Pediatric Anesthesia and Critical Care Journal 2021;9(1):48-53
doi:10.14587/paccj.2021.8

PACCJ

Refractory cardiogenic shock complicating hemolytic uremic syndrome treated by extracorporeal life support and balloon atrial septosomy. A case report

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Keypoints

Myocardial damage in hemolytic uremic syndrome (HUS) can cause severe left ventricular failure resistant to medical treatment for which extracorporeal life support (ECLS) in association with balloon atrial septostomy (BAS) may be necessary.

Abstract

Hemolytic uremic syndrome (HUS) is known to cause kidney damage and bicytopenia can affect many other organs including the cardiovascular system. Although rare, it can be rapidly fatal. HUS causes myocardial vascular damage responsible for acute heart failure, which can progress to a state of refractory cardiogenic shock. The literature on this cardiac complication is sparse and there is no specific treatment. Management of patients with HUS therefore remains a challenge to the clinician. Extracorporeal life support (ECLS) can be used during the acute phase of HUS to help patients recover myocardial integrity. ECLS, which is widely used post-operatively after cardiac surgery, could also be used as rescue therapy to ensure circulatory support during myocardial recovery. We report a case of cardiac arrest secondary to severe heart failure returning to normal cardiac function after ECLS assistance in association with balloon atrial septostomy (BAS). BAS was carried out by an endovascular procedure to decompress the left heart and optimize myocardial vascularization. To our knowledge, no previous case using BAS combined with ECLS in the recovery of cardiac function secondary to HUS has been reported.

Keywords

Hemolytic uremic syndrome; Extracorporeal membrane oxygenation; extracorporeal life support; Balloon atrial septostomy; Cardiac failure

Introduction

Hemolytic uremic syndrome (HUS) is rare, affecting around 10 children each year, and has a poor prognosis with a mortality rate of around 5%, principally due to cardiac damage. Historically described as the triad microangiopathic hemolytic anemia, thrombocytopenia and acute renal failure [1, 2]. Some cases of acute heart failure with rapid progression to refractory cardiogenic shock have been described [3, 5]. Histologic studies have identified coronary microcirculation microthrombi and thrombotic microangiopathy during autopsies of HUS patients [4, 6]. Clinically, HUS induces myocardial ischemia responsible for depressed myocardial function, and rarely myocarditis [4] or tamponade [7, 8]. Standard therapy of cardiogenic shock consists of inotropic agents administration but rarely

needs upgrading to mechanical circulatory support device. However, severe and fatal cardiogenic shock in young patients have been previously reported [3, 5]. Consequently, it is essential to screen patients at risk of severe left ventricular dysfunction and to propose rapid initiation of extracorporeal life support (ECLS) as salvage therapy [9]. ECLS allows to ensure appropriate end-organ perfusion while myocardial recovery. Such device is routinely used to support children with refractory cardiogenic shock from different etiologies [10-12]. However, significant increase in left ventricular loading conditions may be observed under ECLS [13]. Balloon atrial septostomy (BAS) may be used for unloading left cardiac cavities by creating a left to right intracardiac shunt allowing the blood return to the left atrium to be redirected into the right atrium and thus into the ECLS through the venous return cannula [14]. BAS has been previously reported as an effective approach for reducing pulmonary edema, preventing pulmonary hemorrhage, and reducing ventricular distension in patients with severe ventricular dysfunction secondary to myocarditis and dilated cardiomyopathy requiring ECLS [15]. Here, we report here an educative case describing management options of a largely unknown cardiac complication in HUS and requiring ECLS as well as venting.

