Postpartum dilated cardiomyopathy in a patient with systemic lupus erythematosus, nephritis and lupus anticoagulant: a diagnostic dilemma

Daniel Hall BSc (Hons)*, **David New** MBChB FRCP PhD[†] and **Teresa Kelly** MBChB MRCOG[†]

*University of Manchester Medical School, Manchester, UK; [†]Salford Royal Foundation Trust, Greater Manchester, UK

Summary: A 32-year-old Caucasian woman presented with shortness of breath four weeks postpartum. She was known to suffer from systemic lupus erythematosus with cutaneous, joint and minor renal involvement. During pregnancy, the patient had developed nephrotic syndrome for which she was managed with prophylactic anticoagulation and corticosteroid therapy. A leg deep vein thrombosis had arisen following caesarean section following antepartum haemorrhage. Examination revealed a heart murmur, and pulmonary signs. Computed tomography pulmonary angiogram showed cardiomegaly and bilateral pleural effusions but no pulmonary embolus. Echocardiogram demonstrated dilated cardiomyopathy. An initial diagnosis of peripartum cardiomyopathy was considered, with lupus myocarditis and coronary *in situ* thrombosis among the differential diagnoses.

Keywords: perinatal medicine, cardiomyopathy, lupus nephritis

BACKGROUND

Systemic lupus erythematosus (SLE) can cause clinical myocarditis in <10% of patients, which can infrequently progress to dilated cardiomyopathy.¹ Peripartum cardiomyopathy is an idiopathic pathology that can occur around parturition.² Both conditions can cause acute onset heart failure. SLE patients can present with acute heart failure due to myocarditis during or after pregnancy and this can be confused with peripartum cardiomyopathy. Diagnosis of myocarditis in this clinical scenario is difficult but should be sought in order to provide appropriate therapy.

CASE PRESENTATION

A 32-year-old woman presented at 30 weeks gestation with oedema due to nephrotic syndrome (Table 1). There was a history of SLE with skin, joint and renal involvement. A kidney biopsy performed nine years earlier, to investigate microscopic haematuria with mild proteinuria (0.3 g/day), showed immune complex deposition and mild mesangial expansion consistent with lupus nephritis class 2 which had not required specific treatment. Since that time she had had three successful pregnancies and one termination, without significant complication other than a deep vein thrombosis. There had been no renal flares during these previous pregnancies, and in the early second trimester of the current pregnancy urinalysis had been negative for blood and protein on two occasions. The only treatment up to this point in her current pregnancy had been prophylaxis against recurrent venous thrombosis using low-molecular-weight

heparin (tinzaparin 4500 units subcutaneous injection once daily, according to local and national guidelines). Examination showed longstanding cutaneous scarring and mild ankle oedema only. There were no heart murmurs. Blood pressure was not elevated nor had it been at any point throughout pregnancy. She was antinuclear factor positive >1/1000 (homogeneous pattern) with strongly positive anti-DSDNA antibodies. Ro/SSA antibody was positive but La/SSB antibody was negative as were antibodies to other extractable nuclear antigens. Cryoglobulins were absent from the blood. The anticardiolipin antibody was negative but the activated partial thromboplastin time (APTT) time was raised and further testing confirmed strongly positive lupus anticoagulant. Complement C3 levels were low at 0.71 g/L (normal 0.83–1.46 g/L) but C4 was normal. Rheumatoid factor was weakly positive. Mild thrombocytopenia was present. The patient was treated with aspirin and continued prophylactic heparin injections. Because of the advanced stage of pregnancy and the need for prophylactic anticoagulation, a kidney biopsy was deferred. Treatment of suspected active lupus nephritis with high-dose oral prednisolone (40 mg daily) was commenced.

