Anaesthesia. Pain & Intensive Care 2013;17(1):88-90

CASE REPORT – Successful treatment of severe Legionella pneumonia and acute kidney injury with polymyxin B-immobilized fiber column direct hemoperfusion

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ABSTRACT
Legionella pneumonia is often complicated by multiple organ failure. Although acute kidney injury is relatively rare in the context of *Legionella* pneumonia, it is associated with an increase in mortality rate. This report describes a case of a patient with *Legionella* pneumonia and acute kidney injury who was successfully treated with polymyxin B-immobilized fiber column direct hemoperfusion (PMX-DHP). We conclude that PMX-DHP may be a useful therapeutic modality in patients with *Legionella* infection and acute kidney injury.
Key words: *Legionella* pneumonia; Polymyxin B-immobilized fiber column direct hemoperfusion; Acute kidney injury
Citation: Matsuki Y, Matsuki Y, Yasuda Y, Mizogami M, Takakura K, Shigemi K. Successful treatment of severe Legionella pneumonia and acute kidney injury with polymyxin B-immobilized fiber column direct hemoperfusion. Anaesth Pain & Intensive Care 2013;17(1):88-90

INTRODUCTION
Legionella pneumonia was first described following an outbreak of pneumonia among army veterans attending an American Legion convention in Philadelphia in 1976.[1] This pneumonia is often complicated by multiple organ failure, including acute kidney injury and hepatic dysfunction, that is associated with an increase in mortality rate.[2-3] Polymyxin B-immobilized fiber column direct hemoperfusion (PMX-DHP) is a useful treatment modality for patients with organ dysfunction due to severe sepsis.[4] We describe a case of a patient with severe *Legionella* pneumonia and acute kidney injury who was successfully treated with PMX-DHP.

CASE REPORT
A 70 years old man was admitted to our hospital with diarrhea, high-grade fever and dyspnea. He had been on treatment for malignant lymphoma, and had mitral valvuloplasty in the past. Physical examination on admission to our hospital revealed a temperature of 38.8°C, blood pressure of 65/40mmHg, heart rate of 89/min, SpO_2 of 80% (on 15 L/min of O_2 via reservoir mask) and a respiratory rate of 35/min. Glasgow coma scale was 9/15. Fine crackles were audible in the upper lung fields bilaterally. Laboratory tests showed elevations in leukocytes and C-reactive protein at 13,100/μl and 35.20mg/100 ml respectively. BUN (28 mg/100 ml), Creatinine (1.64 mg/100 ml), AST (1019iu/L), ALT (677iu/L) and LDH (1756iu/L) were also elevated, and the Na level (127 mEq/L) was low. Arterial blood gas analysis (taken while O_2 was

being administered at 15 L/min via reservoir mask) showed severe hypoxemia, and metabolic acidosis (pH of 7.06, $PaCO_2$ of 54 mmHg, PaO_2 of 52 mmHg, HCO_3^- of 14.5 mmol/L). Chest x-ray film showed infiltrative shadows in the left upper lung fields, and a chest CT revealed consolidation and ground-glass opacity in the left upper lung field (Fig 1-A&B).

Fig 1-A: Chest radiograph on admission. There is an infiltrative shadow in the left upper lung field.

