Case Report

Use of Direct Hemoperfusion with Polymyxin B-Immobilized Fiber for the Treatment of Septic Shock Complicated with Lemierre Syndrome Caused by *Fusobacterium necrophorum*

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1. Introduction

*Fusobacterium* spp. is an anaerobic gram-negative bacillus present in the oral cavity and gastrointestinal tract [1, 2]. However, this organism rarely causes Lemierre syndrome with thrombophlebitis of the internal jugular vein in healthy young individuals [3]. Although the incidence rate has recently been reported to be 0.6–2.3 cases per million [4], the mortality rate is as high as 4–22% [5]. In this study, we report a case of polymyxin B-immobilized fiber column direct hemoperfusion for the treatment of septic shock complicated with Lemierre syndrome caused by *F. necrophorum*.

2. Case Presentation

A 31-year-old man, with no significant medical history, presented with a chief complaint of fever and altered level of consciousness. On April XX, 2018, cold symptoms first appeared. He was diagnosed with influenza by the family physician, and was treated with oseltamivir. However, the symptoms progressed, and it became difficult for him to move after 10 days; therefore, he was admitted to our hospital. His initial examination revealed symptoms of respiratory distress and an altered level of consciousness. Based on laboratory and imaging results, he was diagnosed with septic shock of unknown origin, disseminated intravascular coagulation, and acute renal and respiratory failure. As soon as PMX-DHP was initiated, 2 days following admission to the ICU, his circulatory instability normalized. *F. necrophorum* was ultimately detected after a culture examination, and contrast-enhanced computed tomography revealed a jugular vein thrombus, which led to the diagnosis of Lemierre syndrome. The patient’s condition gradually improved, and he was discharged from the ICU after 19 days.
were normal and moist rales were detected in the lungs, but there were no anomalies in the abdomen, limbs, or skin.

Multiple nodular shadows and infiltrates were observed in both lung fields on chest X-ray. Chest computed tomography (CT) revealed cavitory lesions in both lung fields, and the nodules primarily occurred under the pleura (Figure 1(a) and 1(b)). A bilateral pleural effusion was noted. The ejection fraction was 63% on transthoracic cardiac ultrasound examination. Wall motion was normal and no obvious vegetations were observed. There were no irregular findings on head and abdominal CT.

Laboratory findings upon admission are given in Table 1 and include the following: WBC: 17880/µL; BUN: 85.1 mg/dL; Cr: 2.76 mg/dL; Platelet count: 24000/µL; CRP: 25.75 mg/dL; P-SEP: 3551.0 pg/mL; PCT: 77.21 ng/mL; Endotoxin: 29.1 pg/mL; PT-INR: 1.52; DD: 1.9 µg/mL; AT3: 58%; HbA1C: 5.8%; Glu: 121 mg/dL; arterial blood gas (10 L oxygenated reservoir) pH: 7.509; PO2: 73.9 mmHg; PCO2: 26.9 mmHg; HCO3: 20.5 mol/L; BE: −0.2 mmol/L; Lactate: 3.4 mmol/L; Influenza test: A(−), B(−), and HIV: (−); Sequential organ failure assessment score: 15; Acute physiology and chronic health evaluation II (APACHE II) score: 32; and Acute DIC score: 5.

The patient’s post-hospitalization course is given in Figure 2. Upon admission to the ICU, he was intubated and placed on a ventilator. Based on Sepsis-3 [6], he was diagnosed with septic shock, and we administered a continuous infusion of noradrenaline (NAD). Although the infection source and causative bacterial species were unknown, the likelihood of the presence of an endotoxin was high; therefore, tazobactam/ piperacillin and levofloxacin were administered. Antithrombin and gabexate mesylate were administered for septic DIC. Despite a high dose of NAD, circulatory insufficiency remained significant; 2 days after admission to the ICU, PMX-DHP (PMX-20R) was administered for about 3 h. His blood pressure began to immediately rise; once his blood pressure was stable, about 3 h after initiation of the infusion, the dosage of NAD was gradually decreased.

