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Normal pregnancy in renal transplant recipient with history of eclampsia and intrauterine death

The only case of eclampsia in a renal transplant recipient was reported in 1979 from this unit.¹ The patient's subsequent pregnancy was not complicated by hypertension and had a normal outcome, as is reported here.

Case report

The patient originally presented in 1973, aged 14 years, with hypertension and the nephrotic syndrome due to mesangiocapillary glomerulonephritis. In 1977 she received a cadaveric renal transplant (with no HLA antigens in common) that functioned well after three rejection episodes.

In 1979 she presented at the antenatal clinic with a 20-week pregnancy. She was normotensive, and the pregnancy progressed uneventfully until 30 weeks, when she developed an acute fulminating hypertensive illness (blood pressure 170/130 mm Hg, proteinuria 1 g/24 h) resulting in eclampsia and intrauterine death. She was treated with diazepam and hydralazine. She was delivered vaginally of a female stillborn infant weighing 2193 g after induction of labour with prostaglandin E₂. Recovery was uneventful, her blood pressure settled to 140/90 mm Hg, and the proteinuria diminished. The figure shows renal function after transplantation.

Serial measurements of plasma creatinine concentration, creatinine clearance, and urine protein excretion after transplantation.

Conversion: SI to traditional units—Plasma creatinine: 1 $\mu\text{mol/l} \approx 0.01 \text{ mg/100 ml}$.

The patient was advised against further pregnancies but conceived again 17 months later, accepted the risks to her kidney, and continued with the pregnancy, which progressed without complication. Clear liquor drained spontaneously at 37 weeks and was followed by a low forceps delivery of a healthy female infant weighing 3530 g. Renal function remained unimpaired during and after pregnancy, blood pressure did not exceed 145/90 mm Hg, and proteinuria remained less than 0.25 g/day.

Drug treatment consisted of immunosuppression with prednisolone 12.5 mg and azathioprine 150 mg daily. Antihypertensive treatment comprised propranolol 160 mg, hydralazine 50 mg, and bendroflumazide 5 mg daily at the time of the first pregnancy and labetalol 300 mg and hydralazine 50 mg daily at the time of the second pregnancy.

Comment

The occurrence and course of hypertension in pregnancy are unpredictable, and this case exemplifies the difficulty in advising patients about the risks. Incorrect advice had initially been given to this patient. In retrospect, the hypertensive illness in the first pregnancy was classical toxæmia of pregnancy and not complicated renal hypertension, which would be expected to recur in subsequent pregnancies.

The risks of damage to the renal transplant associated with pregnancy are well documented.^{2,3} Some patients, however, are willing to accept these in the hope of a successful outcome. Eclampsia in the first pregnancy need not be a contraindication to further pregnancies in renal transplant recipients, even in the presence of mild hypertension.

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Exercise testing in assessment of hypertension

Recently Millar-Craig *et al* claimed that maximal and submaximal exercise measurements of blood pressure may provide a better estimate than casual resting values of blood pressure outside the clinic.¹ We carried out a study of blood-pressure response to exercise testing to define a normotensive and a hypertensive response pattern.

Patients, methods, and results

We studied 28 normotensive volunteers aged 35 ± 2 years and 35 patients with untreated hypertension aged 42 ± 1 years. Hypertension was diagnosed when diastolic blood pressure was ≥ 95 mm Hg on three consecutive occasions. A standard ergometric exercise test was performed, the work load being increased at three-minute intervals from 3000 N m (300 kp m) to 4500 N m (450 kp m) and finally 6000 N m (600 kp m). Blood pressure and pulse were measured at the end of each interval. On conclusion the exercise was stopped abruptly and blood pressure and pulse recorded after one and five minutes' rest. Results are expressed as means $\pm$ SE. Statistical analyses were performed with the one-tailed *t* test.

The data obtained in the normotensive group were used to construct a "one-tailed" nomogram. At every point of the exercise testing mean systolic blood pressure and diastolic blood pressure $+1.65$ SD were plotted (figure). A normotensive response to exercise was defined as diastolic blood pressure < 90 mm Hg at the baseline reading and at a work load of 6000 N m; a hypertensive response was defined as diastolic blood pressure ≥ 95 mm Hg at the baseline reading and > 95 mm Hg at a work load of 6000 N m (figure).

Systolic blood pressure in the normotensive subjects was 116 ± 4 mm Hg before exercise, rising to 168 ± 4 mm Hg at 6000 N m. Diastolic pressure was 77 ± 1 mm Hg initially and remained virtually unchanged; after one and five minutes' rest it was 66 ± 2 and 69 ± 2 mm Hg respectively. In the

patients with hypertension baseline systolic blood pressure was 148 ± 2 mm Hg, rising to 207 ± 5 mm Hg at 6000 N m. Baseline diastolic pressure was 100 ± 1 mm Hg, increasing to 111 ± 2 mm Hg at 6000 N m ($p < 0.01$) and falling to 95 ± 2 mm Hg and 93 ± 3 mm Hg after one and five minutes' rest. The diastolic pressure in the hypertensive compared with the normotensive subjects showed a distinctly different pattern of response at maximum exercise: in the patients it rose by 11 ± 2 mm Hg while in the normotensive subjects there was no change. A repeat test in eight hypertensive patients three to six months later yielded nearly identical results.

