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CASE REPORT

Cardiogenic shock as the initial manifestation of systemic lupus erythematosus

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Abstract

Cardiogenic shock as the initial manifestation of systemic lupus erythematosus (SLE) is an uncommon but catastrophic complication. Because of the lack of typical clinical features, the diagnosis of the disease is challenging. This case report describes a 47-year-old female admitted to the emergency room in refractory cardiogenic shock with dilative cardiomyopathy and a left ventricular ejection fraction (LVEF) of 25.6% of unknown origin. The patient responded poorly to the initial tries of stabilization, and the clinical status continued to deteriorate. Venous–arterial extracorporeal membrane oxygenation (V-A ECMO) was applied to maintain hemodynamic stability. Coronary angiography revealed no obvious stenosis of the coronary artery. Evidence of virus infection was negative. After requestioning about medical history in detail, Reynaud's phenomenon was shown. SLE was suspected. A complete autoimmune laboratory workup was completed and found the positive result of antinuclear antibodies, anti-double-stranded DNA antibodies, anti-phospholipid antibodies, and low C3 and C4. The patient also presented with pericardial effusion and the PLTs <100 000/mm^3. SLE was confirmed according to the 2019 EULAR/ACR criteria. When the diagnosis was established, the immunotherapy was initiated. As a result, the patient underwent a quick recovery and achieved good outcomes. In conclusion, early diagnosis and timely application of immunotherapy is the key to treatment lupus myocarditis. Advanced mechanical support may play a necessary role when patient is in critical situation. For middle-aged female patients presenting with unexplained cardiogenic shock, lupus myocarditis should be considered in the differential diagnosis. In addition, the 2019 EULAR/ACR criteria provide a new, fitting tool for the diagnosis, which is conducive to the earlier and more accurate diagnosis of SLE.

Keywords Shock; Cardiogenic; Myocarditis; Systemic lupus erythematosus; Heart failure

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Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with multisystemic characteristics and a variety of clinical presentations. The pericardium, myocardium, valvular tissue, and coronary arteries may be involved during the course of SLE. Lupus myocarditis or cardiac shock are severe manifestations of SLE[1]; these clinical conditions are a rare but catastrophic complications. Once suspected, an accurate diagnosis and appropriate treatment are needed to avoid fatal consequences.[2] Because of the lack of typical clinical features, the diagnosis of the disease is challenging. We describe a 47-year-old woman without SLE or a cardiovascular disease history who presented to the emergency room with cardiogenic shock and was finally diagnosed with cardiogenic shock caused by SLE. The patient eventually recovered after treatment with venous–arterial extracorporeal membrane oxygenation (V-A ECMO) and immunotherapy. Here, we share the clinical characteristics and treatment process of the patient.

Case report

A 47-year-old woman with an uneventful medical history was admitted to the emergency department of our hospital in October 2019 for complaints of shortness of breath,

palpitations, and fatigue for the last 4 days. In the emergency room, the patient was conscious. Her blood pressure was 80/40 mmHg, and her respiratory rate was 25 per minute. Her pulse rate was 98 beats per minute, and her body temperature was 36.2°C. On physical examination, she presented with cold and clammy skin, jugular venous distension, bilateral oedema of the lower limbs, and bilateral decreased breath sounds. The initial laboratory workup revealed the following: white blood cell (WBC) count, 4.2×10^9/L; haemoglobin (Hb), 140 g/L; platelets (PLTs), 81×10^9/L; myoglobin (MYO), 155 ng/mL; creatine kinase (CK), 768 U/L; creatine kinase isoenzyme (CK-MB), 143 U/L; C-reactive protein, 70.60 mg/L; troponin I (cTnI), 16.87 ng/mL; and N-terminal pro-brain natriuretic peptide (NT-proBNP), 5688.4 pg/mL. Urinalysis was positive (+) for urinary protein. An electrocardiogram (ECG) showed sinus tachycardia, ST-segment elevation in the V1 through V3 leads, and negative T waves in the I, II, III, aVF, V4 through V6 leads. Transthoracic echocardiography (TTE) showed biventricular dysfunction, left ventricular enlargement (54 mm), severe systolic impairment with a left ventricular ejection fraction of 25.6%, and minor pericardial effusion. Tricuspid annular plane systolic excursion (TAPSE) was 14 mm. Chest radiography showed thickened texture blurring in the right lower lung field. Lab data and the reference ranges were showed in *Table 1*.

