CASE REPORT

Case of severe acute lupus myocarditis and multiple-organ failure

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SUMMARY

We report a case of severe lupus myocarditis with rapid, acute deterioration to cardiogenic shock and multiorgan failure, highlighting the importance of early identification and treatment of acute presentations in patients with systemic lupus erythematosus. A 31-year-old woman with previously diagnosed subacute cutaneous lupus erythematosus initially presented with abdominal pain and frank per-rectal bleeding. She deteriorated rapidly with type 1 respiratory failure and acute kidney injury requiring dialysis secondary to acute cardiac failure with a prolonged intensive care unit admission, over a month. A significantly elevated troponin, global hypokinesia on echocardiogram and normal coronary artery angiogram and cardiac MRI lead to the diagnosis of acute lupus myocarditis as the cause for the cardiogenic shock. She was treated with high-dose corticosteroids and eventually made a full recovery, with cardiac function returning to normal.

BACKGROUND

Systemic lupus erythematosus (SLE) is a chronic immune-mediated inflammatory disease with the involvement of multiple organ systems. Clinical presentations vary greatly between individuals, the most common being a combination of cutaneous, musculoskeletal and haematological involvement. Severity can vary from largely asymptomatic to fatal organ failure.¹

Cardiovascular involvement in SLE can affect the endocardium, myocardium and pericardium as well as coronary vessels. While pericarditis is the most common form of cardiac involvement, myocarditis is also a common manifestation of SLE.² Myocarditis in SLE is rarely clinically detected, and while previous autopsy studies found high rates of myocarditis in patients with SLE, more recent findings suggest a reduction since the introduction of steroid treatment.²

We report a case of severe lupus myocarditis with rapid, acute deterioration to cardiogenic shock and multiorgan failure. Presentations of acute lupus myocarditis with organ failure are exceedingly rare in the current literature. This case highlights the importance of early identification and treatment of acute presentations in patients with SLE, as well as the importance of surveillance and detection of subclinical myocarditis in patients before they develop complications.

CASE PRESENTATION

A 31-year-old woman initially presented with 3–4 weeks of frank per-rectal bleeding and mild crampy abdominal pain. Prior to presentation, she had a diagnosis of subacute cutaneous lupus erythematosus managed with hydroxychloroquine 400 mg nocte. However, she fulfilled both the American College of Rheumatology (ACR) and the Systemic Lupus International Collaborating Clinics (SLICC) diagnostic criteria for SLE with discoid rash, photosensitivity, positive antinuclear antibody (ANA) and positive antismooth muscle (anti-Sm) antibody. She was also positive for the antiribonucleoprotein antibody, direct Coomb's test was positive without evidence of haemolysis and had hypocomplementaemia. Prior to this presentation, she had no features of major organ involvement. Other background history was significant for biopsy-proven alcoholic cirrhosis, previous seizures attributable to alcohol withdrawal, chronic pancreatitis with exocrine and endocrine insufficiency requiring insulin therapy and significant smoking.

At presentation, the patient had a haemoglobin (Hb) of 59 g/dL but was haemodynamically stable. External haemorrhoids were present on examination (which were not actively bleeding). CT of the abdomen revealed colitis of the ascending and proximal transverse colon. The patient had no clinical features of pneumonia or heart failure. While in hospital the patient deteriorated rapidly, developing significant dyspnoea and desaturation to an O₂ saturation of 70% on pulse oximetry and with chest X-ray showing left lower lobe opacity at this time. ECG showed ST segment depression in the anterior and inferior leads with T-wave inversion in leads V1–V2 (figure 1). Both troponin I and creatine kinase were significantly elevated (table 1). CT pulmonary angiography showed no evidence of pulmonary emboli but demonstrated consolidation and ground glass changes in the lower lobes bilaterally (figure 2). Echocardiogram showed an estimated left ventricular ejection fraction of 30%, hypokinesia of the anterior and inferior walls and the anterior and inferior septum and moderate tricuspid regurgitation.

