efforts to increase the dismal deceased renal transplantation (DRT): live renal transplantation (LRT) ratio in our country have gathered momentum recently, with governmental and non-governmental projects focussing on building public awareness and capacity-building, and appropriate legislation. Worldwide, efforts at increasing the number of organs from the deceased pool have focussed on the use of ‘expanded criteria donors’, including deceased cardiac donors (DCD). ‘Reuse’ transplant, where an organ is transplanted after removal from the first recipient, is a rare strategy, used more commonly in liver than in kidney transplantation. Exceptional circumstances, where other organs have been harvested from transplant recipients, are rare. We describe the successful transplants of two renal grafts obtained from a 19-year-old brain-dead liver transplant recipient; this is probably the second case in English-language literature. A 19-year-old male patient with hepatitis E-induced fulminant hepatic failure underwent live-related liver transplantation. On post-operative day 2, cerebral edema set in, and the patient was declared brain-dead. Despite the economical and emotional trauma, the family opted for donation of the well-perfused kidneys. The kidneys were transported in HTK solution (histidine-tryptophan-ketoglutarate) to our centre. Recipient 1 was a 32-year-old woman (B positive) and recipient 2 was a 29-year-old man (also B positive); the kidneys were placed extraperitoneally and anastomosed end-to-side to the external iliac artery and vein. Recipient 2 experienced delayed graft function; however, both are doing well 15 months posttransplant.

Keywords Deceased donor renal transplant · Reuse transplant · Liver recipient as kidney donor · Cadaver renal transplant · Cerebral edema

Introduction

The rate of deceased renal transplantation (DRT) in India continues to be dismal. The annual number of live renal transplants (LRT) done in India in absolute numbers is about 6000, which in absolute numbers is the second highest in the world after the USA [1]. Renal transplantation started at our centre, a tertiary care hospital in north India, about 3 years back, yet we had not performed a deceased renal transplant even after more than 100 LRT cases. Efforts to increase the DRT: LRT ratio in India have gathered momentum over the last few years with many governmental and non-governmental organizations [2, 3] focussing on building public awareness and capacity-building, along with appropriate legislation.

In established transplant centres around the world, efforts at increasing the number of organs from deceased pool have focussed on the use of ‘expanded criteria donors’, which also include deceased cardiac donors (DCD) [4]. ‘Reuse’ transplant, where an organ is transplanted after removal from the first recipient, is a rare strategy to combat the scarcity of organs for transplantation. This has been used more commonly in liver [5, 6] than in kidney transplantation [7, 8]. A few authors have described exceptional circumstances where other organs have been harvested from transplant recipients [9–11]. We describe the successful transplants of two renal grafts obtained from a 19-year-old brain-dead liver transplant recipient. To the best of our knowledge, this is only the second such case reported in English-language literature.

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Case

A 19-year-old male patient was admitted to the emergency department of a tertiary care liver transplant unit in north India with a 2-week history of fever and jaundice progressing to fulminant hepatic failure and coma (grade 3). The patient's serum was positive for anti-HEV IgM antibodies at the time of admission. The patient underwent emergency live-related liver transplantation on the 4th day of admission; the donor was his elder brother. Induction immunosuppression was performed with basiliximab, methylprednisolone and tacrolimus. In the postoperative period, the patient maintained hemodynamic parameters, regained consciousness and demonstrated a functioning liver graft (normal liver function tests) till day 2. On postoperative day 3, the patient developed severe cerebral edema leading to brain-stem death despite all efforts including mannitol and diuretics. The cause of cerebral edema was probably electrolyte imbalance and/or intracranial haemorrhage postoperatively, and not continuing coma of the hepatic failure.

Despite extreme physical, economical and emotional trauma (two brothers undergoing simultaneous surgery, resulting in failure and death of one of them), the family opted for organ donation as their moral duty to society. The blood group was a common B positive and both the kidneys were well-perfused, with a serum creatinine of 0.8 mg/dL. Two blood samples tested after declaration of brain death had undetectable levels of HEV RNA, signifying lack of infectivity of Hepatitis E virus. Due to these reasons, it was decided to harvest both kidneys for transplantation. A call was sent to the major centres in the city; we communicated our assent and reached the index hospital with our team. Through a midline thoracoabdominal incision, we performed in situ perfusion using HTK solution (histidine-tryptophan-ketoglutarate) through suprarenal aortic cannulation. The thorax and mediastinum was opened to provide a low-resistance vent of the perfusate returning via the inferior vena cava (IVC). Both kidneys were harvested with a single renal artery on an aortic patch, and a single renal vein with an IVC cuff. The thoracic incision also enabled harvest of the entire abdominal aorta till the diaphragm for cryopreservation. The kidneys were preserved in HTK solution and slush, and transported to our centre.

