Systemic lupus erythematosus complicated by heart failure: A case series

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Abstract

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease with diverse cardiovascular manifestations, among which heart failure (HF) remains underrecognized. Although diastolic dysfunction is more common, systolic dysfunction due to lupus myocarditis or medication-related cardiotoxicity can lead to significant morbidity and mortality. We describe three young female patients with SLE who developed reduced ejection fraction (EF) and global hypokinesia, likely secondary to myocarditis. Clinical presentations ranged from mild symptoms to severe decompensated HF, with variable laboratory evidence of inflammation and disease activity.

Overall, two patients had improvement in cardiac function following immunosuppressive therapy and guideline-directed HF management, while one had a progressive clinical decline and died despite treatment. These findings highlight the heterogeneity in presentation, disease activity, and outcomes of SLE-associated cardiomyopathy. Lupus myocarditis, though uncommon, should be suspected in SLE patients presenting with new-onset HF, particularly in the absence of ischemic disease. Diagnosis is typically clinical, supported by biomarkers and imaging, as endomyocardial biopsy is rarely performed. Early recognition and a multidisciplinary approach targeting both HF and underlying autoimmune activity are essential to improve outcomes.

Keywords: Systemic lupus erythematosus, heart failure, myocarditis

Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease. Cardiovascular (CV) manifestations in SLE include premature atherosclerosis, valvular disease, and pericarditis. Heart failure (HF) is less well-recognized. Its incidence is estimated to be 9.7 events per 1000 person-years with a prevalence of 1–10%.[1–3] Although SLE has a female predominance, male patients have a higher incidence of HF.[1,4] In the majority of SLE patients with HF, the cause is attributed to active disease (50%), and only 21% was due to atherosclerotic coronary artery disease (CAD). Diastolic dysfunction is a prominent feature of HF in SLE with heterogeneous etiologies. However, systolic dysfunction due to lupus myocarditis and medication-induced cardiotoxicity can also lead to cardiomyopathy, resulting in HF.[5]

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Herein, we report 3 young female patients with global hypokinesia likely due to myocarditis. Two patients demonstrated improvement of ejection fraction on treatment, while the third patient died as an outpatient.

Case 1

An 18-year-old female with Sjögren's Syndrome and SLE presented to the hospital with shortness of breath with chest pressure. She described her pain as being worse with inspiration with burning substernal chest pain radiating to the back and neck. The patient had been on prednisone 40 mg daily, mycophenolate mofetil 1.5 g daily, hydroxychloroquine 400 mg daily, and rituximab.

Table 1. Laboratory Investigation

	Normal Range	Case 1	Case 2	Case 3 (1st admission)
Complete blood count				
WBC (K/uL)	3.98–10.04	3.51	4.82	1.6
Hemoglobin (g/dL)	11.2–15.7	10.7	9.2	8.9
Hematocrit (%)	34.1–44.9	33	28.5	26.8
Platelets (K/uL)	182–369	315	438	90
Blood chemistry				
BUN (mg/dL)	6–20	12	18	54
Cr (mg/dL)	0.5–1.2	0.4	0.6	3.4
Creatinine kinase (IU/L)	26–308	39	175	NA
ESR (mm/hr)	0–20	3	95	NA
CRP (mg/dL)	0.0–0.5	0	0.8	0.4
BNP (pg/ml)	≤124	81	29680	50,024
Troponin (ng/l)	≤19	<0.1	157	0.01
Immunology				
C3 (mg/dL)	90–180	96	60	34
C4 (mg/dL)	10–40	15	20	4
ANA	Neg	Pos	Pos	Pos
dsDNA	<4	<1	39	93
Smith antibody	0.2–1	1.1	7.4	>8
RNP antibody	0.2–1	>8	NA	>8
SSA-Ab	0.2–1	NA	>8	>8
SSB-Ab	0.2–1	NA	<0.2	0.4

On physical examination, she was tachycardic, saturating above 95% at room air, and afebrile. Cardiovascular and respiratory examinations appeared unremarkable except for Raynaud and capillary refill of more than 3 seconds. Chest wall tenderness was noted.

