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Case Report

Canada's First Successful Paediatric Total Artificial Heart Implant

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Cardiac allograft vasculopathy and antibody-mediated rejection after heart transplant result in an inflammatory process that can cause systolic and diastolic dysfunction and recalcitrant arrhythmias. Haemodynamic supports in this context are challenging as retransplant is not always feasible with active rejection. Standard mechanical circulatory support in the form of a left ventricular assist device supports systolic function but is higher risk with arrhythmias and diastolic dysfunction. Ongoing immunosuppression adds to infection risk. Therefore, total artificial heart support has been used in failing allografts. We present the first Canadian paediatric total artificial heart as a successful bridge to retransplantation.

Case

An 11-year-old girl 3 years after heart transplant for a history of Ebstein's anomaly with left ventricular noncompaction presented with persistent tachycardia, diastolic dysfunction, mildly reduced systolic function (ejection fraction 48%), and severe mitral regurgitation. The clinical course after her initial transplant was unremarkable despite a slightly longer total ischemic time of 5 hours 14 minutes. Crossmatch at the time of transplant was negative, and there was no cytomegalovirus mismatch.

After admission on this occasion, her haemodynamics revealed raised right- and left-sided filling pressures (left ventricular end-diastolic pressure 27 mm Hg and right atrial pressure 17 mm Hg). Coronary angiography showed moderate cardiac allograft vasculopathy (CAV) with no narrowing in the left main coronary artery and mild stenosis in the proximal left anterior descending and circumflex arteries. Biopsy findings were consistent with pAMR2 (histology and immunopathologic positivity) with no evidence of cellular rejection. *De novo* class II donor-specific antibody, DQ6, developed during this time. Findings were consistent with severe antibody-mediated rejection (AMR) and moderate CAV. She received pulse intravenous steroids, thymoglobulin, intravenous immunoglobulin, retuximab and plasmapheresis. Maintenance immunosuppression was augmented to the combination of tacrolimus and sirolimus with mycophenolate mofetil. She was discharged with weekly plasmapheresis cycles, tapering dose of steroids, and outpatient follow-up. However, despite these therapies, she re-presented 1 month later with an out-of-hospital cardiac arrest with a rapid response to bystander cardiopulmonary resuscitation. Repeat angiography demonstrated a significant progression of CAV, with diffuse distal disease in all branches and the paucity or absence of distal branches in some regions. She was admitted to the intensive care unit (ICU) and required milrinone and epinephrine infusion to maintain cardiac output and developed a secondary acute kidney injury necessitating dialysis, which improved over the following week.

Despite the augmented immunosuppression, she remained in a marginal state and experienced a brief arrest with pulseless electrical activity 1 week after admission with rapid return of spontaneous circulation. After multidisciplinary discussion, she was assessed for a potential total artificial heart (TAH) implant to allow for stable cardiac output and end-organ perfusion, with cessation of antirejection medications and resolution of the overall inflammatory state before retransplantation. Given borderline age and size (body surface area

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Novel Teaching Points

- SynCardia 50 cc TAH allows for durable biventricular MCS in patients with low BSA.
- The use of SynCardia TAH provides a unique opportunity for durable MCS with cessation of immunosuppression in the context of rejection.

[BSA] 1.16 m^2), a virtual fit test for TAH was reviewed, and it was determined that a 50 cc pump should suitably fit based on the 3D modeling (Fig. 1). She proceeded to TAH insertion with the SynCardia 50 cc device 2 weeks after admission.

Despite extensive dissection of the mediastinal space after explanation of the heart, including taking down the left-sided pleura and pericardium, and the anterior part of the diaphragm, there was anterior compression of the inferior vena cava (IVC) and left pulmonary vein due to the stiff nature of the device compared with native cardiac tissue. The intraoperative course was complicated by lung reperfusion injury coming off cardiopulmonary bypass with difficult oxygenation, which improved with inhaled nitric oxide. There were additional challenges such as high central venous pressure (20-25 mm Hg) and fluctuating pump flow, necessitating frequent volume infusion to maintain cardiac output through the pump. Postimplantation cardiac output was approximately 2.5-3 L/min.

After prolonged haemostasis, she returned to ICU with the sternum stented open. Her initial postoperative course was complicated by haemodynamic instability, manifested by low urine output and lactic acidosis (peak 11 mmol/L), attributed to profound systemic inflammatory response. She required volume resuscitation and vasopressors to maintain systemic perfusion. Oxygenation slowly improved with high ventilatory pressures. Immunosuppression was discontinued on the day of TAH insertion. She received antibiotic and antifungal prophylaxis for cardiac surgery and delayed sternal closure. Anticoagulation was initiated on day 1 postoperatively with therapeutic heparin.