Polyhydramnios was observed from the 28th week fetal growth scan onwards, while at 32 weeks gestation an antepartum haemorrhage prompted emergency caesarean section with delivery of a premature but otherwise healthy child with no cardiac sequelae of maternal Ro/SSA antibody. A maternal right leg deep vein thrombosis occurred in the early postoperative period and was treated by therapeutic anticoagulation with heparin (tinzaparin 10,000 units [175 units/kg] by subcutaneous injection once daily according to local and national guidelines).

Four weeks postpartum she developed dyspnoea. The examination found the patient to be apyrexial with heart rate 140 per

Correspondence to: Daniel Hall
Email: daniel_hall09@hotmail.co.uk

Table 1 Laboratory results

	Presentation 30 weeks gestation	2 weeks postpartum	5 weeks postpartum	12 weeks postpartum (during cyclophosphamide therapy)	20 weeks postpartum (cyclophosphamide therapy completed)
Anti-dsDNA (units/mL)	26	12	19	6	7
Albumin (g/L)	28	22	31	38	40
eGFR (mL/minute/1.73 m ²)	87	79	59	>90	>90
Platelets ($\times 10^9 \text{L}^{-1}$)	100	78	220	156	219
Urine protein/creatinine ratio (gmol ⁻¹)	985	453	413	170	221

minute, blood pressure 130/80 mmHg, raised jugular venous pressure and minimal peripheral oedema. Cardiac auscultation now demonstrated a pansystolic murmur, suggestive of mitral regurgitation. Chest percussion was dull at the bases and there were basal crepitations. ECG showed sinus tachycardia, reduced R waves in leads V₁–V₃ along with ST interval and T-wave changes in the inferolateral leads. Arterial blood gases revealed no abnormality. Troponin I level was not elevated. A computed tomography (CT) pulmonary angiogram was performed the same day, which found no evidence of pulmonary embolus although there were bilateral small pleural effusions and cardiomegaly. Oxygen therapy was initiated and glyceryl trinitrate (GTN) was infused by vein. Echocardiogram demonstrated a dilated left ventricle with severely impaired systolic function; left ventricle internal dimension during diastole (LVIDD) was 7.6 cm and during systole (LVIDS) was 6.5 cm. There was severe mitral regurgitation and moderate aortic regurgitation. The mitral valve was thin and mobile and the left atrium dilated at 3.9 cm. The right ventricle showed impaired function. There were no previous echocardiogram assessments with which to make comparison as the patient had suffered no symptoms or signs of cardiac disease prior to this presentation.

A provisional diagnosis of postpartum cardiomyopathy was made, although the patient had no known risk factors other than a recent pregnancy. Additional treatments with loop diuretic infusions and oral ACE inhibitor were started. Rheumatology and renal opinions were sought, after which the possibility of active lupus myocarditis was also considered.

A percutaneous renal biopsy was undertaken which confirmed the presence of mesangial proliferative (class II) lupus nephritis (Figure 1). There was no evidence of membranous lupus nephropathy, and no features to suggest lupus-related renal thrombotic microangiopathy. Because of the presence of nephrotic syndrome, and considering possible extra-renal lupus manifestations including myocarditis, immune thrombocytopenia and lupus anticoagulant, therapy with intravenous methylprednisolone followed by oral prednisolone and pulsed intravenous cyclophosphamide was commenced. Cyclophosphamide was dosed at 10 mg/kg on five occasions over three months. At six weeks postpartum, a CT scan of the thorax was performed to assess for pulmonary involvement of SLE, following a minor episode of haemoptysis. There were no signs of pulmonary involvement, although the cardiac diameter had reduced from 15.8 to 12 cm and the pleural effusions had resolved. Anticoagulant treatment continued as did oral diuretics and ACE inhibitor. The patient reported improved exercise tolerance and resolution of breathlessness.

An echocardiogram performed 20 weeks postpartum showed only moderate mitral regurgitation and mildly impaired left ventricular systolic function. LVIDD was 6 cm and LVIDS

Figure 1 Renal biopsy sample taken while nephrotic and during investigation of acute postpartum myocardial dysfunction, demonstrating WHO class II lupus nephritis (mesangial proliferative glomerulonephritis)

was 3.3 cm. The left atrium, at 3.1 cm, was no longer dilated and the mitral valve was again seen to be thin and mobile. The right heart function was now normal.

