

# Systemic lupus erythematosus with coronary vasculitis and massive myocardial infarction

## A case report

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### Summary

A 32-year-old white woman presented with angina pectoris and an acute myocardial infarction (MI) complicated by congestive cardiac failure. Other symptoms and results of immunological investigation were highly suggestive of systemic lupus erythematosus (SLE). Thallium-201 scintigraphy confirmed an extensive MI, as initially suspected from an ECG. Cardiac catheterization delineated a poorly contracting left ventricle secondary to MI. Selective coronary angiography showed features suspicious of coronary arteritis involving the left anterior descending and left circumflex coronary arteries. Right ventricular endomyocardial biopsy failed to show any 'small-vessel disease', vasculitis or myocarditis.

We suggest that the acute MI was caused by coronary arteritis due to SLE. Overview of the literature indicates that coronary arteritis is not as rare a complication of SLE as previously believed; however, acute MI is most unusual.

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### Case report

An unemployed 32-year-old white woman, divorced and with 2 children, smoked 20 cigarettes daily and had frequent attacks of anxiety and depression. At the age of 12 years she had had transient arthritis after varicella. She was later told that she had a 'leaking heart' but refused to take medication. At 15 years of age she was told her heart was normal. Her two pregnancies were apparently uncomplicated. A few years ago she was diagnosed as having psoriasis and gout.

Towards the end of 1983 she began experiencing a burning left-sided chest pain unrelated to effort, sometimes nocturnal and occasionally associated with asthma-like attacks. She was

given anti-inflammatory drugs for musculoskeletal chest pain with no real improvement. In February 1984 she was treated for chronic salpingo-oophoritis at Tygerberg Hospital, and referred to the general outpatients' department with numerous complaints, including symmetrical arthralgia and swelling of the right ankle. The leucocyte count was  $17 \times 10^9/l$  (71% neutrophils), the erythrocyte sedimentation rate (ESR) 55 mm/h (Westergren) and the haemoglobin level and platelet count normal. Immunological tests revealed the following: antinuclear antibody (ANF) — positive in a titre of 1:80, anti-double-stranded DNA — positive, extractable nuclear antigens (ENA) — negative, and auto-antibodies against mitochondria, smooth muscle and parietal cells — negative. Abnormal biochemical findings included slightly raised urea and creatinine levels, a moderate rise in the aspartate transaminase level, and a markedly elevated lactate dehydrogenase level. A resting ECG on 27 February 1984 revealed the following: sinus rhythm 98, P-R interval 0.14 second, mean QRS axis  $-10^\circ$ , incomplete right bundle-branch block, poor R-wave progression over the anteroseptal leads, pathological Q waves and raised ST segments in leads I and aVL. A chest radiograph was normal. The patient was treated with an anti-inflammatory agent and an antidepressant, and seen again on 13 March 1984 and 24 April 1984, at which stage her symptoms were slightly improved.

In August 1984 she began experiencing nonspecific right-sided chest pain which radiated down the right arm. She also complained of occasional haemoptysis. The patient visited a day hospital on 1 October 1984 with swelling and pain of the right knee and ankle, nonspecific chest pain, cough and haemoptysis, and was referred to Tygerberg Hospital on 2 October 1984; clinical examination revealed a murmur characteristic of mitral incompetence, no mitral stenosis and no evidence of cardiac failure. A resting ECG now demonstrated QS waves in V1-V3 with abnormal ST-T segments in leads I, aVL, and V4-V6. The possibility of a previous transmural anteroseptal and high lateral myocardial infarction (MI), with a possible nontransmural lateral extension, was now entertained. A chest radiograph demonstrated bilateral pleural effusions with slight left ventricular (LV) cardiomegaly. Echocardiography (M-mode and two-dimensional) delineated marked LV dilatation and decompensation with a reduced ejection fraction of 44%. Repeat immunological investigations were now positive for ANF (in a titre of 1:160) and negative for anti-double-stranded DNA. Other tests remained negative. A differential diagnosis of dilated cardiomyopathy, myocarditis, and LV dysfunction secondary to previous MI was considered. The possibility of an underlying collagen disorder was favoured.

