Renal artery thrombosis and hypertension in a 13 year old girl with antiphospholipid syndrome

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Abstract

The case of a 13 year old girl with renal artery thrombosis and hypertension is described. A cerebrovascular accident and a probable occlusion of the superior mesenteric artery also occurred. Very high levels of 'lupus anticoagulant', anticardiolipin antibodies as well as false positive Venereal Disease Research Laboratory tests were repeatedly shown. Moreover, the patient fulfilled at least four classification criteria for systemic lupus erythematosus, but only a slight positivity for antinucleolar antibodies was present. The striking relation between antiphospholipid antibody levels and clinical events and the treatment of this complex syndrome are discussed.

Renovascular hypertension is one of the commonest forms of secondary hypertension. In the young the most usual pathological finding underlying the disease is fibromuscular dysplasia, whereas in the elderly atherosclerosis is the major cause.^{1,2} Less commonly reported is renal artery thrombosis, which usually occurs after lesions of the artery wall.¹

In the past few years the relation between thrombosis and antiphospholipid antibodies has been increasingly reported.³⁻⁹ 'Lupus anticoagulant' and anticardiolipin antibodies have been found to be associated with both venous and arterial thrombosis,^{3-6,10} as well as with recurrent fetal loss,^{3,6} thrombocytopenia,⁷ false positive tests for syphilis,¹¹ and Coombs' positivity.⁸

Since, to our knowledge, renal artery thrombosis has never been reported in association with antiphospholipid antibodies, in this paper we describe the case of a 13 year old girl with renal artery thrombosis and severe hypertension associated with lupus anticoagulant anticardiolipin antibodies, and false positive Venereal Disease Research Laboratory (VDRL) tests.

Case report

In April 1986 a 13 year old girl suddenly complained of severe cramping abdominal pain, accompanied by vomiting and a slight fever (37.5°C). After a few days gastrointestinal symptoms disappeared, while hypertension developed (blood pressure 180/140 mmHg) together with fever (39°C), convulsive seizures, oliguria, and haematuria.

Owing to the persistence of these symptoms despite antihypertensive and steroid treatment the patient was admitted to our institute in May 1986.

At entry she presented with blood pressure 180/120 mmHg, nystagmus, stupor-like unconsciousness, and palmar erythema. A systolic diastolic periumbilical bruit was heard. Electrocardiogram and chest x ray showed respectively left ventricular hypertrophy and a moderate enlargement of the cardiac shadow, and the echocardiogram showed a small pericardial effusion. An electroencephalogram showed severe and diffuse abnormalities, while cerebrospinal fluid and ophthalmoscopic examination as well as brain computed tomography were normal. Laboratory tests showed haemoglobin 94 g/l, erythrocyte sedimentation rate 78 mm/1st h; blood urea 19.2 mmol/l, serum creatinine 97 µmol/l, prothrombin 0.71, partial thromboplastin time 27 s. Liver enzyme levels were raised: serum aspartate transaminase 45 U/l, serum alanine transaminase 82 U/l, γ-glutamyl transferase 244 U/l, alkaline phosphatase 901 U/l. Microhaematuria and slight proteinuria (up to 0.9 g/day) were also found. Dilute Russell's viper venom time¹² was 37.4 s (control 23.7 s). Very high levels of IgG anticardiolipin antibodies (1680 EU—quantitative enzyme linked immunosorbent assay (ELISA) technique)¹³ and a false positive VDRL test were also detected. Antinucleolar antibodies by immunofluorescence (1/80) and immune complexes by Raji cell assay (IgG 1/32; IgM 1/8; IgA 1/4) were also found, while white blood cell count, platelets, CH₅₀, C3, and C4 were all normal and Coombs' test was negative.

Plasma exchange was started in association with prednisone and antihypertensive drugs (β blockers, prazosin, and enalapril).

Renal echotomography and angiophotoscintiscan showed a small and poorly perfused left kidney, while the right one presented cortical irregularities. Selective angiography showed a high grade stenosis of both renal arteries at their origin (fig 1). The left artery also had several filling defects extending into the intrarenal branches, which were interpreted as revascularised thrombosis (fig 2). Distal to the ostial stenosis, the right artery and its branches were normal. Riolan's arch was very prominent, probably owing to stenosis of the superior mesenteric artery (fig 1). Transluminal angioplasty by Grüntzig catheter was performed, obtaining an apparently appropriate dilatation of the right renal artery ostium, whereas the attempt made to insert the catheter into the left artery was unsuccessful. On the other hand, surgical revascularisation was discouraged owing to the diffuse involvement of the intraparenchymal vessels. After angiography and angioplasty the renal function deteriorated

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further. A subsequent renal scintiscan showed reduced blood flow also involving the right kidney. Treatment with oral anticoagulants (warfarin) was therefore added.

Figure 1: Renal angiography shows marked stenosis of both renal arteries at their origin. The left one presents several filling defects. Hypertrophic Riolan's arch is also evident.

Figure 2: Selective angiography of the left renal artery: the magnification shows filling defects extending into the intrarenal branches.

One month later the patient developed neurological symptoms related to a cerebrovascular accident. Computed tomography showed an ischaemic area in the temporal lobe, suggestive of arterial thrombosis. Prednisone dose was increased and cyclophosphamide added. Subsequently, two episodes of leucopenia (white blood cells $<10^9/l$) occurred. Firstly (December 1986), enalapril, then (May 1987) cyclophosphamide were withdrawn, and a normal white blood cell count was obtained rapidly in both cases.

