Acute adrenal failure secondary to bilateral infarction of the adrenal glands as the first manifestation of primary antiphospholipid antibody syndrome

Adrenal insufficiency is an uncommon, life threatening complication of the primary antiphospholipid antibody syndrome (PAPS), secondary to either adrenal haemorrhage or infarction.[1–6] Adrenal failure more often follows other PAPS thromboembolic manifestations, and has to be clearly differentiated from other PAPS abdominal emergencies, including mesenteric and hepatic infarction.[1 3–5] The pathological mechanisms involved are still not clearly understood, but the hypercoagulable state in patients with PAPS supports the concept that adrenal haemorrhagic infarction may possibly be related to adrenal vein thrombosis.[7] We recently observed a new case, which is of particular interest as the patient developed an acute adrenal failure, revealing bilateral adrenal infarction, as a first manifestation of the PAPS.

A 70 year old patient presented with diffuse abdominal pain persisting for 15 days. He had no previous history of thromboembolic or connective tissue disease. On admission, he was dehydrated with pulse 120/min, blood pressure 9/4 mm Hg, and abdomen palpation was tender. Laboratory findings were: haemoglobin 6.3 mmol/l, white cell count 6.4 $\times 10^9$/1, platelets were 90 $\times$ 10^9/l, ESR 18 mm 1st h. Blood electrolytes were abnormal for natraemia 118 mmol/l, kaliaemia 6.3 mmol/l, glycaemia 2 mmol/l. Acute adrenal failure diagnosis was suspected, and was confirmed by a low plasma cortisol concentration 20 nmol/l and an adrenocorticotrophichormone (ACTH) test that failed to raise plasma cortisol over 25 nmol/1. The serum ACTH concentrations were 300 pg/1 (normal range 10–50). Coagulation studies found a pronounced prolonged activated partial thromboplastin time (APTT) (95 s; normal: 32 s) with normal prothrombin time. D-Dimers were 230 ng/ml (normal < 320). Lupus-like anticoagulant (LAC) was quantified with the dilute thromboplastin time inhibition test with a high dilution of thromboplastin (1:500)[8]; the confirmatory test for LAC was positive. Anticardiolipin antibodies IgG were positive (IgG-aCL: 18GPL U/ml; normal < 15) and IgM were negative. The presence of aCL was determined by solid phase enzyme linked immunosorbent assay according to international standardised methods.[9] Examination of antiphospholipid antibodies (asserachrom APA-Diagnostica Stago) was negative. The results of autoantibody screening, including *Treponema pallidum* haemagglutination, Veneral Disease Experimental Laboratory test, antinuclear and anti-DNA antibodies, cryoglobulin, and rheumatoid factor were negative. The complement profile was normal. Abdominal computed tomography showed bilateral enlarged adrenal glands, secondary to adrenal haemorrhagic infarction (fig 1). The diagnosis of PAPS was made, because of the presence of LAC and IgG-aCL, associated with bilateral adrenal infarction, which was probably secondary to thrombosis of the adrenal gland veins. The patient was treated with cortisone acetate and aspirin, with rapid improvement of his clinical status. Three months later, and while APTT, IgG-aCL, and LAC titres were still raised, the patient developed an extensive deep venous thrombosis of the right forearm, confirmed by venous Doppler echography. Anticoagulation treatment was begun.

