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CASE REPORT

Application of decellularized allograft for primary repair of congenital heart disease in Japan

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Abstract

A 6-month-old infant with a double outlet right ventricle, doubly committed ventricular septal defect, and right ventricle outflow tract (RVOT) stenosis underwent intracardiac repair with RVOT reconstruction using a fresh decellularized allograft derived from a 1-year-old heart transplant recipient in Japan. Early postoperative evaluation via echocardiography and cardiac magnetic resonance imaging revealed that the pulmonary allograft and cardiac function were stable. This is the first case report on using a decellularized heart valve, which was resected from a heart transplant recipient, for primary repair of congenital heart disease in Japan.

Keywords Congenital heart disease · Tissue engineering · Decellularization

Introduction

It has been reported that the technique of decellularization of the heart valve can suppress immunological reactions, while maintaining a structural scaffold [1]. Several reports suggest that this type of valve has superior durability and growth potential because it reseeds the patient's own cells [2]. However, for using this treatment method in Japan, securing a heart valve within the country is very important.

We report the first clinical application of a decellularized fresh pulmonary allograft from a Japanese heart transplant recipient for the primary repair of congenital heart disease in a Japanese infant.

Case

This clinical study was performed with the approval of the Ethics Committee of the Osaka University Graduate School of Medicine, Osaka, Japan (No. 12318). Informed consent was obtained from the guardians of the heart transplant recipient (who provided the heart allograft) and the patient who had the pulmonary allograft replacement.

The patient was a 6-month-old infant with double outlet right ventricle, doubly committed ventricular septal defect and right ventricle outflow tract (RVOT) stenosis. The preoperative percutaneous oxygen saturation was approximately 85% in room air. The diameter of the pulmonary allograft was 5 mm, which was 50% of a normal pulmonary valve size. We recommended using a fresh, decellularized pulmonary allograft for RVOT reconstruction, as part of our clinical study.

The diameter of the fresh decellularized allograft was 10 mm, 100% of the normal size for the patient's body surface area (Fig. 1a). The allograft was provided from a 1-year-old girl with dilated cardiomyopathy who was on a left-ventricular assist device (Berlin Heart Excor®). We dissected her pulmonary allograft at the time of her heart transplant at Osaka University Hospital. The decellularization process was performed by CorLife GbH (Hannover, Germany). The decellularization procedure was certified by transplant organizations in Germany (approval no.: PEI.G.11634.01.1) [3]. We transported the removed pulmonary allografts to CorLife GbH under controlled temperature conditions (0–15 °C). In brief, pulmonary allografts were treated under shaking conditions with a solution of 0.5% sodium deoxycholate and 0.5% sodium dodecyl sulfate for 36 h. The allografts were then washed with NaCl 0.9% solution. The created decellularized heart valves were transported back

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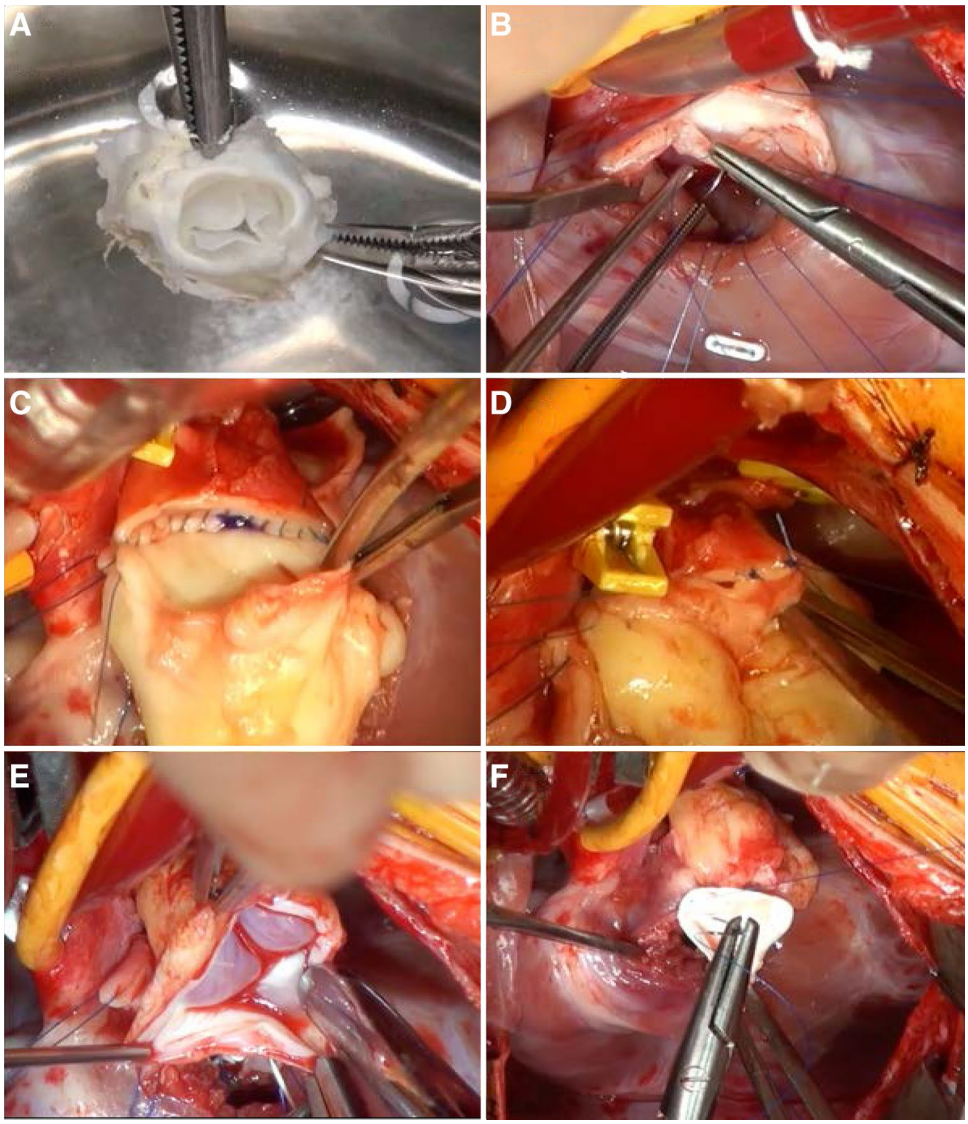