The patient required mechanical ventilation and inotropes to maintain her blood pressure. Sputum samples, nasopharyngeal viral PCR testing and bronchial lavage sampling were initially negative for bacteria and viruses. She developed large bilateral pleural effusions, consistent with an exudate. Pleural fluid cytology, microscopy and culture were unremarkable.

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Figure 1 ECG showing evidence of ST segment depression in the anterior and inferior leads with T-wave inversion in leads V1–V2.

Given the echocardiographic findings of left ventricular systolic dysfunction with regional wall motion abnormalities across multiple vascular territories, a diagnosis of acute myocarditis was favoured at this point rather than acute coronary syndrome. She was commenced on intravenous methylprednisolone 1g for 3 days followed by a weaning regimen of oral prednisone from 50mg daily. Although she was initially commenced on piperacillin–tazobactam for presumed community-acquired pneumonia as a source of sepsis, this was ceased after no improvement and lack of evidence of infection. The overall impression was heart failure in the context of acute myocarditis with pulmonary oedema and bilateral pleural effusions and possible lupus-associated pneumonitis.

The patient developed a severe oliguric dialysis-dependent acute kidney injury (AKI) over the first week of admission. Renal ultrasound found no evidence of obstruction. A renal biopsy was performed to rule out lupus nephritis and other causes of severe AKI but demonstrated features consistent with acute tubular necrosis (ATN).

OUTCOME AND FOLLOW-UP

The patient had a prolonged intensive care unit (ICU) and hospital stay. A repeat echocardiogram on day 7 of ICU admission demonstrated recovery of left ventricular function with an ejection fraction of 60% and no regional wall motion abnormalities.

While in ICU, the patient developed atrial fibrillation with rapid ventricular rate likely triggered by a dobutamine infusion. This resolved with cessation of dobutamine.

Following a period of significant improvement, the patient deteriorated again on day 10 due to a hospital-acquired *Pseudomonas aeruginosa* pneumonia which was treated with intravenous piperacillin–tazobactam and meropenem.

Other issues during hospitalisation included three separate episodes of viral gastroenteritis, with norovirus, rotavirus and adenovirus, and dyselektrolytaemia in the form of hypokalaemia and hyperkalaemia, and depression. Gastroscopy and colonoscopy showed only mild congestive gastropathy, non-bleeding internal haemorrhoids and no visible evidence of colitis.

Commencement of mirtazapine and sertraline for depression was complicated by hyponatraemia which resolved on cessation of the medications. The patient had normal left ventricular function on echocardiography prior to discharge.

A dobutamine stress echocardiogram performed 7 months after discharge found inducible global hypokinesia with some regional variation at peak dobutamine dose, consistent with either proximal multivessel coronary artery disease or cardiomyopathic response. The patient developed a junctional tachycardia at peak dobutamine dose and the test was terminated early. An echocardiogram the following day revealed left ventricular ejection fraction of 40%, severely hypokinetic basal anterior

Table 1 Pathology results

Lupus anticoagulant	Anti-dsDNA (IU/mL)	ANA	Anti-Sm	Anti-RNP	C-ANCA	P-ANCA	C3 (g/L)	C4 (g/L)	Creatinine (max) (μmol/L)	Hb (min) (g/L)	Troponin I (max) (μg/L)	CK (max) (U/L)
-ve	3 (<7)	+ve	+ve	+ve	-ve	-ve	0.33	0.07	454	59	30	13000

Anti-dsDNA, double-stranded DNA antibodies; anti-RNP, antiribonucleoprotein antibodies; anti-Sm, antismooth muscle antibodies; C-ANCA, cytoplasmic antineutrophil cytoplasmic antibodies; CK, creatine kinase; C3 and C4, complement factors 3 and 4; Hb, serum haemoglobin; P-ANCA, perinuclear antineutrophil cytoplasmic antibodies.

