CASE REPORT

Successful Treatment of Protein-Losing Enteropathy and Plastic Bronchitis by Biphasic Cuirass Ventilation in a Patient with Failing Fontan Circulation

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Summary

We present a 16-year-old male patient with hypoplastic left heart syndrome who developed protein-losing enteropathy (PLE) and plastic bronchitis (PB) after a Fontan operation. He received medical therapies, including albumin infusion, unfractionated heparin, and high-dose anti-aldosterone therapy but could not obtain clinical relief. Biphasic cuirass ventilation (BCV) led to expectoration of bronchial casts and prompt resolution of PB. Notably, clinical symptoms related to PLE were dramatically improved after starting BCV. A brief period of BCV increased stroke volume from 26 ± 1.4 to 39 ± 4.0 mL. This case suggests that BCV could be an effective treatment for PLE in patients with failing Fontan circulation.

(Int Heart J Advance Publication)

Key words: Central venous pressure, Congenital heart disease, Continuous negative extrathoracic pressure, Functionally univentricular circulation, Low cardiac output

Since the Fontan operation was first reported in 1971, it has been performed as a final definitive palliative procedure to improve survival in patients born with a functionally univentricular circulation.[1-3] More than 40 years after the first operation, short-term outcomes of these patients have improved dramatically.[1] Nonetheless, because of a lack of subpulmonary ventricle, elevated central venous pressure (CVP) and low cardiac output (CO) can cause various chronic complications in multiple organs, especially the hepatorenal and intestinal functions.[1,2,4] Protein-losing enteropathy (PLE) is a characteristic feature of Fontan failure, leading to peripheral edema, ascites, pleural effusions, malabsorption, and loss of immunoglobulins.[5] Various therapies have been tried for the treatment of PLE, but the management strategy for this complex pathophysiology is not yet established.[2,5]

Biphasic cuirass ventilation (BCV), a form of noninvasive extrathoracic mechanical ventilation, is an advanced model of the iron lung.[6] It consists of a cuirass and a pressure source capable of providing both positive and negative pressure, which supports spontaneous breathing in a more physiological manner than does positive pressure ventilation.[6] Presently, it is used not only for respiratory failure but also for impaired hemodynamics after surgery of congenital heart disease (CHD).[3,6-8]

Here, we describe a 16-year-old male patient who suffered from PLE and plastic bronchitis (PB), a rare but potentially fatal condition noted in patients with failing Fontan circulation.[9] BCV enabled successful management of dyspnea related to PB. Notably, PLE was also dramatically improved after the treatment with BCV.

Case Report

A 16-year-old male patient with a 7-day history of intractable cough and severe edema was hospitalized. He was diagnosed as having hypoplastic left heart syndrome at birth and received Fontan procedure (total cavopulmonary connection: TCPC) when he was 21-month-old. PLE occurred 11 years after TCPC. He had been receiving periodic administration of albumin and gamma-globulin (IgG) on an outpatient basis and had been hospitalized on and off because of failing Fontan circulation. Stent implantation for left pulmonary artery and coarctation of the aorta was performed when he was 13-year-old. On admission, he presented with persistent nonproductive cough, pallor, and coldness. The puffy face, distended jugular veins, and hepatomegaly were remarkable (Figure 1A). Vital signs were as follows: blood pressure, 98/61 mm Hg; pulse rate, 104/minute; respiratory rate, 34/minute; body temperature, 36.8℃; and percutaneous oxygen saturation, 78% with oxygen therapy supplied via nasal cannula. He had no history of arrhythmia. Complete blood counts showed polycythemia with the following values:

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Received for publication May 24, 2017. Revised and accepted September 13, 2017.

Released in advance online on J-STAGE May 23, 2018.

