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Intraoperative Endotoxin Adsorption as a New Therapeutic Option for Mycotic Aortic Aneurysm

Toshinori Totsugawa, MD; Masahiko Kuinose, MD; Hidenori Yoshitaka, MD; Satoko Ishii, MD*; Yoshimasa Tsushima, MD; Atsuhisa Ishida, MD

An 82-year-old man with a mycotic aortic aneurysm of the distal arch underwent urgent surgery because of sepsis. The infected aortic arch was excised, replaced with a rifampicin-bonded prosthetic graft, and covered with omentum. Direct hemoperfusion using polymyxin B-immobilized fiber (PMX-DHP) was intraoperatively carried out in parallel with the cardiopulmonary circuit. Intraoperative PMX-DHP dramatically reduced the level of plasma endotoxin, and ameliorated hemodynamic instability and oxygenation, resulting in smooth weaning from cardiopulmonary bypass. Intraoperative endotoxin adsorption is technically simple and easy, effective in hemodynamic stabilization, and so could be a new therapeutic option for mycotic aortic aneurysm. (*Circ J* 2008; **72:** 161 – 163)

Key Words: Endotoxin adsorption; Mycotic aortic aneurysm; PMX-DHP; Polymyxin B-immobilized fiber; Sepsis

Mycotic aortic aneurysm is a rare, life-threatening condition. Omentopexy and in-situ replacement using rifampicin-bonded prosthetic grafts or homografts have been reported as effective therapeutic options,[1–3] but there are still many cases in which infectious complications occur after surgery. We have reported 3 cases of mycotic aortic aneurysm complicated with *Klebsiella pneumoniae*;[4] 1 of the patients developed septic shock before surgery and was successfully treated by in-situ replacement with a rifampicin-bonded prosthesis but also with direct hemoperfusion using polymyxin B-immobilized fiber (PMX-DHP) connected to the cardiopulmonary bypass circuit. To our knowledge, there have been no other reports of intraoperative PMX-DHP for sepsis.

Case Report

An 82-year-old diabetic man was admitted to hospital complaining of high-grade fever in December 2005. On computed tomography (CT) scan, he was diagnosed as having an aortic aneurysm, with hazy aneurysmal wall, of the distal arch. On admission, his body temperature was 38.1°C, heart rate 100 beats/min, and blood pressure 70/35 mmHg. Laboratory tests revealed: leukocytes 22,100/mm^3; C-reactive protein, 24.6 mg/dl; and plasma endotoxin level 196 pg/ml (cut-off value 1.0 pg/ml with limulus turbidimetric time assay). Antimicrobial chemotherapy using sulbactam/ampicillin was introduced at 6 g/day after admission because of the low risk of aneurysmal rupture. Preoperative blood culture grew *Klebsiella pneumoniae* and CT scan revealed increased pericardial effusion and an inflamed, thickened aneurysmal wall (Fig 1). His blood pressure gradually decreased, despite antibiotic chemotherapy. He underwent urgent surgery on the 6th day under a diagnosis

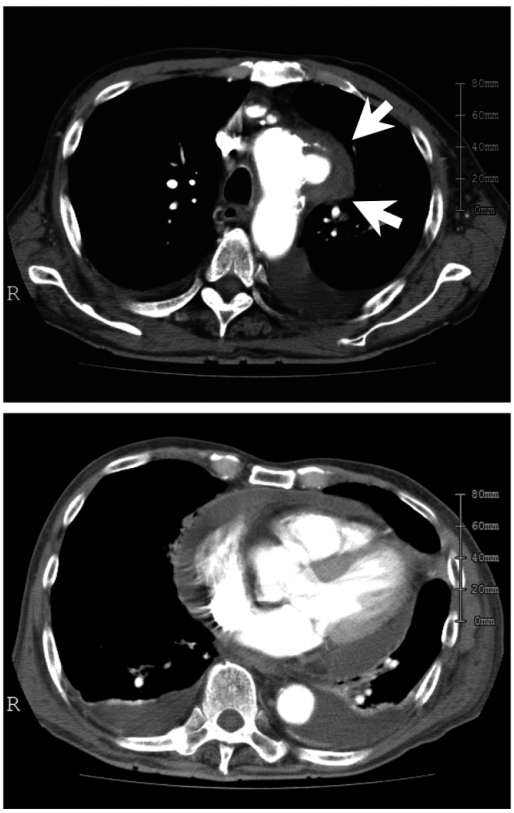

Fig 1. Preoperative computed tomography scan shows the aortic aneurysm of the distal arch with inflamed thickened aneurysmal wall (arrows) and remarkable bilateral pericardial effusion.

