

Veno-Arterial Extracorporeal Membrane Oxygenation in the Treatment of Hemodynamically Unstable Lupus Myocarditis: A Retrospective Case Series Study

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Objective: The clinical manifestations and treatment of three patients with hemodynamically unstable lupus myocarditis (LM) were analyzed.

Methods: The clinical data of three patients with LM with hemodynamic instability, who were admitted to the emergency ICU of the south hospital of the Renji Hospital, School of Medicine, Shanghai Jiao Tong University of Medicine from January 2018 to December 2021, were collected and analyzed, and relevant literatures were reviewed.

Results: Two of the three patients had the first onset of systemic lupus erythematosus. The other patient had mixed connective tissue disease in the past, and lupus was the main manifestation of this disease. At the onset of the disease, all patients had chest tightness and shortness of breath; two patients had a fever, and the markers of myocardial injury increased. Cardiac color Doppler ultrasound indicated that left ventricular ejection fraction decreased significantly. Cardiac insufficiency with cardiogenic shock rapidly appeared as the main manifestation. Two patients immediately started veno-arterial extracorporeal membrane oxygenation (VA-ECMO), and ECMO was also started in one patient after a pacemaker placement was ineffective. For all three patients, high-dose hormones were given to control the primary disease, and then the ECMO machines were removed successfully.

Conclusion: VA-ECMO treatment should be implemented in patients with hemodynamically unstable LM as soon as possible to maintain the patient's hemodynamics and help them overcome the crisis of cardiac dysfunction, allowing more time for primary disease treatment.

Keywords: VA-ECMO, lupus myocarditis, hemodynamic instability

Introduction

Systemic lupus erythematosus (SLE) is an immune-mediated systemic connective tissue disease involving the skin, joints, kidneys, and other tissues and organs. In up to 50% of patients, SLE may involve the heart.¹ Lupus myocarditis (LM) is a severe manifestation of SLE.² Some patients' conditions may rapidly develop into malignant arrhythmia, dilated cardiomyopathy, and severe heart failure, which require early diagnosis, intervention, and treatment.³

Extracorporeal membrane oxygenation (ECMO), a cardiopulmonary support technique, has been widely used in clinics. ECMO can be used for cardiac arrest, refractory cardiogenic shock, and ventricular tachycardia caused by a variety of reasons or for shock after cardiac surgery and the bridging of heart transplantation.⁴ Especially in the treatment of fulminant myocarditis, it has achieved good curative effect.

The onset of LM is acute, and patients may quickly develop hemodynamic instability. There is an urgent need for a support means to replace the patient's heart, so that the heart can rest while organ function perfusion is maintained. We conducted this retrospective case series study to describe the clinical process of three patients with LM who developed acute myocardial failure and received veno-arterial ECMO (VA-ECMO), and we subsequently reviewed the relevant literatures.

Data and Methods

The clinical data of three patients with LM with hemodynamic instability, who were admitted to the emergency ICU of the south hospital of the Renji Hospital affiliated to the Shanghai Jiao Tong University School of Medicine from January 2018 to December 2021, were collected. SLE was diagnosed according to the antibody spectrum, complements, and clinical manifestations. The antiphospholipid antibody spectrum was negative in all three patients. LM is defined as new or worsening changes, including new wall motion abnormalities, a left ventricular ejection fraction (LVEF) less than 45%, and impaired left ventricular function, observed in echocardiography or cardiac magnetic resonance imaging (CMRI) in patients with SLE. Patients with previous heart diseases, such as coronary artery disease, valve disease, cardiomyopathy, or congenital heart disease, were excluded. Data were collected through charts. The participants provided informed consent to the publication of their case details.

Clinical Data

The demographic characteristics, clinical manifestations, and various clinical test indices of the patients are presented in [Table 1](#). Relevant clinical data during ECMO treatment are presented in [Table 2](#). The primary diseases and related adjuvant treatments are presented in [Table 3](#).