The sternum was closed on postoperative day 4 with some fluctuation of haemodynamics with residual moderate lower-left pulmonary vein and IVC compression and 1-2 cm of the lower sternum left open. Follow-up computed tomography to delineate the extent of venous compression showed a large mediastinal haematoma. As such, she returned to the operating room on day 10 for mediastinal exploration and haematoma evacuation. The posterior aspect of the sternum was also thinned by cautery as it was noted to be tight between the device and the chest wall to allow for chest closure. No additional interventions were required to address the IVC or pulmonary veins.

The subsequent ICU course was marked by hypertension and 1 episode of pulmonary haemorrhage that was likely related to the TAH "full filling." She was extubated 2 weeks postoperatively and transitioned to the ward 4 weeks postoperatively. After a period of rehabilitation with physiotherapy and improved nutritional intake, she was activated on the waitlist and received a second heart transplant 2 months after TAH insertion. TAH removal at the time of retransplant necessitated careful planning for sternal re-entry and dissection. Additional challenges included the presence of an old thrombus and adhesions in the chest cavity, difficulty visualizing the IVC due to the right-sided pump, and challenges establishing a plane between the aorta and the pulmonary artery due to the existing pulmonary artery graft. Cardiopulmonary bypass was initiated ascending aortic and 2 venous cannulae. The air tube for the right pump was transected, which allowed us to cannulate the IVC; then both pumps were completely explanted. The intraoperative course thereafter was otherwise unremarkable.

Our patient remained off immunosuppression for the course of her TAH support. At the time of retransplant she had one class II donor-specific antibody (DR4). She received routine perioperative steroids and one volume of plasma exchange while on pump.

Remarkably, she was discharged home only 9 days after the transplant. She was treated with pulse steroids for AMR but remains well at home 18 months after retransplant.

Discussion

This case documents the first paediatric use of TAH in Canada, with a successful bridge to retransplant. End-stage heart failure and refractory arrhythmias due to CAV presented a significant management dilemma for which the SynCardia 50 cc TAH represented a unique opportunity to provide durable mechanical circulatory support (MCS). Specific challenges in this case included inotrope dependence, recalcitrant arrhythmias, small body size, and the need for ongoing immunosuppression.

CAV involves a complex multifactorial inflammatory process, contributed to by ischemia reperfusion injury, cellular rejection, donor-specific antibody, and lifestyle-mediated disease such as hyperlipidemia, hypertension, and diabetes, and remains the primary indication for retransplant in paediatrics.[1] Our patient had early-onset aggressive CAV in association with AMR despite a relatively low-risk profile, with the only risk factor of note being a prolonged ischemic time after her initial transplant. Despite her previous surgeries, she was not sensitized before her initial transplant, had a negative retrospective crossmatch, no cytomegalovirus mismatch, no prior rejection episodes, no additional lifestyle risk factors, and had been managed with statin therapy before her graft failure.

However, managing our patient's combination of AMR and severe CAV was additionally challenging due to the potential for immunosuppressive agents to potentiate vasculopathy.[2] The deleterious consequences of CAV in association with rejection have been well described, with studies demonstrating a significant increase in risk of mortality in those with AMR and CAV vs AMR without CAV.[3] Our patient had been treated with standard maintenance immunosuppression with mycophenolate mofetil and tacrolimus. Sirolimus was added after the diagnosis of CAV, as mammalian target of rapamycin inhibition demonstrated slower disease progression.[4]

Selection criteria for cardiac retransplantation remain controversial with many centres not offering paediatric retransplant for early graft failure due to the low likelihood of long-term survival.[1] However, recent adult data have