The patient finally consented to admission on 23 October 1984, when she was very depressed and emotionally labile, with no cutaneous features of collagen disease. The pulse rate was 100 with all peripheral pulses palpable. The jugular venous pressure was not elevated and her blood pressure was

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130/80 mmHg. The apex beat felt dyskinetic and was palpated in the fifth left intercostal space, just outside the midclavicular line. Heart sounds were normal with a grade 2/6 pansystolic murmur characteristic of mitral incompetence. A resting ECG was unchanged. Radiography demonstrated that the large right-sided pleural effusion was no longer present, and that there was some pleural thickening on the right and slight blunting of the left costophrenic angle. The heart was minimally enlarged. A leucocytosis of  $14 \times 10^9/l$  was still present and the ESR was raised at 42 mm/h. Immunological tests were persistently positive for ANF (titre of 1:80) and C-reactive protein (CRP) ( $20 \mu\text{g/ml}$ ). Rheumatoid factor was absent, as were auto-antibodies to mitochondria, smooth muscle, parietal cells and thyroid microsomes, anti-double-stranded DNA antibodies and ENA. Serum C3 and C4 levels were normal to low. Circulating immune complexes showed a 69% inhibition (normal: 15-37%). All other bacteriological and virological tests were negative, as were biochemical studies and lung function tests. A gallium scintiscan was negative. The likelihood of a previous MI was confirmed by a resting thallium-201 scintiscan on 25 October 1984, which delineated a large 'cold area' in the lateral part of the LV which also appeared enlarged. A technetium-99m gated blood pool scintiscan demonstrated a normal right ventricle (RV), and a large LV which contracted very poorly in its apical and anterior segments. The ejection fraction was quite markedly reduced at 22%. Hence the patient was not suffering from a dilated (congestive) cardiomyopathy but rather a post-MI condition. An exercise ECG (Bruce protocol) on 29 October 1984 was negative.

Definitive clinical diagnosis was difficult, but it was felt that the patient was suffering from a collagen disease, most likely systemic lupus erythematosus (SLE). The exact cause of her previous MI was unknown, but very likely due to a coronary arteritis caused by a systemic disease. Despite negative gallium scintigraphy, an associated myocarditis could not be excluded with certainty. The patient was subjected to cardiac catheterization and RV endomyocardial biopsy on 1 November 1984.

### Cardiac catheterization

This procedure was undertaken from the right groin using the percutaneous Seldinger technique. Intracardiac pressures

(all in mmHg) were as follows: right atrium — mean 5, RV — 48/0-6, main pulmonary artery — 48/21 (mean 33), pulmonary capillary wedge — mean 31, LV — 120/0-31, central aorta — 120/80 (mean 100); these results indicated moderate pulmonary hypertension secondary to LV failure. The cardiac output was significantly reduced at 2.4 l/min and both systemic and pulmonary vascular resistances were elevated. The LV dp/dt was unexpectedly normal. LV cine angiography demonstrated anterolateral akinesia with normal contractility of the interventricular septum and inferoposterior segments. RV cine angiography in the right anterior oblique (RAO) view showed normal contractility. Aortic cine angiography in the left anterior oblique (LAO) projection demonstrated no evidence of aortic arteritis and no aortic valve abnormality. Selective dye injection into the right coronary artery (RCA), in the LAO and RAO projections, delineated a dominant vessel free of disease, but there was evidence of right-to-left collateral flow indicative of a left coronary artery (LCA) lesion (Fig. 1). Selective LCA cine angiography in multiple projections showed a most striking picture (Figs 2 and 3). The left mainstem coronary artery appeared normal but both the left anterior descending (LAD) and left circumflex (LC) coronary arteries were diffusely diseased with a narrow lumen, particularly the LAD. Some left-to-left collateral vessels were visualized. There was no calcification.