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*Departments of Cardiovascular Surgery, *Anesthesiology, The Sakakibara Heart Institute of Okayama, Okayama, Japan*
Mailing address: Toshinori Totsugawa, MD, Department of Cardiovascular Surgery, The Sakakibara Heart Institute of Okayama, 2-1-10 Marunouchi, Okayama 700-0823, Japan. E-mail: toshinoritotsugawa@mac.com

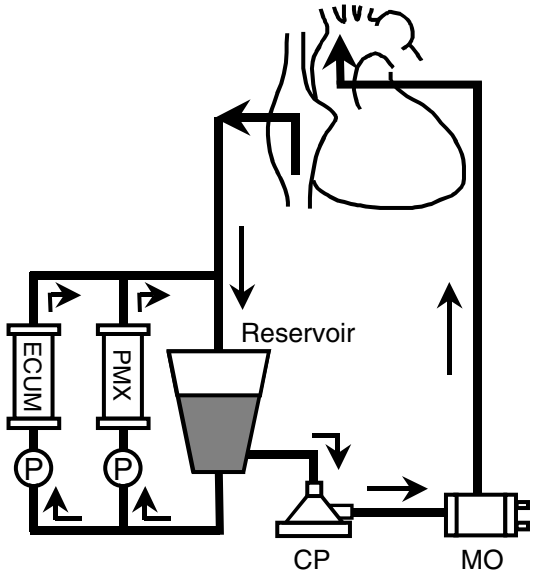

Fig 2. Schematic of the cardiopulmonary bypass circuit combined with direct hemoperfusion using polymyxin B-immobilized fiber. The endotoxin adsorbent column is incorporated into the extracorporeal circulation in parallel with a hemoconcentration column. CP, centrifugal pump; ECUM, hemoconcentration column using extracorporeal ultrafiltration method; MO, membrane oxygenator; P, roller pump; PMX, column of polymyxin B-immobilized fiber.

of progressive septic shock because of the mycotic aortic aneurysm.

The patient's chest was entered through a median sternotomy. There was remarkable retention of purulent effusion in the pericardial space. Cardiopulmonary bypass was instituted using ascending aortic and single right atrial cannulation. The PMX-DHP circuit, which uses a column of polymyxin B-immobilized fiber (Toraymyxin, Toray Industries, Tokyo, Japan), is a medical device that removes circulating endotoxin by adsorption, and was incorporated into the cardiopulmonary bypass in parallel with a hemoconcentration column (Fig 2). PMX-DHP was carried out during the surgery at a blood flow rate of 100 ml/min. Heparin was used as the anticoagulant for PMX-DHP in the usual manner of cardiopulmonary bypass. The aortic aneurysm and surrounding infected tissue were widely excised under conditions of circulatory arrest, with selective cerebral perfusion at a rectal temperature of 21.5°C. The aortic arch was replaced with a 4-branched gelatin-impregnated Dacron graft (Gelseal 4 branch plexus, Vascutek, Renfrewshire, Scotland) soaked for 1 h in rifampicin solution (Wako Pure Chemical Industries, Osaka, Japan) at a concentration of 1 mg/ml. The omental flap was harvested and transposed to cover the prosthetic graft and anastomoses. The respective times of cardiopulmonary bypass, selective cerebral perfusion, circulatory arrest, and aortic cross-clamping were 184, 146, 66, and 114 min. Intraoperative PMX-DHP dramatically ameliorated hemodynamic instability and the patient was easily weaned from cardiopulmonary bypass without any cardiopulmonary support device, even with a septic status, requiring only with some support with catecholamines.

