Failure of captopril to reverse the renal crisis of scleroderma

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SUMMARY Captopril, an oral inhibitor of angiotensin converting enzyme, has recently been described as causing a dramatic reversal of the renal crisis in scleroderma in 2 patients¹. We report here 2 patients with scleroderma, hypertension, and rapidly deteriorating renal function who were given captopril. Despite good blood pressure control, captopril had no effect on renal function, both patients requiring long-term haemodialysis.

Case reports

CASE 1

A 63-year-old white woman, known to have had Raynaud's phenomenon in her hands for at least 20 years, was found to have skin changes typical of scleroderma in her hands in May 1977. At that time renal function and blood pressure were normal. By January 1978 the scleroderma was involving her face and trunk, and she was started on D-penicillamine. In June 1978 proteinuria was noted for the first time, and her blood pressure was mildly raised at 140/98 mmHg. The glomerular filtration rate, as measured by EDTA clearance, was impaired at 53 ml/min. A renal biopsy showed changes consistent with chronic interstitial fibrosis. There were no arterial or glomerular changes suggestive of scleroderma. Electron microscopy revealed subepithelial deposits suggestive of early membranous glomerulonephritis. In view of the renal changes, the penicillamine was stopped and treatment with melphalan and cryoheptidine was given for 3 months. In November 1979, when she was off all treatment, her blood pressure was 140/90 mmHg.

However, in December 1979 she was feeling unwell and her blood pressure had risen to 180/110 mmHg and her fundi showed papilloedema, haemorrhages and exudates. She was admitted to hospital for control of her blood pressure. Propranolol was started, but her blood pressure remained poorly controlled, and 10 days later she went into left ventricular failure and had a cardiac arrest. Her plasma creatinine by then had risen to 177 $\mu\text{mol/l}$. Attempts were made to control her blood pressure with increasing doses of diuretics and hydralazine, but her

creatinine continued to rise to 230 $\mu\text{mol/l}$ and her blood pressure was not well controlled. Plasma renin activity measured at this time was 29.9 ng/ml/h (normal range 0.5-2.5). A diagnosis of renal scleroderma crisis was made.

Captopril was started at an initial dose of 3 mg and then gradually increased over the next few days to 25 mg t.d.s. Blood pressure was well controlled, but her renal function continued to deteriorate. Her plasma creatinine had risen to 849 $\mu\text{mol/l}$. She was oliguric, and haemodialysis was started 10 days after starting captopril. Captopril was continued at a dose of 12.5 mg t.d.s. for the next 6 months, with good control of her blood pressure but with no improvement in renal function or scleroderma. The patient remains on long-term haemodialysis.

CASE 2

A 49-year-old white woman was first seen in October 1978 when she complained of Raynaud's phenomenon that had been getting worse over several months. At that time thickening of her skin was noted over her fingers, hands and distal forearm. A skin biopsy confirmed the diagnosis of scleroderma. Her blood pressure at this time was 140/90 mmHg and her plasma creatinine was 69 $\mu\text{mol/l}$. She was started on D-penicillamine and followed up regularly in the clinic. The scleroderma progressed to involve her face, trunk and lower limbs. Blood pressure and renal function remained normal. In March 1980 she presented in the Casualty Department with a history of nausea and dyspnoea for 10 days and ankle swelling for 4 days. Her blood pressure was 200/120 mmHg and her fundi showed papilloedema and exudates. Plasma creatinine was 863 $\mu\text{mol/l}$, and plasma renin activity was 8.28 ng/ml/h (normal range

0.5–2.5). In view of the left ventricular failure and renal impairment she was dialysed.

Captopril was started that evening at a dose of 12.5 mg q.d.s. This resulted in good control of her blood pressure, but there was no improvement in renal function or scleroderma, and she remains on haemodialysis.

Discussion

Sudden and rapid deterioration in renal function associated with severe hypertension is a well recognised complication of scleroderma and is referred to as the renal scleroderma crisis. Fifteen of the 210 patients (7%) with scleroderma seen at Columbia Presbyterian Medical Center from 1952 to 1972 developed this complication². Hyper-reninaemia occurs during the renal scleroderma crisis² and has been suggested as being an important factor in the pathogenesis of this crisis³. Captopril, an oral inhibitor of angiotensin converting enzyme, has been reported to reverse the renal crisis in 2 patients to whom it was given¹. The first patient was given captopril at a time when creatinine clearance was 39 ml/minute; good blood pressure control was achieved, and 2 weeks later the creatinine clearance was 65 ml/minute. The second patient had a creatinine clearance of 15 ml/minute when started on captopril, and one week later it had risen to 33 ml/minute. However, in neither of these 2 patients was there evidence of rapidly deteriorating renal function. Return of renal function has also been described in patients with renal scleroderma crisis when blood pressure control has been achieved by conventional treatment even after the patient has been on dialysis for some months⁴.

In the 2 patients reported on here there was evidence of activation of the renin-angiotensin systems, and in both the blood pressure was well controlled with small doses of captopril. Despite blockade of the formation of angiotensin II, renal function continued to deteriorate in the first and failed to improve in the second patient, and there was no improvement in either patient's scleroderma. Both these patients had evidence of advanced disease at the time captopril was started. There is evidence that the renin-angiotensin system is activated in patients with scleroderma whose renal biopsies show vascular abnormalities but whose renal function is normal.^{5,6} This suggests that, if the raised angiotensin II levels contribute to the deterioration in renal function, captopril should if possible be given at an early and more reversible stage.

References

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