Antiphospholipid syndrome presenting as cardiac failure

Sir,

Antiphospholipid syndrome (APS) is a thrombophilic disorder commonly associated with venous and arterial thrombosis, recurrent fetal loss and thrombocytopenia. Even though cardiac manifestations are well recognized, congestive cardiac failure (CCF) as an initial presenting feature is very uncommon. We present three cases presenting predominantly as cardiac failure where the diagnosis of APS emerged later.

Patient 1, a 67-year-old woman, presented with increasing dyspnoea and uncontrolled hypertension of a few weeks duration. Past medical history included dermatomyositis, mastectomy for carcinoma of the breast and a left total hip replacement. There was no previous history of hypertension. Her drug therapy comprised of prednisolone 5 mg a day, ranitidine and prothiaden. On examination she was hypertensive (BP 190/112 mmHg), with papilloedema and signs of congestive cardiac failure. Electrocardiogram (ECG) revealed sinus tachycardia and evidence of left ventricular hypertrophy. Chest X-ray (CXR) showed bilateral pleural effusions and pulmonary congestion. Urine examination showed haematuria and proteinuria. Urea and creatinine were elevated at 8.8 mmol/l and 245 mmol/l, respectively. Haemoglobin was 8.8 g/dl and platelet count was $90 \times 10^9$/l. Clotting screen and C-reactive protein (CRP) were normal. Blood film showed fragmented red cells. Antinuclear antibody (ANA) was positive at 1 : 640, but antibody to double-stranded DNA (dsDNA) and antineutrophil cytoplasmic antibody (ANCA) were negative. A diagnosis of congestive cardiac failure due to malignant hypertension was made, and she was treated with intravenous diuretics and nitrates. However, renal function deteriorated rapidly (creatinine 697 mmol/l) and haemodialysis was initiated. She then developed ischaemia of the left ring finger, and was treated with low-molecular-weight heparin. Echocardiogram revealed left ventricular hypertrophy but no thrombus. Renal biopsy revealed thrombotic microangiopathy without any evidence of lupus nephritis. Lupus anticoagulant and anti-cardiolipin antibody (ACA) was positive (IgG 80 units). She was commenced on anticoagulation but renal function did not improve, necessitating long-term renal replacement therapy.

Patient 2, a 32-year-old woman, was admitted with acute onset dyspnoea. She had no previous medical illnesses and was not on any medication. Examination revealed a normal blood pressure and signs of cardiac failure. CXR showed cardiomegaly and pulmonary oedema. ECG showed sinus tachycardia. Urine analysis was normal. She was commenced on intravenous diuretics and angiotensin-converting-enzyme inhibitors. Echocardiogram showed dilated globally impaired left ventricle and moderate aortic and mitral insufficiency. Some 72 h later, she developed multiple painful ischaemia of her digits, livedo reticularis, hemiparesis and bilateral branch retinal artery occlusions. Blood count showed thrombocytopenia. Clotting screen was normal. There was a mild increase in urea and creatinine. Computed tomography (CT) of the brain did not show any abnormalities.ANA, ds-DNA and hepatitis screen was negative. ACA was positive (IgG 90 units). She was treated with anticoagulation, steroids, diuretics and angiotensin-converting-enzyme inhibitors, and her symptoms gradually improved.

Patient 3, a 62-year-old woman with rheumatoid arthritis was admitted with pleuritic chest pain and increasing shortness of breath. Examination revealed signs of cardiac failure. Investigations showed raised white cell count, CRP and fibrinogen, positive D-dimer and a slight increase in urea and creatinine. Clotting screen was normal. ECG revealed sinus tachycardia and CXR showed cardiomegaly and bilateral airspace shadowing. A ventilation/perfusion scan showed matched defects, suggesting a low probability of pulmonary embolus. She was treated with diuretics and antibiotics. However, her symptoms did not improve and a repeat CXR showed cavitation in the left midzone and consolidation in right middle lobe with pleural effusion. A few days later she developed livedo...
reticularis and a diagnosis of vasculitis was suspected. A CT scan of the chest showed wedge consolidation within lingular and right lower lobe segments, with cavitation on the left, suggesting peripheral pulmonary emboli. It also showed cardiomegaly and a filling defect in the left atrium and ventricle. Echocardiogram showed global impairment of left ventricle with apical thrombus and mild mitral insufficiency. A diagnosis of APS was suspected, and she was commenced on anticoagulation. ACA was positive (IgG 30 units). ANA, ANCA and dsDNA were negative. Her symptoms improved gradually on diuretics, angiotensin converting enzyme inhibitors and warfarin.