Fig. 1 **a** Fresh decellularized pulmonary allograft. **b** Doubly committed type of ventricular septal defect was closed with an ePTFE patch. **c** The peripheral site of the allograft was anastomosed with a continuous suture. **d** The anterior wall was anastomosed with an interrupted suture. **e** The proximal end of the allograft was anastomosed at the pulmonary allograft annular position. **f** Augmentation with an ePTFE patch was performed

to Japan under controlled temperature conditions (0–10 °C) and transplanted within 4 months after preparation.

The operation was performed using mild hypothermic cardiopulmonary bypass and mechanical cardiac arrest. The RVOT was opened longitudinally and passed through the pulmonary valve annulus. A doubly committed type of ventricular septal defect was closed with a polytetrafluoroethylene (ePTFE) patch using a 6-0 Prolene mattress suture (Fig. 1b). The decellularized heart valve function was determined to be good by the water test, and a 10-mm bougie could just pass though the allograft.

The peripheral site of the allograft was anastomosed with a 6-0 Prolene continuous and interrupted suture (Fig. 1c, d). The proximal site of the allograft was anastomosed at the native pulmonary valve annular position with a 5-0 Prolene continuous suture (Fig. 1e). Augmentation with an ePTFE patch was performed on the anterior surface of the right ventricle (Fig. 1f). Weaning from cardiopulmonary bypass was uneventful.

She was discharged on postoperative day 21 without any postoperative complications. Two types of antiplatelet drugs were used; no immunosuppressant drugs were administered. Postoperative cardiac MRI examination and catheter examination revealed that the cardiac function as well as valve function was maintained. The velocity of blood flow through the pulmonary allograft was 2.5 and 2.6 m/s at postoperative 6 and 12 months, respectively, on MRI examination (Table 1). The pressure gradient through the pulmonary allograft was 32 mmHg on catheter examination at postoperative 12 months.

Table 1 Result of cardiac magnetic resonance imaging

	Baseline	3 months	6 months	12 months
LVEDVI	49.6	103.1	–	85.4
LVESVI	31.3	46.8	–	39
RVEDVI	66.3	65.6	–	82.9
RVESVI	31.3	40.6	–	51.2
RF	0	0	0	10
Valve flow	–	1.9	2.5	2.6
Annulus diameter	10	10	11	12.2
BSA	0.3	0.32	0.34	0.41

LVEDVI left ventricle enddiastolic volume index, ml/m^2, *LVESVI* left ventricle end-systolic volume index, ml/m^2, *RVEDVI* right ventricle enddiastolic volume index, ml/m^2, *RVESVI* right ventricle end-systolic volume index, ml/m^2, *RF* regurgitant fraction, %, *Valve flow* m/s, *Annulus diameter* mm, *BSA* body surface area, m^2

Comment

To our knowledge, this is the first case report of the use of a fresh decellularized heart allograft from a Japanese hear transplant recipient for primary repair of congenital heart disease in Japan. We believe that there are two important points to note in this case.

The first is that we used a pulmonic allograft from a heart transplant recipient in Japan. To use this treatment method in Japan, harvesting the heart valve in our own country is very important. In Europe, approximately one-third of homografts are heart allografts taken from the heart removed from the recipient of the heart transplant [4]. Therefore, the ability to use a Japanese cardiac transplant recipient's heart allograft is very useful from the viewpoint of medical resources in Japan.

The second point is that a fresh decellularized heart valve has the potential for self-regeneration by self-cells in the transplanted tissue [2]. In addition, Cebotari et al. have reported that when implanting this type of tissue into a child, the diameter of the valve annulus is maintained normally according to the patient's growth, and valve function is maintained [5].

Moreover, the decellularized allograft used in this case was not to be cryopreserved after being decellularized and was to be transplanted within 4 months. The structure of the extracellular matrix is deteriorated after performing cryopreservation [6], and it is speculated that the efficiency of cells entering (recellularization) after transplantation improves and the durability is maximum when using decellularized allografts under fresh conditions. These facts suggest that this valve is likely to grow after transplantation as the patient grows. In this case, regarding the function of the implanted pulmonary valve, it was confirmed that it was good even in the catheter examination and MRI examination 1 year postoperatively, and the valve annulus diameter was also larger than the diameter of the annulus in the sixth month after the operation. Moreover, comparing postoperative 6 months and 1 year, even if BSA increased, there was no change in the rate of blood flow through the transplanted pulmonary artery graft. On the other hand, the pressure gradient across the transplanted pulmonary grafts has not worsened but has elapsed with flow velocity that was the upper limit of the permissible range. Thus, we think that it is necessary to follow up on the progress of stenosis in the future.

In summary, we report early results of intracardiac repair for a double outlet right ventricle using a fresh decellularized pulmonary allograft derived from the heart of a Japanese transplant recipient. Long-term follow-up is necessary; however, the use of this allograft may be an alternative primary surgical technique for the treatment of congenital heart disease in Japanese infants.

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