Shortness of breath in systemic lupus erythematosus: a diagnostic and therapeutic dilemma

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CASE HISTORY
A 30 year old woman with systemic lupus erythematosus (SLE) was admitted to hospital complaining of shortness of breath, orthopnoea, swelling of ankles, and increased weight over the preceding eight days. She otherwise felt well, and reported that her lupus was inactive. She denied any associated chest pain, cough, or fever. A similar presentation had occurred three months previously, when she went to another hospital with the same symptoms, associated with a raised temperature (38.4°C). Investigations performed at that time included a complete blood picture, cardiac enzymes, and the measurement of antibodies against double stranded DNA (dsDNA). Blood and urine cultures were normal and a chest x-ray examination was normal. All blood tests were normal with the exception of a raised troponin-t level of 0.62 µg/l (normal <0.1 µg/l). An echocardiogram and high resolution computed tomography (HRCT) chest scan were also done. She was discharged from hospital and given oral diuretics without a definite diagnosis being made. Two weeks later, her case was reviewed in our hospital and in view of the recent history, a repeat chest x-ray examination, echocardiogram, and HRCT scan of the chest were performed. The only abnormality was seen on echocardiography, which showed a hypokinetic inferior, inferoposterior, and inferoapical left ventricle wall, with some mild to moderate left ventricular dilatation and systolic dysfunction. There was a small pericardial effusion with some mild to moderate left ventricular dilatation and septal/inferior wall akinesis, with an ejection fraction estimated at 28% and a left ventricular end diastolic diameter of 6.45 cm (normal <5.3).

A diagnosis of cardiac failure was made on the basis of clinical and investigative findings. A number of potential causes were considered including increased SLE disease activity complicated by myocarditis or coronary arteritis, hypertensive heart disease, drug related causes such as coronary atherosclerotic disease secondary to corticosteroid usage or cyclophosphamide cardiotoxicity and viral myocarditis.

Treatment was started with furosemide (frusemide) 120 mg daily, perindopril 4 mg daily, and digoxin 250 µg daily and proceeded to cardiac catheterisation, coronary angiography, and myocardial biopsy. The coronary angiogram was normal with no evidence of aneurysmal dilatation or atherosclerosis. The cardiac catheter showed raised arterial blood pressure, LV end diastolic pressures and right heart pressures. Six endomyocardial biopsy samples were taken from the right ventricle. The histopathology disclosed marked interstitial oedema, vacuolation, and variations in fibre size, but no haemorrhagic changes. Additionally, mild vascular inflammation was seen, mainly with polymorphonuclear cells with only occasional mononuclear cells. One of the six biopsies demonstrated a focus of myocyte necrosis with an associated mononuclear cell infiltrate (fig 1).

Three days after the treatment described above was started, the clinical signs had resolved and repeat echocardiography showed significant improvement in LV systolic function and global LV wall motion, with only mild residual septal hypokinesia. The ejection fraction had risen to 52% and the LV end diastolic diameter had reduced to 6.3 cm. The patient remains stable with an angiotensin converting enzyme inhibitor, furosemide, hydroxchloroquine, and prednisolone, with no symptoms of dyspnoea. Repeat echocardiography four months after discharge showed an LV ejection fraction of 67% and an end diastolic diameter of 5.8 cm.

Abbreviations: HRCT, high resolution computed tomography; LV, left ventricle; SLE, systemic lupus erythematosus
DISCUSSION
Cardiac involvement is a well recognised manifestation of SLE, and includes pericarditis reported in 50–74% of patients, endocardial involvement in 50–63%, premature atherosclerosis and primary myocardial involvement (myocarditis) in 8–81%, depending on series and diagnostic criteria.\(^1\) Necropsy studies suggest that myocardial involvement is common, affecting up to 40% of cases, with areas of myocardial inflammation, necrosis, and fibrosis seen.\(^2\) An endomyocardial biopsy is required for a confident diagnosis before death of myocarditis secondary to active SLE. It has been known for some time that myocardial function is impaired in patients with SLE, in particular those with coexistent hypertension.\(^3\) Abnormalities in systolic and diastolic LV function have been demonstrated on echocardiography\(^4\) and cardiac catheter studies.\(^5\) It is unclear from published reports how much of this impaired function is related to primary myocardial involvement with SLE and how much relates to drug toxicity from long term corticosteroid use, including hypertension and accelerated atherosclerosis affecting coronary arteries. Cyclophosphamide used in the treatment of vasculitic and renal complications of SLE is also a well known cause of cardiotoxicity and myocardial necrosis, usually presenting with acute pericarditis, acute cardiomyopathy, and congestive cardiac failure.\(^6\) Cardiotoxicity is thought to be related to the dose of cyclophosphamide and has been infrequently reported at doses <200 mg/kg.\(^6\)

It is against this background that we present this case of SLE complicated by cardiac disease, where the cause of the cardiac failure was unclear and potentially multifactorial. It was felt necessary to proceed to an endomyocardial biopsy to exclude cyclophosphamide cardiotoxicity and to obtain evidence of myocarditis secondary to active SLE, as these results would significantly affect future therapeutic decisions about this patient. The cumulative cyclophosphamide dose for this patient was 100–150 mg/kg, which together with the endomyocardial biopsy result, suggested that cyclophosphamide was not the cause of her cardiac failure. Based on laboratory evidence of active SLE and the histopathological evidence of myocarditis, it was decided cautiously to resume treatment with intravenous cyclophosphamide and corticosteroids.

THE LESSONS
- Cardiac involvement in SLE is common and often unsuspected.
- The cause of cardiac disease in patients with SLE is potentially multifactorial, including disease related, treatment related, and unrelated causes.
- Hypertension is commonly seen in SLE, but is rarely the sole cause for congestive cardiac failure in patients with SLE.
- Invasive procedures including cardiac catheterisation and endomyocardial biopsy may be necessary to investigate fully and make decisions about the treatment of patients with SLE presenting with shortness of breath.

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UNUSUAL AND MEMORABLE

Case Number 24: Scalp necrosis in giant cell arteritis

A 73 year old woman was referred with two weeks’ history of temporal headaches, jaw claudication, and painful rash on both temples (fig 1). The jaw claudication was so intense that she could take fluids only and could not chew solid food. She had no visual symptoms. The erythrocyte sedimentation rate was 50 mm/1st h and C reactive protein 70 mg/l.

Diagnosis of scalp necrosis in giant cell arteritis (GCA) was made on clinical grounds. Biopsy was not undertaken as she had already been receiving oral corticosteroids and because of the risk (perhaps theoretical) of worsening the scalp necrosis. Treatment with corticosteroids led to a resolution of symptoms and complete healing of the scalp.

Scalp necrosis in GCA is a rare but recognised complication. It may represent a subset of severe disease. Of the 24 cases reported in English, 16 had visual loss, four gangrene of the tongue, and one nasal septal necrosis.1

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Reference