F. necrophorum (Table 1) was detected in the blood culture on the 6th day after admission to the ICU. On the same day, cervical contrast-enhanced CT, neck echocardiography, and intraoral examination were performed. Cervical contrast-enhanced CT and neck echocardiography revealed a thrombus in the right internal and external jugular veins, and emboli were present in both lung fields on chest CT (Figure 1(c)). Intraoral examination revealed periodontal disease and multiple caries in the oral cavity (Figure 1(d)). These findings led to the diagnosis of Lemierre syndrome caused by F. necrophorum. With continued oral care and antimicrobial treatment, his respiratory condition gradually improved, and he was removed from the ventilator on the 16th day after admission to the ICU, and moved to the general ward on the 20th day.

3. Discussion

In Lemierre syndrome, thrombophlebitis of the internal jugular vein is caused by acute pharyngitis and abscess in the
amygdala. In severe cases, bacterial emboli from the internal jugular vein spread to the lung, liver, kidney, bone, and joints. Lemierre syndrome is more common in healthy young individuals, and the male-to-female ratio was 1:2 [7]. In addition, among the 114 cases of Lemierre syndrome, it has been reported that the proportion of the 1st decade to 3rd decade was 79% [7]. Even in this case, it was an inherently healthy young person.

Notably, *F. necrophorum* has been identified as the causative species in at least 80% of patients with Lemierre syndrome [8]. In our case, in addition to periodontitis and numerous dental caries, pharyngitis caused by the influenza virus may have triggered the onset of the syndrome. Furthermore, the infection route is consistent with that reported previously [9, 10].

Lemierre syndrome is characterized by (1) a history of recent oropharyngeal infection, (2) clinical or radiological evidence of internal jugular vein thrombosis, and (3) isolation of anaerobic pathogens, mainly *Fusobacterium necrophorum* [11]. The patient did fulfill these characteristics.

For several days after admission to the ICU, although the infection source and causative bacterial species were unknown, the endotoxin levels were high, and intensive care was provided based on the presumed diagnosis of septic shock from gram-negative bacteria. We believe that the initial treatment was appropriate because it took 6 days before the culture was positive for *F. necrophorum*; this suggests the diagnosis of Lemierre syndrome. To the best of our knowledge, this is the first report of PMX-DHP being used for the successful treatment of septic shock with Lemierre syndrome caused by *F. necrophorum*. In our case, the endotoxin level decreased from 6.8 pg/mL before PMX-DHP infusion to 2.6 pg/mL after infusion. In addition, his blood pressure was quite unstable prior to PMX-DHP infusion, with 74/44 mmHg before infusion to 113/47 mmHg after infusion, after which it stabilized. As a result, the infusion of NAD could be gradually decreased from 0.23 µg/kg/min to 0.08 µg/kg/min. *F. necrophorum* tends to form a septic thrombus by destroying red blood cells and aggregating

| Hematology          |            |            |
|---------------------|------------|------------|
| WBC                 | 17880/µL   |            |
| RBC                 | 3.54 million/µL |  |
| Hb                  | 11.5 g/dL  |            |
| Hct                 | 32.9%      |            |
| Plt                 | 24000/µL   |            |

| Coagulation tests   |            |            |
|---------------------|------------|------------|
| PT                  | 19%        |            |
| PT-INR              | 1.52       |            |
| APTT                | 43.9 s     |            |
| D-dimer             | 1.9 µg/mL  |            |
| AT3                 | 58%        |            |

| Biochemistry        |            |            |
|---------------------|------------|------------|
| AST                 | 66 U/L     |            |
| ALT                 | 46 U/L     |            |
| LDH                 | 472 U/L    |            |
| γ-GTP               | 36 U/L     |            |
| T-BIL               | 4 mg/dL    |            |
| D-BIL               | 3.1 mg/dL  |            |
| CK                  | 107 U/L    |            |
| TP                  | 5.1 g/dL   |            |
| Alb                 | 2 g/dL     |            |
| BUN                 | 85.1 mg/dL |            |
| Cre                 | 2.76 mg/dL |            |
| Na                  | 128 mEq/L  |            |
| K                   | 3.7 mEq/L  |            |
| Cl                  | 89 mEq/L   |            |