Initial supportive management included anticoagulants, antiplatelet drugs, and intravenous (IV) diuretics treatment. Dobutamine (12 μg/kg/min) and noradrenaline (0.4 μg/kg/min) infusions were administered to maintain haemodynamic stability.

Despite optimal medical therapy, the patient's clinical status continued to deteriorate. One day later, the patient's blood pressure was 86/44 mmHg, although the doses of multiple vasopressor agents increased dramatically, and elevated serum lactate was observed; the blood lactate level was 7.36 mmol/L. Further evaluation and treatment were needed. She endured refractory cardiogenic shock, and her situation deteriorated. In order to combat the adverse situation, the patient's medical history and clinical data were evaluated in depth, and the treatment plan was adjusted. V-A ECMO was introduced to enhance circulatory support to maintain haemodynamic stability and recover organ function. When her haemodynamics were relatively stable, coronary angiography was performed, and obvious stenosis of the coronary artery was not found. Evidence of virus infection by using polymerase chain reaction technology was negative. Identifying the cause of cardiogenic shock is challenging sometimes. Repeated analysis of emerging conditions and medical history is a necessary step. After we requestioned about her medical history in detail, we found that the patient occasionally experienced Reynaud's phenomenon after contact with cold water when living in a remote rural area 6 years ago. Later, the patient relocated to a city with improved living conditions, where she lived currently, and she was no longer exposed to cold water, so these symptoms did not occur again. Considering the medical history, a connective tissue disease was suspected. A complete autoimmune laboratory workup was performed immediately.

Table 1 Lab data and the reference ranges

Laboratory test index	Results	Reference ranges
WBC	4.2×10^9/L	$(3.5–9.5) \times 10^9$/L
Hb	140 g/L	115–150 g/L
PLTs	81×10^9/L	$(125–350) \times 10^9$/L
MYO	155 ng/mL	0–85 ng/mL
CK	768 U/L	40–200 U/L
CK-MB	143 U/L	0–24 U/L
CRP	70.60 mg/L	0–8 mg/L
cTnI	16.87 ng/mL	0–0.08 ng/mL
NT-proBNP	5688.4 pg/mL	0–250 pg/mL
C3	0.39 IU/mL	0.80–1.60 IU/mL
C4	0.08 g/L	0.16–0.38 g/L

Abbreviations: CK, creatine kinase; CK-MB, creatine kinase isoenzyme; CRP, C-reactive protein; cTnI, troponin I; Hb, haemoglobin; MYO, myoglobin; NT-proBNP, N-terminal pro-brain natriuretic peptide; PLTs, platelets; WBC, white blood cell count.

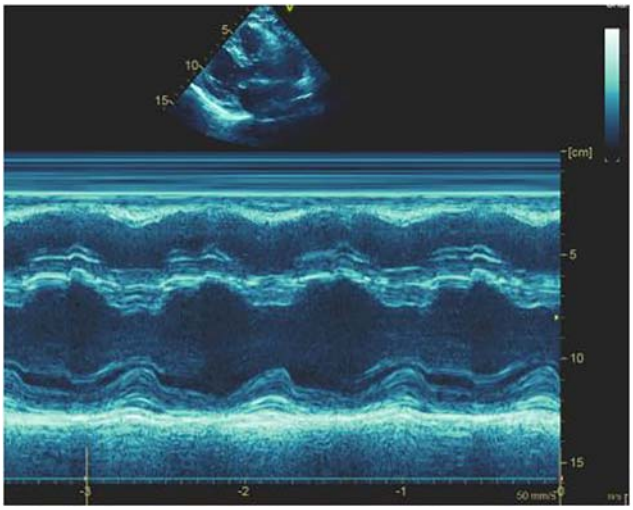
Serum was positive for antinuclear antibodies (ANAs), anti-double-stranded DNA antibodies, lupus anticoagulant, antineutrophil cytoplasmic antibodies, and on Coombs' (direct antiglobulin) test. C3 and C4 were decreased to 0.39 IU/mL and 0.08 g/L, respectively. Anticardiolipin antibody and anti-beta 2 glycoprotein I antibodies were negative.