Multiple endomyocardial specimens were taken from the interventricular septum and RV apex and free wall. On light microscopy the myocardium appeared to be within normal limits, apart from areas of dense interstitial fibrosis. There was no evidence of myocarditis or small-vessel vasculitis. Electron microscopy confirmed a regular arrangement of myofibrils, mitochondriosis and some lipofuscin pigment (Fig. 4). Definite extensive interstitial fibrosis was encountered and there was no evidence of vasculitis (Fig. 5).

### Further clinical course and follow-up

In view of what appeared to be a spontaneous remission of the disease process, and lack of evidence of myocarditis in the biopsy material, it was decided against steroid treatment. Her oral contraceptive was discontinued and the patient was advised to stop smoking. She was also to continue on maintenance isosorbide dinitrate, digoxin and diuretic therapy.

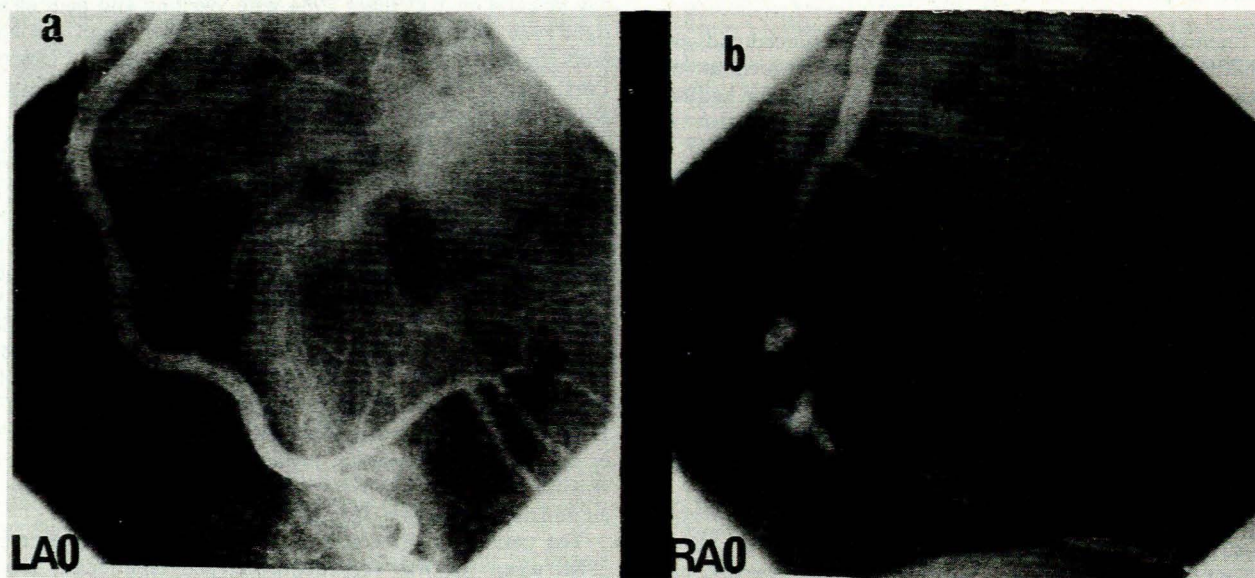


Fig. 1. RCA cine angiograms in the (a) LAO and (b) RAO views. The vessel is dominant and free of obstructive disease or aneurysm formation. Right-to-left collateralization is present, opacifying the LAD coronary artery territory.



