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Case Report

First case report of multivisceral transplant from a deceased cardiac death donor

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ABSTRACT

The current shortage of pediatric multivisceral donors accounts for the long time and mortality on the waiting list of pediatric patients. The use of donors after cardiac death, especially after the outbreak of normothermic regional perfusion, has increased in recent years for all solid organs except the intestine, mainly because of its higher susceptibility to ischemia-reperfusion injury. We present the first literature case of multivisceral donors after cardiac death transplantation in a 13-month-old recipient from a 2.5-month-old donor. Once exitus was certified, an extracorporeal membrane oxygenation circuit was established, cannulating the aorta and infrarenal vena cava, while the supra-aortic branches were clamped. The abdominal organs completely recovered from ischemia through normothermic regional perfusion (extracorporeal membrane oxygenation initially and beating heart later). After perfusion with the preservation solution, the multivisceral graft was uneventfully implanted. Two months later, the patient was discharged without any complications. This case demonstrates the possibility of reducing the time spent on the waiting list for these patients.

1. Introduction

Multivisceral donors are particularly critical in pediatric transplantation and shortages are responsible for the high mortality rate on the waiting list (WL).[1-3] Despite the increasing use of donors after cardiac death (DCD) in other solid organ transplants, with results similar to those of donors after brain death (DBD),[4-9] this option has not been tried in intestinal transplantation owing to susceptibility to ischemic damage.[10]

Abbreviations: DBD, donor after brain death; DCD, donor after cardiac death; ECMO, extracorporeal membrane oxygenation; MVT, multivisceral transplantation; NRP, normothermic regional perfusion; POD, postoperative day; SD, standard deviation; WL, waiting list.

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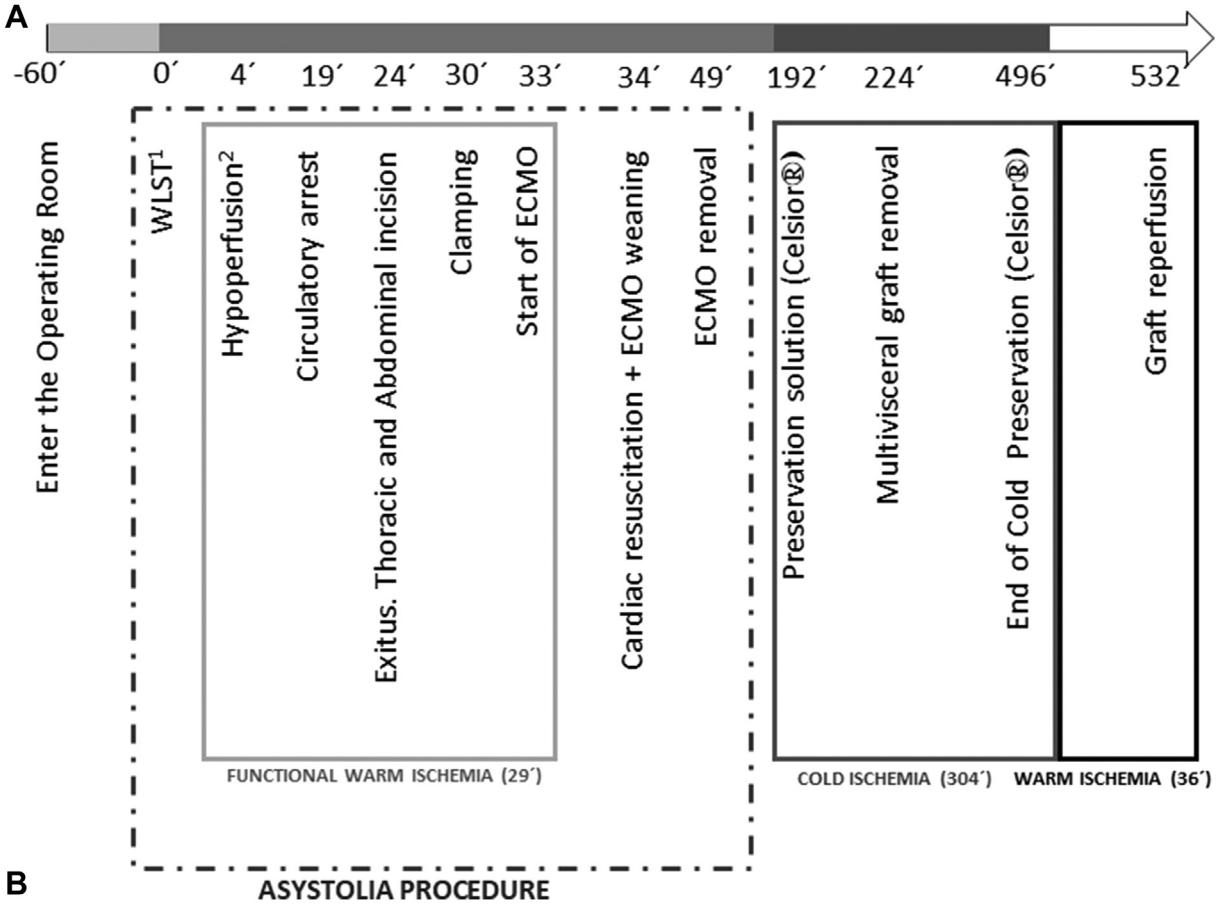