Case 1

This patient was a 43-year-old female, hospitalized for fever and chills for more than three weeks and chest tightness for one day. Her maximum body temperature was 40°C. Her symptoms were complicated with joint pain in both elbows and lower limbs, as well as Raynaud's phenomenon. Anti-infective treatment was ineffective. Admission examination results included the following: anti-Chrome+, anti-SSA-52kd antibody+, anti-SSA-60+, anti-SmRNP+, anti-RNP-68 antibody+, anti-RNPA antibody+, decreased C3 and C4. Brain natriuretic peptide (BNP) was 1911 pg/mL. A B-ultrasound indicated pericardial effusion and bilateral pleural effusion. The patient was diagnosed with SLE with cardiac insufficiency. Dexamethasone (7.5 mg, q8h) was given to control the primary disease; the fever of the patient subsided, but cardiac function continued to worsen. Pericardial tamponade was considered, and the blood pressure was still low after pericardiocentesis. The patient had chest tightness, cold limbs, and a low heart rate. Her blood pressure was 80/50 mmHg under treatment of dopamine at a dose of 20 µg/min/kg. An echocardiography revealed that the left ventricular wall was diffusely thickened, the overall systolic activity of the left ventricular wall was weakened, and the LVEF was 36%. VA-ECMO was launched. The patient's blood pressure gradually stabilized after using the ECMO machine. Concurrently, the primary disease was treated with a shock treatment with 500 mg of methylprednisolone, which was gradually reduced after three days. The patient's cardiac function improved gradually, and the machine was successfully removed after nine days of conscious ECMO operation. After one month, a 200 mg dose of rituximab injection was given. After the condition became stable, the hormone was reduced to seven prednisone tablets taken orally, and the patient was discharged from the hospital.

Case 2

This patient was a 32-year-old female, hospitalized because of fever, chest tightness, and shortness of breath for four days. She had suffered from Raynaud's phenomenon for 11 years, joint pain for more than 10 years, and had a previous diagnosis of mixed connective tissue disease. The patient took her medication irregularly on ordinary days. Admission examination results included the following: anti-Chrome+, anti-SSA-52kd antibody+, anti-SmRNP+, anti-RNPA antibody+, decreased C3 and C4, and impaired myocardial and renal function. An acute onset of lupus erythematosus was considered. The patient was treated with methylprednisolone; the fever subsided, but the peripheral circulation was

Table 1 Basic Information of Patients

	Case 1	Case 2	Case 3
Demographic characteristics			
Age, years	41	32	22
Gender	Female	Female	Female
BMI, kg/m ²	21.2	20.9	20.7
Underlying diseases	–	–	–
Chief complaint	Fever for 3 weeks	Fever and shortness of breath for 4 days	Chest tightness and shortness of breath for half a month
Characteristics of connective tissue diseases			
Arthralgia	Yes	Yes	Yes
Raynaud phenomenon	Yes	Yes	Yes
Rheumatic antibody	Anti Chrom ⁺ , Anti SS-A52kd ⁺ , Anti SS-A60 ⁺ , Anti SmRNP ⁺ , Anti RNP-68 ⁺ , Anti RNPA ⁺	Anti Chrom ⁺ , Anti SS-A52kd ⁺ , Anti SmRNP ⁺ , Anti RNPA ⁺	Anti SSA ⁺ , Anti Ds-DNA ⁺
WBC, 10 ⁹ /L	8.06	13.24	28.45
Hemoglobin, g/L	122	120	91
PLT, 10 ⁹ /L	159	204	149
CRP, mg/L	32.86	96.17	19.59
PCT, ug/L	0.12	9.05	2.207
ESR, mm/h	5	33	87
CK max, U/L	58	767	167
CK-MB, U/L	3.6	30.4	1
cTNI, ng/mL	0.212	34.27	0.11
BNP, pg/mL	1911	>5000	>5000
MYO, ng/mL	58.1	155.7	>500
ALT, IU/L	124	4092	1535
AST, IU/L	63	8559	3333
Bilirubin, μmol/L	60	13	51
Alb, g/L	23.5	24.5	37.3
LDH, U/L	557	10,597	6560
Cr, umol/L	24	385	277
BUN, mmol/L	4.76	24.17	30.74
eGFR, mL/min	80	50	70
Urine protein	-	++	+
Ferritin, ng/mL	1434	52.9	>15,000
C3, g/L	0.368	0.443	0.36
C4, g/L	0.062	0.112	0.34

Notes: The complement in all 3 patients decreased; Troponin was significantly elevated in 1 patient. -, negative; +, 0.3-0.5g/L; ++, 0.7-1.0g/L.