Blood-pressure response to graded exercise in untreated hypertensive subjects ($n=35$) plotted against nomogram obtained from results in normal individuals ($n=28$). Unbroken line of nomogram represents mean blood pressures; broken line represents mean $+1.65$ SD; and hatched area shows upper boundary of 95% confidence limit.

Conversion: SI to traditional units—1 N m ≈ 0.1 kp m.

Comment

It has recently been claimed that changes in blood pressure during exercise may be better correlated with ambulatory measurements than with casual resting blood pressure.¹ Moreover, assessment of ambulatory pressure may have a predictive value for cardiovascular risks (M Soklow, D Perloff, R Cowan, unpublished observations). Hamer *et al*² suggested that during exercise the effect of nervous influences on arterial tone is abolished; therefore, measurements made during exercise may offer a more reliable estimate of the degree of hypertensive vascular changes.

The present study serves as a model for evaluating the blood-pressure response to exercise in normotensive and hypertensive subjects. Hypertensive patients were characterised by a rise in diastolic pressure, while in normotensive subjects diastolic pressure remained unchanged. This rise in diastolic pressure may be attributable to an inability of hypertensive patients to reduce peripheral resistance to the same extent as normotensive subjects during exercise, a phenomenon reported by other workers.³ In contrast to these findings, Lund-Johansen³ reported a rise in diastolic blood pressure in normotensive subjects, but other workers have observed a fall.⁴ The discrepancy between these studies may be partly due to different methodological approaches, since the position of the body during exercise influences the pattern of response.³

In the present study the mean age was slightly higher in the hypertensive than the normotensive subjects; therefore a comparison was made with an age-matched group of normotensive subjects. The pattern of response showed the same differences, excluding the possibility of age as a contributing factor to the different responses.

Fourteen hypertensive patients retested after drug treatment had achieved normal resting blood pressures. On repeat exercise testing six manifested a normotensive response while eight maintained a hypertensive response irrespective of type or dose of medication. These preliminary data indicate that exercise testing may be a useful tool for assessing hypertension and evaluating the efficacy of treatment.

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Transient monoclonal gammopathy in hydralazine-induced lupus erythematosus

Hydralazine-induced lupus erythematosus was observed commonly when the drug was used at high doses, and the daily dose is now customarily limited to 200 mg to avoid this complication. The syndrome still, however, occurs in 3-4% of patients when the dose is limited in this way.^{1,2} It occurs almost exclusively in slow acetylators. We describe a case of hydralazine-induced lupus erythematosus with transient monoclonal gammopathy, an association that to our knowledge has not been reported before.

Case report

Severe hypertension (250/140 mm Hg) was diagnosed in 1972 in a woman aged 57 years. She had stable mild renal impairment (blood urea concentration 13-15 mmol/l (78-90 mg/100 ml)) and in 1979 suffered a small stroke. In January 1979 hydralazine was started, and she was maintained on 50 mg twice daily from April 1979. In addition she took atenolol, methyldopa, and cyclopentiazide. In July 1980 (when aged 65 years and after 18 months of treatment with hydralazine, the total dose being about 52 g) she was admitted with a further small stroke, from which she made an uncomplicated recovery. She complained also of anorexia and general ill health and had lost 15 kg in weight over 18 months (table). She had noted mild pain in her right shoulder but did not have pleurisy or a rash.

On examination she was ill and anaemic and had hepatosplenomegaly. Blood pressure was 160/80 mm Hg. Investigations showed a high erythrocyte sedimentation rate (130 mm in the first hour); pancytopenia (haemoglobin concentration 7.8 g/dl, white cell count $3.4 \times 10^9/l$, and platelets $108 \times 10^9/l$); low serum albumin concentration (24 g/l); high globulin concentration (43 g/l); presence of antinuclear factor (titre of 1/500); and a weak positive titre of antibody to double-stranded DNA. She was a slow acetylator. Tests for haemolysis and deficiency of iron, vitamin B₁₂, and folate yielded negative results. An IgM kappa monoclonal was present at a concentration of 16.7 g/l. Further investigation suggested that this was a benign monoclonal as concentrations of IgG (12.6 g/l) and IgA (2.3 g/l) were normal, Bence-Jones protein was absent, skeletal x-ray films showed no evidence of myeloma, and the bone marrow showed plasma cells normal in both number and morphology. Plasma viscosity was slightly raised at 1.94 mPa s (cP) (normal 1.5-1.72 mPa s).

A presumptive diagnosis of hydralazine-induced lupus erythematosus with a coincidental benign monoclonal gammopathy was made, and hydralazine was stopped. The symptoms, signs, and laboratory abnormalities associated with the lupus syndrome resolved completely over the next few months (table). During the same period the concentration of the IgM monoclonal decreased and eventually disappeared. She subsequently remained in good health.

Comment

An illness characterised by weight loss, ill health, hepatosplenomegaly, a high erythrocyte sedimentation rate, pancytopenia, low albumin and high globulin concentrations, and a high titre of antinuclear factor occurring in a slow acetylator 18 months after the start of treatment