Figure 2 CT chest of the patient on admission to the intensive care unit.

wall and mildly akinetic mid-anterior and antero-septal walls. A coronary angiogram performed subsequently showed angiographically normal coronary arteries (figure 3). Therefore, the changes that occurred during the dobutamine stress echocardiogram were thought to be a form of Tako-Tsubo or stress-induced cardiomyopathy which has been documented in the literature. Repeat echocardiogram 5 months later showed a return to normal ejection fraction of 60% and no regional wall motion abnormalities. Holter monitor 3 months later was normal, with no significant arrhythmias recorded. A cardiac MRI performed 15 months after the initial presentation showed a mildly dilated

Figure 3 Coronary artery angiogram demonstrating no significant coronary arterial stenosis.

Figure 4 Cardiac MRI showing a small septal segment of post-gadolinium delayed enhancement consistent with lupus myocarditis.

left ventricle with preserved left ventricular function, no focal regional wall motion abnormalities, no convincing evidence of myocardial oedema on T2-weighted imaging, normal right ventricle, normal systolic function and moderate dilation of both right and left atria. There was a thin stripe of enhancement in the septum on post-gadolinium delayed enhancement imaging (figure 4). Even though this is a non-specific finding, sometimes seen in dilated cardiomyopathy, in her situation, this may represent some scarring from the myocardial inflammation during myocarditis and subsequent healing. A repeat chest X-ray performed a couple of months later demonstrated complete resolution of the pleural effusions.

On discharge, the patient was prescribed a tapering dose of prednisolone, initially commenced at 30 mg daily and reduced slowly over 6 months. She continued her original maintenance therapy with hydroxychloroquine 400 mg.

DISCUSSION

We have presented a case of acute severe lupus myocarditis with a precipitous decline secondary to cardiogenic shock and multi-organ failure including type 1 respiratory failure requiring ventilation and severe dialysis-dependent AKI due to ATN.

Prior to this presentation, the patient had been managed as subacute cutaneous lupus erythematosus. On presentation, she already met the ACR diagnostic criteria for SLE, meeting at least four of the criteria required for diagnosis prior to developing the acute symptoms presented in this case.³ A thick erythematous raised plaque-like rash consistent with discoid rash was present over her face and forehead, she had had long-term photosensitivity managed by her rheumatologist, she had a positive ANA and she had positive anti-Sm muscle antibodies. Additionally, she met the SLICC diagnostic criteria for SLE.⁴ These criteria were photosensitive rash, chronic discoid rash, positive ANA, positive anti-Sm and a positive direct Coomb's test in the absence of haemolytic anaemia and hypocomplementaemia with low C3 and C4. On this basis, a diagnosis of SLE rather than SCLE was made, supporting the conclusion that her acute decline

was precipitated by an acute lupus myocarditis. A 2005 review found that up to 10%–15% of patients with SLE alone go on to develop severe SLE, which is consistent with this patient's clinical course.⁵

Myocarditis in SLE is often asymptomatic, though clinically evident signs and symptoms can be present in 10% of cases.⁶ It is especially rare to present with acute cardiogenic shock and multiorgan failure, as this case reports. Two similar cases, one with acute cardiogenic shock, although without the associated multiorgan failure and another with acute myocarditis and associated respiratory failure were reported in 2015.^{7,8} A Chinese case-control study of 24 patients with lupus myocarditis over a 10-year period reported one case of severe cardiogenic shock resulting in death and six cases requiring mechanical respiratory ventilation as a result of cardiac failure.⁹ Other cases with less severe acute presentations have been reported previously.^{10,11} Milder myocarditis has been identified clinically in around 10% of patients with SLE, with a far higher proportion (up to 37%) showing evidence histologically in large autopsy studies.¹²

Making the diagnosis of lupus myocarditis is not always simple, given that SLE can involve all three layers of the heart as well as the coronary arteries.

In this case, the diagnosis of myocarditis was made based on a combination of clinical and echocardiographic findings. The global hypokinesia found on echocardiogram was not consistent with any specific coronary artery territory. The subsequent coronary angiogram confirmed lack of involvement of the coronary arteries. The relatively rapid improvement in the regional wall motion abnormalities and ejection fraction following intravenous administration of methylprednisolone lends further support to a diagnosis of myocarditis. Cardiac MRI finding of septal enhancement on post-gadolinium delayed enhancement imaging was non-specific but supported this diagnosis. As the MRI was performed several months after the acute event, many of the acute changes of myocarditis are likely to have resolved. While a myocardial biopsy could have provided further information, it is often not confirmatory. In the case of our patient, it was felt that the risks of the procedure outweighed the benefits.