Case report

A previously healthy 6-year-old boy was admitted to a local pediatric department with a 2-day history of mucous and bloody diarrhea, dehydration without fever, and asthenia. The first blood sample showed normal renal function, normal blood count, and no inflammatory syndrome. The following day, he developed oliguria without peripheral edema, elevated blood pressure, and fever with increased asthenia. Biochemical tests revealed acute renal failure with elevated serum creatinine (177 µmol.L^{-1}) and urea (17.4 mmol.L^{-1}), hyponatremia with sodium 123 mmol.L^{-1}, normal kaliemia, normal hemoglobin (16 g. L^{-}), thrombocytopenia (85 G.L^{-1}), and inflammatory syndrome with raised CRP (64 mg.L^{-1}). Troponin as well as lipase levels were normal. Mild hepatic involvement with increased ASAT (120 UI. L^{-1}) and ALAT (26 UI.L^{-1}) was observed. He was treated with intravenous fluids consisting of dextrose 5% with 0.9% Sodium Chloride. Antibiotherapy was initiated by ***intravenous ceftriaxone*** because of suspected sepsis and platelets were given. The patient was transferred to a tertiary care facility. On admission to the pediatric ICU, the child had become anuric and presented with elevated blood pressure (121/90 mmHg) and tachycardia (141 bpm). A cutaneous-mucous paleness with signs of dehydration were noted while his neurologic status was normal. Biological results were similar to previous results indicating acute renal failure, increased thrombocytopenia after transfusion, lactate dehydrogenase of 1901 UI. L^{-1}, haptoglobin of 1.1 g. L^{-1}, and no schistocytes. Bedside transthoracic echocardiography (TTE) revealed a structurally normal heart with preserved left ventricular ejection fraction (LVEF) of 68%. A low stroke volume with a preload reserve was noted as well as mild pericardial and left pleural effusions. Electrocardiogram (EKG) did not reveal any abnormalities. A hemodialysis was rapidly initiated through a jugular catheter due to persistent anuria. Serum creatinine and urea levels decreased respectively to a value of 82 µmol. L^{-1} and 6.2 mol. L^{-1}. The blood pressure gradually normalized as did the remaining of biological test. HUS was confirmed with a positive stool culture yielding Escherichia coli serotype O157:H7, which carries the virulence genes Stx2, in addition to schistocytes in blood smears (1%). The patient was started on a 15-day course of azithromycin. On ICU day 1, he developed neurological problems with hallucinations, inconsistent speech, fluctuating awareness, and diffused reflexes. Magnetic resonance imaging (MRI) revealed specific damage to the basal ganglia integrating into a thrombotic microangiopathy. The patient became comatose despite the absence of sedation. An electroencephalogram (EEG) was performed and revealed encephalopathy without paroxysmal abnormalities. A dose of eculizimab (600 mg IV) was given. On ICU day 2, his clinical condition deteriorated with breathing problems, desaturation requiring

oxygen, and moderate arterial hypotension (83/54 mmHg) without signs of shock. Chest X-rays revealed a stable left pleural effusion and his troponin level was 538 $ng.L^{-1}$ (48 $ng.L^{-1}$ the day before). His neurological status did not improve. With this background of multiorgan failure, it was decided to sedate and intubate him. At this time, he developed severe bradycardia followed by cardiac arrest, requiring cardiac compression and an epinephrine IV bolus. The reference center for cardio-pediatric resuscitation was contacted during resuscitation. His heartbeat restarted after 22 min of cardiopulmonary resuscitation. He required extensive inotropic support including 20 $\mu g.kg^{-1}.min^{-1}$ dobutamine and 1.8 $\mu g.kg^{-1}.min^{-1}$ epinephrine. A bedside descrambling TTE showed severe left ventricular dysfunction (LVEF ≈15%). Regarding to the profound ventricular dysfunction, the mobile cardiac assistance team was called and a peripheral jugular carotid venoarterial ECLS was rapidly implanted. The patients was then transferred to the cardio-pediatric ICU under ECLS. Immediately after the arrival in ICU, TTE showed dilated left chambers and confirmed the profound left ventricular dysfunction (LVEF≈10%). A severe pulmonary edema could be observed on the chest X-ray. In order to unload left cardiac cavities, an endovascular balloon atrial septostomy (BAS) was performed (Figure 1). Transseptal puncture was carried out from a femoral venous approach and guided by trans-esophageal echocardiography. Decompression of the left atrium was successfully achieved after withdrawing the septal sheath as evidenced by left right shunt through the septal defect (Figure 1). To optimize cardiac function recovery, levosimendan 0.2 $\mu g.kg^{-1}.min^{-1}$ was introduced in association with 0.3 $\mu g.kg^{-1}.min^{-1}$ norepinephrine while dobutamine infusion could be then rapidly stopped. On ECLS day 2, the value of LVEF was near form 40% while indexed blood flow was reduced to 1.5 $L.min^{-1}.m^{-2}$. The obtaining of arterial pulsatility meaning ventricular ejection, the decreased oxygen dependency on ECLS, the disappearance of pulmonary edema on the chest X-ray (Figure 2)