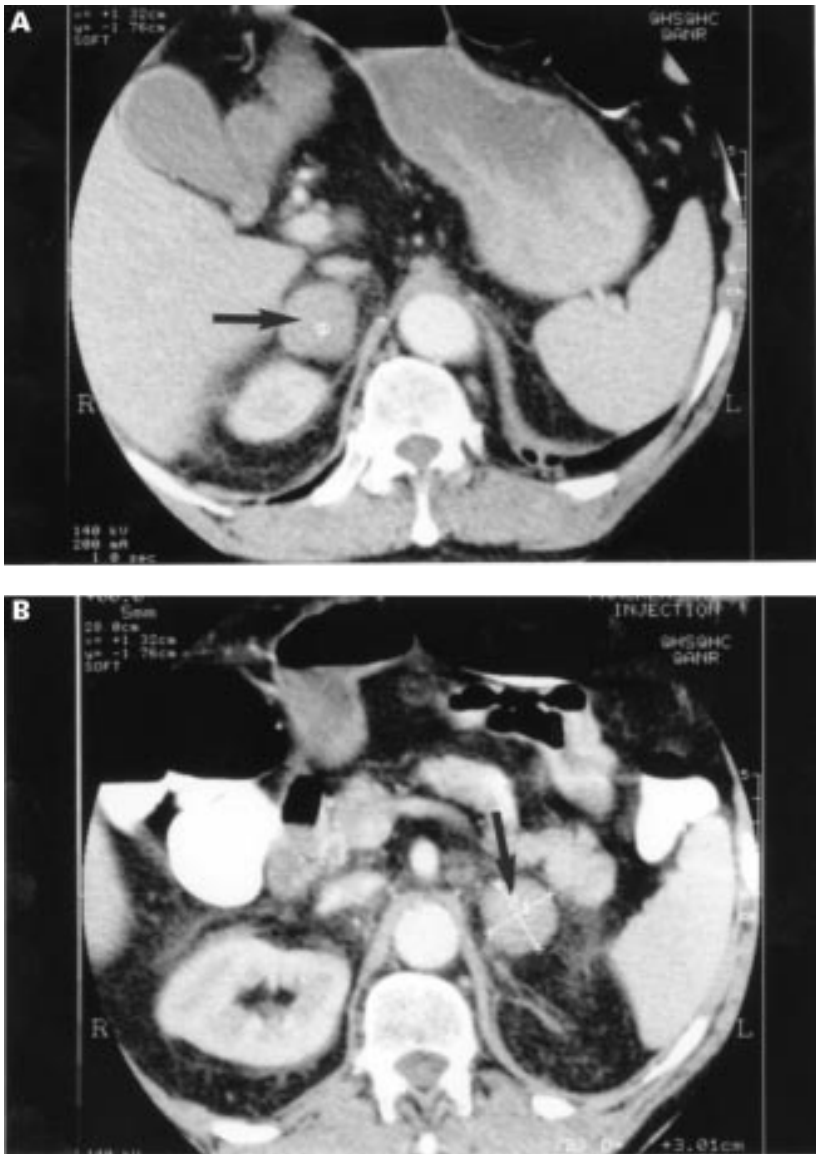

Figure 1 (A) and (B) Bilateral enlarged adrenal glands, secondary to adrenal haemorrhagic infarction confirmed by computed tomography.

The PAPS is characterised by recurrent venous or arterial thrombosis, or both, or repeated fetal loss, associated with the persistent presence of anticardiolipin antibodies or LAC, in the absence of connective tissue disease (notably systemic lupus erythematosus). Our case report is original in that the acute adrenal failure, secondary to bilateral adrenal haemorrhagic infarction, was the first clinical manifestation of a typical PAPS. We suggest therefore, that PAPS may be suspected in patients with either acute or chronic adrenal failure, even if they have no previous history of thromboembolic disorders. Because haemorrhagic infarction may precede other thromboembolic events, when this type of complication is noted, an evaluation for PAPS with a search for antiphospholipid antibodies should be systematically done. Moreover, adrenal haemorrhagic infarction secondary to PAPS should be excluded in all patients presenting with enlarged adrenal glands shown by abdominal compted tomography. Our findings further emphasise that diagnosis of adrenal insufficiency should be considered in patients with PAPS and acute abdominal pain.

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Echocardiographic findings in primary Sjögren's syndrome

Primary Sjögren's syndrome (pSS) is a chronic autoimmune disease characterised by lymphocytic infiltration of the salivary and lacrimal glands.[1] Similar lymphocytic infiltrates may invade visceral organs, and this results in several extraglandular manifestations.[1] Among these, a clinically overt heart disease is very rare.[2–4] However, recent echocardiographic studies showed that asymptomatic cardiac involvement is frequent in pSS. Thus, Rantapää-Dahlqvist and colleagues[5] reported signs of present or previous pericarditis in nine of 27 (33%) pSS patients. Of the echocardiographic measurements, the right ventricular anterior wall and the left ventricular posterior wall were significantly smaller in patients with pericarditis than in those without pericardial serositis. Moreover, in the pericarditis patients, the regional fractional shortening of the left ventricle was significantly higher and the hypokinesia of the left ventricle significantly more frequent, when compared with those without pericarditis. Sclerosis of the aortic cups and a slight aortic regurgitation were seen in 11 and three patients, respectively. No patient had mitral valve prolapse or indirect signs of pulmonary hypertension. Mita *et al*[6] evaluated 112 patients with SS, primary in 33 and secondary in 79, by two dimensional echocardiography. They reported abnormal findings in 69 (61.6%) of the total cohort and in 55.5% of the pSS patients. In this second group, pericardial effusion was seen in 21.2%, thickening/calcification of the aortic valve in 10.3%, decrease in the diastolic descent rate of mitral valve in 6.9%, thickening/calcification of mitral valve in 3.4%, mitral regurgitation in 3.3%, and mitral prolapse in 3.2%. No pSS patient had pulmonary hypertension. Gyöngyösi *et al*[7] examined 64 pSS patients and showed an echogenic pericardium in 21 (33%). Pulmonary pressure was significantly higher in the patients group than in controls, probably because of interstitial lung disease. Left systolic parameters and left atrial diameter did not differ between the pSS patients and controls. On the contrary, the E:A wave ratio, the main Doppler index of left ventricular diastolic function, was abnormal in 21 of 42 (50%) patients, in 17 of whom other parameters of diastolic function were significantly changed. No correlation between the left ventricular diastolic dysfunction and presence of an echogenic pericardium was found.

