Case report

Aortic occlusion in systemic lupus erythematosus associated with antiphospholipid antibodies

P DREW,¹ R A ASHERSON,² R J ZUK,¹ F J GOODWIN,¹ AND G R V HUGHES

From the ¹Department of Nephrology and Morbid Anatomy, The London Hospital, Whitechapel; and the ²Lupus Arthritis Research Unit, The Rayne Institute, St Thomas's Hospital, London

SUMMARY The patient, a Caucasian woman of 22 years, developed malignant hypertension at the age of 16 years. An abdominal bruit was found on routine examination. She had two spontaneous abortions and systemic lupus erythematosus was diagnosed at age 21 years. She was found to have a persistently low positive VDRL and antibodies to mitochondria were also present on repeated examinations, to a titre of 1/160. Because of angiographic findings, demonstrating an occlusion of the aorta, an endarterectomy of the descending thoracic and upper abdominal aorta was performed. This showed mainly intimal thickening and the presence of thrombus. She then had four further spontaneous abortions (with good blood pressure control). The lupus anticoagulant and antibodies to cardiolipin were found to be positive at this time.

Key words: aortic coarctation, recurrent abortions.

The thrombotic manifestations occurring in association with the antiphospholipid antibodies ('lupus anticoagulant', antibodies to cardiolipin and the false positive test for syphilis—Venereal Disease Research Laboratory (VDRL)) are usually found in the venous system.^{1,2} They include, not only deep vein thromboses, affecting mainly leg veins, but other veins as well, such as renal,³ axillary,⁴ or superficial thrombophlebitis.⁵ Retinal vein occlusions, uncommon in systemic lupus erythematosus (SLE), have also been reported in association with these antibodies, and in these patients they occurred together with retinal arterial involvement.^{6,7}

Large vessel arterial occlusions are unusual in SLE and may be vasculitic in origin. Vasculitis is also usually responsible for smaller vessel distal infarctions which occur in the vicinity of the nail fold. Occasionally they may be more extensive, resulting in larger gangrenous areas of the fingers or toes.

It has become evident since the introduction of

the anticardiolipin antibody test that there are patients who do not have vasculitic lesions on histological examination who have raised levels of anticardiolipin antibodies, show the presence of the 'lupus anticoagulant', and perhaps show other manifestations of the antiphospholipid syndrome.⁸ These patients present with or develop large vessel occlusive disease during the course of classical SLE or even more commonly during a 'lupus-like' illness.¹⁰

Case report

In 1971 a 16 year old girl presented to hospital complaining of severe headaches and was found to have malignant hypertension. Apart from a blood pressure of 200/150 mmHg and a grade IV hypertensive retinopathy she was also noted to have an abdominal bruit. Preliminary investigations showed normal plasma urea and electrolytes, a negative VDRL test, and normal chest x ray and intravenous pyelogram (IVP). Both the patient and her parents declined further investigations at this stage. Her blood pressure was well controlled by treatment with methyldopa and a thiazide diuretic, and she was discharged for outpatient review.

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Correspondence to Dr R A Asherson, The Rayne Institute, St Thomas's Hospital, London SE1 7EH.

Over the next few years she suffered intermittently from depression. Methyldopa treatment was withdrawn and blood pressure satisfactorily controlled with diuretic therapy alone, but despite

Fig. 1a

Fig. 1b

Fig. 1 (a) Proximal aortography showed occlusion of the aorta just above the diaphragm (partly obscured by the spine in the photograph) with dilatation of the proximal aorta and a collateral circulation. The internal mammary artery is marked with an arrow. (b) Distal aortography showed patent renal arteries but occlusion of the aorta just above the level of the coeliac axis. This distal aorta appears hypoplastic and the splenic artery is enlarged.

