Enteroviral Myocarditis Requiring Extracorporeal Membranous Oxygenation in a 2 Week Old Girl

Naama Elisha MD, Gideon Paret MD, Marina Rubinsthein MD and Ishay Salem MD

Department of Pediatric Intensive Care, Safra Children's Hospital, Sheba Medical Center, Tel Hashomer, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

KEY WORDS: myocarditis, levosimendan, enterovirus, extracorporeal membranous oxygenation

IMAJ 2013; 15: 387–388

Viral myocarditis and acute heart failure requiring intensive pharmacological and mechanical support can be a devastating complication of enteroviral disease. Recent studies have shown that levosimendan is a potent cardioprotector in viral myocarditis: it preserves left ventricular function and inhibits apoptotic cell death, thereby preventing cardiomyocyte loss [2]. Although little is known about the use of levosimendan in cases of viral myocarditis, there are many reports of severe myocarditis treated successfully with extracorporeal membranous oxygenation. We present a case of severe enteroviral myocarditis with fulminant heart failure where levosimendan in combination with ECMO life support was effective.

PATIENT DESCRIPTION

The patient was an 11 day old girl born at full term without complications to a 33 year old G2P2 mother. At the time of delivery the mother had fever and nasal congestion and was treated with intravenous amoxicillin. She reported that her 1 year old child had been diagnosed a week earlier as having a viral disease. The newborn received a hepatitis B vaccine and vitamin K at birth but was not treated with antibiotics after delivery.

The infant initially presented with fever to our pediatric department on the 5th day of life and underwent a complete sepsis workup. She was diagnosed as having enterovirus and was treated with wide-spectrum antibiotics (IV ampicillin at a dose of 130 mg/kg/day and IV gentamycin 2.6 mg/kg/day) for 5 days until all bacterial cultures (blood, urine and cerebrospinal fluid) returned negative. CSF polymerase chain reaction returned positive for enterovirus (coxsackie B2) and negative for herpes simplex virus 1 and 2. She was discharged home in good general condition. On day 11 she was brought to the emergency room of another hospital with symptoms of hyperthermia and poor feeding. The vital signs on arrival were 120 beats/minute, 55 breaths/minute and saturation level 88%. Her blood pressure was undetectable. She was immediately intubated and given inotropic support and antibiotics. Emergent echocardiography showed severely decreased systolic function. She was then transported to our pediatric intensive care unit for further treatment.

Upon arrival at our ward, heart rate was 130 beats/minute and mean arterial pressure 40 mmHg. Blood gases showed pH 69. and lactate > 160. Follow-up echocardiography demonstrated a severe decrease in left ventricular function, mild aortic insufficiency, mild tricuspid regurgitation, mild-moderate pericardial effusion and a shortening fraction estimated at 5% (normal range 25–40%). She was also suffering from acute renal failure (blood creatinine 1.37 mg/dl, urea 30 mg/dl) and hepatic failure (liver enzymes reaching 2000 U/L). She underwent 2 hours of cardiopulmonary resuscitation, including mechanical ventilation, continuous chest compressions, IV adrenaline, IV dexamethasone, IV terlipressin and IV bicarbonate and calcium boluses. She was also started on IV antibiotics (meropenem and vancomycin 40 mg/kg/day). Head and abdominal ultrasound evaluations and chest X-ray were normal.

The neonate was hooked up to ECMO with a flow of 640 ml/kg/min including hemofiltration, and was given one dose of levosimendan IV on the first day (she was given a loading dose of 6 µg/kg over 10 minutes followed by 0.05–0.2 µg/kg/min as a continuous infusion for a total of 24 hours). She was on ECMO for 6 days during which she needed cardiovascular support with dopamine and milrinone (continuous IV infusion at a rate of 12.5 µg/kg/min and1 µg/kg/min, respectively). She was safely taken off the ECMO on day 6 of treatment. The echocardiography showed paradoxical septal movement, mild tricuspid regurgitation, mild-to-moderate mitral regurgitation and poor systolic function. She was kept intubated and under continuous inotropic support. She was successfully extubated on day 14 post-ECMO. During her ensuing hospitalization, serial echocardiograms showed clinical improvement with a gradual increase in ventricular systolic function and shortening fraction. Her troponin levels decreased gradually and returned to normal. The repeat head ultrasound was normal. The results of a full neurological assessment prior to discharge were entirely normal, as were her creatinine and

ECMO = extracorporeal membranous oxygenation

CSF = cerebrospinal fluid

liver function tests. She was discharged home hemodynamically stable and in good general condition.