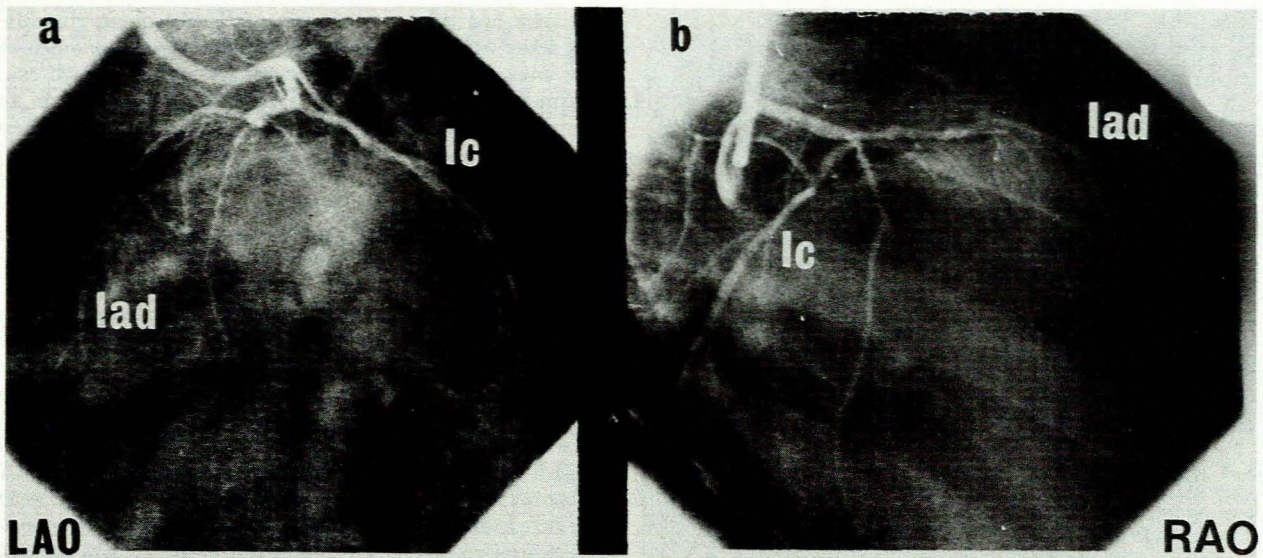


Fig. 2. LCA cine angiograms in the (a) steep LAO and (b) steep RAO projections. The LAD and LC coronary arteries are diffusely diseased and have a uniformly very narrow lumen.

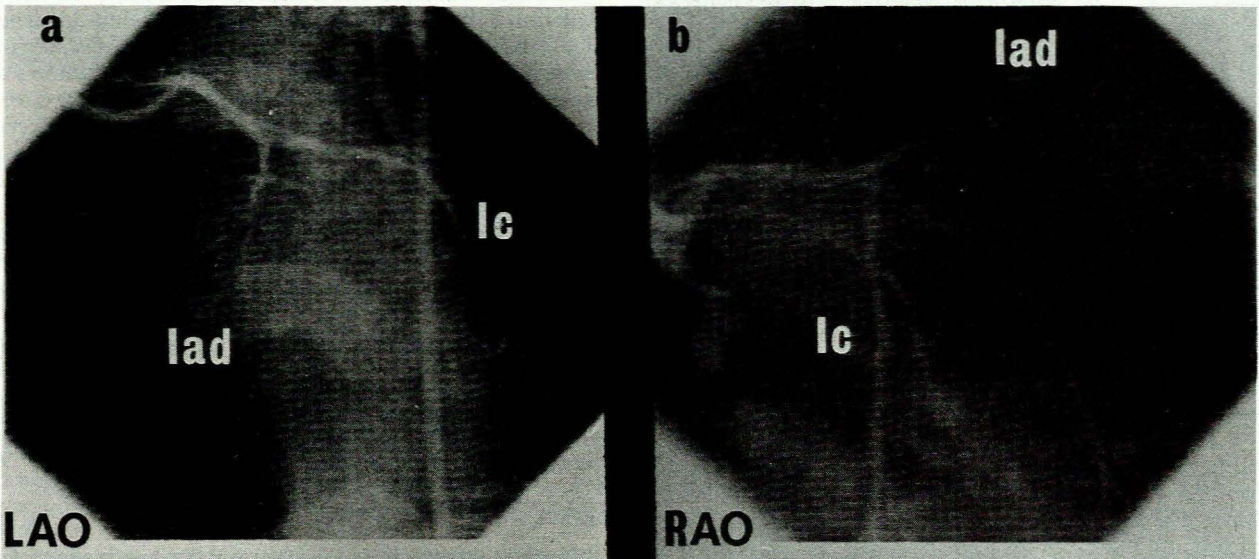


Fig. 3. LCA cine angiograms in the (a) shallow LAO view with cranial tilt and (b) shallow RAO view with caudal angulation. Both the LAD and LC coronary arteries are very diseased, especially the former vessel.