The patient's recovery was uneventful, except for mild aspiration pneumonia because of recurrent nerve palsy. The postoperative level of plasma endotoxin was 1.1 pg/ml; furthermore, the levels of lactate and base excess indicating peripheral tissue circulation were almost within normal limits and there was no progression of multi-organ distress syndrome. Both the continuous administration of catecholamines and mechanical ventilation were stopped 80 h after surgery (Fig 3). *Klebsiella pneumoniae* was cultured from both the aneurysmal wall and pericardial effusion. We administered intravenously 1 g of imipenem and 4 g of fosfomycin per day for 10 days and then 600 mg of ciplofroxan per day for 25 days; subsequently, he began to take 600 mg/day of oral levofloxacin. He recovered from the aspiration pneumonia with antimicrobial chemotherapy and was discharged from hospital 45 days after surgery. He continues to take levofloxacin and remains well without recurrent prosthetic infection 11 months after surgery.

Discussion

There are numerous reports of endotoxin adsorption treatment being successfully used for sepsis[5,6] Although a randomized controlled study failed to demonstrate a significant difference in the blood endotoxin level, the authors indicated that PMX-DHP improved hemodynamic status and that further studies were needed to establish its effec-

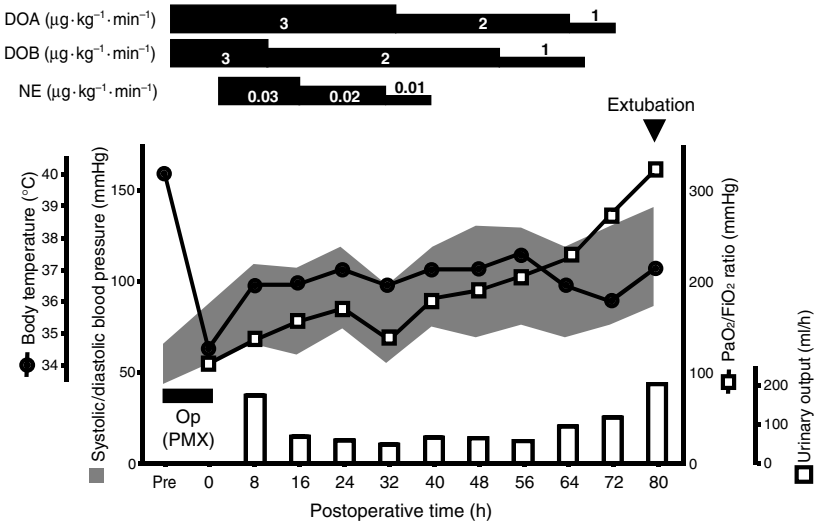

Fig 3. Perioperative course of the patient shows ameliorated general status. Blood pressure gradually elevated, despite decreased administration of catecholamine, and body temperature also stabilized in parallel with the heart rate (data not shown). Surgical intervention, including intraoperative direct hemoperfusion using polymyxin B-immobilized fiber (PMX) dramatically improved the arterial partial pressure of oxygen/fraction of inspired oxygen (PaO_2/FiO_2) ratio indicating respiratory status, and he was able to be weaned from mechanical ventilation 80 h after surgery. DOA, dopamine; DOB, dobutamine; NE, norepinephrine; Op, operation.

tiveness[7] There are a few reports regarding PMX-DHP for the treatment of sepsis in cardiovascular surgery[8,9] Furthermore, we rarely encounter a report regarding intraoperative endotoxin adsorption by a combination of cardiopulmonary bypass and endotoxin absorbent column. Asano et al reported a case, in the Japanese literature, demonstrating that PMX-DHP incorporated into the extracorporeal circulation circuit was effective for the treatment of infective endocarditis[9] However, both the causative microorganism and plasma endotoxin levels were unknown and cardiogenic shock because of valve destruction would mainly cause hypotension, and so it is unclear if PMX-DHP contributed to hemodynamic stabilization. Therefore, this is the first report of intraoperative endotoxin adsorption for the treatment of septic shock in the field of cardiovascular surgery.