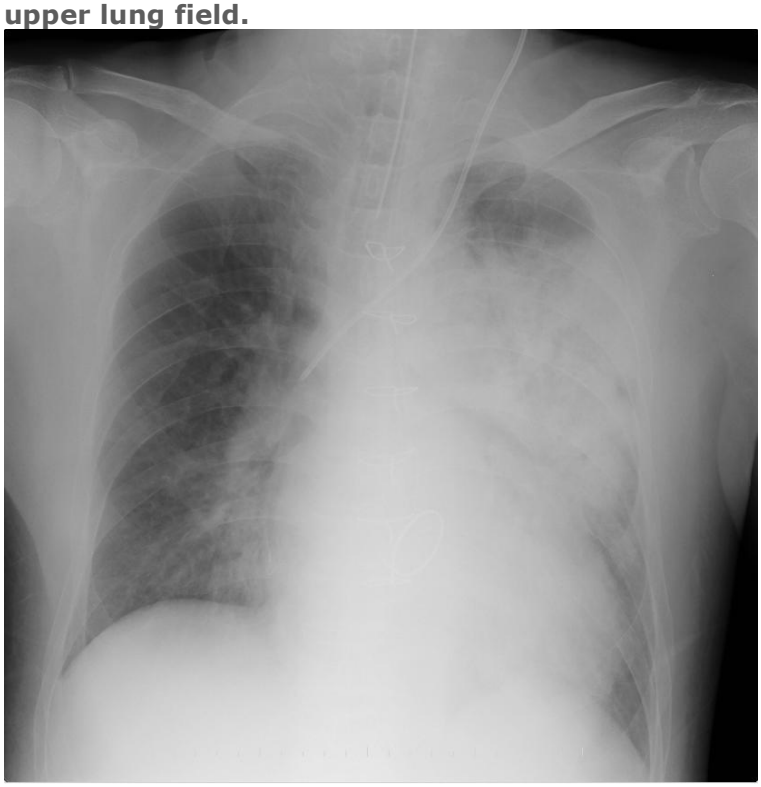
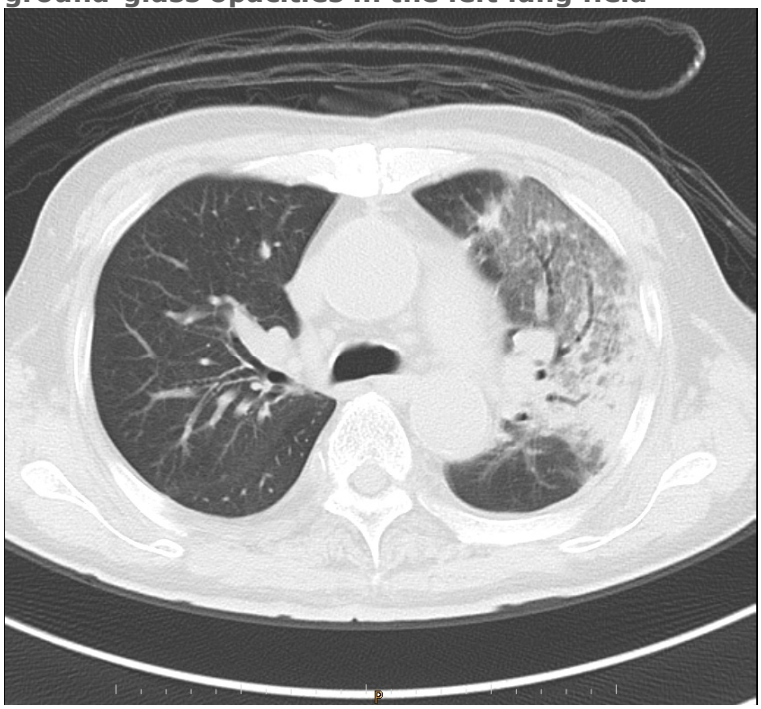
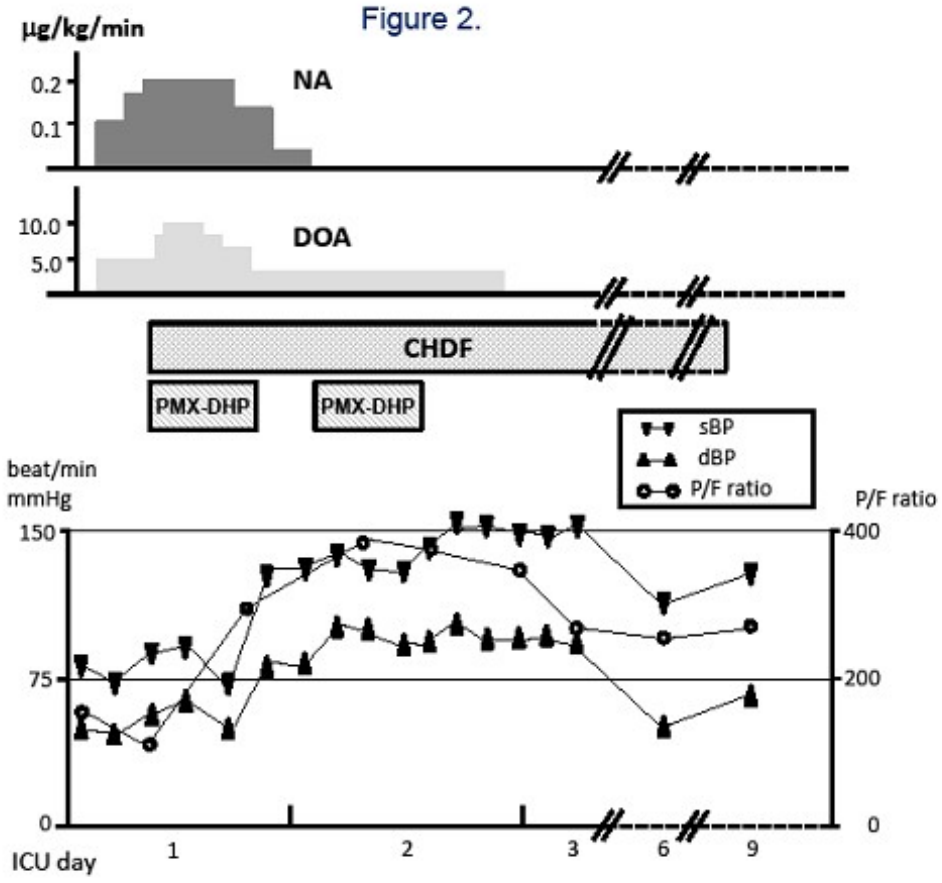