At her first outpatient visit on 15 January 1985 she no longer complained of angina pectoris, but had slight swelling of her right leg attributed to venous obstruction secondary to the catheterization procedure. A chest radiograph now delineated a normal-sized cardiac silhouette and clear lung fields. A resting ECG demonstrated features of an old transmural anterolateral MI, persisting left axis deviation and incomplete right bundle-branch block, but no evidence of left atrial enlargement or sinus tachycardia. The ESR was normal, as were the rest of the haematological studies. The test for CRP was now negative and renal and hepatic function values were within normal limits. Repeat immunological tests were positive for ANF (titre of 1:160), positive for anti-double-stranded DNA and negative for ENA.

The patient was last seen on 6 February 1985; she was free of angina pectoris and dyspnoea, but still complained of slight generalized arthralgia; there was a slight decrease in the leg swelling. A resting ECG now showed additional first-degree atrioventricular heart block, accepted as being due to digoxin

therapy. Serum digoxin levels were therapeutic. She will be followed up regularly to determine her long-term course and prognosis.

## Discussion

The diagnosis of SLE was based on the symptoms and results of immunological testing, particularly the repeatedly positive anti-double-stranded DNA test and circulating immune complexes. A superimposed infection was strongly suspected in view of the markedly elevated neutrophilic leucocyte count and raised CRP. ESR fell in concert with a return to normal of the leucocyte count, and the patient felt better despite persistently positive signs of immunological abnormality.

Cardiovascular abnormalities are encountered in up to 60% of patients suffering from SLE,<sup>1-3</sup> but a rather difficult complication to explain is congestive cardiac failure, a clinical feature of our case. The better recognized cardiovascular manifestations



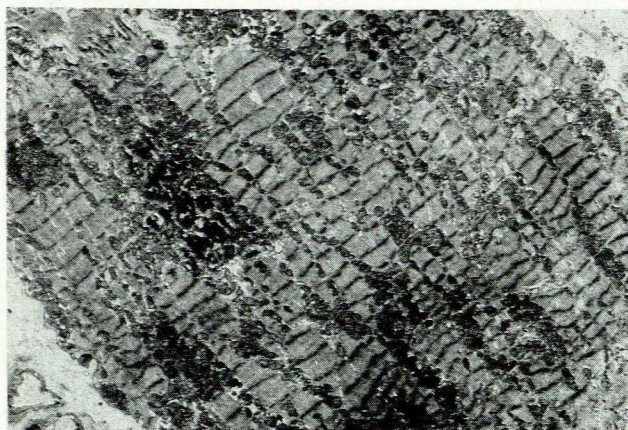


Fig. 4. Electron photomicrograph of the RV endomyocardial biopsy material. Regular arrangement of myofibrils, mitochondria and some lipofuscin pigment is in evidence (uranyl nitrate and lead citrate stain x 7 500).

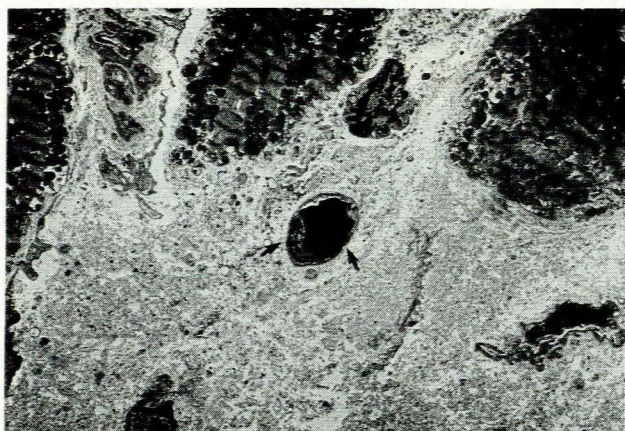


Fig. 5. Electron photomicrograph of the RV endomyocardium. There is extensive interstitial fibrosis. The blood vessel (arrowed) appears normal (uranyl nitrate and lead citrate stain x 6 000).

of SLE are Libman-Sacks endocarditis, pericarditis and myocarditis.