Abbreviations: BMI, body mass index; WBC, white blood cell; PLT, platelet; CRP, C-reactive protein; PCT, procalcitonin; ESR, erythrocyte sedimentation rate; CK, creatine kinase; cTN, cardiac troponin; BNP, brain natriuretic peptide; MYO, myoglobin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Alb, albumin; LDH, lactate dehydrogenase; Cr, creatinine; BUN, blood urea nitrogen; eGFR, epithelial growth factor receptor.

poor. The patient had cold limbs, a blood pressure of 30/10 mmHg, and a heart rate of 58 beats/minute, and she lost consciousness after a few minutes. Auscultation showed that the heart sound was low and blunt, and there was no rale in both lungs. An electrocardiography showed a III° atrioventricular block. Blood creatine kinase, cardiac troponin I (cTNI), liver enzyme, and creatinine levels increased, while urine was reduced. A temporary pacemaker placement/

Table 2 ECMO-Related Data

	Case 1	Case 2	Case 3
Clinical data before ECMO			
PH	7.36	7.46	7.404
Lactate, mmol/L	7.1	11.4	10.1
Blood pressure, mmHg	80/50	70/40	68/40
ECG	Sinus tachycardia, low and flat T-wave	Sinus bradycardia, inverted T wave	Sinus tachycardia, inverted T wave
Chest radiograph	Bilateral lung exudates, pleural effusion. Enlarged heart shadow	Blurred the texture of both lungs, enlarged heart shadow	Blurred the texture of both lungs, decreased transparency, bilateral pleural effusion and enlarged heart shadow
FS, %	16	15	17
LVEF, %	36	32	36
Ventricular septal thickness, mm	14	9	10
Pulmonary artery pressure, mmHg	38	17	44
Pericardial effusion	A small volume	A small to medium volume	A small volume
ECMO-related parameters			
Intubation (percutaneous peripheral)	Femoral vein-femoral artery	Femoral vein-femoral artery	Femoral vein-femoral artery
ECMO flow, L	3.2	3.5	3.3
Mechanical ventilation	Sober	Trachea cannula	Sober
Ventilation mode	Noninvasive assisted ventilation	PC-PSV	-
ECMO operation time, days	9	10	5
Clinical data after ECMO			
PH	7.45	7.45	7.579
Lactate, mmol/L	2.7	5.2	2.3
Blood pressure, mmHg	106/69	98/60	100/67
ECG	Sinus rhythm, inverted T wave	Sinus rhythm, T wave changes	Sinus rhythm, T wave changes
Chest radiograph	Enlarged heart shadow	The heart shadow is slightly full	A small volume of bilateral pleural effusion. Enlarged heart shadow
FS, %	29	24	29
LVEF, %	52	48	56
Ventricular septal thickness, mm	10	7	10
Pulmonary artery pressure, mmHg	37	22	30
Pericardial effusion	No	A small volume	A small volume

Notes: Two patients have pleural effusion and pericardial effusion; One patient has pericardial effusion.

Abbreviations: ECMO, extracorporeal membrane oxygenation; ECG, electrocardiogram; PSV, pressure support ventilation; FS, left ventricular systolic fraction; LVEF, left ventricular ejection fraction.

coronary angiography/left ventriculography was performed. No obvious stenosis was found in the coronary artery during the operation, and the right coronary artery was dominant. A temporary pacemaker was successfully placed, but the pacing effect was poor, with a heart rate of 55 beats/minute. When dopamine was continuously pumped at a rate of