DISCUSSION

SLE typically affects the joints and skin; however, complications such as glomerulonephritis and myocarditis can occur.^{1,3} When nephrotic syndrome occurs as a complication of lupus nephritis the underlying renal lesion can either be a proliferative nephritis (class 2, 3 or 4), as in this case, or more usually a membranous nephritis (class 5). Nephrotic syndrome is rare in class 2 lupus nephritis and in the judgement of the authors this mandated more aggressive treatment, with high-dose corticosteroids and intravenous cyclophosphamide, than would ordinarily be indicated for this lesion.

Myocardial dysfunction in SLE is often related to coronary disease,⁴ although this was ruled out by the clinical assessment and by the normal troponin level. Peripartum cardiomyopathy is an idiopathic disease presenting as heart failure in late pregnancy or the early postnatal period.² It is a diagnosis of exclusion with criteria demanding a lack of a demonstrable cause of heart failure and the absence of known heart disease before the last month of pregnancy. Known risk factors include age over 30 years, black racial origin, obesity, preeclampsia, hypertension and twin/multiple pregnancy.

Peripartum cardiomyopathy was the initial diagnosis. However, lupus myocarditis was an alternative possibility. Many cases of reported peripartum cardiomyopathy may actually be due to myocarditis, with a possible autoimmune

aetiology.⁵ There are previous reports of patients with SLE presenting with acute heart failure postpartum in whom an incorrect diagnosis of peripartum cardiomyopathy lead to a detrimental outcome.^{6–9} Although the incidence of peripartum cardiomyopathy in lupus patients specifically is unknown, the incidence in general maternal population is between 1 in 1300 and 1 in 15,000 live births.⁵ The incidence of lupus myocarditis in SLE patients is one in 10,¹ and on that basis the more likely diagnosis would be lupus myocarditis.

This is a diagnostic dilemma for the clinician. Investigations to achieve the diagnosis of lupus myocarditis can be challenging. Echocardiography, ECG and chest radiography are largely unhelpful in diagnosing lupus myocarditis,⁴ although ST/T wave abnormalities are the most likely ECG changes to occur, as was observed in this case.^{8,9}

In this particular case, evidence for active SLE was obtained through a kidney biopsy, prompting immunosuppressive treatment and thereby removing any absolute requirement to obtain a definitive diagnosis⁴ of lupus myocarditis. The favourable clinical course that followed immunosuppressive therapy does not guarantee any particular diagnosis; peripartum cardiomyopathy may have been present yet improved spontaneously in spite of immunosuppressive therapy, or, as is sometimes reported, immunosuppression with corticosteroid therapy may have had beneficial effect on peripartum cardiomyopathy.

The role for endomyocardial biopsy in peripartum cardiomyopathy remains unclear. A proportion of patients have histological evidence of myocarditis, while other features include myocardial fibre hypertrophy/degeneration, fibrosis or interstitial oedema. Hence there are no pathognomic findings and yet there is risk in performing endomyocardial biopsy, particularly in a dilated failing ventricle.

The negative troponin value observed in our patient argued against myocardial infarction, which occurs with greatly increased prevalence in SLE patients. However, the absence of a rise in cardiac troponin I would not necessarily discount myocarditis due to either SLE or peripartum cardiomyopathy; in a study of patients from the Myocarditis Treatment Trial, only 18 (34%) of 53 patients with proven myocarditis demonstrated raised values of troponin I.¹⁰

Cardiac magnetic resonance imaging would be useful in the evaluation of myocardial damage in this case. In addition to being able to distinguish ischaemic cardiomyopathy, as might have arisen from coronary *in situ* thrombosis secondary to lupus anticoagulant for example, from non-ischaemic cardiomyopathy, it may also differentiate tissue changes in various non-ischaemic cardiomyopathies.¹¹

The possibility of pre-existing undetected mitral valve regurgitation, exacerbated by fluid overload occurring as a result of pregnancy and the nephrotic syndrome, should also be considered in the differential diagnosis as there were no pre-existing echocardiogram assessments to exclude this possibility. Nevertheless, there was no heart murmur prior to this presentation, and echocardiography found no structural abnormality

of the valve to suggest anything other than functional regurgitation.

