Correspondence

We have arbitrarily chosen our recommended W.-K. Chan reduced dosage of thrombolytic therapy as few T.-F. Chan studies address this issue. The largest study was by Goldhaber et al. 6 comparing reduced rtPA bolus (0.6 mg/kg/15 min, maximum 50 mg) and rtPA infusion (100 mg over 2 h) in 87 patients, a double-blind Hong Kong randomized multicentre controlled trial. All patients had baseline, 20-h and 28-h follow-up nuclear scans. Some patients in centres with angiography services had baseline and 2-h pulmonary angiography, and some patients had baseline, 3-h, 20-h and 28-h echocardiogram. There was no significant difference and ... in acute major pulmonary embolism: Results of a Multicentre Registry. J Am Coll Cardiol 1997;30:1165–71. Another study compared rtPA and Streptokinase in 66 patients with acute massive pulmonary embolism. Circulation 1997;96:882–8. A substudy in 48 patients, there was less fibrinogenolysis in the bolus between thrombolytic treatment and the prognosis of hemodynamically stable patients with major pulmonary embolism. Chest 1997;111:1241–5.

Because of the small sample size of our study group, and lack of matched controls, we can draw no definite conclusion about the efficacy and safety of our reduced dosage of thrombolytic therapy for acute massive pulmonary embolism thrombolysis. An international multicentre randomised trial. The Bolus Ateplase Pulmonary Embolism group. Chest 1994;106:718–24. The antiphospholipid syndrome (APS), first described in 1983, has become recognized not only as a major cause of venous and arterial thrombosis, but as a model for accelerated arterial disease. In this prothrombotic condition, all organs are potentially targeted. The renal manifestations have included intraglomerular thrombi (thrombotic microangiopathy) and renal infarcts. Renal artery stenosis has only rarely been reported. In 1991, we reported a case of renal artery thrombosis associated with the syndrome. We here report five cases with documented renal artery stenosis and antiphospholipid antibodies (aPL) (Table 1).

Antiphospholipid syndrome and renal artery stenosis

Sir,
The antiphospholipid syndrome (APS), first described in 1983, has become recognized not only as a major cause of venous and arterial thrombosis, but as a model for accelerated arterial disease. In this prothrombotic condition, all organs are potentially targeted. The renal manifestations have included intraglomerular thrombi (thrombotic microangiopathy) and renal infarcts. Renal artery stenosis has only rarely been reported. In 1991, we reported a case of renal artery thrombosis associated with the syndrome. We here report five cases with documented renal artery stenosis and antiphospholipid antibodies (aPL) (Table 1).

Case 1. A 37-year-old female patient presented with mild renal impairment and hypertension, blood pressure 170/100. She was initially diagnosed with ds-DNA-positive SLE in 1980. In 1993, she developed a cerebral infarct and a miscarriage, and was aPL positive. In 1995, she had aortic and mitral valve replacements performed. She was hypertensive in 1998. A captopril renal scan showed symmetrical renal function, and a renal ultrasound was also unremarkable. A spiral CT scan of her renal arteries revealed a right ostial renal artery stenosis. In addition to aPL, her vascular risk factors include smoking, mild hypercholesterolaemia and steroid usage. Her BP has been controlled with amlodipine. To date,
Table 1  Patient characteristics

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Renal artery stenosis</th>
<th>Other vascular event</th>
<th>Echocardiogram</th>
<th>Risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>37</td>
<td>F</td>
<td>SLE/APS</td>
<td>Unilateral</td>
<td>Yes</td>
<td>Abnormal</td>
<td>Lipids, steroids</td>
</tr>
<tr>
<td>47</td>
<td>F</td>
<td>SLE/APS</td>
<td>Bilateral</td>
<td>Yes</td>
<td>Abnormal</td>
<td>Lipids, steroids</td>
</tr>
<tr>
<td>62</td>
<td>F</td>
<td>SLE/APS</td>
<td>Bilateral</td>
<td>No</td>
<td>Abnormal</td>
<td>Steroids</td>
</tr>
<tr>
<td>33</td>
<td>F</td>
<td>PAPS</td>
<td>Unilateral</td>
<td>Yes</td>
<td>Abnormal</td>
<td>Smoking</td>
</tr>
<tr>
<td>22</td>
<td>M</td>
<td>PAPS</td>
<td>Bilateral</td>
<td>Yes</td>
<td>Normal</td>
<td>Nil</td>
</tr>
</tbody>
</table>

PAPS, primary antiphospholipid syndrome.

no intervention of her renal artery lesion has been attempted.