Fig 1-B: Chest computed tomography on admission showing consolidation with ground-glass opacities in the left lung field



The patient's clinical course is summarized in Fig 2. He was admitted to the intensive care unit (ICU) with a blood pressure of 78/42 mmHg despite administration of 5 μg/kg/min of dopamine hydrochloride and 0.1 μg/kg/min of noradrenaline. He was immediately intubated and ventilated with 100% oxygen and was treated with sivelestat sodium hydrate, intravenous fluids of volume and antibiotics (tazobactam/piperacillin, pazufloxacin). A diagnosis of legionellosis was made on the basis of positive specific urinary antigen. Antibiotics were switched to erythromycin, but blood pressure and the PaO_2/FiO_2 (P/F) ratio continued to decrease. He became anuric, and continuous hemodiafiltration (CHDF) (CH-1.0®; Toray Medical Co., Tokyo, Japan) was started to maintain body water balance. In addition, PMX-DHP (Toraymyxin 20R®; Toray Medical Co., Tokyo, Japan) was performed for 4 hours on days 1 and 2 to adsorb endotoxin. After the introduction of PMX-DHP, blood pressure and urinary output were gradually increased, and catecholamines were tapered off. The P/F ratio improved from 173 to 386 on day 3, and CHDF was terminated on day 8. The patient was extubated on day 9 after careful weaning from mechanical ventilation.

Fig 2: Clinical course after initiation of PMX-DHP. Catecholamines (noradrenaline and dopamine) were tapered off, and blood pressure and the PaO_2/FiO_2 (P/F) ratio gradually improved.



(**Legend:** NA: noradrenaline, DOA: dopamine, CHDF: continuous hemodiafiltration, PMX-DHP: polymyxin B-immobilized fiber column direct hemoperfusion, sBP: systolic blood pressure, dBP: diastolic blood pressure)

DISCUSSION

The bacterium, *Legionella*, got its name after a 1976 outbreak, when many people who went to a Philadelphia convention of the American Legion suffered from this disease, a type of pneumonia (lung infection). Although this type of bacterium was around before 1976, more illness from Legionnaires' disease is being detected now. The report describes the case of a patient with Legionella pneumonia and acute kidney injury who was successfully treated with PMX-DHP. *Legionella pneumophila* is one of the three most common causes of severe community-acquired acute pneumonia and comprises 3-6% of all cases of community-acquired pneumonias.[5,6] Although radiologic and clinical findings alone are not sufficient to establish a diagnosis of *Legionella* pneumonia, if these are accompanied by diarrhea, neurological signs, a temperature >39°C, hyponatremia and hepatic dysfunction, these are strongly suggestive of legionellosis.[7-9] Diarrhea, hyponatremia and hepatic dysfunction were noted in our present case. The patient was ultimately diagnosed with legionellosis on the basis of positive specific urinary antigen.

Although *Legionella* pneumonia complicated by acute kidney injury is a rare disease, it is associated with a mortality rate greater than 50%.[2,3] In our case, rhabdomyolysis was not observed, and we speculated that direct microbial toxicity,[10] endotoxemia, inflammatory cytokines[11] and/or hypotension was the cause of acute kidney injury. *L. pneumophila* is a Gram-negative aerobic bacterium that is an intracellular parasite, and produces beta-lactamase and many other potential endotoxins.

PMX-DHP can lower the plasma level of endotoxin and inflammatory cytokines,[12,13] and can significantly improve hemodynamics and organ function in patients with severe sepsis and/or septic shock arising from Gram-negative bacterial infections.[4,14] In the present case, early use of PMX-DHP resulted in improved hemodynamics and kidney function. PMX-DHP exerts a therapeutic effect in patients with pneumonia by absorbing cytokines (e.g. IL-8) and neutrophil elastase produced by activated neutrophils PMX-DHP,[15,16] and this was the likely mechanism of therapeutic action in our patient.

CONCLUSION

We conclude that PMX-DHP may be a useful therapeutic modality in patients with *Legionella* infection and acute kidney injury.

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