Once the diagnosis of lupus myocarditis was established, methylprednisolone was commenced and subsequently changed to oral prednisolone for 6 months. She was continued on hydroxychloroquine long term. The patient responded quickly and effectively to this treatment, eventually making a near full recovery. Corticosteroids are the mainstay of treatment for lupus-induced myocarditis. While other immunosuppressants, including azathioprine or cyclophosphamide, can be considered, this patient responded well to corticosteroid treatment and no further escalation of therapy was required. This highlights the importance of early recognition and commencement of treatment once a diagnosis of acute SLE exacerbation or lupus myocarditis is established.

The patient developed transient atrial fibrillation during the admission, which seemed to be secondary to dobutamine administration. Atrial fibrillation is common in SLE and is usually associated with other cardiac involvement.¹³ Whether conduction abnormalities in SLE are caused by an immune-mediated disease process or are a consequence of the myocardial involvement of the disease is unclear.²

The patient rapidly developed type 1 respiratory failure with consolidation, bilateral ground glass changes and pleural effusions on CT and required mechanical ventilation. While an infective aetiology was considered, sputum, nasopharyngeal swab and bronchial washings were all negative for infectious

microbial causes. While the respiratory failure may have been secondary to the cardiogenic shock, pneumonitis and pleuritis are both known complications of SLE and can occur in conjunction with other organ system involvement in an acute flare.¹⁴ Given the exudative pleural effusion, ground glass changes on CT and lack of any microbial growth as a cause, there was a high suspicion for pneumonitis and pleuritis playing a role in addition to myocarditis. Conversely, the rapid deterioration and clinical features of fluid overload were more consistent with cardiogenic shock. The second deterioration in respiratory status with type 1 respiratory failure was clearly associated with a hospital acquired pneumonia due to *P. aeruginosa*.

This case was also complicated by severe dialysis-dependent AKI. Given the rapidity and severity of renal impairment and the fact that the kidneys are commonly involved in SLE, a renal biopsy was performed. The demonstration of ATN on the renal biopsy is again consistent with renal hypoperfusion secondary to cardiogenic shock. This further highlights the severity of this presentation and the importance of prompt management of lupus myocarditis with intravenous corticosteroids.

The initial presentation of colitis remains of unclear aetiology. During her admission, she returned positive stool PCR results for norovirus, rotavirus and adenovirus. These could explain her initial presentation with colitis. SLE has been associated with colitis caused by intestinal vasculitis.¹⁵ While this is a possible cause for the colitis presented in this case report, there was no conclusive evidence to confirm this diagnosis. The patient's colitis had resolved during the admission and has had no further episodes since. Her colonoscopy performed during the admission was normal.

While there are no clinical trials on the effectiveness of corticosteroids in the treatment of acute lupus myocarditis, several case reports have reported good clinical effect.^{16,17}

Learning points

- ▶ Systemic lupus erythematosus (SLE) can involve all three layers of the heart. Myocarditis, although often asymptomatic, can be a cause of heart failure in SLE.
- ▶ Corticosteroids are the mainstay of treatment for lupus-induced myocarditis. Initial high-dose methylprednisolone followed by an extended tapering course of prednisolone had good effect in this case. Other immunosuppressants, including azathioprine or cyclophosphamide, can be considered in patients not responding to corticosteroids.
- ▶ Early recognition of acute lupus myocarditis and commencement of early corticosteroids is important given the possibility of rapid deterioration to multiorgan failure. This patient had a fast and positive response to corticosteroids making a near-full recovery.
- ▶ Determining the cause of acute heart failure in SLE can be a diagnostic challenge as multiple pathologies can co-exist.
- ▶ Limited cutaneous forms of lupus can progress to significant systemic involvement and clinicians should remain alert to this possibility.

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finished manuscript. All the above authors are in agreement to be accountable for the article and to ensure that all questions regarding the accuracy or integrity of the article are investigated and resolved.

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