First Heart Transplantation in a Small Child in Romania

H. Suciu¹, M. Oprisă², M. Suciu², M. Ispas³, A. Sglimbea¹, R. Deac³

¹Department of Cardiovascular Surgery for Children and Adults, University of Medicine and Pharmacy Tg. Mureș, Romania
²University of Medicine and Pharmacy Tg. Mureș, Romania
³Department of Cardiology, Tg. Mureș, Romania

Abstract
Heart transplantation is a life-saving procedure for irreducible heart failure in children as in adults. Worldwide there is a great amount of experience with this procedure, while Romania is only at the beginning. The authors are presenting the experience concerning the first small child heart transplantation in Romania, underlining the pre-operative and post-transplantation experience. The patient, a 3 year-old girl, diagnosed with class IV NYHA functional classification congestive heart failure secondary to an idiopathic dilated cardiomyopathy, has received an isogroup isoRh donor heart on the 14th of January 2011. The operative technique used was an orthotopic bicaval technique. In-hospital postoperative evolution was favourable, the child receiving triple immunosuppressive therapy and prophylaxis therapy against cytomegalovirus, fungi, and pneumocystis carinii bacteria. Myocardial biopsy performed 1 month after transplantation showed no signs of rejection. The child is in good health at 31 months (2 years, 8 months) after the transplantation. Heart transplantation in children is the result of teamwork, while the procedure can be performed with low mortality and morbidity in centers with large experience in heart transplantation and pediatric cardiovascular surgery.

Key words: heart transplantation, child

Corresponding author: Associate Prof. Suciu Horia
Department of Cardiovascular Surgery
Institute for Cardiovascular Diseases and Transplantation, Tîrgu Mureș, Romania
50 Gh. Marinescu Street
E-mail horisuciu@gmail.com
Introduction

Heart transplantation entered the scene of medical therapy 40 years ago. During this time, advances were made that transformed this treatment in a feasible solution for end-stage heart failure in adults and children. Heart transplantation started in Romania 14 years ago, but pediatric cases are very rare due to several more or less objective reasons. Two pediatric heart transplants have been performed in Romania: one in 2000, in a 11 years old girl and one in a small child, the case presented in this paper. Both cases were operated in the Cardiovascular Surgery Clinic, Institute for Cardiovascular Diseases and Transplantation, Tirgu Mures.

Case report

The patient is a 3 year-old girl, diagnosed with dilated cardiomyopathy at the age of 6 months. After several heart failure periods, the girl ended up in congestive heart failure (CHF) NYHA IV class, with extremely reduced exercise tolerance, failure to thrive, 10 kg weight at the age of 3, with reduced pulse volume and pressure on palpation at all extremities, pallor, diminished heart sounds, heart rate 120 BPM, Blood Pressure - 80/50 mmHg, systolic murmur of III/6 degree at the apex, moderate respiratory distress, no pulmonary rales, hepatomegaly at 3 cm below the right rib cage, no splenomegaly, no neurologic impairment.

EKG showed: Sinus rhythm, HR- 130/min, QRS axis +80, left and right ventricular hypertrophy and left atrial enlargement.

On thoracic X-ray: Cardiothoracic ratio 0.63, significant cardiomegaly, enlarged middle and inferior margins of the left heart border, no acute pleural or pulmonary lesions (Fig. 1).

Cardiac ultrasound: Enlarged left and right atria. Significantly enlarged left ventricle with globally depressed contractility, with an ejection fraction (calculated using volumes) of 15% and spontaneous echo contrast. Significant mitral regurgitation. Estimated systolic pulmonary pressure = 60 mmHg (1).

At this point, while the child was in a hemodynamic stable period, a potential donor heart became available. The donor was a 5 year-old child, 15 kg in weight, in brain dead status. Negative crossmatch for B and T lymphocytes.

After the parents consented for organ donation, the heart was harvested from the donor, being preserved with a Celsior solution. Ischemia time was 196 minutes.

In the meantime, assessment of our recipient patient revealed a systolic pulmonary artery pressure of 60 mmHg by echocardiography, establishing the need for an invasive hemodynamic assessment. Cardiac catheterisation was performed under general anesthesia, without complications, the result confirming adequate hemodynamic data for heart transplantation (2).

The transplantation procedure was performed using the bicaval technique, with a heart-lung by-pass time of 148 min and an ischemic time of 196 minutes (3 hours and 16 minutes) without any significant complications (3).

Standard median sternotomy was performed and total cardiopulmonary by-pass installed. In moderate hypothermia at 32°C the aorta was cross clamped and the recipient heart was explanted in bicaval fashion, leaving a cuff of the posterior wall of the left atrium with the four pulmonary veins, the distal part of the two vena cavae, main pulmonary artery and the ascending aorta (Fig. 2, 3). At this point, the implantation of the donor heart was performed using the modified anastomotic sequences used routinely and reported by our surgical team (3). Instead of performing first the left atrial anastomosis, as in the classic Shumway technique, in order to reduce the ischemic time
of the donor heart, we started with the aortic termino-terminal anastomosis, followed by aortic cross-clamp removal and reperfusion of the heart. On the beating heart, with great care for avoiding air embolism, the remaining four anastomoses were performed using Polypropylene running suture - left atrium, inferior vena cava, superior vena cava and pulmonary artery. Great care was taken to avoid right ventricle dilatation during the filling of the heart and suppression of the cardio-pulmonary by-pass (Fig. 4).

