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Report

Severe Acute Respiratory Failure due to 2009 Influenza A (H1N1) Infection Treated by Extracorporeal Membrane Oxygenation

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Here, we describe the validity of extracorporeal membrane oxygenation (ECMO) in treating severe respiratory failure due to 2009 influenza A (H1N1) viral infection. The patient was 59-year-old man. Cough and fever developed 3 days before admission. Two days before admission, he attended a neighborhood hospital where the influenza rapid (IR) test proved negative for influenza A and B antigens. He was admitted and administered antibiotics. However, dyspnea and respiratory distress worsened over the next 2 days when the IR test had become positive for influenza A antigen. A physician administered inhaled laninamivir and accompanied the patient to our hospital by ambulance.

The patient appeared critically ill and dyspneic upon arrival but was conscious, and a chest examination revealed generalized rales and rhonchi. A chest X-ray revealed an infiltration shadow over the whole lungs. We immediately inserted tracheal intubation and managed respiration under controlled mechanical ventilation with 100% oxygen and positive end expiratory pressure 15 cm H_2O. Under the condition, the tidal volume was 160 ml, and arterial blood gas analysis revealed PaO_2 49 torr and $PaCO_2$ 87 torr. We started ECMO therapy. We also administered peramivir, gammaglobulin, sivelestat, methylprednisolone, meropenem, gabexate mesilate. His medical course rapidly improved.

Key Words: 2009 influenza A (H1N1), extracorporeal membrane oxygenation, acute respiratory failure

Introduction

Infection with 2009 influenza A (H1N1) can result in rapidly progressive, severe respiratory failure and death[1]. Extracorporeal membrane oxygenation (ECMO) is one method of treating infected patients who are resistant to conventional mechanical ventilation[2]. Here, we describe the validity of ECMO in treating severe respiratory failure due to 2009 influenza A (H1N1) viral infection.

Case

A 59-year-old man was transferred from another hospital to our emergency and critical care center with respiratory failure in January 2011. His body mass index (BMI) was 24.2 kg/m^2, and he was a nonsmoker. He had a history of diabetes mellitus, bronchial asthma and allergies to contact medium and chub mackerel. He had not been vaccinated against H1N1 or seasonal influenza.

Cough and fever developed 3 days before admission. Two days before admission, he attended a local hospital where the influenza rapid (IR) test proved negative for influenza A and B antigens. He was admitted and given tazobactam/piperacillin. However, dyspnea and respiratory distress worsened over the next 2 days when the IR test had become positive for influenza A antigen. A physician administered inhaled laninamivir and accompanied the patient to our hospital by ambulance.

The patient appeared critically ill and dyspneic upon arrival but was conscious, with blood pressure of 170/80 mmHg, an irregular heart rate of 113 beats/min, labored respiration at a rate of 36 breaths/min and a body temperature of 39.0℃. Oxygen saturation was 80% under 10 *l* of inspira-

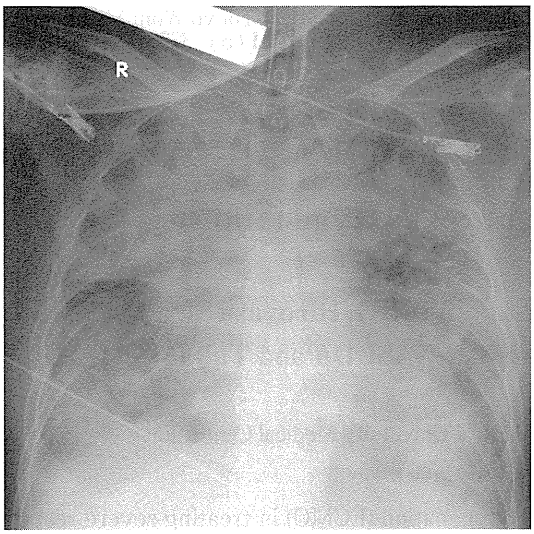

Fig. 1 Chest X-ray film on arrival
X-ray image revealed an infiltration shadow over the whole lungs.