ECG showed sinus tachycardia. The CT angiography was unremarkable. EGD demonstrated reflux esophagitis. The transthoracic echocardiogram (TTE) showed an ejection fraction (EF) of 45–49% (normal EF ≥ 50%) with mild global hypokinesia. Rheumatology and cardiology services were consulted due to concern of SLE exacerbation and reduced EF secondary to SLE. Cardiology initiated carvedilol 3.125 mg twice daily for reduced EF. Hydroxychloroquine was held due to concerns it could be implicated in impaired ejection fraction. A short course of high-dose methylprednisolone 500 mg daily intravenous was initiated. Laboratory studies revealed normal ESR (3 mm/hr), CRP (0 mg/dl) and complement levels (C3 95 mg/dl, C4 15 mg/dl) as shown in Table 1. Troponin-T was unremarkable (<0.01 ng/mL). She had suspected pleuritic chest pain and myofascial pain. Systemic lupus erythematosus disease activity index (SLEDAI)-2000 (SLEDAI-2K) score was 2 (pleuritis). Naproxen was also initiated. The patient reported improved pain.

During hospitalization, the patient also complained of severe knee pain requiring hydromorphone. Magnetic resonance imaging of the lower extremities showed evidence of early avascular necrosis (AVN) on the left distal femur. Steroids were tapered down to avoid worsening AVN and were discontinued in 2 months. A repeat TTE 2 months later showed an EF of 60–64% with no regional wall motion abnormality and normal RV systolic function.

Case 2

A 31-year-old female with known SLE with class V lupus nephritis (on MMF 1 g daily and HCQ 200 mg daily), and pulmonary embolism (on apixaban) presented with difficulty breathing for 2 days, worse with exertion and lying flat. She was recently admitted a month prior due to pericardial effusion and pleural effusions secondary to SLE and nephrotic syndrome. She denied fever, chest pain, dizziness, joint pain, or rashes. On examination, the patient was hemodynamically stable but desaturated to 84% on ambient air, requiring oxygen supplementation, and had tachycardia with an HR of 116. Crepitations in bilateral lungs and peripheral edema were noted.

Troponin was elevated and peaked at 513. ESR and CRP were elevated, and C3 level was low (71 mg/dl). Systemic lupus erythematosus disease activity index (SLEDAI)-2000 (SLEDAI-2K) was 18. Other laboratory investigations are summarized in Table 1 and the complement level trend in Figure 1. An ECG demonstrated sinus tachycardia. The CT pulmonary embolism protocol did not show acute pulmonary embolism but again demonstrated pericardial and pleural effusions with pulmonary edema. She was treated with furosemide intravenously. A TTE showed EF at 20–24% with severe global hypokinesia and small to moderate pericardial effusion without tamponade physiology. Cardiology was consulted for evaluation. Her elevated troponins were considered secondary to troponin leakage from pericarditis and/or myocarditis rather than ischemia due to the absence of chest pain. She underwent an exercise stress test, which demonstrated no ischemia. She was given a diagnosis of non-ischemic cardiomyopathy (NICM). She did not undergo cardiac catheterization, and treatment was continued for SLE, including MMF 3 g daily, HCQ 200 mg daily, and prednisone 40 mg daily. She was also treated with carvedilol and lisinopril with continued diuresis, then discharged home with a wearable cardioverter defibrillator (WCD).

At the 4-week rheumatology clinic follow-up, a decision was made to treat the patient with cyclophosphamide for 3 doses due to presumed cardiac involvement (myocarditis) of SLE while remaining on MMF 3 g daily, HCQ 400 mg daily, and prednisolone 20 mg daily. During her follow-up in the cardiology clinic, lisinopril was switched to sacubitril/valsartan, and spironolactone was added. A TTE repeated 6 months after discharge showed improvement of EF to 40–44%, and she was taken off WCD.

Case 3

A 25-year-old female with known SLE (on MMF 3 g daily, prednisone 10 mg daily) with class V LN (treated with cyclophosphamide) and hypertension presented with shortness of breath (SOB) for 2 weeks. She visited an emergency room once and was prescribed furosemide with no clinical improvement. Dyspnea on exertion became worse for 2 days, with orthopnea and paroxysmal nocturnal dyspnea. She also complained of intermittent sharp chest pain, radiating to the neck and left breast, lasting 15 minutes each episode. Troponin-T was normal, and low C3 and C4 (34 mg/dl and 4 mg/dl, respectively) were noted; other blood work is summarized in Table 1 and the complement level trend in Figure 1. The SLEDAI-2K was 16.