doi: 10.1536/ihj.17-292

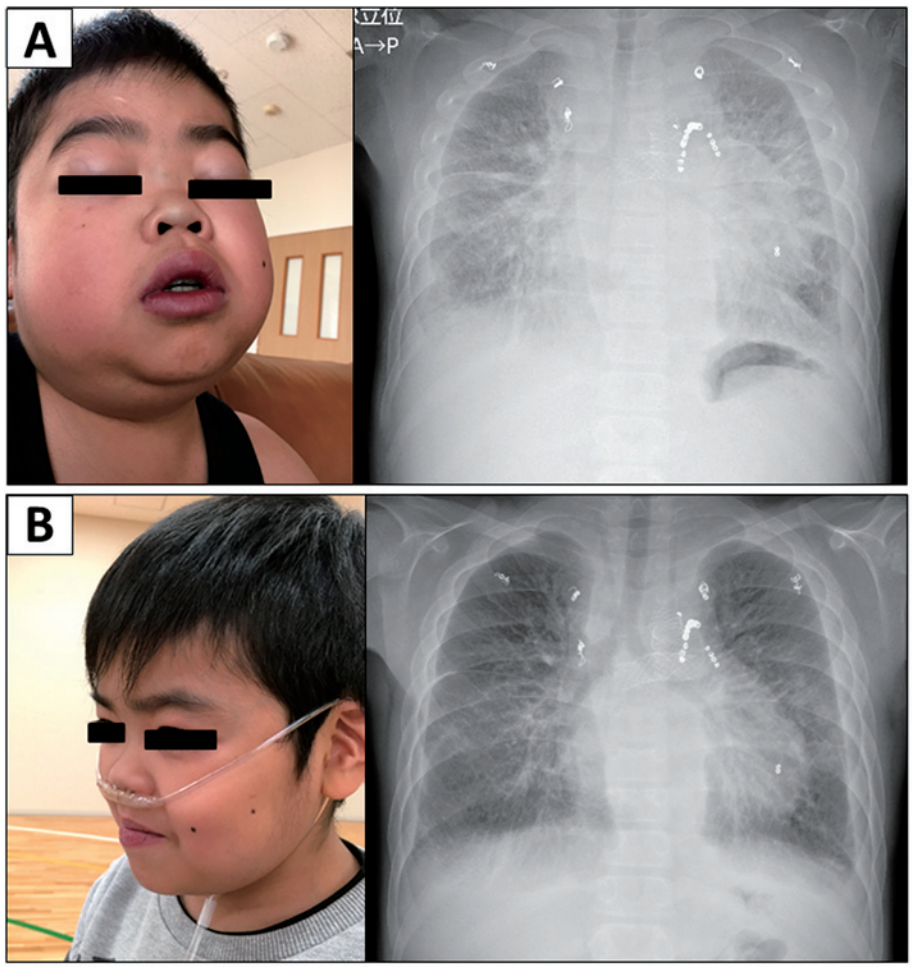

Figure 1. The patient's appearance and chest radiography before and after the treatment of BCV. **A:** Before the treatment. He suffered from PLE. Facial puffiness is a remarkable symptom. His body weight and the serum albumin level are 28.6 kg and 2.2 g/dL, respectively. Chest radiography reveals cardiomegaly (CTR of 0.56), marked pulmonary congestion, and pleural thickening and effusion. **B:** Three months after the treatment. Various symptoms related to PLE are dramatically improved. His body weight is decreased to 26.1 kg, and the serum albumin level is increased to 3.0 g/dL. Chest radiography shows improvement of the symptoms related to pulmonary congestion (CTR of 0.52). Written permission was obtained from the patient and his parents for appearing in the photographs. BCV indicates biphasic cuirass ventilation; CTR, cardiothoracic ratio; and PLE, protein-losing enteropathy.

hemoglobin, 17.7 g/dL and hematocrit, 56%. Blood chemistry values were as follows: albumin, 2.1 g/dL; IgG, 342 mg/dL; aspartate aminotransferase, 22 IU/L; alanine aminotransferase, 20 IU/L; cholinesterase, 129 IU/L; gamma-glutamyl transpeptidase, 26 IU/L; C-reactive protein, 0.02 mg/dL; and B-type natriuretic peptide, 31 pg/mL (rr < 18.4). Echocardiography revealed a reduced contraction of the right ventricle (RV) (ejection fraction 40%), grade II of regurgitation of the tricuspid valve, and back-streaming flow of the inferior vena cava and the hepatic vein. Chest radiography revealed cardiomegaly (cardiothoracic ratio of 0.56), marked pulmonary congestion, and pleural thickening and effusion (Figure 1A). Cardiac catheterization data were as follows: CVP, 15 mm Hg; pulmonary arterial pressure, 14 mm Hg; pulmonary capillary wedge pressure, 7 mm Hg; pulmonary arterial resistance, 2.1 WU · m^2; systolic pressure of the RV, 67 mm Hg; end-diastolic pressure of the RV, 8 mm Hg; pressure of the aorta, 67/37 mm Hg; and cardiac index, 3.3 L/minute/m^2. These determined the diagnosis of PLE related to failing Fontan circulation. This condition prompted us to start the treatment for PLE, which includes the administration of albumin, high-dose aldosterone antagonist (4 mg/kg per day), intravenous furosemide, and continuous heparin infusion, but these treatments did not improve the symptoms relating to PLE. The intractable cough got worse, and the patient complained of difficulty of phlegm expulsion and of sleeping. Budesonide inhalation and oral codeine phosphate were added but were not effective. Hence, we started an additional therapeutic strategy on the 6th day of hospitalization using the RTX® respirator (Medivent Ltd., London, UK) to assist in phlegm expulsion and Fontan circulation. Two days after the start of RTX, bronchial casts were expectorated spontaneously on

