Nitric Oxide Inhalation and V-V ECMO for Severe Respiratory Failure after Acute Type A Aortic Dissection Surgery

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A 65-year-old man was admitted to our hospital with acute type B aortic dissection that extended into both common iliac arteries with an occluded right common iliac artery and large bullae in bilateral upper lung fields. Femoro-femoral arterial bypass surgery with an artificial blood vessel was performed. Two days postoperatively, acute type B aortic dissection progressed to acute type A aortic dissection. Emergency total arch graft replacement (TAR) was performed through a median sternotomy on the same day. Immediately following TAR, the patient experienced hypoxemia. Acute respiratory distress syndrome (ARDS) was diagnosed following TAR for acute aortic dissection with pneumonia. Nitric oxide inhalation (NOI) therapy was commenced at 20 ppm from the fourth day post-surgery. However, 6 d following TAR, he developed bilateral pneumothorax due to ruptured bullae requiring chest tube management and thoracoscopic left upper lobe bullectomy. Eight days following TAR, veno-venous extracorporeal membrane oxygenation (V-V ECMO) was initiated and NOI therapy was completed. V-V ECMO was withdrawn 18 d after TAR. Postoperatively, after 2 years 3 months, the patient remains ambulatory without assistance, walking to the outpatient clinic.

Key words: Acute type A aortic dissection, Nitric oxide inhalation, Veno-venous extracorporeal membrane oxygenation

INTRODUCTION

Arteriosclerosis, associated with aging and lifestyle habits such as smoking, contributes to acute aortic dissection. Inoue *et al.*[1] reported that out of 1217 patients in the Japan registry, 63% with acute type A aortic dissection (ATAAD) had hypertension, 14% had dyslipidemia, and 2.3% had chronic obstructive pulmonary disease (COPD) [1]. Especially among patients with COPD, postoperative respiratory management is difficult because of the cytokine storm associated with aortic dissection. Herein, we present a case in which combination therapy of nitric oxide inhalation (NOI) and veno-venous extracorporeal membrane oxygenation (V-V ECMO) was implemented for severe respiratory failure following surgery for ATAAD, on the background of pre-existing COPD. To our knowledge, there are no prior reports of severe respiratory failure following surgery for ATAAD treated by combination therapy with NOI and V-V ECMO.

CASE REPORT

A 65-year-old man with emphysema was admitted to our hospital 3 h after experiencing symptoms of coldness and pallor of the right lower limb. Initial computed tomography (CT) demonstrated acute type B aortic dissection that extended into both common iliac arteries with an occluded right common iliac artery; large bullae were also visualized in the bilateral upper lung fields (Fig. 1A, B). A femoro-femoral arterial bypass surgery with an artificial blood vessel (FUSION Vascular Graft [MAQUET Cardiovascular LLC, Wayne, NJ, USA]) was performed 5 h 20 min after the onset, and the right lower limb was spared through reperfusion. Two days postoperatively, acute type B aortic dissection progressed to ATAAD with thrombosis of a false lumen in the ascending aorta (Fig. 1C, D). Emergency surgery was performed through a median sternotomy on the same day as the onset of new symptoms. Cardiopulmonary bypass was initiated via ascending aortic cannulation using the Seldinger technique and bicaval drainage to establish complete antegrade perfusion using previously reported methods [2]. Hypothermic circulatory arrest was established at < 17.5°C by the temperature of blood in the venous drainage cannula. The lowest rectal temperature achieved was 21.3°C. Subsequently, the entry tear was identified in the aortic arch, and total arch graft replacement (TAR) using an arch-first technique was performed using a 4-branched Triplex vascular prosthesis (Terumo, Tokyo, Japan). The duration of the operation, extracorporeal circulation, and circulatory arrest were 408, 226, and 32 min, respectively. Immediately following surgery, the patient experienced hypoxemia with decreased permeability of bilateral lung fields on chest radiography (Fig. 2A). Increased sputum production was noted on clinical examination. $PaO2/FiO_2$ (P/F) ratio on arterial blood gas measurement through the arterial line was 48 mmHg under the following ventilator settings: assist