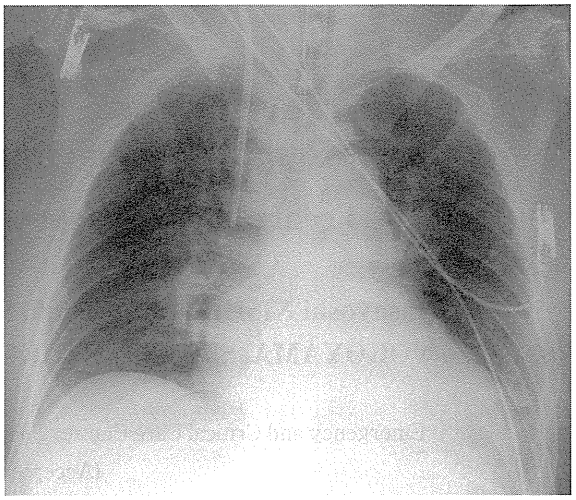

Fig. 2 Chest X-ray film on the sixth day
The lung shadow decreased.

tion through an oxygen mask. The conjunctivae were normal, but a chest examination revealed generalized rales and rhonchi. We immediately intubated the trachea. Thereafter, a chest X-ray revealed an infiltration shadow over the whole lungs (Fig. 1). Computed tomography images could not be obtained because the patient was too ill. A diagnosis of 2009 influenza A (H1N1) infection was confirmed by real-time RT-PCR. Bacterial cultures of blood and sputum at admission were negative.

Laboratory data showed the following: white blood cells, 17,400/μl; hemoglobin, 15.3 g/dl; platelets, 15.2×10^4/μl; C-reactive protein, 7.27 g/dl; creatinine, 1.69 mg/dl; creatinine kinase, 830 IU/*l*; aspartate aminotransferase (AST), 48 IU/*l*; alanine aminotransferase (ALT), 23 IU/*l*; and lactate dehydrogenase (LDH), 563 IU/*l*. We immediately performed tracheal intubation and managed respiration under controlled mechanical ventilation with 100% oxygen and positive end expiratory pressure of 15 cm H_2O. Under the condition, the tidal volume was 160 ml, peak intratracheal pressure was 40 cm H_2O, and arterial blood gas analysis revealed PaO_2 49 torr and $PaCO_2$ 87 torr. We therefore started the patient on veno-venous ECMO therapy using CAPIOX EBS (Terumo Co. Ltd., Tokyo, Japan). Extracorporeal blood flow and gas flow through the artificial lung were initially established at 2.0 *l*/min and at 5 *l*/min of oxygen, respectively.

We also administered peramivir (600 mg) as a single intravenous (IV) bolus, gammaglobulin (5 g) for 3 days, sivelestat (300 mg) for 6 days, methylprednisolone (1 g) for 3 days, meropenem (2.0 g) for 10 days, gabexate mesilate (1,500 mg) for 10 days and continuous IV insulin.

The patient's medical course rapidly improved and the lung shadow decreased daily (Fig. 2). Urine volumes ranged from 1,700 to 4,000 ml/day and no severe complications were directly attributable to ECMO. The ECMO was stopped on day 5, and the intratracheal tube was removed 2 days later. He returned to the previous hospital on day 12 and was finally discharged from that institution on day 19.

Discussion

The 2009 influenza A (H1N1) initially appeared in March 2009, then rapidly spread worldwide, sometimes causing respiratory failure[1].

Pregnancy, immunosuppression, obesity, cardiovascular disease, diabetes, asthma and chronic obstructive pulmonary diseases are known risk factors for severe or fatal 2009 influenza A (H1N1) infection[1]. Our patient had diabetes and asthma.