| Serology            |            |            |
|---------------------|------------|------------|
| CRP                 | 25.75 mg/dL|            |
| Presepsin           | 3551 pg/mL |            |
| Procalcitonin       | 77.21 ng/mL|            |
| Endotoxin           | 29.1 pg/mL |            |
| β-D glucan          | ≤3.50 pg/mL|            |
| HbA1C               | 5.8%       |            |
| Glu                 | 121 mg/dL  |            |
| HBs-Ag              | (−)        |            |
| HCV-Ab              | (−)        |            |
| HIV                 | (−)        |            |

| Arterial blood gases|            |            |
|---------------------|------------|------------|
| pH                  | 7.509      |            |
| pCO₂                | 26.9 mmHg  |            |
| pO₂                 | 73.9 mmHg  |            |
| HCO₃⁻                | 20.5 mEq/L |            |
| BE                  | −0.2 mEq/L |            |
| Lac                 | 3.4 mmol/L |            |

| Urinalysis          |            |            |
|---------------------|------------|------------|
| Pneumococcal-Ag     | (−)        |            |
| Legionella-Ag       | (−)        |            |

| Influenza           |            |            |
|---------------------|------------|------------|
| Type A              | (−)        |            |
| Type B              | (−)        |            |

| Laboratory data upon hospital admission. |
|------------------------------------------|
| Hematology                               |
| WBC 17880/µL                             |
| RBC 3.54 million/µL                      |
| Hb 11.5 g/dL                             |
| Hct 32.9%                                |
| Plt 24000/µL                             |

| Coagulation tests                        |
| PT 19%                                   |
| PT-INR 1.52                              |
| APTT 43.9 s                              |
| D-dimer 1.9 µg/mL                        |
| AT3 58%                                  |

| Biochemistry                              |
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| ALT 46 U/L                                |
| LDH 472 U/L                               |
| γ-GTP 36 U/L                              |
| T-BIL 4 mg/dL                             |
| D-BIL 3.1 mg/dL                           |
| CK 107 U/L                                |
| TP 5.1 g/dL                               |
| Alb 2 g/dL                                |
| BUN 85.1 mg/dL                            |
| Cre 2.76 mg/dL                            |
| Na 128 mEq/L                              |
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| Serology                                  |
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| β-D glucan ≤3.50 pg/mL                   |
| HbA1C 5.8%                               |
| Glu 121 mg/dL                            |
| HBs-Ag (−)                               |
| HCV-Ab (−)                               |
| HIV (−)                                  |

| Arterial blood gases (10 L reservoir oxygen) |
| pH 7.509                                    |
| pCO₂ 26.9 mmHg                               |
| pO₂ 73.9 mmHg                                |
| HCO₃⁻ 20.5 mEq/L                             |
| BE −0.2 mEq/L                               |
| Lac 3.4 mmol/L                              |

| Urinalysis                                  |
| Pneumococcal-Ag (−)                         |
| Legionella-Ag (−)                           |

| Influenza                                   |
| Type A (−)                                  |
| Type B (−)                                  |

Acid-fast
Smear (−)
Culture (−)

Culture
Sputum and blood

**Fusobacterium necrophorum**

| Antibiotics                  | MIC    |
|-----------------------------|--------|
| Ampicillin                  | 0.12S  |
| Penicillin G                | 0.06S  |
| Sulbactam/ampicillin        | ≤0.06S |
| Cefmetazole                 | ≤1S    |
| Meropenem                   | ≤0.25S |
| Levofloxacin                | ≤2S    |
| Clindamycin                 | ≤0.12S |
| Tazobactam/piperacillin     | ≤16S   |

β-D glucan ≤5.0 pg/mL
platelets and bacteria by producing endotoxins [12]. Therefore, PMX-DHP was considered to be effective based on this mode of action.

We describe a report in which PMX-DHP was used for the treatment of septic shock complicated with Lemierre syndrome caused by *F. necrophorum*. In addition to the early use of appropriate antimicrobial therapy, PMX-DHP should be considered a supportive therapy in similar situations.

**Consent**

This is an anonymous case report based on the Personal Information Protection Law, and the consent for publication was obtained from the patient and his family.

**Conflicts of Interest**

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

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