Additionally, blood culture and HIV testing were negative. There was no history of recent infection. Combined with her medical history and laboratory examination results, we suspected shock introduced by SLE.

After the diagnosis was made, on the third day of admission, the patient began treatment with IV immunoglobulin (25 g once daily for 5 days) and IV methylprednisolone (500 mg once daily for 5 days and later decreased to 80 mg once daily for 3 days), followed by oral methylprednisolone (1 mg/kg/d).

After 7 days of V-A ECMO treatment combined with 6 days of immunotherapy, there was significant clinical improvement. TTE exhibited obvious recovery of heart function (the left ventricular ejection fraction was 47.5%). The clinicians successfully weaned the patient off V-A ECMO support. Noradrenaline and dobutamine were discontinued. Prior to her discharge, repeat TTE showed a significant improvement, with a left ventricular ejection fraction of 56%. Drugs in treatment are oral methylprednisolone (dosage reduced by 10% every 2 weeks) and IV cyclophosphamide (500 mg every 2 weeks for 3 months). After 3 months, the patient underwent an additional TTE examination, which showed a significant improvement of the left ventricle in size and function, with an ejection fraction of 74% (*Figure 1*).

Figure 1 Parasternal long-axis view and an M-mode echocardiogram recorded in the patient 3 months after discharge.



Discussion

SLE is a chronic autoimmune inflammatory disease, occurring more frequently in women than in men; up to 57% of cases involve the heart, and there is a variety of clinical presentations.[3–5] Lupus myocarditis, with a clinical prevalence of approximately 9%,[6] is a severe manifestation of SLE,[7] which is often asymptomatic but may manifest as fever, dyspnoea, palpitations, and nonexertional chest pain.[8]

However, the diagnosis of lupus myocarditis remains challenging in clinical practice. Cardiac magnetic resonance imaging (CMR) is a sensitive noninvasive technique to investigate myocarditis. However, CMR alone is insufficient to clarify the cause of myocarditis. Although endomyocardial biopsy (EMB) is considered to be the gold standard for the diagnosis of myocarditis, it is not performed routinely because endocardial biopsy is invasive and has a risk of possible sampling error. Currently, the most reasonable strategy in clinical practice is considering the medical history combined with a positive laboratory test when SLE is suspected.[9]

Myocardial infarction patients need to receive reperfusion therapy expeditiously and effectively according to the 2017 ESC Guidelines.[10] However, in our case, the patient received the coronary angiogram 1 day later. In China, about only 25% patients with acute myocardial infarction received reperfusion therapy timely.[11]

In clinical practice, the differences of culture have brought difficulties to clinical standard treatment. In traditional Chinese culture, family members usually play a decisive role in a patient's treatment plan and undertake the role of giving informed consent.[12] In our case, patients' family were filled with many concerns and scruples when faced invasive operations with potential risks. Obtaining the consent of patients' family in time was difficult, which led to EMB and CMR not performed and the coronary angiography delayed. EMB and CMR play an important role and make the diagnosis more perfect in patients with suspected of lupus myocarditis under the background of the evidence-based medicine. If the patient and family members approve of the procedure, EMB and CMR should be performed to consolidate the diagnosis although there are potential risks and difficulties.

Cardiogenic shock is rare but potentially fatal manifestation of SLE and has been reported in recent literature. Serum markers of myocardial injury may be elevated, similar to acute myocardial infarction, myocarditis, or stress cardiomyopathy.[13–15]

In our case, the patient's main clinical manifestations were palpitation, shortness of breath, fatigue without fever, and rapid deterioration to cardiogenic shock. The initial diagnosis was considered myocarditis or myocardial infarction due to the clinical symptoms, ECG characteristics and significant increase in myocardial enzymes and troponin I. After a detailed medical history, it was discovered that the patient experienced Raynaud's phenomenon; patients with two-handed Raynaud's phenomenon (RP) occasionally present skin discoloration with cold water contact. RP is caused by vasospasm of the small muscular arteries and arterioles of the digits,[16] triggered by cold and/or emotional stress. Although RP is a nonspecific skin change that appears in 18–46% of SLE patients.[17,18]The prevalence of RP in patients with connective tissue disease is significantly higher than that in the normal population. The presence of RP provides important cues of association with SLE diagnosis.