B

Minutes	0	60´	90´	120´	150´	210´
Hemoglobin (g/dl)	11.2	14.4	12.1	8.6	12.0	13.2
Leucocytes (x10^3/µl)	14.06	8.64	5.21	5.06	6.30	7.01
Lymphocytes(%)	13.4%	45.5%	61.8%	52.4%	38.6	37.3
Platelets (x10^3/µl)	463	172	247	235	163	158
Prothrombine activity	104%	65%	68%	55%	71%	72%
INR	1.0	1.3	1.3	1.3	1.2	1.1
Prothrombine time (seconds)	10.7	16.4	17.0	17.2	12.6	12.4
AST[3](UI/L)	14	82	172	138	129	133
ALT[4] (UI/L)	20	59	126	97	95	93
GGT[5] (UI/L)	140	66	67	69	69	73
Alcaline phosphatase (UI/L)	63	66	68	72	75	77
Total Bilirubin (mg/dl)	<0.15	<0.15	<0.15	<0.15	0.15	0.22
Amilase (UI/L)	<20	<20	<20	22	29	28
Creatinine (mg/dl)	0.11	0.15	0.15	0.22	0.20	0.15

Figure 1. (A) Chronogram of the procedure; [1]WLST, withdrawal of life-sustaining treatment; [2]Definition of significant hypoperfusion: mean arterial pressure: <60 mmHg in adults, <50 mmHg in >10 year-old children, <40 mmHg in 1-10 year-old children, and <30 mmHg in children <1 year old. (B) Liver and intestine function monitoring after beginning extracorporeal membrane oxygenation (ECMO) and cardiac resuscitation. [3]AST, aspartate transaminase; [4]ALT, alanine transaminase; [5]GGT, Gamma-glutamyl-transferase; INR, international normalized ratio.

However, normothermic regional perfusion (NRP) has decreased this complication.[8,11] Furthermore, preliminary reports in experimental models have shown that DCD intestinal grafts are viable.[12] We present the first case of DCD multivisceral transplantation (MVT), with excellent short-term results. We previously demonstrated the feasibility of this procedure in rat and porcine models (in press).

2. Case report

The ethical committee and organ-allocating authorities approved the procedure before launching the clinical program. The donor's and recipient's parents signed informed consent forms.

The recipient was a 13-month-old girl referred at 1 month of age with short bowel syndrome secondary to jejunal atresia. On admission, her weight and height were 2.320 kg (standard deviation [SD], −4.1) and 45 cm (SD, −4.4), respectively; she had duodenocolic anastomosis, left subclavian vein thrombosis, and history of catheter-related sepsis with mild nonbridging portal fibrosis. There were no cardiologic, pulmonary, or neurologic contraindications; therefore, she was listed for MVT at 4 months of age. Meanwhile, she received total parenteral nutrition with fractionated oral feeding shots. Anti–human leukocyte antigen antibodies and Epstein-Barr virus/cytomegalovirus IgG/IgM were negative. During transplantation, severe malnutrition was evident: weight, 3.88 kg (SD, −5.8) and height, 65 cm (SD, −4.6). She spent 9 months on the WL.

The donor was 2.5 months old without past medical history. He was admitted because of neurologic deterioration that progressed to refractory epileptic status. Brain magnetic resonance imaging confirmed necrotizing encephalopathy. The medical team and parents agreed to withdraw mechanical support treatment. The patient was intubated without inotropic support and had normal cardiac, renal, and liver function. Once the donation offer was accepted, morphine perfusion was initiated to ensure comfort. He was placed in the operating room and monitored, and the sterile surgical field was prepared without additional invasive maneuvers. Heparin (3 mg/kg) was administered intravenously. The extracorporeal membrane oxygenation (ECMO) circuit (Maquet Rotaflow I System, Getinge) and left cavity vent line extension were prepared and recirculated to prevent thrombosis. The recovery team then left the room to make way for the parents, who entered through a separate corridor with the coordinators and the physician responsible for the patient.