Table 3 Primary Disease and Related Treatment

	Case 1	Case 2	Case 3
Glucocorticoid	MP 0.5g	MP 0.5g	MP 1.0g
Immunosuppressants	Rituximab	Tocilizumab	Rituximab
IVIG	20g* 5 days	20g* 5 days	20g* 5 days
IABP	No	No	No
PCI	No	Yes	No
Pacemaker	No	Yes	No
Blood purification	No	CRRT	Artificial liver
Infection	No	Pulmonary infection	Bloodstream infection
ECMO removal	Successful	Successful	Successful
ECMO complications	No	No	No
ICU stay, days	11	14	12
Outcome	Survived	Dead	Dead

Abbreviations: ECMO, extracorporeal membrane oxygenation; IVIG, intravenous immunoglobulin; IABP, intra-aortic balloon pump; PCI, percutaneous coronary intervention; ICU, intensive care unit; CRRT, continuous renal replacement therapy.

20 µg/min/kg, the blood pressure was 70/40 mmHg, and blood oxygen saturation was 95%. Cardiac color Doppler ultrasound revealed that LVEF was 32%, and there was a little to moderate amount of pericardial effusion. LM and acute cardiac insufficiency were considered. VA-ECMO was immediately launched. Concurrently, shock treatment with 500 mg of methylprednisolone was given to control the primary disease. However, the patient's renal function could not be recovered and continuous renal replacement therapy was needed. Gastrointestinal bleeding and aspiration occurred. Emergency endotracheal intubation and ventilator-assisted ventilation were performed. BNP and TnI decreased gradually and cardiac color Doppler ultrasound revealed that LVEF was 52%. ECMO was successfully removed 10 days after the operation. However, the patient's pulmonary infection worsened, and she died of septic shock two days later.

Case 3

This patient was a 22-year-old female, hospitalized for edema with chest tightness and shortness of breath for half a month. Physical examination results included the following: gallop rhythm, joint pain, Raynaud's phenomenon, and the moist rales of the left lower lung could be heard. Rheumatic antibodies included anti SSA+, and anti Ds-DNA+. Cardiac color Doppler ultrasound revealed that LVEF was 36%. The patient developed cardiogenic shock. When dopamine was continuously pumped at a rate of 20 µg/min/kg, her blood pressure was 68/40 mmHg. Non-invasive auxiliary ventilation was needed to maintain an oxygen saturation >90%. The patient was considered to have SLE and acute cardiac insufficiency. VA-ECMO was immediately launched. The patient was given shock treatment with methylprednisolone (1g/2 days), which was gradually reduced to 30 mg after three days. Concurrently, Rituxan was added to control the primary disease. Mepem and ganciclovir were given for anti-infection. The patient's cardiac function gradually improved, and a cardiac ultrasound revealed that LVEF was 56%; the ECMO machine was successfully removed after five days. The patient's renal and liver function recovered gradually. After 10 days, the patient developed a high fever and a blood culture was positive. The patient was treated with Mepem + tigecycline + caspofungin + levofloxacin for anti-infection, and then the patient's fever subsided. However, her liver enzymes and bilirubin increased, and the effect of the liver protection treatment was poor. After 20 days, the patient had coagulation dysfunction and a progressive increase of liver enzymes and bilirubin. The artificial liver treatment was ineffective as well. Finally, multiple organ failure occurred, and the patient was discharged voluntarily. Indications for the artificial liver support device: 1. Severe hepatitis; 2. Hyperbilirubinemia; 3. Hepatic encephalopathy; 4. Diseases such as drug poisoning.

Results

All three patients in this study were young women, with no significant difference in demographic data among them. SLE was diagnosed according to clinical manifestations, antibody spectrum, complements, and damage of organ function. The

rapid increase of BNP, the decrease of left ventricular systolic activity, and the decrease of LVEF met the diagnostic criteria of LM. VA-ECMO was started, the cardiac function was recovered, and then the ECMO machine was removed successfully. Among them, one patient survived and was discharged successfully, one patient developed liver failure and died after an ineffective artificial liver treatment, and one patient developed renal failure due to contrast-induced nephropathy and needed continuous bedside hemodialysis, later dying as a result of a pulmonary infection.