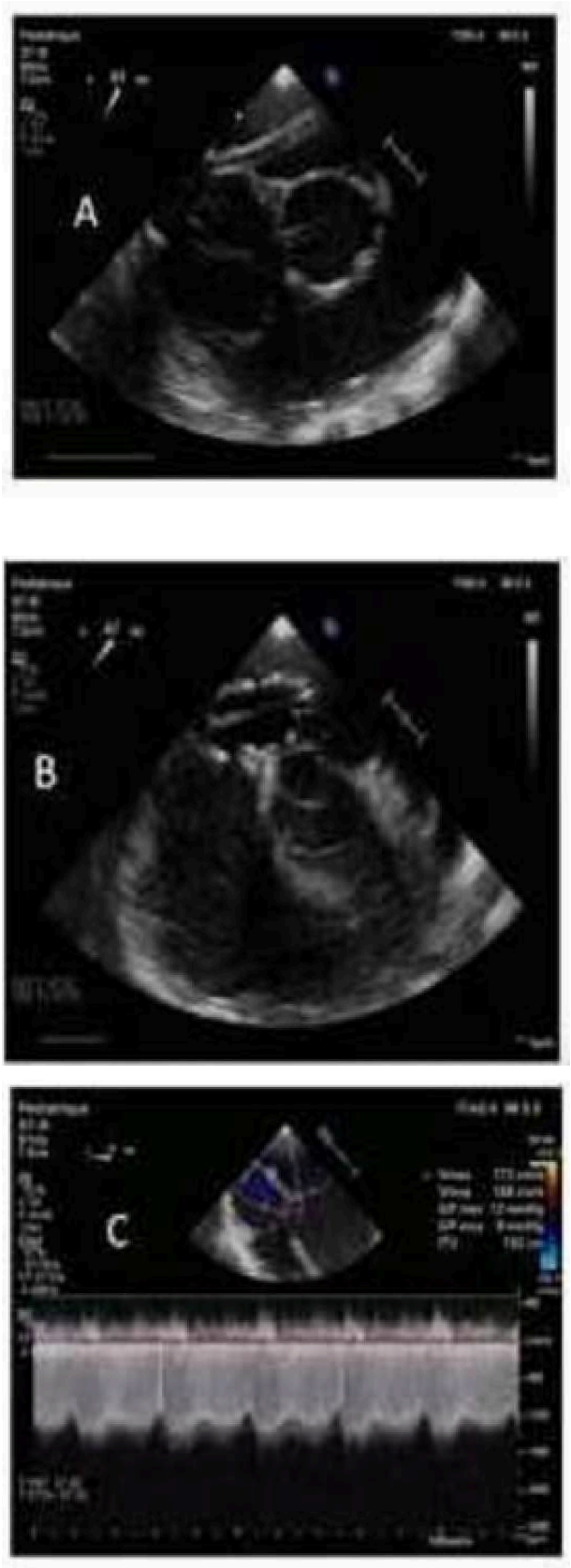

Figure 1. Introduction (A) and inflation (B) of the balloon catheter into the left atrium through a patent foramen ovale on a mid-esophageal inflow-outflow view of the right ventricle. Large septal defect (C) that allowed mixing of oxygenated and deoxygenated blood in the four cavities.

reflecting an efficient left cardiac discharge by the atrial shunt as well as the significant decrease in troponin allowed us to progressively decrease the ECLS indexed blood flow rate up to minimum flow rate of 0.8 L.min.m^2 from ECLS Day 3 (Table 1).