We evaluated 18 female patients diagnosed as suffering from pSS according to the EEC criteria[8] by M-mode and two dimensional echocardiography. The mean age (SD) was 55.3 (7.4) years (range 46–67) and the mean disease duration (SD) was 6 (4.8) years (range 6 months–20). The control group consisted of 18 age matched healthy women. No patient or control had history of cardiovascular diseases, such as arterial hypertension or ischaemic heart disease. Echocardiography was carried out with an ATL Apogee 800 instrument and normal values of the measured parameters were taken from Feigenbaum.[9] Transmitral diastolic flow velocities were recorded by pulsatile Doppler method. Moreover, the left ventricular diastolic function was evaluated according to Choong.[10] Statistical analysis was performed using the Student's *t* test and Scheffe's method for multiple comparison among means. The results show that only the deceleration of the E wave was significantly reduced in pSS (mean (SD)) (360 (84.02) cm/s^2) compared with controls (462 (84.25) cm/s^2) ($p<0.0009$), and remained significantly different when five subjects older than 60 years were excluded from both groups. No significant valvular disease was found in both groups. Additionally, present or previous pericarditis and pulmonary hypertension were not detected in pSS.

In conclusion, although overt heart involvement in pSS is very rare echocardiography shows an unexpectedly high frequency of cardiac manifestations, mainly pericarditis and diastolic dysfunction. These findings suggest that cardiac involvement must be included in the spectrum of extraglandular manifestations of pSS.

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An acute multiorgan thrombotic disorder associated with antiphospholipid antibodies; two 'catastrophic' cases

Over the past decade the antiphospholipid syndrome (APS) was defined by the presence of antiphospholipid antibodies (aPL) and clinical manifestations including thrombosis, recurrent fetal loss, thrombocytopenia, chorea, livedo reticularis, heart valve lesions, and renal involvement.[1] Asherson *et al* first drew attention to a catastrophic variant of APS (CAPS) that is characterised by multiple widespread vascular occlusions, leading to multiple organ failure and often death.[2] We describe two non-systemic lupus erythematosus (SLE) patients with a strikingly similar clinical presentation of CAPS and emphasise the difficulties in differentiating CAPS from other thrombotic angiopathies.

Case reports

CASE REPORT ONE

A 20 year old woman presented with transient hemichorea in 1993. Computed tomography of the brain was normal. From June 1995, episodes of hemichorea reoccurred together with severe frontal headaches. In November 1995 she was admitted to our hospital with rapid deterioration of vision and behavioural changes.

Physical examination showed subcoma, blood pressure 150/115 mm Hg, livedo reticularis, ischaemic skin ulcerations, and a systolic cardiac murmur. Fundoscopy showed arteriolar occlusions, bleeding, and exudates.

Laboratory findings included: platelet count 47×10^9/l, creatinine 176 µmol/l, fibrin degradation products 1.0 mg/l (normal <0.5), fibrinogen 4.0 g/l (normal range 2.0–4.0), haptoglobin 0.2 g/l (0.3–1.8), reticulocytes 62% (7–30), positive direct Coombs test, microscopic haematuria and proteinuria (3.9 g/day). Both Lupus anticoagulant (LAC; dRVVT; IL Test LACscreen and LACconfirm, Instrumentation Laboratory, Milan, Italy)) and high titre IgG and IgM anticardiolipin antibodies (aCL) were present; ANA were negative. Echocardiography showed mitral regurgitation but no vegetations. Brain magnetic resonance imaging showed multiple ischaemic infarctions. A skin biopsy specimen from a livedo-reticularis lesion showed thrombotic occlusions of arterioles and venules with partial recanalisation.

Treatment consisted of high dose corticosteroids, plasma exchange, anticoagulation, cyclophosphamide (1000 mg intravenous), and platelet transfusions. After three weeks she gradually regained consciousness and renal