On examination, she was hemodynamically stable. Cardiovascular and respiratory examinations were normal. No edema was appreciated. CXR showed cardiomegaly. The TTE showed EF 30–34% with global hypokinesis. She was diagnosed with systolic heart failure. She was underwent diuresis and was discharged home with carvedilol 6.25 mg BID, lisinopril 20 mg BID, which was later switched to sacubitril/valsartan in clinic, and WCD.

At clinic follow-up, she had worsening SOB during a 6-minute walk with elevated JVD at the angle of the mandible and pitting edema 1+. The patient underwent right heart catheterization which demonstrated elevated right atrial pressure (26 mmHg), and sildenafil was initiated. Despite all treatment, she had frequent hospital admissions with SOB due to acute heart failure, which had consistently improved with intravenous furosemide. The stress test showed moderate ischemia in the inferior wall (intermediate risk). However, angiography was not feasible due to rising creatinine. The patient was followed in the heart failure clinic and scheduled for furosemide infusions every 2 weeks, which reduced recurrent hospitalization. Her

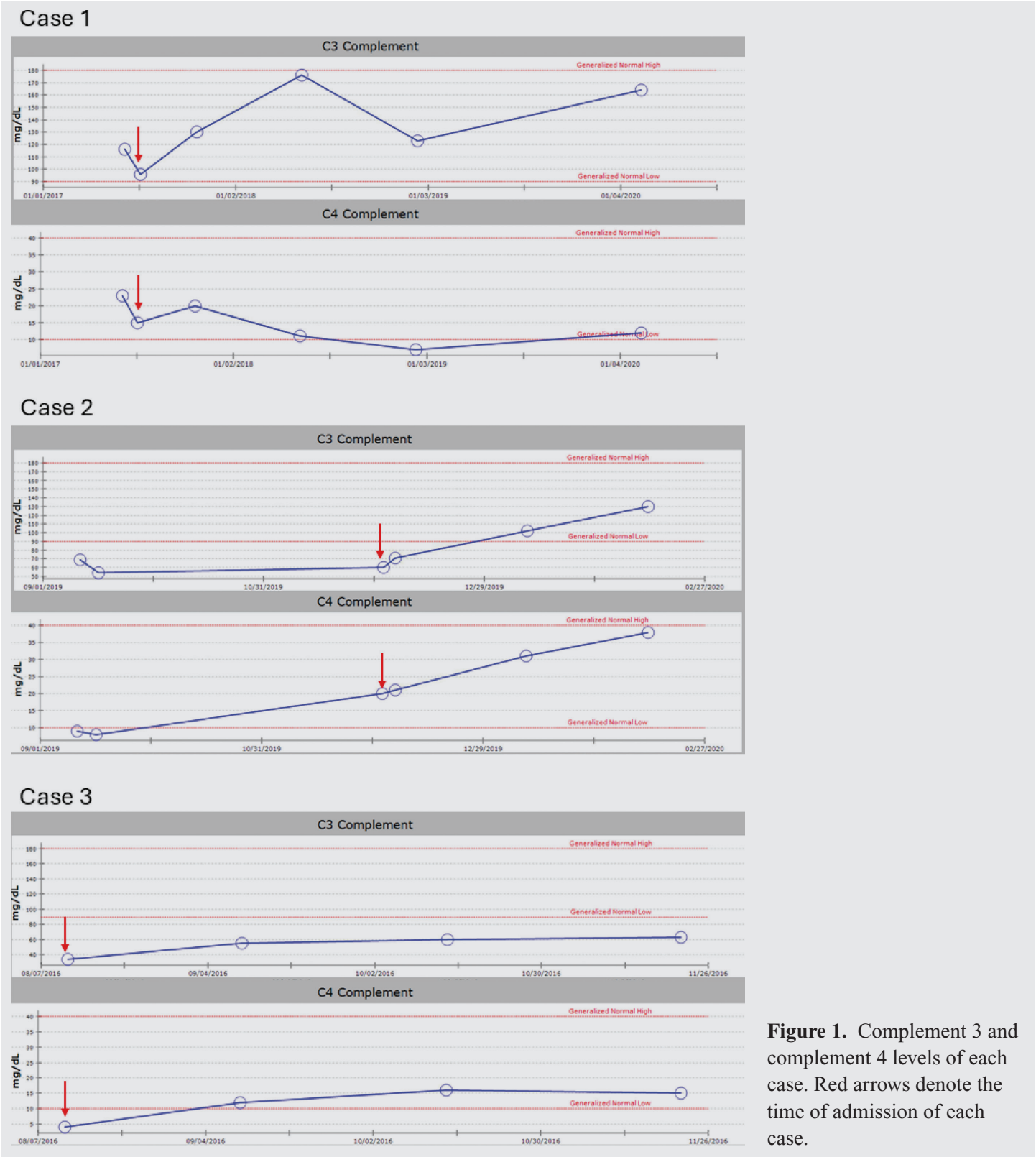

Figure 1. Complement 3 and complement 4 levels of each case. Red arrows denote the time of admission of each case.

immunosuppressive treatment remained unchanged. Subsequently, she died as an outpatient.