The patient was extubated, and vital functions were monitored. Significant hypotension appeared at 4 min, and circulatory arrest was confirmed 19 min after withdrawal of mechanical support treatment. The parents left the room, and 5 min later, the retrieval team began organ recovery.

The cardiac and abdominal teams worked simultaneously to perform sternotomy and ligation of the supra-aortic trunks and cannulation of the infrarenal aorta and vena cava. After cannulation, the arterial and venous lines were connected, and NRP (36°C-37°C) began 9 min after cardiac

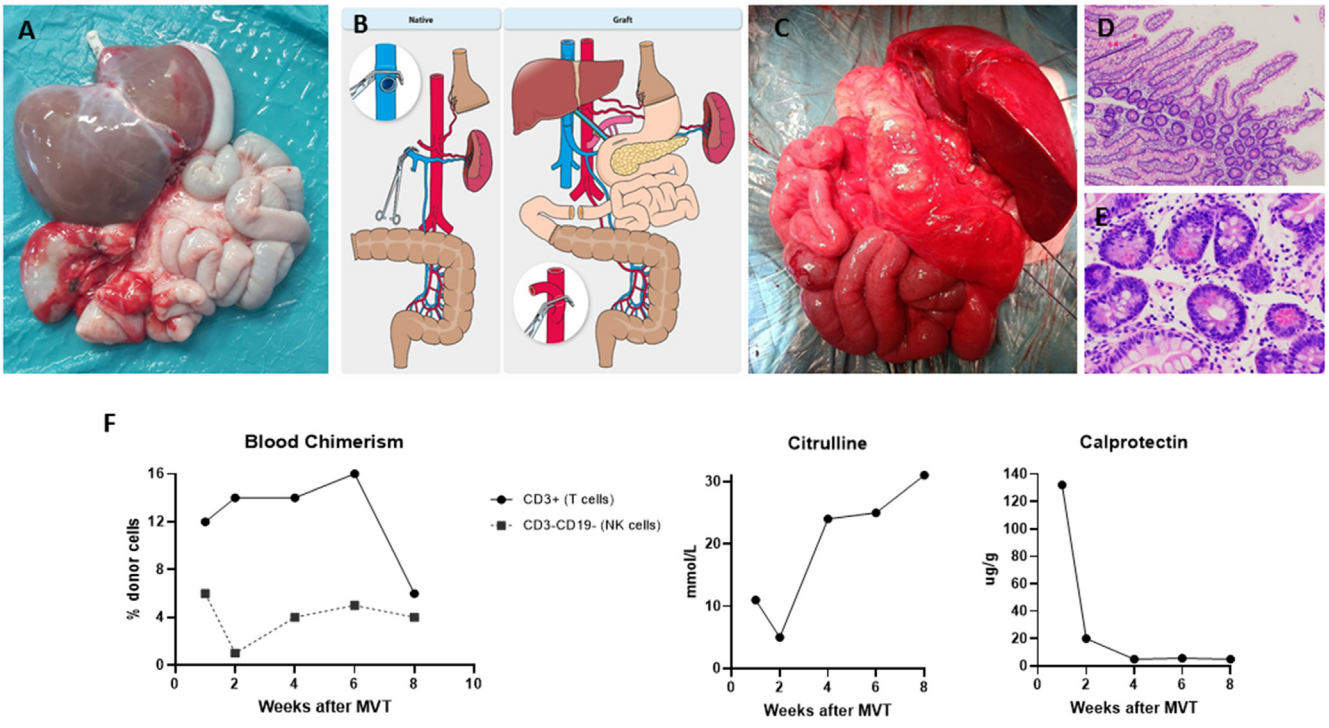

Figure 2. (A) Multivisceral graft during the back table surgery: The graft includes a cluster comprising stomach, small bowel, large bowel, liver and pancreas in bloc, with the abdominal and thoracic aorta. The excess tissue is removed from the donor, the intercostal and lumbar branches of the aorta are clipped, followed by cholecystectomy and splenectomy. (B) Transplant procedure: 1. Subcostal bilateral laparotomy. 2. Dissection of the bloc formed by the short bowel including the duodenum and part of the stomach as well as the liver, with particular attention to preserve the splenic artery and vein, as well as the left gastric artery and vein. The cava vein was fully preserved with a piggyback technique. 3. Placement of an arterial graft from the donor thoracic aorta in the recipient infrarenal aorta. 4. Completion of the enterectomy and hepatectomy. 5. Once in the anhepatic phase, anastomosis of the donor's suprahepatic veins to the recipient's suprahepatic cava and anastomosis from the donor's thoracic aorta to the aortic graft is performed. The donor's inferior vena cava is used for portocaval anastomosis, to preserve the native spleen and left colon.[13] 6. Reperfusion. 7. End-to-end gastro-gastric and ileocolic anastomoses, pyloroplasty, and loop ileostomy. In this case an ileocolonic anastomosis was made since there was an abscess in the donor's colon and the recipient had native colon so this was not used. 8. Placement of a Gore-Tex mesh for abdominal wall closure. (C) Multivisceral graft aspect 5 min after reperfusion. (D) and (E) Two-week-protocol biopsy through the stoma showing normal small bowel mucosa without histologic lesions or apoptosis or viral cytopathic changes. (F) Measurement of chimerism in peripheral blood, as well as fecal calprotectin, and citrulline levels at the time of transplantation, and at 2, 4, 6, and 8 weeks after transplantation. Reference value for fecal calprotectin: <100.0 μg/g; reference value for citrulline: 9-38 μmol/L. CD; MVT, multivisceral transplantation.

death was certified (Fig. 1A). The venting cannula in the left atrium was connected to a Y-circuit. The flow was progressively increased to reach a target of 2.6 L/min/m^2. After a cardiac massage, the heart began to beat spontaneously 1 min after NRP began without requiring defibrillation.

Samples of venous and arterial blood gases were drawn before the procedure, 5 min after starting ECMO, and 20 min before leaving the NRP. Gasometry showed hemoglobin, minimum 10.3 mg/dL, lactic acid, maximum 10.3 mmol/L (reduced to 2.7 mmol/L before Celsior), and pH 6.9, which was corrected with $HC03^{-1}$M until normalization. As the organ perfusion was optimal and the donor was stable with good blood pressure and cardiac contractility, the flow progressively decreased until withdrawal 16 min later. At this point, communication between surgeons and perfusionists was essential for maintaining hemodynamics during weaning from ECMO.