this she required periods of psychiatric treatment. She married, but after an unsuccessful pregnancy, which was complicated by hypertension, she was referred to The London Hospital for a second opinion. When seen she was pregnant for the second time and hypertensive with systolic blood pressure recordings greater than 200 mmHg in both arms. Again she was noted to have a loud abdominal bruit and was found to have greatly diminished pulses in both legs. Systolic pressures in both legs were recorded at less than 100 mmHg. There was no evidence of exudative retinopathy and routine urine analysis was normal. She was admitted to hospital and subsequently had a spontaneous abortion. Further investigations showed normal renal function; VDRL test positive 1/4; fluorescent treponemal antibody (FTA) test and *Treponema pallidum* haemagglutination (TPHA) test negative; the antinuclear factor (ANF) diffuse positive at 100 U/ml; antimitochondrial antibodies positive 1/160; deoxyribonucleic acid (DNA) binding normal; diffuse hypergammaglobulinaemia on serum electrophoresis; reduced levels of serum complement, with C4 component of 70 mg/l (normal range 200–550 mg/l) and CH₅₀ of 27 U/ml (normal range 30–50 U/ml) but slightly raised C3 component at 1550 mg/l (normal range 650–1450 mg/l) (Table 1). Selective renal arteriography showed no evidence of a renal artery stenosis, but aortography showed almost complete obliteration of the aorta over a 6 cm segment immediately above the take off of the coeliac axis. The lower intercostal arteries on the left and the internal mammary artery on the right were found to be moderately dilated, supplying a collateral circulation around the obliterated segment of the aorta (Figs 1a and b).

In May 1979 an endarterectomy of the descending thoracic and upper abdominal aorta was performed, a large section of grossly thickened cartilaginous vessel was removed and a Dacron patch inserted over the defect. Histology of the resected specimen showed that it was mostly intima, thickened with fibrous tissue and focal calcification and with adherent recent thrombus. There were no other diagnostic features (Fig. 2).

Postoperatively, her blood pressure fell to levels of around 110/80 mmHg, and she required no drug treatment. Over the next four years she had three spontaneous abortions; none of the pregnancies were associated with development of high blood pressure. Further investigations were performed and included VDRL positive 1/16; FTA and TPHA negative, ANF positive 1/40, with nucleolar pattern; antimitochondrial antibodies positive 1/40; DNA binding 21 U/ml, repeated 10 U/ml (normal range 0–25 U/ml); IgM anticardiolipin antibodies strongly

Table 1 Laboratory investigations

Test	Units	May 1979	July 1984	March 1986
VDRL	Positive titre	1/4	1/16	1/8
ANF	Positive titre	1/40	1/40	1/160
C4 complement	mg/l (normal 200-550)	70	—	100
C3 complement	mg/l (normal 650-1450)	1550	—	820
CH ₅₀ complement	U/ml (normal 30-50)	27	—	18
DNA binding	U/ml (normal 0-25)	25	21	30
Anticardiolipin antibodies (IgM)	Standard deviations above mean (n <2.25)	—	10	4.5
Dilute thromboplastin test for lupus anticoagulant	Positive/negative	—	Strongly positive	Weakly positive
IgM cryoglobulins	mg/l	—	—	180

positive, IgG anticardiolipin antibodies negative; dilute thromboplastin test for lupus anticoagulant positive (Table 1). During the course of these investigations she was found to have carcinoma in situ of the uterine cervix and underwent cone biopsy. Consideration was given to the possibility of steroid treatment in an attempt to produce a

successful pregnancy, but the patient and her husband decided that they did not want to proceed with any further pregnancies and her husband underwent vasectomy.

During 1984 she again developed a high blood pressure with diastolic recordings consistently above 100 mmHg. Atenolol treatment was started with a satisfactory result. In March 1986 she presented with an ulcer under her right great toe which was subsequently biopsied. Histology of the biopsy specimen showed an area of epidermal necrosis overlying dermis which contained several small and medium sized blood vessels. There was marked perivascular mononuclear cell infiltration with destruction of vessel walls. Two medium sized veins contained organising thrombi and also appeared to be involved in the vasculitic process. No fibrinoid necrosis was seen (Fig. 3). Further investigations at this stage confirmed the presence of the lupus anticoagulant and again showed the serum ANF positive at a titre of 1/160 with a nucleolar pattern. DNA binding was minimally raised at 30 U/ml. Anticardiolipin antibodies were positive and an IgM cryoglobulin was detected in a concentration of 180 mg/l. Serum C4 and CH₅₀ complement were again

Fig. 2 Representative area of endarterectomy specimen showing (1) thickened fibrotic intima with focal calcification; (2) adherent recent thrombus; (3) thin outer rim of media.