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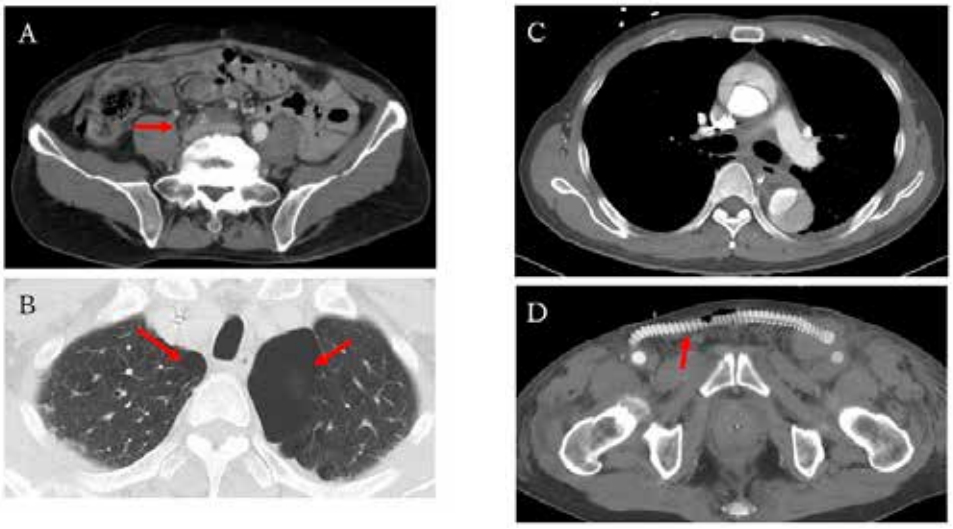

Fig. 1 Preoperative computed tomography. (A) Right common iliac artery is occluded (red arrow). (B) Bilateral bullae are seen (red arrow). Preoperative retrograde acute type A aortic dissection was documented upon computed tomography. (C) A new dissection is seen in the ascending aorta. (D) The femoro-femoral bypass is intact (red arrow).