Recipient 1: The first crossmatch negative, B positive recipient was a 32-year-old woman, with a history of CKD for 4 years as a result of contrast-induced nephropathy. She had been on maintenance hemodialysis for 2 years. Her native urine output was about 1 L/day.

Recipient 2: The second recipient was a 29-year-old male student, also B positive and crossmatch negative, with ESRD for 2 years due aetiology chronic glomerulonephritis. He was also on maintenance hemodialysis. His native urine output was less than 100 mL/day.

Both recipients were negative on standard virology and cancer screening. The ileofemoral vessels were found to have

normal flow on Duplex scans. After extensive bench dissection on the grafts, the kidneys were placed extraperitoneally in the right lower quadrant in both recipients. The renal artery was anastomosed end-to-side to the external iliac artery, and the renal vein similarly to the external iliac vein. The neoureterocystostomies were fashioned over D-J stents. Table 1 summarizes the intraoperative and postoperative course in both recipients.

Discussion

The perpetual shortage of organs for transplantation has led transplant team to evolve newer strategies to overcome this problem. Donation after cardiac death (DCD) is an established strategy which has shown equivalent results to donation after brain death (DBD) [12]. Reuse of organs is a non-traditional approach, which has been used more frequently for liver transplants, both in the early postoperative period and also after many years. Cerebral edema and intracranial haemorrhage may contribute to brain death in liver transplant recipients, without affecting the perfusion of viscera [5, 9, 13]. Tanaka and colleagues have shown in a systematic review of 28 such cases that outcomes of transplantation using previously

Table 1 Intraoperative and postoperative course of both recipients

	Recipient 1	Recipient 2
Induction immunosuppression	Inj. ATG 4.5 mg/kg	Inj. ATG 6 mg/kg
Immunosuppression	Tacrolimus + Mycophenolate mofetil + Prednisolone	Tacrolimus + Mycophenolate mofetil + Prednisolone
Warm ischemia	0 min	0 min
Cold ischemia	6 h	20 h
Urine production	Immediate on table	Delayed graft function; acute tubular necrosis on graft biopsy
Postoperative complications	Superficial surgical site infection	Laryngitis; lymphocele (resolved on expectant management in 4 weeks)
Hospital stay	12 days	35 days
Follow-up	Well at 14 months (urine: 6 L/day, serum creatinine = 0.9 mg/dL)	Well at 14 months (urine: 4.5 L/day, serum creatinine = 1.1 mg/ dL)
HEV status during follow-up (2 weeks, 3 months, 9 months)	HEV RNA undetectable Anti-HEV IgG-negative LFT normal	HEV RNA undetectable Anti-HEV IgG-negative LFT normal

transplanted grafts are similar to those seen with conventional grafts [13]. Judicious use of mannitol, saline and diuretics is important to prevent cerebral edema in emergency liver transplant recipients.

Reuse of kidney allografts has not been reported frequently. Kamar and colleagues describe a case where the index recipient developed intractable recurrent thrombotic microangiopathy (TMA), which necessitated nephrectomy. The well-preserved graft was then successfully transplanted into a recipient with polycystic kidney disease [8]. Kadambi et al. have described the case of a 42-year-old man who received a kidney from a deceased recipient, who had undergone transplantation 7 years previously; the new recipient was well 5 years later despite suffering from ganciclovir-resistant cytomegalovirus (CMV) infection. The authors have reviewed the scanty literature available on this subject, and concluded that since most renal transplant recipients die with a functioning graft, re-transplant of the organ, though challenging, is feasible. [7, 14].

Romatowska and colleagues performed a successful liver harvest and transplant from a 26-year-old male patient, who had undergone kidney transplant 6 years previously and was on triple immunosuppressive regimen with cyclosporin, rapamycin and prednisone. Despite the potential hepatotoxicity of these drugs, the authors reported a favourable postoperative outcome. In the same paper, they have depicted data from the United Network for Organ Sharing (UNOS) from 2000 to 2012 showing the large number of organs retrieved from 718 deceased transplant recipients—762 organs (264 kidneys, 368 livers, 79 lungs, 36 hearts, 13 pancreases and two intestines). However, there is no data on the further utilization of these organs. [9].