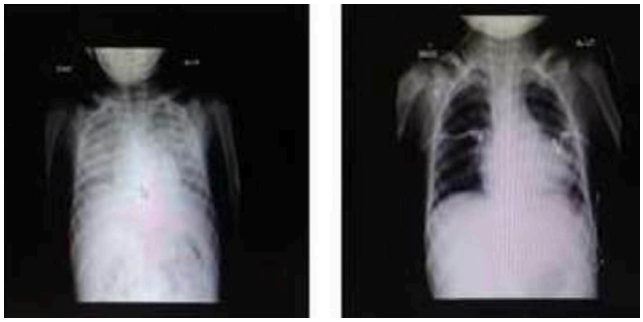

Figure 2. Chest X-ray before (left) and after (right) extracorporeal life support (ECLS) and balloon atrial septostomy (BAS) management.

Time in days from onset of symptoms	Troponin ng.L^{-1}	BNP pg.mL^{-1}	Lactates mmol.L^{-1}	Créatinine µmol.L^{-1}	ECMO* L.min^{-1}.m^{-2}	Dialysis	EF %
4	7	-	-	186	N	N	68
5 (ICU admission)	48	-	-	-	N	Y	-
6 (before CA)	538	-	-	-	N	Y	-
6 (after CA)	1170	-	4.5	-	2.2	Y	10
7 (after BAS)	1789	1655	1.1	85	2	Y	-
8	1926	2589	0.9	82	1.5	Y	40
9	1551	2160	1.5	76	1.1	Y	40
10	1382	2050	1.6	81	1.0	Y	60
11	1125	3387	1.7	76	0.8	Y	-
12	547	6834	1.1	-	N	Y	65
13	224	11500	-	91	N	Y	70
14	140	-	-	-	N	Y	-
19	66	-	-	-	N	Y	-
23	26	-	-	-	N	Y	-

*indexed blood flow CA= cardiac arrest. Y= yes N= no

Table 1. Changes in biological markers and organ supports from the onset of symptoms.

In conjunction with the decrease in ECLS blood flow, epinephrine could be stopped twelve hours later. The patient could be successfully weaned from ECLS after five days of supply. The next day the patient could be transferred back to the original pediatric center. Epinephrine infusion had to be reintroduced on arrival in pediatric intensive care because of a new circulatory failure, but it was rapidly weaned the next day. He progressed favorably with recovery of normal contractile function (LVEF =65%) on follow-up TTE. Nevertheless, there was still an ultrasound diastolic dysfunction objectified by high left ventricular filling pressures, right cardiac overload with tricuspid insufficiency and dilatation of the inferior vena cava, and biology by the persistence of high levels of brain natriuretic peptide (BNP). TTE also shows a thickened aspect of the left ventricular myocardium, suggesting an aspect of myocarditis (no picture available). Antihypertensive drugs were introduced to maintain normal blood pressure. No atrial shunt or secondary complications to BAS were reported. A tracheal extubation could be successfully performed nine days after the readmission to the pediatric ICU despite a fluctuating state of consciousness. Although the weaning from all sedative drugs, a vegetative state persists. An EEG revealed a pattern of diffuse cerebral damage. Cerebral MRI revealed many ischemic brain lesions and persistence of thrombotic microangiopathy lesions in the basal ganglia. In parallel, the anuric acute kidney injury persists without any recovery of renal function and hemodialysis was continued. Despite the administration of six doses of eculizumab there was no improvement in his condition and he died 60 days after his initial hospital admission.