COMMENT

Most children with enteroviral infections present with hand, foot and mouth disease or herpangina, and only a few are likely to progress to more serious symptoms, such as central nervous system manifestations, pulmonary edema, acute myocardial failure, rapid shock, or death. Despite the many available therapeutic strategies for severe enteroviral infection, the mortality rate remains between 10 and 25.7% [5]. Acute heart failure is a potentially fatal manifestation of viral myocarditis. Because the disease is potentially reversible, ECMO is a reasonable course of action to maintain patients until recovery or transplantation. A recent study [1] reviewed the course and outcome of 12 children with acute fulminant myocarditis diagnosed solely by clinical and echocardiographic data who were managed by ECMO because of refractory circulatory collapse. The results of that study showed that ECMO can be safely and successfully used in children with acute fulminant myocarditis who require mechanical support. The outcome was usually favorable (10/12 patients), with the regaining of normal or near-normal heart function without the need for heart transplantation.

The development of myocardial damage in myocarditis involves cardiomyocyte apoptosis. Levosimendan is a novel calcium-sensitizing inotropic agent with anti-apoptotic properties. The results of a recent study showed that it improves ventricular function and inhibits cardiomyocyte apoptosis, and those authors considered it a potentially feasible therapeutic approach in cases of acute heart failure caused by viral myocarditis [2]. Little is known about the use of levosimendan in pediatric patients, and even less in neonates. There are only a few case reports describing the use of levosimendan in viral myocarditis-induced heart failure, and most studies were done on patients who developed acute heart failure after cardiac surgery [3,4]. Momeni et al. [4] compared the hemodynamic and biochemical parameters of levosimendan to milrinone after corrective open-heart surgery in 41 neonates and infants. They found that levosimendan is at least as efficacious as milrinone after corrective congenital cardiac surgery in neonates and infants. Another study [3] reported that levosimendan was safely administered to 15 children aged 7 days to 18 years (median age 38 months) who had severe myocardial dysfunction secondary to end-stage heart failure, or acute heart failure, and who were inotrope-dependent (requiring at least one catecholamine). Levosimendan enabled substantial reduction in catecholamine infusions in the children with end-stage or acute heart failure and also led to an objective improvement in myocardial performance in the children with acute heart failure.

Our patient required ECMO therapy and was additionally given a trial of levosimendan. We suggest that the combination of levosimendan with extracorporeal life support to treat children with enteroviral infection-related cardiopulmonary failure will help to decrease the mortality rate. Given the success of ECMO in neonates and children with enteroviral myocarditis, as reported in recent studies, prolonged quality cardiopulmonary resuscitation is warranted until access can be obtained and ECMO initiated. We also recommend the simultaneous use of levosimendan as a cardiomyocyte apoptosis inhibitor and for the improvement of ventricular function.

Corresponding author:
Dr. G. Paret
Director, Dept. of Pediatric Intensive Care , Safra Children's Hospital, Sheba Medical Center, Tel Hashomer 52621, Israel
Phone: (972-3) 530-2885
Fax: (972-3) 530-3188
email: gparet@post.tau.ac.il

References

1. Nahum E, Dagan O, Lev A, et al. Favorable outcome of pediatric fulminant myocarditis supported by extracorporeal membranous oxygenation. *Pediatr Cardiol* 2010; 31: 1059-63.
2. Latva-Hirvelä J, Kytö V, Saraste A, Vuorinen T, Levijoki J, Saukko P. Effects of levosimendan in experimental acute coxsackievirus myocarditis. *Eur J Clin Invest* 2009; 39: 876-82.
3. Namachivayam P, Crossland DS, Butt WW, Shekerdemian LS. Early experience with Levosimendan in children with ventricular dysfunction. *Pediatr Crit Care Med* 2006; 7: 445-8.
4. Momeni M, Rubay J, Matta A, et al. Levosimendan in congenital cardiac surgery: a randomized, double-blind clinical trial. *J Cardiothorac Vasc Anesth* 2011; 25 (3): 419-24.
5. Sheng-Ling J, Shing-Jong L. Extracorporeal life support for treatment of children with enterovirus 71 infection-related cardiopulmonary failure. *Intensive Care Med* 2010; 6 (3): 520-7.

"Flatter me, and I may not believe you. Criticize me, and I may not like you. Ignore me, and I may not forgive you. Encourage me, and I will not forget you"

William Arthur Ward (1921-1994), American college administrator and one of the most quoted writers of inspirational maxims

"My pain may be the reason for somebody's laugh. But my laugh must never be the reason for somebody's pain"

Charlie Chaplin (1889–1977), English comic actor and filmmaker who became a worldwide icon through his screen persona "the Tramp." His films are characterized by slapstick combined with pathos, and often feature the Tramp struggling against adversity. Many contain social and political themes, with *The Gold Rush*, *City Lights*, *Modern Times*, and *The Great Dictator* often ranked among the greatest films of all time