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Brief Report

An infant with out-of-hospital cardiac arrest secondary to enteroviral myocarditis surviving up to cardiac transplantation

Eimear McGovern,[1] Ethel Ryan,[2] Colin J. McMahon[1]

[1]*Department of Paediatric Cardiology, Our Lady's Hospital for Sick Children, Crumlin, Dublin;* [2] *Department of Paediatrics, University Hospital Galway, Galway, Ireland*

Abstract We report the case of a 13-day-old infant with enteroviral myocarditis surviving an out-of-hospital cardiac arrest. She underwent orthotopic cardiac transplantation three months later. A year after the transplantation, she is alive and well. Enteroviral infection is common in neonates with high mortality in cases of enteroviral myocarditis. Cardiac transplantation is a treatment option for infants who fail to recover and remain dependent on inotropic support. This is the first report of an infant with out-of-hospital cardiac arrest secondary to enteroviral myocarditis surviving up to cardiac transplantation.

Keywords: Myocarditis; out-of-hospital cardiac arrest; transplantation

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Case report

We report the case of a 13-day-old female neonate presented with cardiorespiratory arrest to the local hospital. In the early morning, she had been found unresponsive by her parents. There had been no viral prodrome or respiratory symptoms reported. An ambulance arrived five minutes later and cardiopulmonary resuscitation was commenced after confirming cardiorespiratory arrest. Cardiac rhythm demonstrated ventricular fibrillation. The infant arrived at the local emergency department only five minutes after the ambulance arrived. By this time, her rhythm was pulseless electronic activity and cardiopulmonary resuscitation was resumed. The infant received one round of intraosseous and one round of intravenous adrenaline, 60 ml/kg crystalloid fluid, intravenous antibiotics, and acyclovir. Her cardiac rhythm normalised after 20 minutes of cardiopulmonary resuscitation. On examination, her pulses were weak, there was a gallop rhythm, and a 3 cm hepatomegaly. An echocardiogram performed locally demonstrated a dilated left ventricle with severely impaired left ventricular systolic function.

She was immediately transferred to the national paediatric cardiac intensive-care unit. Echocardiogram at the tertiary hospital confirmed a structurally normal heart, severe left ventricular systolic dysfunction, with a left ventricular shortening fraction <10%, and moderate mitral regurgitation. The origin and proximal course of the coronary arteries were normal on transthoracic echocardiography. The B natriuretic peptide level measured 3060 pg/ml, troponin T 3032 ng/L, AST 265 U/L, and ALT 142 U/L. Urea and creatinine levels were normal, albumin 23 g/L, and prothrombin time was 24.1 seconds. The infant was commenced on intravenous milrinone, noradrenaline, and adrenaline. Viral myocarditis was suspected, and therefore intravenous immunoglobulin was administered. The mother had a history of coryzal symptoms, sore throat, and cough starting five days before delivery. Polymerase chain reaction studies of the infant's blood, nasopharyngeal aspirate, and stool sample were positive for enterovirus RNA. All other microbiological, metabolic, and genetic testings for cardiomyopathy were negative.

After two months, the infant remained dependent on intravenous milrinone, noradrenaline, adrenaline,

Correspondence to: Dr C. J. McMahon, Cardiac Department, Our Lady's Hospital for Sick Children, Crumlin, Dublin 12, Ireland. Tel: +01-4096160; Fax: +01-4096181; E-mail: cmcmahon992004@yahoo.com

and invasive ventilation. Mild-to-moderate mitral regurgitation persisted and left ventricular shortening fraction remained <10%. Further, two courses of levosimendan were administered without any beneficial effect. Earlier in her course, an electroencephalogram showed moderate-to-severe bilateral cerebral dysfunction, and an magnetic resonance imaging (MRI) scan of the brain demonstrated two small areas of haemorrhage in the posterior fossa. A repeat MRI of the brain one and a half months after the event showed no change in the lesions, and the infant was neurologically normal on examination. Liver synthetic function had normalised and transaminase levels were normal.

She was listed for orthotopic cardiac transplantation two months after the initial presentation. It was decided not to place her on a ventricular assist device due to her small size, risk of thromboembolism/stroke, limited availability, and the difficulty in transporting the patient on a ventricular assist device by fixed-wing aircraft to the cardiac transplantation centre. In addition, despite her dependence on mechanical ventilation and inotropic support, she maintained reasonable end-organ perfusion. A month later, she received an orthotopic heart transplantation after fixed-wing air transport to Great Ormond Street in the United Kingdom. She did not require bridging to transplant in Ireland with extracorporeal membranous oxygenation or a left ventricular assist device, as she remained haemodynamically stable on intravenous inotropes and invasive ventilation. The surgery was uncomplicated and the infant recovered well. She received the standard immunosuppression and antimicrobial prophylaxis regimens in addition to co-trimoxazole and intravenous ganciclovir, as the donor was positive for toxoplasmosis and cytomegalovirus. Echocardiography demonstrated normal biventricular function with a left ventricular shortening fraction of 38%. Endomyocardial biopsy three months after the transplantation demonstrated no evidence of rejection. She has been discharged home, is asymptomatic, and making normal developmental progress.