Much has been written about the increased incidence of coronary atherosclerosis in patients with SLE, particularly if they have been treated with long-term corticosteroid therapy.<sup>4,5</sup> Some authors even claim that the disease accelerates coronary atherosclerosis.<sup>6</sup> Our patient was a heavy smoker and on oral contraceptives, a combination well established as a serious risk factor combination for coronary atherosclerosis, yet the coronary angiographic features were not those of obstructive coronary atherosclerotic disease. Thus, we do not believe that our patient's angina pectoris and extensive acute MI were due to the latter.

Acute MI is rare in SLE. Meller *et al.*<sup>6</sup> reported 3 young patients who experienced this event, 1 dying from ventricular fibrillation. Wei and Bulkley<sup>7</sup> also stressed the importance of non-atheromatous diseases such as SLE in acute MI in young women below the age of 36. Bignold *et al.*<sup>8</sup> documented a 24-year-old female with acute MI and papillary muscle dysfunction causing mitral incompetence in the absence of coronary atherosclerosis or coronary arteritis. They suggested that the cause of the acute MI was most likely multiple hyaline thrombi.

In our patient coronary arteritis may have been secondary to SLE. Several autopsy studies have documented focal fibrinoid deposits and fibroplastic proliferation with subsequent luminal narrowing of the small arteries and arterioles in SLE,<sup>3,9,10</sup> but the larger epicardial coronary arteries were less commonly involved. Bonfiglio *et al.*<sup>10</sup> reported the case of a 16-year-old

girl who had coronary arteritis with subsequent thrombosis and acute MI, and described a further 3 young women with cine angiographic features of coronary arteritis which caused angina pectoris in all and a probable acute MI in one. Hejtmancik *et al.*<sup>2</sup> reported 6 patients with coronary arteritis but no acute MI. Kong *et al.*<sup>11</sup> documented acute MI following coronary arteritis in SLE, as did Benisch and Pervez.<sup>12</sup> In a most elegant case study Heibel *et al.*<sup>13</sup> performed repeated coronary cine angiography on a woman aged 45 years who had suffered repeated episodes of acute MI and showed features of coronary arteritis. They said: 'the diagnosis of coronary arteritis due to systemic lupus erythematosus is seemingly suggested by the established diagnosis of this connective-tissue disease, an absence of predisposing factors to atherosclerotic heart disease, an absence of predisposing factors to atherosclerotic heart disease in a young patient, and the occurrence of angina pectoris or myocardial infarction, or both'. Coronary arteritis in SLE was also reported by Taubenhaus *et al.*<sup>14</sup> and Keat and Short.<sup>15</sup> Luminal obliteration in coronary arteritis due to SLE can be explained by thrombosis or subendocardial connective tissue proliferation which subsequently extends into the lumen through gaps in the arterial wall. Pathological Q waves are most uncommon in SLE, even when MI is demonstrated at autopsy.<sup>1</sup>

The RV endomyocardial biopsies in our case showed no evidence of 'small-vessel disease' or vasculitis, but this type of biopsy is not very reliable for such detection, especially with sampling of the RV. Furthermore, no histological features of a myocarditis due to SLE could be recognized. Because of these considerations, as well as the likelihood of a secondary infection, it was decided against corticosteroid or immunosuppressive therapy. The patient's transient congestive cardiac failure could be explained on the basis of extensive MI secondary to coronary vasculitis. It would appear that this young woman has a poor prognosis and must be managed symptomatically. Stopping smoking and oral contraception may help somewhat.

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