Discussion

HUS is a serious disease due to potential cardiac and neurologic involvement [16]. Our patient developed encephalopathy 3 days after the first symptoms of HUS, followed by severe myocardial dysfunction leading to cardiac arrest and hemodynamic compromise requiring ECLS as well as venting ensured by BAS. The occurrence of cardiac arrest has probably multifactorial origin including myocardial ischemia, hypoxemia by pulmonary alveolar-interstitial oedematous damage and potentially vasoplegia induced by anesthetic drugs.

The pathophysiology of thrombotic microangiopathy is now well know, and can be described as damage to the vascular endothelium as primum movens, which leads to platelet adhesion and then aggregation leading to the formation of fibrinoplatelet thrombi [6]. When it affects the coronary microvessels it induces myocardial ischemia [2]. The acute phase of the disease is at high risk of life-threatening cardiac involvement but requiring rarely short term mechanical circulatory support [3]. Under ECLS, the left ventricular loading conditions may be

profoundly modified and thus aggravate the pulmonary edema induced by acute heart failure. In our case, in immediate left heart decompression has clearly allowed to limit cardiac congestion, ventricular dilation and ischemia of subendocardial myocardial layers. We chose to use the endovascular approach of BAS because we have a team of experts in this technique with many years of experience. Multiple strategies may be used to unload the left ventricle during ECLS[17]. The BAS present the advantage to be minimally invasive and with a low risk of complications (most commonly bleeding and myocardial perforation very rarely in 0,01% of cases) [18]. Intra-aortic balloon pump (IABP) and Impella are two others efficient and minimally invasive devices to discharge left ventricle during ECLS but cannot be used in the pediatric population [13]. Moreover, the BSA allows a long-term discharge contrary to others decompression techniques such as the transseptal cannula, consists of a percutaneous placement of a transseptal left atrial drain incorporated in the ECLS circuit [19]. This permanent atrial shunt is particularly indicated in cases of chronic diastolic dysfunction as is the case with HUS. The BAS is an interesting alternative to surgical atrial or ventricular vent requiring a thoracotomy at high risk of complications, in particular hemorrhagic in the context of HUS-related anemia and thrombopenia. Its main disadvantage is the risk of reduced ECLS effectiveness due to the recirculation of oxygenated blood from the left atrium to the ECLS. However, in our patient any clinical impact could be observed. Already used in some congenital heart diseases (especially transposition of the great arteries), myocarditis, and dilated cardiomyopathy associated with severe left ventricular dysfunction, atrial septostomy successfully reduces pulmonary edema and permits left heart decompression without major complications [11].

The increased troponin level prior cardiac arrest and ECLS initiation means a possible early cardiac involvement in HUS. Our case report confirms the necessity to screen cardiac involvement by monitor cardiac specific enzymes [20]. Although Troponin level decreased rapidly, BNP continues to rise under ECLS including efficient venting by BAS. Some authors reported the interest to monitor BNP levels to confirm the efficacy of left ventricular venting under ECLS [21]. There is a discrepancy between the rapid myocardial recovery and the persistence of high BNP levels. One explanation should be a possible persistent microvascular myocardial lesion inducing chronic diastolic dysfunction partly limited by the BAS. Beware, heart function recovery is not synonymous with myocardial recovery. As kidney and brain sequelae persist -a long time, myocardial sequelae could also exist. It may be advantageous to maintain a permanent interatrial shunt in this case in order to fight the chronic overload of the left ventricle. If troponin level may be considered as an early biomarker of cardiac involvement in HUS, BNP appears to be a biomarker of myocardial sequelae and chronic cardiac overload. The place of TTE for optimal management of these patients is crucial. The transfer of the patient to a cardio-pediatric center able to provide intensive supportive care like ECLS should be performed at the first signs of heart failure.

Source of funding: Support was provided solely from institutional sources.

Conflicts of interests: The authors declare no competing interests.

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