Combined with thrombocytopenia and pericardial effusion, which did not initially attract the clinical physician's attention, SLE was suspected. Research findings on the presence of Raynaud's phenomenon and positive autoimmune antibodies, such as ANAs, anti-double-stranded DNA antibodies, antiphospholipid antibodies, anti-Smith antibodies, anti-Sjögren's syndrome-related antigen antibodies, anti-ribonucleoprotein antibodies, and lupus anticoagulant, are necessary to diagnose myocarditis in SLE.[9,19]

In our case, we enabled establishing the diagnosis of SLE according to the 2019 EULAR/ACR classification criteria. The new classification criteria have defined positive anti-nuclear antibody (ANA) as required entry criterion, and the clinical manifestations of various systems/organs and multiple immunological abnormalities as additive criteria. The differential weighting of criteria better represents their relative contribution to SLE. In our case, laboratory screening found that ANAs at a ratio of 1:1000 fit the entry criterion, then additive criteria were applied. Clinical criteria were pericardial effusion and PLTs <100 000/mm^3. Immunology criteria consisted of positive anti-double-stranded DNA antibodies and antiphospholipid antibodies, and low C3 and low C4. The total score was >10 points. According to 2019 EULAR/ACR classification criteria, SLE was diagnosed.

Compared to the 1997 ACR criteria and the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria, the new classification criteria show excellent sensitivity and specificity.

The evidence of viral infection was negative. No obvious stenosis was found on coronary angiography. No obvious change in the heart structure was found by echocardiography. Based on these negative results, the common causes of cardiogenic shock were excluded, and the patient's shock was confirmed to be caused by SLE.

During the course of treatment, due to biventricular dysfunction and steady deterioration of the condition under routine treatment, we finally adopted ECMO instead of Impella support to treat the patient. ECMO can be applied in cases of cardiac arrest, refractory cardiogenic shock and ventricular tachycardia, or shock after cardiac incision.[20] After the diagnosis of SLE and the administration of immunotherapy combined with ECMO support, the patient recovered quickly. High-dose corticosteroid treatment is the most common therapy used for lupus myocarditis.[21,22] In this case, the prognosis was good with ECMO support and immunotherapy, and heart function recovered quickly. Echocardiographic follow-up for 3 months showed a significant improvement of biventricular dysfunction. The subsequent therapeutic effects also support the diagnosis of cardiogenic shock caused by SLE to some extent. We describe the successful application of V-A ECMO and glucocorticoids in a patient with cardiogenic shock induced by systemic lupus who achieved good outcomes.

The clinical manifestations of SLE are complex and heterogeneous. Early detection, early intervention, an accurate diagnosis, and correct treatment are major challenges for clinicians. We should improve our understanding of SLE, especially in middle-aged female patients with unexplained cardiogenic shock. Detailed history collection and keen insight are of great significance for the diagnosis of the disease. In the clinic, we should pay attention to atypical symptoms and signs of SLE, which provide necessary support for the final diagnosis. A reasonable analysis of clinical history data, such as SLE-related glomerulonephritis, arthritis, skin or mucosal lesions, or connective tissue disease, should be performed when diagnosing a patient for whom SLE is highly suspected.

Conclusions

In conclusion, early diagnosis and timely application of immunotherapy prompt a quick recovery from lupus myocarditis and achieve good outcomes. Advanced mechanical support may play a necessary role in critical situation. For middle-aged female patients presenting with unexplained cardiogenic shock, lupus myocarditis should be considered in the differential diagnosis. 2019 EULAR/ACR criteria provide a new, fitting tool for the diagnosis, which is conducive to the earlier and more accurate diagnosis of SLE.

Conflict of interest

None declared.

Author contributions

Liang Liu and Yanling Dong contributed equally to this paper and should be regarded as co-first authors. Hengbo Gao is the second author. He was the attending in charge of the patient. Dongqi Yao, Rui Zhang, and Tuokang Zheng are other residents taking part in caring for the patient. Yingli Jin and Baopu lv spent time performing echocardiography and supervising patient care. Professor Yingping Tian provided the detailed treatment regimen for the patient and reviewed the manuscript, and he is our corresponding author.

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