The donor was reintubated and hemodynamically stable and underwent optimal diuresis for the remainder of the procedure. Perfusion used norepinephrine, epinephrine, plasma, red blood cells, calcium chloride, and sodium bicarbonate. The abdominal viscera showed good perfusion. Transaminases moderately increased but progressively improved after 2 hours (Fig. 1B), and the intestine showed minimal petechial patching with no changes during dissection maneuvers. These 2 parameters were the main decision-making points.

Multivisceral graft procurement was similar to that in DBD. Briefly, the distal esophagus and colon were stapled, and the abdominal bloc was removed after transection of the thoracic aorta and inferior vena cava. Intravenous heparin (300 IU/kg) was administered immediately before perfusion with Celsior solution.

MVT was performed according to the standard procedure (Fig. 2A, B).[13] This was preferred over combined liver–small bowel grafting, owing to the greater simplicity. The cold ischemia time was 340 min, with an excellent macroscopic graft appearance after reperfusion (Fig. 2C). The heart was successfully implanted in a 2-month-old infant with dilated myocardiopathy from birth; unfortunately, that patient died 2 days later.

The immediate postoperative days (PODs) were uneventful, and the stoma began functioning within the first hour. The cross-match test results were negative. There was a maximum peak of transaminase levels on POD 1 (aspartate transaminase, 1182 IU/L: alanine transaminase, 512 IU/L), with normal values until discharge. On the sixth POD, the Gore-Tex mesh was removed, showing an excellent graft appearance. She was fed fractionated elemental formula on the ninth POD, and oral intake progressively increased.

The patient received standard immunosuppression,[14] basiliximab for induction and tacrolimus and steroids for maintenance. Usual antibiotic and antiviral prophylaxes were administered for 14 days. Figure 2C-E shows the 2-week-protocol biopsy, chimerism in peripheral blood, fecal calprotectin, and citrulline levels.

Two months after transplantation, the patient returned home, was able to eat orally, was asymptomatic (5.1 kg), and had stable tacrolimus levels and digestive losses of approximately 55 mL/kg/day, although she remained on parenteral nutrition for a catch-up, with a view to its withdrawal in the coming weeks.

This case report presents the first case of a DCD intestinal/multivisceral transplant. NRP allowed control of the liver's biochemical and macroscopic recovery of the MVT graft. This technique has never been described before in such as young donor.[15] We observed no additional difficulties or adverse events during the postoperative period of grafting from a DBD donor. This case report could pave the way for reducing the time spent and mortality of patients on the WL.

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Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the American Journal of Transplantation.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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