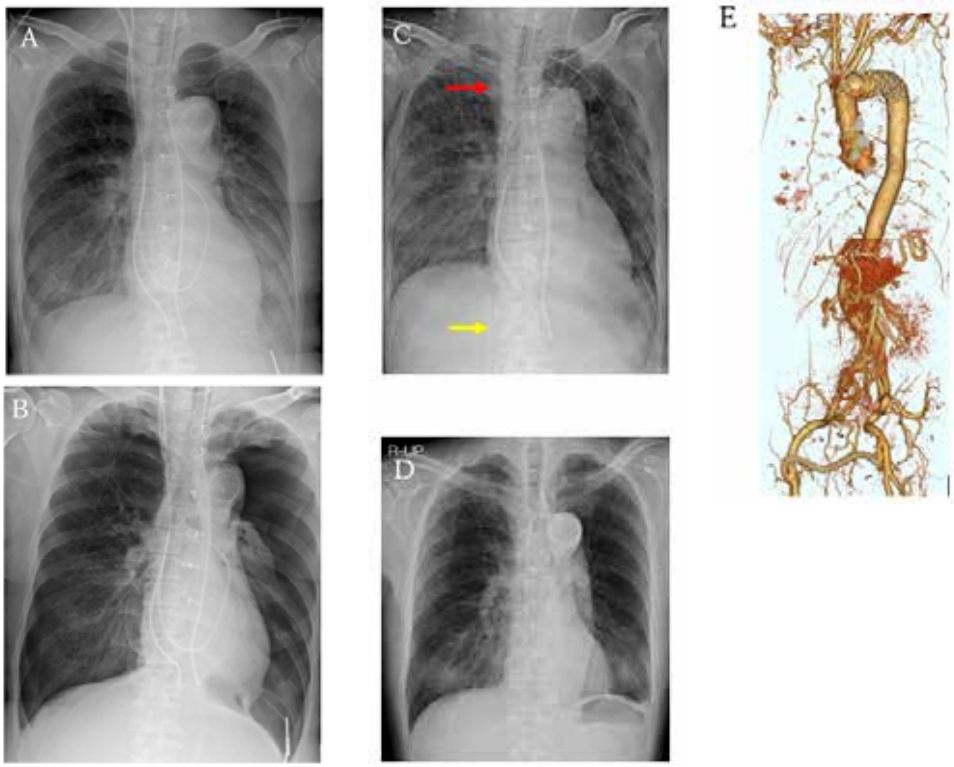

Fig. 2 Postoperative chest radiography. (A) Immediately after surgery. (B) Bilateral pneumothorax. (C) When veno-venous extracorporeal membrane oxygenation is introduced. The cannula of outlet flow (*red arrow*) and the cannula of inlet flow (*yellow arrow*) are observed. (D) Chest radiograph. (E) 3D-computed tomography image following discharge.

Fig. 3 Changes in white blood cell (WBC) and C-reactive protein (CRP).
TAR: total arch replacement, CEZ: cefazolin, TAZ/PIPC: tazobactam/piperacillin

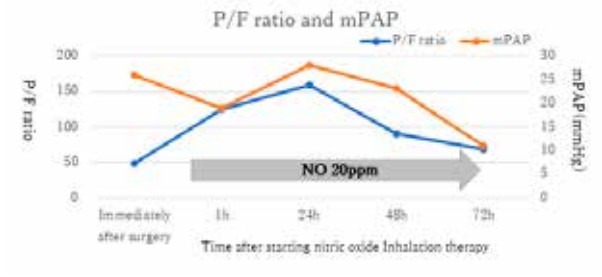

Fig. 4 Changes in $PaO2/FiO_2$ (P/F) ratio and mean pulmonary artery pressure (mPAP).
NO: nitric oxide