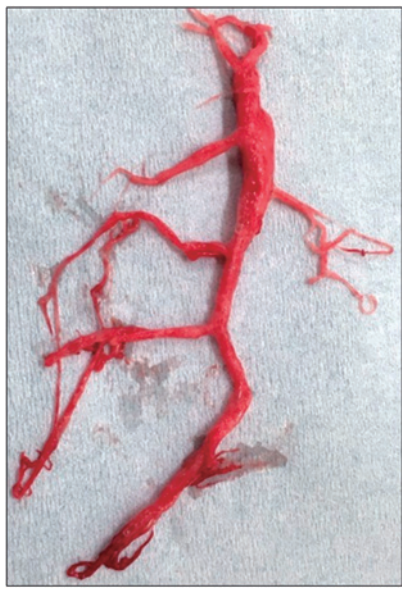

Figure 2. Patient's expectorated cast due to plastic bronchitis. Histology reveals an acellular mucinous fibrin collection.

the following days (Figure 2). The intractable cough dramatically improved after the expectoration of the bronchial casts. Furthermore, hypoalbuminemia and congestive symptoms also improved (Figure 1B), and he was discharged on the 15th day. No signs of recurrent circulatory failure have since been observed, and now he has not received albumin infusion or has been rehospitalized.

To date, the patient is continuously undergoing cardiac rehabilitation using RTX twice a week. We are using the noninvasive electrical velocimetry Aesculon® monitor (Osypka Medical GmbH, Berlin, Germany) to evaluate the hemodynamic effects of RTX on Fontan circulation. Written informed consent was obtained from the patient's parents. A brief period of RTX increased the stroke volume from 26 ± 1.4 mL to 39 ± 4.0 mL, with a mean increase of 51%. Heart rate was not changed during RTX. Furthermore, peripheral skin temperature (measured using THERMOFOCUS® [Tecnimed Srl, Varese, Italy]) was elevated from 33.1 ± 0.2℃ to 33.6 ± 0.1℃ after RTX.

Discussion

This paper is the first case report of a successful treatment of PLE with BCV. Although this is the first time that BCV was used for the treatment of intractable dyspnea related to PB, it unexpectedly improved the symptoms related to PLE. The noninvasive hemodynamic monitor indicated that BCV might increase CO leading to the improvement of the hemodynamics of the patient with Fontan circulation.

PLE is one of the most serious complications in patients with Fontan circulation. Once PLE occurs, the patient's outcome is quite poor. The survival rates 5 and 10 years after the PLE onset were 50% and 20%, respectively.[2] Although PLE may successfully resolve after cardiac transplantation, early survival rate is lower in patients with PLE than those without PLE.[2,5] Medical therapies include unfractionated heparin, high-dose anti-aldosterone therapy, oral budesonide, loperamide, and targeted pulmonary vasodilators (nitric oxide, prostacyclin, and endothelin), but none are reliably effective.[2,5] Although the precise mechanisms of PLE onset remain unclear, high CVP is thought to be closely associated with the onset.[2] It is now well known that spontaneous inspiration enhances pulmonary blood flow and stroke volume in Fontan circulation.[10] If positive end-expiratory pressure becomes more than 6 cmH_2O, CO is significantly decreased.[3] Previous studies showed that BCV provided a short-term improvement in the hemodynamics of Fontan circulation.[3] Another study showed that BCV brought a marked increase of the pulmonary blood flow, and it was achieved by the increase in CO without the increase of heart rate.[10] The hemodynamic changes of our patient were consistent with those of the previous report.[10] Enhanced negative intrathoracic pressure by BCV might be specifically beneficial in improving the hemodynamics of the patient from the malignant cycle of exacerbated Fontan circulation.[3]

PB is a potentially fatal but rare condition. PB in CHD patients varies given the specifics of the cardiac disease and the associated complex hemodynamics.[8] Conceptually, increased CVP may lead to lymphatic obstruction, retrograde flow, and chylous leakage within the airways.[9] There is only anecdotal evidence that any of the abovementioned therapies is beneficial, and this evidence has usually been provided for individual patients only.[11] Even if that is the case, treatment for children with cyanotic CHD and PB should include a careful cardiac evaluation, by looking for evidence of stenosis or thrombosis and optimizing cardiac rhythm and CO.[11] Previously reported successful therapeutic interventions focused on optimizing post-Fontan cardiac hemodynamics and lowering the CVP.[9] In this context, BCV may be beneficial for the treatment of PB because it has the capacities of not only reducing CVP in Fontan circulation but also expectorating casts as an instrument of respiratory physical therapy.[3,7] However, to our knowledge, the use of BCV for PB has never been reported in patients with Fontan circulation.

BCV could be an effective treatment for major problems, such as PLE or PB, long after a Fontan operation. Further studies are needed to evaluate the therapeutic effects of BCV in patients with failing Fontan circulation.

Acknowledgments

We thank Mt. Kazuki Kusano for the data collection of the cardiac catheterization.

Disclosure

Conflicts of interest: There are no conflicts of interest to declare.

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