Fig. 3 Representative area of dermis showing two medium sized veins containing organising thrombi and marked perivascular mononuclear cell infiltration.

found to be reduced, but serum C3 complement was normal (Table 1). Atenolol treatment was stopped and hypertension controlled with a small dose of enalapril. Treatment with prednisolone and azathioprine was started, and the ulcer slowly healed over the next few weeks. After six months' immunosuppressant treatment there was no further ulceration, though she had developed several tender, non-ulcerating nodules on the underside of her toes, which have resolved without further intervention. Blood pressure was satisfactorily controlled at 140/90 mmHg by treatment with enalapril 5 mg/day, and systolic blood pressure was the same in all four limbs. Repeat tests for cryoglobulins have been performed and show that these are still detectable but at a lower concentration of 72 mg/l.

Discussion

The patient reported is a unique case. She had persistently positive 'lupus anticoagulant' and antibodies to cardiolipin and a false positive VDRL test over a number of years. The manifestations of the 'antiphospholipid syndrome' in her case included five spontaneous abortions but, more importantly, obliteration of a 6 cm segment of the aorta immediately above the take off of the coeliac axis. Aortography demonstrated the probable presence of a collateral circulation via the lower left intercostal arteries and the right internal mammary artery (Figs 1a and b). There had been no evidence of renal artery stenosis, but hypertension had been a problem since the age of 16. Ulceration of the toes which occurred subsequently was proved by biopsy to be due to a vasculitic process.

The histology of the resected portion of the vessel showed thickened intimal tissue demonstrating fibrosis and focal calcification with adherent recent thrombus. There was no evidence of aortitis (Fig. 2).

This case represents the first record of a patient who developed aortic occlusion in association with antiphospholipid antibodies. Lesions of the aorta and its branches in SLE have been infrequently reported and are considered as distinctly rare. A report of Lessof and Glynn in 1959 appears to have been the first recorded case of this association, and their patient presented with a 'pulseless syndrome' affecting the upper extremities.¹¹ Interestingly, that patient showed a false positive Wassermann reaction.

Ferrante *et al* described a 19 year old woman with a left subclavian artery occlusion,¹² and Asherson *et al* in 1985 reported a similar patient, who had the lupus anticoagulant, antibodies to cardiolipin, and a false positive VDRL test.¹³ This patient has since

developed recurrent cerebral infarctions and multi-infarct dementia, a not uncommon development in these patients.¹⁴ Another similar patient recently treated by the same group went on to develop gangrene and required amputation of three digits of her left hand.¹⁵ Six patients with large vessel occlusions and gangrene in SLE, four of whom demonstrated antiphospholipid antibodies, were recently recorded by Asherson *et al*,¹⁶ who also described mesenteric occlusions in association with these antibodies.^{17 18} In all patients where histological material was available no evidence of vasculitis was found. Usually the pathology showed the presence of thrombus and severe intimal proliferation similar to that seen in the present case.

The commonest site for arterial occlusions in association with antiphospholipid antibodies is the cerebral vasculature,¹⁹ the middle cerebral artery being most frequently affected, but often multiple vessels are occluded^{20 21} and a variety of central nervous system (CNS) symptomatology is encountered. Transient ischaemic attacks, recurrent strokes, and epilepsy are commonly seen. Migraines are a frequent prodrome or accompaniment of these events.⁸ Whether the other CNS symptomatology such as chorea, transverse myelitis, Guillain-Barré syndrome, or optic neuritis occur on an ischaemic basis or are due to antigen-antibody reaction between brain antigens and antiphospholipid antibodies is unclear.⁹

Takayasu's arteritis can cause a similar clinical picture. Upper abdominal aortic involvement is usually asymptomatic, whereas lower abdominal narrowing may result in intermittent claudication or even gangrene.²² In addition to the case described by Lessof and Glynn,¹¹ LE cells have been reported in two other early cases.²³

Takayasu's arteritis presents a different picture from the present case. Necrosis and fragmentation of the elastic tissue of the media and internal laminae are associated with an irregular pan arteritis with perivascular round cell infiltration in the adventitia. Occasionally granulomatous changes (including multinucleated giant cells) may be demonstrable within the media and calcification may be found. Superimposed atheromatous changes are usually present.²²

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