A clinical syndrome associating antibodies against phospholipids with widespread arterial and venous thrombosis was described between 1983 and 1986.1,2 It was initially called anti-cardiolipin syndrome, but is now very widely known as anti-phospholipid syndrome (APS). APS can be primary or secondary.3 Secondary APS usually occurs in association with other diseases, most commonly systemic lupus erythematosus (SLE). Various clinical manifestations of APS due to the involvement of all systems are increasingly recognized. The most common include arterial/venous thrombosis (86%), recurrent foetal loss (33%) and thrombocytopenia (23%).4

The well-known features of cardiac involvement include valvular lesions leading to insufficiency, vegetations and myocardial infarction. Intracardiac thrombus, pericardial effusion and dilated cardiomyopathy are less well recognized.3 Although all three of our patients presented with cardiac failure, only two showed dilated and globally impaired ventricular function. Diffuse cardiomyopathy in patients with ACA has been reported before, and in these patients widespread thrombus in the intramyocardial arteries and arterioles was found at autopsy.6,7

Symptomatic and asymptomatic cardiac lesions have been found to be more common in patients with ACA. The prevalence of myocardial dysfunction varies from study to study. An echocardiographic study on 75 SLE patients, of whom 23 had ACA, revealed abnormalities in 16 patients. Of these, nine had myocardial dysfunction.8 However, a prospective echocardiographic study on 132 patients with SLE showed that the presence of ACA was associated with a higher prevalence of valvular abnormalities, but did not demonstrate any myocardial dysfunction.9 Similarly, in a series of 20 patients with primary APS, 13 had valvular lesions a few had pulmonary hypertension and pericardial effusion. None exhibited myocardial dysfunction.10

The occurrence of malignant hypertension and hypertension as a presenting feature has been recognized in patients with APS.11–13 Interaction between ACA, platelets and endothelial cells, leading to formation of microthrombi and fibroblast proliferation, is thought to be the mechanism responsible. Acute renal failure due to thrombotic microangiopathy in APS in the absence of SLE has also been reported.14

All our patients had involvement of more than of three organs satisfying the criteria of catastrophic APS (CAPS). A review of 31 patients with CAPS revealed cardiac involvement in about a third.15 Mortality was high in this group (58%) and cardiac disease accounted for more than half the deaths.

### Table 1 Clinical features

<table>
<thead>
<tr>
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<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>67</td>
<td>33</td>
<td>62</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
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<tr>
<td>Initial presentation</td>
<td>CCF + HT</td>
<td>CCF</td>
<td>CCF + PE</td>
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<tr>
<td>Thrombosis</td>
<td>Digital</td>
<td>Retinal artery</td>
<td>Pulmonary emboli</td>
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<tr>
<td>Renal involvement</td>
<td>ARF</td>
<td>Mild</td>
<td>Mild</td>
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<tr>
<td>Echocardiogram</td>
<td>LVH</td>
<td>Dilated CMP</td>
<td>Dilated CMP, thrombus</td>
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<tr>
<td>ECG</td>
<td>LVH</td>
<td>Sinus tachycardia</td>
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<tr>
<td>Thrombocytopenia</td>
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<td>–</td>
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<tr>
<td>Livedo reticularis</td>
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<td>+</td>
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<tr>
<td>Clotting</td>
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<tr>
<td>Anti-cardiolipin (IgG)</td>
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<tr>
<td>Other antibodies</td>
<td>ANA</td>
<td>–</td>
<td>RF</td>
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</table>

CCF, congestive cardiac failure; HT, hypertension; PE, pulmonary emboli; ARF, acute renal failure; LVH, left ventricular hypertrophy; CMP, cardiomyopathy; –, absent; +, present; N, Normal; TE, thromboembolism.

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All our patients predominantly presented with cardiac failure, and a diagnosis of APS was suspected at a later stage when other symptoms appeared. None had previous thrombo-embolic events or miscarriages. Clinical improvement was seen with anticoagulation, diuretics and angiotensin-converting-enzyme inhibitors. Although one patient was treated with a tapering course of steroids, its benefit in APS remains to be proven. We believe that it is important to consider APS in patients presenting with cardiac failure of uncertain aetiology, malignant hypertension or dilated cardiomyopathy. Increased recognition of these associations has an important implication on management of this complex syndrome.

We would like to thank Dr R. Sheers for allowing us to include one of his patients.

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References