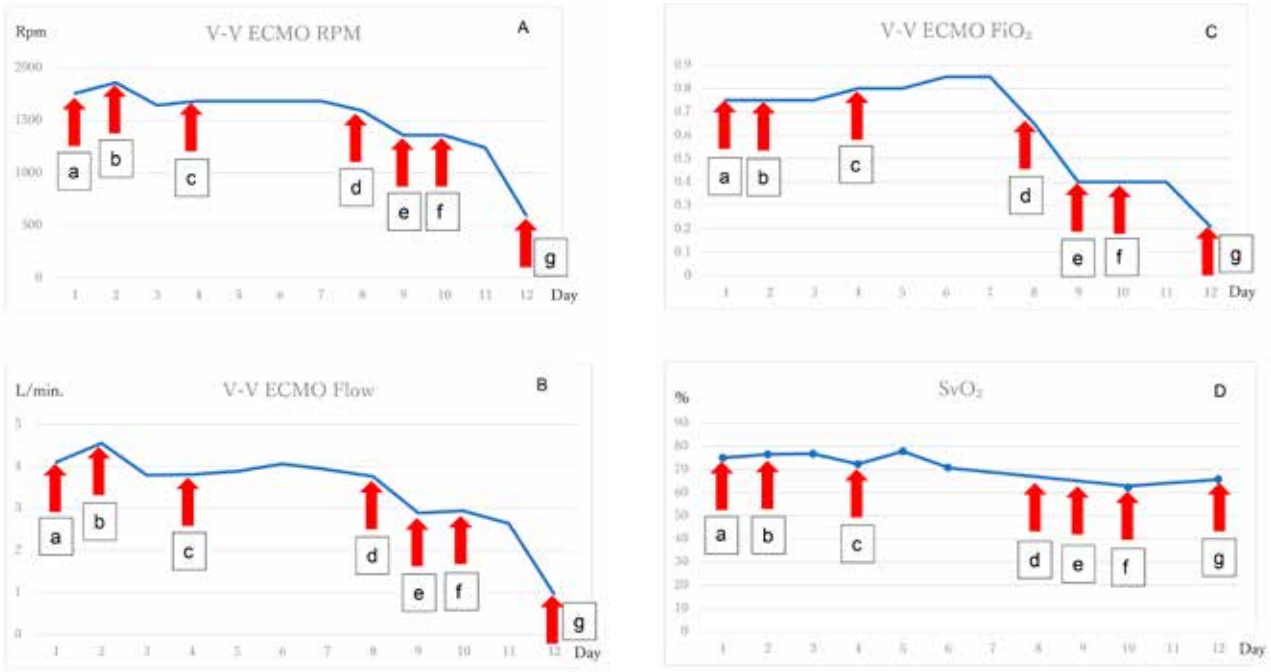

Fig. 5 Changes in the ventilator and V-V ECMO settings, and SvO_2 during the V-V ECMO therapy. (A) V-V ECMO RPM. (B) V-V ECMO flow. (C) V-V ECMO FiO_2. (D) CVP.
a–g show the ventilator settings.
a– mode: A/C, VC; FiO_2: 0.3; PEEP: 5 cmH_2O; RR: 10/min; TV: 400 ml
b– mode: A/C, PC; FiO_2: 0.3; PEEP: 3 cmH_2O; RR: 10/min; Pi: 5 cmH_2O
c– mode: CPAP; FiO_2: 0.3; PEEP: 3 cmH_2O; PS: 5 cmH_2O
d– mode: CPAP; FiO_2: 0.3; PEEP: 7 cmH_2O; PS: 5 cmH_2O
e– mode: CPAP; FiO_2: 0.6; PEEP: 10 cmH_2O; PS: 5 cmH_2O
f– mode: CPAP; FiO_2: 0.6; PEEP: 12 cmH_2O; PS: 5 cmH_2O
g– mode: CPAP; FiO_2: 0.5; PEEP: 12 cmH_2O; PS: 6 cmH_2O
SvO_2: central venous oxygen saturation, A/C: assist control, VC: volume control, PC: pressure control, CPAP: continuous positive airway pressure, FiO_2: fraction of inspiratory oxygen, PEEP: positive end expiratory pressure, RR: respiratory rate, TV: tidal volume, Pi: inspiratory pressure, PS: pressure support

control (A/C), fraction of inspired oxygen (FiO_2): 1.0, and positive end-expiratory pressure (PEEP): 18 cmH_2O. Acute respiratory distress syndrome (ARDS) with pneumonia was diagnosed following surgery for acute aortic dissection, and intravenous administration of antibiotics (cefazolin [CEZ]: 2 g/d, tazobactam/piperacillin (TAZ/PIPC): 13.5 g/d) was initiated (Fig. 3). *Klebsiella pneumoniae* sensitive to the above antibiotics was identified 3 d after TAR by sputum culture examination. Although high PEEP management (PEEP: 18 cmH_2O) was implemented, his respiratory status did not improve. NOI therapy was commenced at 20 ppm from the fourth day after TAR. One hour after initiation of NO inhalation, the P/F ratio improved to 124 (FiO_2: 1.0, PEEP 15 cmH_2O), and 24 h after initiation it improved further to 159 (FiO_2: 1.0, PEEP 12 cmH_2O) (Fig. 4). However, 6 d following TAR, he developed bilateral pneumothorax due to the rupture of bullae detected upon initial CT (Fig. 1B), and his respiratory condition subsequently deteriorated (P/F ratio 67.6, (FiO_2: 1.0, PEEP 10 cmH_2O)); bilateral chest tubes were accordingly inserted. Eight days following TAR, V-V ECMO was initiated (Fig. 5A–D), with no complications associated with bleeding, and NOI therapy was completed. His height was 183 cm, weight was 86.7 kg, and body surface area (BSA) was 2.0. Full flow was estimated to be 4.8 L/min. V-V ECMO was approached via right jugular vein and right common femoral vein cannulation. We used a 22 Fr infusion cannula (OptiSite Aortic Cannula, Edwards Lifesciences, Irvine, CA) and a 28 Fr drainage cannula (VFEM Femoral Venous Cannula, Edwards Lifesciences, Irvine, CA). At the time of V-V ECMO introduction, 2000 units of heparin was administered to achieve an active clotting time (ACT) of 200 s or higher. Subsequently, the heparin was sustained, and ACT measurement was performed after 2 h. ACT was maintained at over 200 s. We monitored the central venous oxygen saturation (SvO_2) to evaluate circulation and oxygen demand. Lung rest was observed (Fig. 5), and V-V ECMO was withdrawn 18 d following TAR. Thoracoscopic left upper lobe bullectomy by general thoracic surgeons, tracheostomy, and ventilator withdrawal were performed at 30, 35, and 37 d, respectively, following TAR. Swallow training and transfer to a rehabilitation hospital were initiated at 43 and 51 d, respectively, following TAR. Tracheostomy was closed at the rehabilitation hospital. Postoperatively, even after 2 years 3 months, the patient remains ambulatory without assistance, walking to the outpatient clinic, with an uneventful post-aortic surgery state (Fig. 2D, E).