Early therapy with a neuraminidase inhibitor might reduce the rate of progressive disease severity requiring ICU admission or resulting in death[1]. However, the clinical sensitivity of commercially available assays that can rapidly detect 2009 influ-

Table The reports of extracorporeal lung support for multiple adult patients of influenza A (H1N1) infection

	NZA[2]	Freed[4]	Roch[5]	Chan[6]	Cianchi[7]	Japan[8]
ICU patients	252	168	18	120	12	57
ECLS patients	68	6	9	7	7	10
(ECMO patients)	68	4	6	7	7	nd
Age (median or mean)	36 (27-45)	22±15.5	49 (26-57)	42 (39-50)	45 (37-46.5)	nd
Duration of ECLS (days) (median or mean)	10	5	9	6	8	nd
Died patients Mortality rate	14 21%	2 33%	5 56%	1 14%	1 14%	2 20%

ECLS: extracorporeal lung support, nd: not described, ECMO: extracorporeal membrane oxygenation.

enza A (H1N1) antigen is poor[1]. Consequently, diagnostic or therapeutic decisions should not be based solely on negative test results[1].

The most important drugs against 2009 influenza A (H1N1) are neuraminidase inhibitors such as oseltamivir and zanamivir, and more recently, laninamivir and peramivir, have also been applied in practice[1]. Laninamivir and peramivir are administered as a bolus, but since laninamivir is administered tracheally, and good absorption by our patient was doubtful, we added IV peramivir.

Treatment using ECMO for severe respiratory failure due to 2009 influenza A (H1N1) infection has been reported[2)~10)]. We summarized the outcomes of extracorporeal lung support (ECLS), which means percutaneous cardiopulmonary support (PCPS) or ECMO, for several adult patients infected with 2009 influenza A (H1N1)[2)~8)] (Table). In Japan, 54 of the 57 patients (mean age, 43 years) treated in the ICU between September 2009 and March 2010, received mechanical ventilation[8]. Among these patients, ten were treated with ECLS and two died.

ECMO is, of course, an invasive and expensive method. Therefore, we must be careful when employing this method. We evaluated the condition of the patient to be critical, because a chest X-ray revealed an infiltration shadow over the whole lungs, and under controlled mechanical ventilation with 100% oxygen and positive end expiratory pressure of 15 cm H_2O, arterial blood gas analysis revealed PaO_2 49 torr and $PaCO_2$ 87 torr.

Our patient was weaned from ECMO after 5 days. We considered his condition to be fatal, judging from blood gas analysis and chest X-ray findings, the rapid disease progression and his age; at 59 years he was somewhat older than infected patients described in other reports. Lactate dehydrogenase is considered a marker of lung damage, and Cianchi et al[7] reported a mean LDH value of 445 IU/*l* in patients on ECMO. The LDH value in our patient before ECMO was 563 IU/*l*. The guidelines of the Extracorporeal Life Support Organization indicated that a P/F ratio of <80 on FiO_2 1.0 is one indication for extracorporeal life support[11].

Conclusion

Extracorporeal membrane oxygenation might be effective for patients who are resistant to conventional mechanical ventilation due to 2009 influenza A (H1N1) infection.

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Extracorporeal membrane oxygenation により救命しえた新型インフルエンザによる呼吸不全の1例

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今回われわれは，extracorporeal membrane oxygenation（ECMO）により救命しえた新型インフルエンザによる呼吸不全の1例を経験したので報告する．患者は59歳，男性．咳と発熱が出現した．翌日近医へ入院した．インフルエンザ簡易検査が陰性だったので抗菌薬を投与された．2日後，呼吸状態が悪化した．簡易検査が陽性となったので，ラニナミビルを吸入した．当センターへ紹介・搬送された．到着時は呼吸状態が非常に不良のため，ただちに気管挿管し人工呼吸（FiO_2 1.0，PEEP 15 cm H_2O）を開始した．この条件下で，一回換気量は160 ml，動脈血ガス分析でPaO_2は49 torrであった．胸部レントゲン撮影では肺野全体に浸潤影が著明であった．このため集中治療室に収容しECMOを導入した．またペラミビル・シベレスタット・メチルプレドニゾロン・グロブリン製剤・メシル酸ガベキサート・抗菌薬などを投与した．状態は急速に改善した．