Modified ultrafiltration was performed for 20 minutes at the end of the extracorporeal circulation, in order to reduce the systemic inflammatory response by removing the specific metabolites (4).

Peri-operative therapy consisted of:
- Induction immunosuppressive therapy with Methylprednisolone iv 250 mg preoperatively and 300 mg/day postoperatively; Rabbit Anti-thymocyte Globulin (ATG) 12.5 mg/day postoperatively for 4 days;
- Inotropics: Milrinone 0.5 μg/kg/min, Dobutamine 10 μg/kg/min, Adrenaline 0.1 μg/kg/min, Noradrenaline 0.1 μg/kg/min;
- Antibiotic prophylaxis: iv Cefuroxime 900 mg/day, iv Diflucan (Fluconazole) 54 mg/day, po Vulganciclovir 225 mg/day, po Sumetrolim (mg on Trimetoprim component).

The patient was extubated after 30 hours and the drain tubes were removed 4 days postoperatively. The ICU stay was 12 days (5).

Immunosuppressive therapy continued with Prednisone 5 mg/day, Tacrolimus 1 mg/day, Myfortic (MMF) 360 mg/day. As CMV (Cytomegalovirus) status of the donor was negative, but transfused blood used was not tested for CMV, prophylactic therapy was started 5 days after the operation. Antifungal prophylaxis was started on the first day, along with prophylaxis against Pneumocystis carinii on the 5th postoperative day, with Sumetrolim.

Antihypertensive therapy was needed, as BP values went up to 140/70 - 150/80 mmHg. Diltiazem 3x10 mg doses, associated with Captopril 3 x 2.5 mg, were administered, resulting in normalization of BP values, in accordance with the child's age.

Echocardiographic follow-up initially showed a normal biventricular systolic function, along with impaired diastolic function, without any localized contractility impairment, with a minimum amount of pericardial fluid, which disappeared over the following days.

On the 12th postoperative day, the child was transferred to the ward. 5 weeks after the transplantation, a myocardial biopsy was performed, showing no signs of rejection.

The child was discharged home on day 33 after transplantation. At 31 months after transplantation (2 years, 8 months) the child is in good health.

Discussion

Pediatric heart transplantation is a complex therapeutic process, involving a multidisciplinary team: cardiovascular surgeons, pediatric cardiologists, anesthesiologists and cardiac intensive care specialists, interventional cardiologists, infectionists, immunologists, transplant coordinators and high quality nursing.

In heart transplantation, an ischemic time under 4 to 5 hours is a prerequisite for success. With the technique used – a modified sequence of anastomoses, as previously published (3) called "aortic anastomosis first’’ we managed to obtain an ischemia under 4 hours. This technique is recommended especially for a distant donor heart, the ischemic time being shorter with nearly 1 hour at reimplantation.

A proper functioning transplantation program has to be organized in detail. A separate unique national transplantation list for children is recommended.

At international level, the indications for transplantation...
are developed in countries which are able to provide complex bridge-to-transplantation care. In a country unable to offer this type of care, indications for transplantation should be adjusted to best fit the needs of the particular population.

Personalized therapy leads to less side effects and better long-term prognosis (6). The major limitation of transplantation is the lack of donor organs. In Romania, this is caused by inadequate information of the population and the lack of information among medical professionals about the opportunity of this therapy. The presented case is a small but unique experience in Romania (7,8).

Conclusions

1. This is the first heart transplantation performed in a small child in Romania.
2. In our experience pediatric heart transplantation in infants and small children is limited by the lack of small age donors.
3. Pediatric heart transplantation is a multidisciplinary activity involving cardiovascular surgeons, pediatric cardiologists, anesthesiologists and intensivists, interventional cardiologists, infectionists, immunologists, laboratory and transplant coordinators and high quality nursing, the results depending on the team work, experience and organization of the Heart Transplantation Program.
4. Two and a half year survival of our patient is encouraging for further experience.
5. The procedure can be performed with low mortality and morbidity in centers with large experience in heart transplantation and pediatric cardiovascular surgery.
6. The success of heart transplantation in small children offers the prospect of a healthy adolescent or adult in the future.

Acknowledgements

This paper is partially supported by the Sectorial Operational Programme Human Resources Development, financed from the European Social Fund and by the Romanian Government under contract number POSDRU/89/1.5/S/60782.

References

1. Canter CE, Shaddy RE, Bernstein D, Hsu DT et al. Indications for Heart Transplantation in Pediatric Heart Disease: A Scientific Statement From the American Heart Association Council on Cardiovascular Disease in the Young; the Councils on Clinical Cardiology, Cardiovascular Nursing, and Cardiovascular Surgery and Anesthesia; and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation. 2007;115:658-76.