Surgical excision of infected tissue is essential for infection control and necessary for hemodynamic stabilization. However, cardiovascular surgery using cardiopulmonary bypass with circulatory arrest is highly invasive, and so is unlikely to remarkably ameliorate the hemodynamic instability after surgical debridement in the case of septic shock. Therefore, weaning from cardiopulmonary bypass becomes difficult under such bad patient conditions, requiring cardiopulmonary support devices, such as intra-aortic balloon pumping, percutaneous cardiopulmonary support and extracorporeal membrane oxygenation, because of hypotension or poor oxygenation. In contrast, the present patient was easily weaned from cardiopulmonary bypass, with only a little support from catecholamines, and cardiopulmonary support devices were not required, even in the septic state. Furthermore, perioperative peripheral tissue circulation, including organ perfusion, was well preserved, and so the patient did not developed multi-organ distress syndrome. A systematic review has demonstrated that PMX-DHP increases arterial pressure while simultaneously reducing the dose of vasoactive agents, improving the ratio of arterial partial pressure of oxygen/fraction of inspired oxygen (PaO_2/FiO_2), and significantly reducing mortality[10] In addition, that review also described the ability of PMX-DHP to reduce the levels of humoral mediators such as interleukin (IL)-6, IL-10 and IL-18, tumor necrosis factor α, metalloproteinase-9, plasminogen activator inhibitor-1, neutrophil elastase, and anandamide, an endogenous cannabinoid. PMX-DHP during surgery enables not only simultaneous elimination of infectious foci and circulating endotoxin, but also concurrent reduction of these cytotoxic mediators. Intraoperative PMX-DHP may contribute to hemodynamic stabilization, amelioration of oxygenation, enhanced organ perfusion and prevention of multi-organ failure by these effects. PMX-DHP is a safe treatment with less adverse effects, as both a pilot study and the systematic review demonstrated[7,10] and incorporation into the cardiopulmonary bypass is technically simple and easy (Fig 2). We conclude that intraoperative PMX-DHP is a valuable option, not only for the treatment of mycotic aortic aneurysm, but also for cardiovascular surgery involving sepsis.

References

1. Shrager JB, Wain JC, Wright CD, Donahue DM, Vlahakes GJ, Moncure AC, et al. Omentum is highly effective in the management of complex cardiothoracic surgical problems. *J Thorac Cardiovasc Surg* 2003; **125:** 526–532.
2. Bandyk DF, Novotney ML, Johnson BL, Back MR, Roth SR. Use of rifampin-soaked gelatin-sealed polyester grafts for in situ treatment of primary aortic and vascular prosthetic infections. *J Surg Res* 2001; **95:** 44–49.
3. Knosalla C, Weng Y, Yankah AC, Hofmeister J, Hetzer R. Using aortic allograft material to treat mycotic aneurysms of the thoracic aorta. *Ann Thorac Surg* 1996; **61:** 1146–1152.
4. Totsugawa T, Kuinose M, Yoshitaka H, Tsushima Y, Ishida A, Minami H. Mycotic aortic aneurysm induced by *Klebsiella pneumonia* successfully treated by in-situ replacement with rifampicin-bonded prosthesis. *Circ J* 2007; **71:** 1317–1320.
5. Shoji H, Tani T, Hanasawa K, Kodama M. Extracorporeal endotoxin removal by polymyxin B immobilized fiber cartridge: Designing and antiendotoxin efficacy in the clinical application. *Ther Apher* 1998; **2:** 3–12.
6. Sato T, Shoji H, Koga N. Endotoxin adsorption by polymyxin B immobilized fiber column in patients with systemic inflammatory response syndrome: The Japanese experience. *Ther Apher Dial* 2003; **7:** 252–258.
7. Vincent JL, Laterre PF, Cohen J, Burchardi H, Bruining H, Lerma FA, et al. A pilot-controlled study of a polymyxin B-immobilized hemoperfusion cartridge in patients with severe sepsis secondary to intra-abdominal infection. *Shock* 2005; **23:** 400–405.
8. Takemoto M, Inada H, Masaki H, Morita I, Ishida A, Miyake T, et al. A case report on the successful treatment of septic shock of a postoperative patient of aortic dissection with blood purification. *Jpn J Endotoxemia Ther* 2000; **4:** 7–11 (in Japanese with English abstract).
9. Asano M, Hanafusa Y, Otake H, Kazuma H. PMX-DHP therapy for a patient with infectious endocarditis. *Jpn J Crit Care Endotoxemia* 2005; **9:** 247–250 (in Japanese with English abstract).
10. Cruz DN, Perazella MA, Bellomo R, de Cal M, Polanco N, Corradi V, et al. Effectiveness of polymyxin B-immobilized fiber column in sepsis: A systematic review. *Crit Care* 2007; **11:** R47.