**Case 2.** A 47-year-old female patient with a 7-year history of SLE was noted to have bilateral renal artery stenosis (50%) at angiography for peripheral vascular disease. She suffered a TIA in 1994 and was lupus-anticoagulant-positive. She commenced anticoagulation at that stage. Ischaemic heart disease was treated with an angioplasty. She had a superficial femoral angiogram performed in 1997 for ischaemic toes. aPL at that stage were positive with an IgG level >80GPL. In 1998, a right carotid endarterectomy was performed but this occluded postoperatively. Echocardiography at the time revealed a mildly thickened mitral valve with reduced leaflet mobility. She was an ex-smoker, had mild hyperlipidaemia and had had steroid therapy for several years.

**Case 3.** A 62-year-old female patient with long-standing SLE and APS, and mild hypertension developed worsening renal function and severe hypertension, BP 190/110. Her hypertension had been treated with enalapril and diuretics for several years. Her creatinine reached 200 µmol/l in 1998. A renal ultrasound showed a small right kidney, and renal angiogram showed an occluded right renal artery with a tight stenosis of the left artery, which was successfully treated by angioplasty. She also suffered a DVT 2 months post angiogram. Echocardiogram showed thickened aortic and mitral valves. Apart from steroids, she had no other vascular risk factors.

**Case 4.** A 33-year-old female patient with primary APS was found to have left renal artery stenosis, mesangio proliferative glomerular nephritis with no immune deposits, and intraglomerular thrombi in 1995. She initially presented in 1973 with immune thrombocytopenia, and had a CVA in 1987. At this stage she was noted to be positive for lupus anticoagulant. Echocardiogram in 1994 showed aortic regurgitation and thickened mitral valve and annulus. Pulmonary emboli were also documented, and in 1998 she experienced a right renal infarct.

**Case 5.** A 22-year-old male patient developed hypertension and was found to have bilateral renal artery stenosis and superior mesenteric artery occlusion. aCL positive (27 GPL units). He had no other vascular risk factors. Cardiovascular examination was unremarkable. Although ANA-positive, he has no other features to suggest SLE. The renal artery stenosis was successfully treated with angioplasty, and he is now anticoagulated.

Thrombosis and arterial occlusion are hallmarks of the antiphospholipid (Hughes) syndrome. Histologically, there is bland intimal proliferation and thrombosis, and no evidence of inflammatory vasculitis. In addition to acute thrombosis, the syndrome has been linked with more widespread arterial disease, the lesions ranging from focal arterial occlusion to more widespread accelerated arterial disease. Although some patients have lupus, it is likely that the majority of patients with APS have no other autoimmune disease, and present with ‘idiopathic’ strokes, coronary arterial disease, and recurrent miscarriage. The percentage of these common conditions associated with APS remains unknown and awaits more detailed epidemiological study. However, to give an example, it has been estimated that up to 18% of strokes in the under-40s are associated with APS.

The contribution of APS to idiopathic renal artery stenosis is unknown. In our experience, labile hypertension has, from the initial description of the syndrome, been a prominent feature in some cases. Renal artery stenosis may have been underestimated, although intraglomerular thrombi and renal infarcts are well documented.

Renal artery stenosis is a well-recognized complication of atheroma in the elderly. Other causes are rare. The first report of APS and renal artery stenosis was in a girl with severe hypertension and bilateral renal artery thrombosis. Our group in 1991 reported a 35-year-old man with APS, hypertension and occlusion of the right renal artery and 80% stenosis on the left. Cacoub reported five SLE
Correspondence

patients with secondary APS who had hypertension and renal impairment due to renal artery lesions. Apart from the 62-year-old patient, the others were all young patients, who had clearly developed lesions at least three decades earlier than would normally be expected. It is possible that the renal artery lesions were multifactorial in the SLE patients. Steroid usage favouring abnormal lipid profiles and glucose intolerance combined with immunological factors have been linked with the development of atheroma in SLE patients. However, the development of disease in two patients with primary APS suggest a direct role for aPL in the pathogenesis of these lesions. Evidence is accumulating to suggest that aPL are directly involved in atherogenesis, possibly through cross-reactivity with oxidized low-density lipoproteins.

In our patients, the renal artery stenosis was associated with generalized vascular disease, with 4/5 having had arterial lesions in different locations and abnormal echocardiograms. One patient needed aortic and mitral valve replacements.

In summary, we report five cases of renal artery stenosis in patients with APS, and suggest that this important cause of venous and arterial thrombosis may also be a significant cause of renal artery stenosis. The contribution of aPL to ‘idiopathic’ renal artery stenosis remains to be elucidated.

T. Godfrey
M.A. Khamashta
G.R.V. Hughes
Lupus Unit
I. Abbs
Department of Nephrology
Guy’s and St Thomas’s Hospital
London

References