Domagala et al. performed successful immediate retrieval and transplanted two kidneys from a 21-year-old brain-dead liver transplant recipient in Poland in 2012, [11] while Peng and colleagues from China in 2013, retrieved and transplanted two kidneys from a liver transplant recipient 5 years post-transplant, with good results [10]. These two cases are the only two in literature similar to our case; early retrieval of the kidneys was a notable feature in our case. Chua et al. from Australia in 2015 have reported the use of four kidneys; two each retrieved from a lung transplant recipient and a lung transplant recipient on the waiting list. Thus, we are seeing this novel strategy taking shape all over the globe [15]. HLA typing in deceased organ transplant is possible only when computerized algorithms are available at the national level matching the pairs; since we do not yet have these systems, we perform HLA (which is expensive) usually just before live donor renal transplant. The use of HLA typing today is not sacrosanct for deceased donors; assuming our recipients as high-immunological risk without HLA matching, we induced them with anti-thymocyte globulin (ATG).

A major emotional and ethical challenge confronts the transplant team when the issue of harvesting organs from a

brain-dead recipient arises. The entire family has recently been through a tumultuous experience, and may be busy with another hospitalized member if a live donor was involved, as in our case. The success of the grafts retrieved may be questioned by the new recipients, in view of the immunosuppression received and the postoperative course of the brain-dead recipient. However, as shown by earlier authors, immunosuppression is not a contraindication for donation [9, 16]. Organ retrieval from transplant recipients has been successfully performed despite years of use of triple immunosuppression [9]. We feel that the transplant team can see the situation as a unique opportunity, since the family involved in transplant is already sensitized to the needs of these patients, and they know how precious organs are to people on the waiting list. Also, by reporting more such cases, physicians around the world can gather courage for entering unknown territory. However, despite the satisfactory results of a few such cases, we are still a long way from advocating previous transplant recipients to be conventional organ donors.

Another point of debate while accepting the liver transplant recipient as an organ donor was the presence of hepatitis E virus, as the donor had suffered fulminant hepatitis E-induced liver failure. The donor was tested twice in different laboratories for HEV RNA, which was undetectable in both. The case was discussed with experts in both hospitals, who concluded that since there was no similar precedence, we would have to decide on the available evidence. Hepatitis E is a hepatotropic virus, which can cause acute fulminant liver failure by an immune-mediated process. Being a self-limiting infection, viremia clears by the second week, as evidenced by HEV RNA levels. HEV RNA is also a marker of infectivity. The progression to chronic hepatitis E is rare (<1 %). Only recently, it has been shown that chronic hepatitis E can occur in a few patients, especially liver transplant recipients as they are immunosuppressed. The exposure might have occurred earlier either by occult infection in blood transfusions, or by the virus persisting in liver cells. Detection of hepatitis E persistence necessitates antiviral therapy for 20 weeks [17, 18].

We reasoned that since HEV RNA was undetectable, that chronic hepatitis is a rare event, and, in any case, the kidneys were unlikely to harbour the virus (which mostly persists in liver cells and consequently excreted in stools), it would be prudent to offer these kidneys to willing recipients. The scenario was explained to the potential recipients, who gave informed consent both for the procedure and the subsequent screening for HEV RNA and IgG anti-HEV. Since immunization against hepatitis E for recipients on the waiting list is still not recommended by the WHO due to non-standardization of the vaccine, no vaccine was offered [19]. The follow-up is ongoing and the recipients are negative for evidence of hepatitis E infection (HEV RNA undetectable, LFT normal) more than a year later.

We need to strengthen co-ordination between hospitals and build infrastructure capable of utilization of organs available at odd hours. In our scenario, the call was received close to midnight; till early morning, one team assisted organ retrieval while another prepared the operating room for renal transplant at our hospital. Since no national or regional matching is available, potential recipients on the hospital waiting list were individually contacted, called to the hospital, and evaluated clinically and with cross-match; all within a span of a few hours. Out of five, two were finalized (two patients higher on the waiting list were cross-match positive). Due to these obstacles, the second kidney was utilized 10 h later, when the second recipient was ready. All aspects of this co-ordination including transport, specialized laboratory tests, and drugs (HTK solution) were managed individually. We realized the acute need of ‘prior readiness’ at our hospital and all government hospitals, including readiness of the traffic police for creation of ‘green corridors’.

Conclusions

This case highlights the need for novel strategies and increased sensitivity amongst all practising physicians to the problem of organ shortage in our country. Whenever possible, we must identify potential donors in the intensive care units and contact transplant personnel to motivate the family members, within the prescribed guidelines. Capacity building in government institutions must be on a war footing to benefit the large number of poor patients with organ failure. We have thus described a rare and implausible scenario where a transplant recipient turned into an organ donor, and how this was accomplished by laudable efforts of the doctors and the family, despite many systemic shortcomings.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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