Discussion

We present three young female lupus patients with diffuse wall motion abnormalities. In two patients, wall motion abnormalities reversed over time. While it is possible Case 1 represented Takotsubo cardiomyopathy as she was in considerable pain due to avascular necrosis, we presume that at least Cases 2 and 3 had global hypokinesis due to myocarditis. No biopsy was obtained for a definite diagnosis in any case. The condition was likely mediated by immune-mediated inflammation, as evidenced by elevated cardiac biomarkers, specific serologies, and echocardiographic/imaging findings, leading to HF.

Risk factors for HF in SLE include myocardial dysfunction, conduction system disease, carditis, anemia, chronic kidney disease, and pulmonary hypertension (as in Case 3).[6] However, myocardial dysfunction in SLE can be a consequence of other conditions, especially coronary artery disease, valvular disease, and toxicity from medications such as chloroquine,[6,7] as was considered in Case 1. The characteristics of hydroxychloroquine cardiotoxicity on TTE, including diffuse ventricular wall thickening, bi-atrial enlargement, and restrictive physiology, were not observed in Case 1.[7] However, ischemic cardiomyopathy should be excluded as a cause of cardiomyopathy leading to HF, when feasible, as in Cases 2 and 3.

Lupus myocarditis (LM), suspected in all cases, is the most characteristic myocardial involvement in SLE.[8] It is uncommon and reported in 7–10% of cases, with a mortality of approximately 10%.[8,9] The gold standard for diagnosis is endomyocardial biopsy (EMB), which is not routinely performed due to low sensitivity and risk of complications.[10]

Diagnostic criteria for LM remain a matter of debate. A study by Thomas et al. described the features of LM. The most common presentation is reduced LVEF (≤45%), followed by pericardial effusion. An antinuclear antibody test (ANA) was positive in all studied cases and dsDNA in almost all cases. The most common ECG finding is tachycardia.[9] Some reports have noted an association between myocarditis and anti-Ro/SSA and anti-La/SSB antibodies.[11]

All our cases had positive ANA. Significantly reduced EF, positive dsDNA, SSA-Ab, low complement levels, and pericardial effusion were found in Cases 2 and 3. Sinus tachycardia was documented in Cases 1 and 2. The likelihood of lupus myocarditis was high, even without cardiac MRI or myocardial biopsy. Thomas et al. even recommended against EMB in established SLE patients.[9]

Diagnosis is therefore based on clinical findings, cardiac markers, imaging, and classically echocardiography. An alternative to EMB is cardiac magnetic resonance imaging (cMRI), which has proven effective in localizing inflammation and distinguishing inflammatory from ischemic lesions.[12,13] However, cMRI is not widely available; none of our patients underwent cMRI, as it was unavailable at our institution during the time of presentation, and two improved with appropriate treatment.

Very few studies have described prognosis and outcomes regarding cardiac recovery. Cases 1 and 2 had improved EF, but no follow-up TTE was available for Case 3, who had frequent readmissions due to HF exacerbation. High-dose corticosteroids remain the mainstay of treatment for LM, and cyclophosphamide can be reserved for severe cases or markedly reduced EF, as seen in Case 2.

Our patients were diagnosed with systolic heart failure, that did not appear to correlate with SLEDAI score or disease duration, consistent with findings by Merfeizi et al.[14] Management required optimization of heart failure therapy with beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers,[15] along with control of SLE disease activity, underscoring the importance of multidisciplinary collaboration.

Conclusion

SLE-related HF secondary to myocarditis is a rare but severe complication that requires early recognition and prompt initiation of targeted therapy. Cardiac MRI is a reliable modality to detect underlying cardiac

pathophysiology in SLE, when available. Management should be directed toward the specific HF phenotype while simultaneously suppressing autoimmune disease activity.

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