Discussion

SLE is a chronic inflammatory disease with an unknown etiology, and it most often affects young women. It is a connective tissue disease that can affect many organs in the body, with immune complex deposition as the pathological feature. The heart has become one of the target organs of SLE because it is rich in connective tissues. LM is a rare complication of SLE with an incidence rate of 9%.⁵ To date, there is no recognized international guideline or expert consensus to formulate unified clinical diagnostic criteria for SLE complicated with cardiac involvement. LM may exhibit a variety of clinical manifestations, such as dyspnea, fever, or chest pain/palpitations. Serum myocardial injury markers may be elevated, similar to acute myocardial infarction, myocarditis, or stress cardiomyopathy.^{6–8} The gold standard for diagnosis is still an endomyocardial biopsy. However, its low sensitivity and potential complications make clinical use more difficult. CMRI has been evaluated for the diagnosis of myocarditis and appears to be effective.⁹ However, it is difficult to move the patient due to hemodynamic instability. Therefore, the diagnosis of myocarditis is usually determined by clinical manifestations, biomarkers, imaging, and classical echocardiography.¹⁰

The diagnosis of LM is based on myocardial dysfunction caused by SLE activity, excluding other causes, especially coronary atherosclerosis and hypertensive cardiomyopathy. The existence of Raynaud's phenomenon and positive autoimmune antibodies, such as ANAs, anti-double stranded DNA antibody, antiphospholipid antibody, anti-Smith antibody, anti-Sjogren's syndrome associated antigen antibody, anti-ribonucleoprotein antibody, lupus anticoagulant, and pericardial effusion, are the necessary conditions for the diagnosis of SLE.^{11,12} In this report, all three patients were positive for corresponding antibodies. Case 1 had cardiogenic shock and pericardial effusion, so we considered the possibility of pericardial tamponade; pericardiocentesis was conducted, and symptoms were not improved. Case 2 had cardiogenic shock, loss of consciousness, and a significant increase of troponin, so we considered sick sinus or acute coronary insufficiency. A pacemaker was placed, but could not pace normally, and there was no positive finding in the coronary angiography; the angiography also exacerbated renal failure. Case 3 quickly showed cardiogenic shock. All three patients had pericardial effusion and two patients had pleural effusion. Heart color Doppler ultrasound of the patients revealed that the systolic activity of the left ventricular wall decreased overall and the LVEF decreased significantly. After ECMO support, the ejection fraction was improved, and finally, the machine was successfully removed. No ECMO-related complications were found in any patient.

The treatment goal of acute LM is to control SLE activity, heart failure, and arrhythmia. High-dose corticosteroid therapy is the most commonly used treatment for LM.^{5,13} In this study, the treatment option was high-dose glucocorticosteroids, as well as Rituximab and tocilizumab. Cyclophosphamide and azathioprine were also used in some studies. These corticosteroid drugs have proven to be beneficial in strengthening the treatment of SLE.^{14–18} Other researchers have described the efficacy of pulse-dose corticosteroid therapy on LM.¹⁹ However, there are few literatures on the best immunosuppressive regimen for LM treatment. The treatment of LM is based on high-dose glucocorticoids combined with immunosuppressants, such as intravenous cyclophosphamide. In this report, three patients were treated with immunoglobulin and biological agents, two patients were treated with rituximab, and one patient was treated with tocilizumab.

Conclusion

The clinical manifestations of SLE are complex and strongly heterogeneous. Early detection, early intervention, accurate diagnosis, and correct treatment are the main challenges faced by clinicians, especially for middle-aged female patients with unexplained cardiogenic shock. The collection of detailed medical history is of great significance for the diagnosis

of the disease. In cases of obvious hemodynamic instability, VA-ECMO treatment should be started quickly to increase the probability of patient survival.

This report was merely a retrospective case analysis. Moreover, LM in all patients was not confirmed by histology, thus limiting the certainty of diagnosis in this study.

Ethics Approval

The study was conducted in accordance with the Declaration of Helsinki (as was revised in 2013). The study was approved by Ethics Committee of the Renji Hospital.

Consent to Participate

The written, informed consent was obtained from the participants for the publication.

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Disclosure

The authors declare that they have no competing interests.

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