The sections from the myocardium of the explanted heart showed extensive areas of myocyte loss with replacement fibrosis. These areas had a stellate outline with an irregular distribution throughout the full thickness of the myocardium. They corresponded to yellow areas noted macroscopically and affected the ventricular myocardium, predominantly on the left side, and also affected the atrial myocardium and septum (Fig 1). The affected areas showed extensive granular calcification and a moderate-to-heavy infiltrate of inflammatory cells, particularly plasma cells. In some areas, there were multinucleated giant cells, although well-formed granulomata were not present.

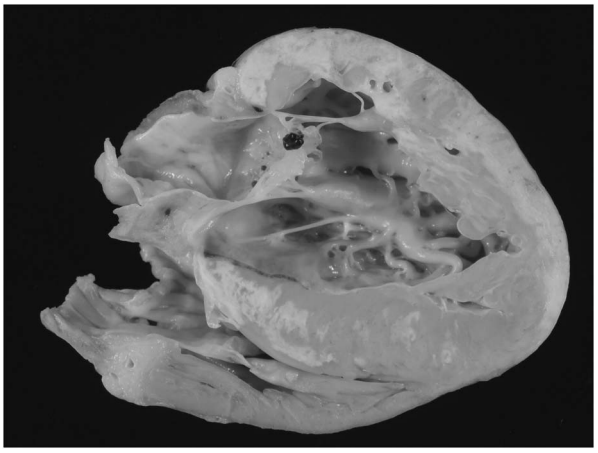

Figure 1.
Macroscopic image of the explanted heart demonstrating dilated left ventricular cavity with extensive areas of myocyte loss with fibrosis (yellow areas), predominantly on the left side. There was a large blood cyst in the anterior leaflet of the mitral valve.

The vessels were normal. There were mild dysplastic changes in the atrioventricular valves, and the mitral valve showed a large blood cyst in the anterior leaflet (Fig 1). There was a scattered chronic inflammatory cell infiltrate in the endocardium and epicardium. The atrioventricular conduction axis showed necrosis and focal haemorrhage. The appearances were those of extensive myocardial necrosis with inflammatory cell infiltration and calcification, in keeping with previous myocarditis.

Discussion

There have been no other reported cases of infants with out-of-hospital cardiac arrest, who have survived up to cardiac transplantation. Incidence of out-of-hospital cardiac arrest amongst infants is significant and higher than that seen for older children and adolescents.[1] According to a North American multisite database, the incidence of non-traumatic infant out-of-hospital cardiac arrest was 73 per 100,000 persons per year compared with 4 per 100,000 for older children and 6 per 100,000 for adolescents.[1] Survival and neurological outcome after 1 month is better for paediatric than for adult out-of-hospital cardiac arrests; however, survival rate is less for infants compared with older children.[1,2] A retrospective Japanese study identified that factors including <18 minutes to reach the hospital and less than seven minutes for an ambulance to arrive at the scene were factors that related to higher survival in out-of-hospital cardiac arrests in infants.[3]

Paediatric out-of-hospital cardiac arrests with ventricular fibrillation or ventricular tachycardia as the initial rhythm have been associated with higher

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incidence of survival to discharge.[1] Our patient was attended to by paramedics within five minutes of being found unresponsive, she had a shockable rhythm recorded at her home by the ambulance crew, and received defibrillation. She was admitted to the emergency department 10 minutes after the event. All these factors are felt to have contributed to her survival.

Enterovirus infection is a common viral infection in neonates. Incidence rate of 13% in neonates has been reported, with 79% being reported as asymptomatic.[4] Although most infections are asymptomatic or mild, severe disease such as viral sepsis syndrome, myocarditis, hepatitis, and meningoencephlaitis may occur.[5] Neonatal mortality from the infection vary widely, but enteroviral myocarditis is associated with particularly high mortality.[5,6] A report on the prognosis of 35 neonates with enteroviral myocarditis demonstrated a mortality of 31%.[7] One patient was awaiting cardiac transplantation at the time of writing. Between 2000 and 2008, there were 24 neonates with enteroviral myocarditis on the Extracorporeal Life Support Organisation Registry, who required extracorporeal membrane oxygenation support.[6] Survival rate to discharge in this group was only 33%, and there were no cases of cardiac transplantation reported in these infants. There has been one published report of a successful cardiac transplantation in a neonate affected by enteroviral myocarditis.[8]

Cardiomyopathy is an increasing indication for cardiac transplantation in children. A 24-year single-centre experience with 307 paediatric cardiac transplantations reported 39% of transplantations for cardiomyopathy, of which 7% were viral-induced cardiomyopathies.[9] It has become widely recognised that survival after transplantation is significantly better for patients with cardiomyopathy compared with patients with congenital heart disease.[9] Overall infant mortality after cardiac transplantation is higher compared with older children and adults due to a higher prevalence of death from early graft failure, but ongoing mortality for one-month survivors is similar.[10]

In conclusion, this report highlights the potential of an infant to survive up to cardiac transplantation following an out-of-hospital cardiac arrest secondary to enteroviral myocarditis.

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Conflicts of Interest

None.

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