Exacerbation of SLE, particularly renal flares, is not uncommon as a result of pregnancy.¹² Successful treatment of lupus myocarditis has been documented with corticosteroids, often coupled with cyclophosphamide therapy.^{4,6–9} Prognosis is often good, with recovery of normal ventricular function.^{4,6–9}

This case report illustrates the difficulty in differentiating between peripartum cardiomyopathy and lupus myocarditis. It highlights the need for appropriate investigation and careful clinical judgement to appropriately treat women with acute peripartum heart failure. The incidence of lupus myocarditis in known SLE patients is relatively high compared with the incidence of peripartum cardiomyopathy in the general population, and this has to be an important consideration in making a diagnosis in a complex patient such as this.

DECLARATIONS

Competing interests: None.

Funding: None.

Ethical approval: None. The patient gave her consent for this report.

Guarantor: DH.

Contributorship: DH and DN researched literature and wrote the manuscript. TK reviewed it.

Acknowledgements: None.

REFERENCES

- 1 Doria A, Laccarino L, Sarzi-Puttini P, Atzeni F, Turriel M, Petri M. Cardiac involvement in systemic lupus erythematosus. *Lupus* 2005;**14**:683–6
- 2 Abboud J, Murad Y, Chen-Scarabelli C, Saravolatz L, Scarabelli MT. Peripartum cardiomyopathy: a comprehensive review. *Int J Cardiol* 2007;**118**:295–303
- 3 Agrawal N, Chiang L, Rifkin I. Lupus nephritis. *Semin Nephrol* 2006;**26**:95–104
- 4 Chung WJ, Joe YD, Park HJ, Kim AH, Park SH, Sue HC. Clinical characteristics of lupus myocarditis in Korea. *Rheumatol Int* 2008;**28**:275–80
- 5 Felker GM, Jaeger JC, Klodas E, et al. Myocarditis and long term survival in peripartum cardiomyopathy. *Am Heart J* 2000;**140**:785–791
- 6 Woo SI, Hwang GS, Kang SJ, et al. Lupus myocarditis presenting as acute congestive heart failure: a case report. *J Korean Med Sci* 2009;**24**:176–8
- 7 Raskin RJ, Haddock JB, Lawless JO. Systemic lupus erythematosus with myocarditis complicating pregnancy. *South Med J* 1983;**76**:259–60
- 8 Cheng SM, Chang DM, Lee WH, Ding YA. Acute myocarditis as an initial manifestation of systemic lupus erythematosus: a case report. *Chin Med J* 1996;**58**:205–8
- 9 Sandrasegaran K, Clarke CW, Nagendran V. Sub-clinical systemic lupus erythematosus presenting with acute myocarditis. *Postgrad Med J* 1992;**68**:475–8
- 10 Smith SC, Ladenson JH, Mason JW, Jaffe AS. Elevations of cardiac troponin I associated with myocarditis. *Circulation* 1997;**95**:163–8
- 11 Wassmuth R. Cardiac magnetic resonance imaging for myocarditis and nonischemic cardiomyopathies. *Minerva Cardioangiol* 2009;**57**:511–20
- 12 Carvalheiras G, Vita P, Marta S, et al. Pregnancy and systemic lupus erythematosus: review of clinical features and outcome of 51 pregnancies at a single institution. *Clin Rev Allergy Immunol* 2010;**38**:302–6

(Accepted 21 March 2011)