In August 1987 she was promptly readmitted to our institute because of severe hypertension (blood pressure 240/140 mmHg) with a further impairment of renal function. Diffuse erythema and arthritis of the right elbow, wrist, metacarpophalangeal, and proximal interphalangeal joints were also present. Steroid dose and plasma exchange rate were increased, and treatment with furosemide, spironolactone, and azathioprine was added. Within two weeks a good remission was achieved.

In December 1987 the hypertension and renal function worsened again. Angiotensin converting enzyme inhibitors were restarted, but leucopenia (white blood cells $1.5 \times 10^9/l$) and severe anaemia (haemoglobin 7 g/l) arose. Plasma exchange, azathioprine, and angiotensin converting enzyme inhibitors were withdrawn and the prednisone dose increased, resulting in a slow rise in haemoglobin concentration and white blood cell count.

The patient is now (January 1989) receiving prednisone (30 mg daily), β blocking agents, and anticoagulants, and her general condition remains satisfactory.

Figure 3 shows the variation in blood pressure, serum creatinine, lupus anticoagulant, and anticardiolipin antibodies with time and the effect of the major treatments.

Figure 3: Variation of blood pressure, serum creatinine, 'lupus anticoagulant', and anticardiolipin antibodies over two years. Major treatments are also indicated. RVVT=Russell's viper venom time; aCL=anticardiolipin; ELISA=enzyme linked immunosorbent assay; BP=blood pressure; S-CREAT=serum creatinine; CYCLOPH=cyclophosphamide; PREDN=prednisone; PE=plasma exchange; AZA=azathioprine.

Discussion

Recently, the term 'antiphospholipid syndrome' has been introduced to describe patients presenting venous and arterial thrombosis, recurrent abortions, and thrombocytopenia, associated with antiphospholipid antibodies, namely lupus anticoagulant and anticardiolipin antibodies.¹⁴

The various localisations of arterial thrombosis include cerebral,^{5-8 15 16} retinal,¹⁷ coronary,¹⁸ mesenteric,^{10 19} and peripheral vessels,^{16 20} but to the best of our knowledge renal artery thrombosis has never been reported. Only two cases of renal infarction have been described: one patient presented with asymptomatic segmental infarction²¹ and the other with haematuria and severe loin pain, which were attributed to infarct of the kidney.²²

Renal artery thrombosis is a rather rare condition occurring after abdominal trauma and, less commonly, after direct lesions of the renal artery.¹ It has been also reported in polyarteritis nodosa²³ and a single case of spontaneous thrombosis has also been described.²⁴ In all these reports no data are available about the presence of antiphospholipid antibodies.

In our patient thrombosis of the renal artery was associated with hypertension and renal failure. The case also fulfilled sufficient American Rheumatism Association classification criteria for systemic lupus erythematosus²⁵—namely, erythema, pericarditis, arthritis, and a false positive serological test for syphilis. Renal involvement, seizures, and leucopenia also appeared, but they might have been related to the concurrent hypertension or treatment, or both. Antinuclear antibodies with a nucleolar pattern were also present, and, although rare, they have been detected in systemic lupus erythematosus.²⁶

Absence of a relation between antiphospholipid antibodies anti-double-stranded DNA and anti-extractable nuclear antigen antibodies has been reported in several studies.^{7 9 27} Similarly, there seems to be no relation between antiphospholipid antibodies and circulating immune complexes or decreased complement levels.²⁷ Furthermore, multiple and severe arterial and venous thrombosis has been described in cases with clinically and serologically quiescent systemic lupus erythematosus.^{7 20 28} Our patient also developed multiple thrombosis, as shown by the cerebrovascular accident and the probable mesenteric artery occlusion demonstrated by the Riolan's arch hypertrophy and acute abdominal pain and vomiting.

Increasing evidence suggests that a cause and effect relation between antiphospholipid antibodies and thrombosis exists.^{6 16}

It has also been reported that the increase of antiphospholipid antibody levels has a predictive value for thrombosis.²⁹ Our case confirms this view as increased levels of lupus anticoagulant were detected in several blood samples just before the disease relapsed.

Surgery, which is the definitive treatment for renovascular hypertension,² was not attempted in our patient owing to the diffuse involvement of intrarenal arteries. Transluminal angioplasty

was not successful and caused further renal damage. Thus the control of high blood pressure was achieved with rather high doses of several antihypertensive drugs. Angiotensin converting enzyme inhibitors were particularly useful, but both captopril and enalapril were suspected to have produced leucopenia. Oral anticoagulants were also continuously given to prevent recurrent thrombosis, as suggested by Asherson *et al*,³⁰ but cerebral injury supervened two months after warfarin was started. Steroids, immunosuppressive drugs (cyclophosphamide or azathioprine), and plasma exchange were used to reduce the production and increase the removal of antiphospholipid antibodies.²⁸ This therapeutic regimen brought about a slow but definite reduction of lupus anticoagulant and anticardiolipin antibody levels.

Our report deals with the first case of renal artery thrombosis and hypertension occurring in a young patient with antiphospholipid syndrome and systemic lupus erythematosus, further extending the group of conditions which can determine renovascular hypertension and severe high blood pressure in systemic lupus erythematosus. Plasma exchange, immunosuppressive drugs, steroids, and anticoagulants may be useful in the antiphospholipid syndrome where no clear therapeutic guidelines seem yet available.

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