DISCUSSION

Causes of respiratory failure following aortic dissection include pneumonia associated with long-term intubation, ARDS due to cytokine storm (caused by dissection), and exacerbation of underlying lung disease. Deep hypothermic circulatory arrest duration and perioperative transfusion are independent risk factors for postoperative ARDS [3]. In addition, increase in vascular permeability associated with surgical invasion forces respiratory management into a wet state, thus rendering treatment difficult. For sustained hypoxia under mechanical ventilation, administration of support through an extracorporeal circulation device should be considered. Giovanni *et al.* introduced veno-arterial extracorporeal membrane oxygenation (V-A ECMO) for cardiogenic shock after acute aortic dissection and reported a 37.1% withdrawal rate and 74.2% hospital mortality [4]. In this case, the introduction of ECMO with systemic heparinization was considered likely to cause postoperative bleeding and was not introduced immediately following surgery.

In Japan, NOI therapy has been covered by insurance since 2010 for hypoxic respiratory failure for neonatal pulmonary hypertension and has been covered for pulmonary hypertension since 2016, including for use among adults during the perioperative period. Pulmonary hypertension is defined as a mean pulmonary arterial pressure (mPAP) of 25 mmHg or higher per right heart catheter; however, there are few reports of its use following acute aortic dissection. Hang *et al.* reported that NOI therapy improved oxygenation among patients resulting in reduction of time under respiratory support and length of stay in the intensive care unit [5]. It is speculated that NO acts selectively on lung smooth muscle cells to reduce vascular resistance and improve ventilatory and circulatory imbalance, thereby improving oxygenation [6]. Additionally, since NO binds to hemoglobin and is immediately inactivated outside the lungs, it does not affect systemic circulation, and its metabolites are presumed to have anti-inflammatory effects. Similarly, in this case, a decrease in mPAP (immediately after the operation: 26 mmHg; 1 h after the start: 19 mmHg) and an increase in the P/F ratio (immediately after the operation: 48; 1 h after the start: 124) were observed after initiation of NOI therapy. Although it was difficult to continue NOI therapy because of the pneumothorax, it was effective as a bridging treatment for hypoxemia immediately following surgery, when bleeding was likely to occur. With V-V ECMO initiated on the sixth day after surgery and a reduced risk of postoperative bleeding, it was possible to continue treatment for pneumonia and ARDS. High PEEP management is used for ARDS cases with poor oxygenation, but pneumothorax is a possible complication of PEEP that should always be anticipated. The risk of pneumothorax is high in cases with giant bullae such as in this case. We suggest that early initiation of NO inhalation and V-V ECMO may have been necessary in this case.

CONCLUSION

The combination therapy of NOI and V-V ECMO for severe respiratory failure after surgery for ATAAD is effective.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest associated with this manuscript.

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ETHICAL APPROVAL

Written informed consent was obtained from the patient for publication of this case report.

PROVENANCE

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