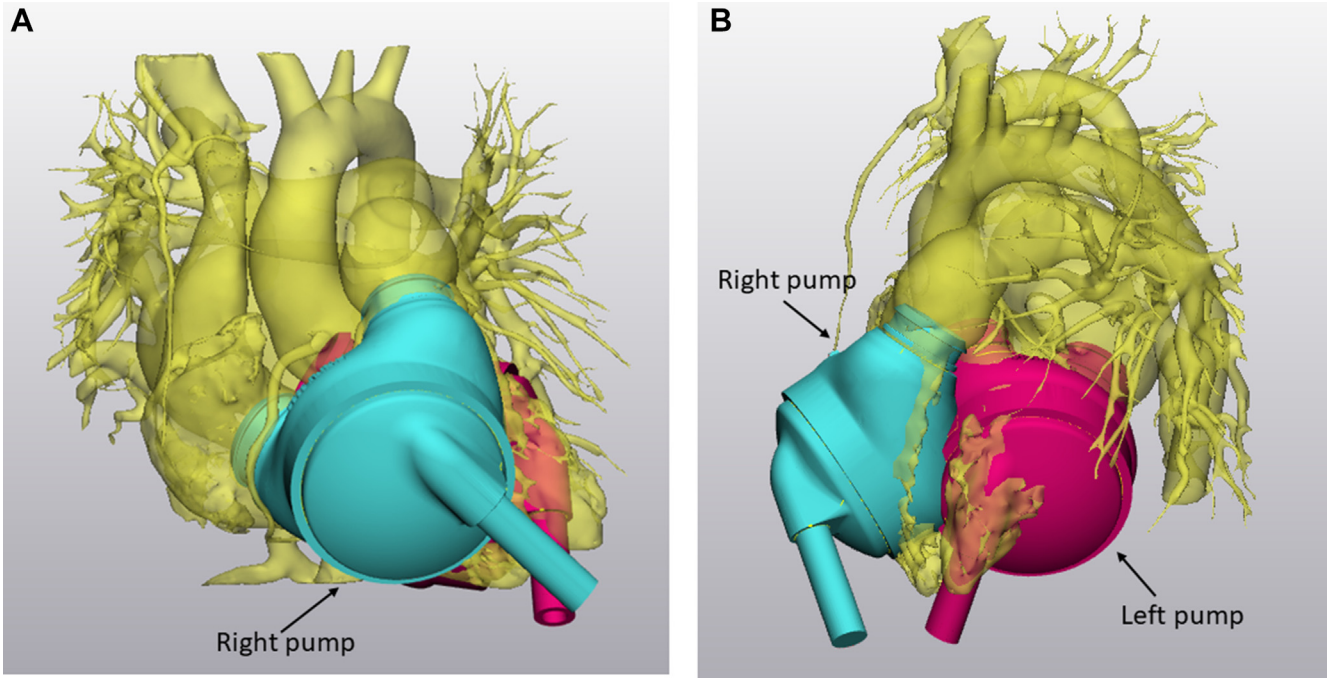

Figure 1. Virtual fit test for the SynCardia 50 cc Total Artificial Heart. (**A**) Virtual fit test for the SynCardia 50 cc Total Artificial Heart; frontal view. (**B**) Virtual fit test for the SynCardia 50 cc Total Artificial Heart; left lateral view.

demonstrated improvements in outcomes after retransplant in those who can achieve rehabilitation on MCS. Moreover, survival after retransplant in those bridged with a ventricular assist device or TAH was superior to those treated with extracorporeal membranous oxygenation or medical management.[1] During support, our patient demonstrated good end-organ function and remained a reasonable candidate for retransplant. However, supporting her to retransplant and facilitating rehabilitation presented a unique challenge. Historically, Berlin Heart EXCOR has been a mainstay support for children requiring durable long-term biventricular support, although data support an increase in mortality for this cohort. Thus, over the last decade, the frequency of use of biventricular support has declined as implant strategies have evolved including timing of implant and supportive measures based on specific patient characteristics and severity of illness.[5] However, conventional ventricular assist device support in the context of active rejection in our patient would have necessitated continued high levels of immunosuppression, with significant associated infection risk, and likely ongoing inflammation.

MCS in paediatric populations presents the additional challenge of smaller patient size relative to device size. The development of the SynCardia 50 cc device designed to support patients with BSA as low as 1.2 m^2 has expanded opportunities for viable biventricular MCS. Since the advent of the Syncardia 50 cc device, TAH has been successfully used in paediatric patients as a bridge to transplant with BSA as small as 0.9 m^2.[6] The largest paediatric case series to date describes 15 cases, of which 2 were inserted for cardiac allograft failure.[7] Given our patient's borderline BSA and chest size, a virtual fit test was completed accurately predicting device fit before surgery.

This case supports the effective use of the SynCardia 50 cc TAH as a bridge to retransplant, providing a unique option for biventricular MCS and cessation of immunosuppression with resolution of the inflammatory process in this case.

Ethics Statement

This report has adhered to the relevant ethical guidelines.

Patient Consent

The authors confirm that a patient consent form(s) has been obtained for this article.

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Disclosures

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