SHORT REPORTS

Therapeutic venous infarction of an aldosterone producing adenoma (Conn’s tumour)

Primary aldosteronism accounts for about 1% of the hypertensive population. It may be due to an aldosterone producing adenoma (Conn’s tumour), adrenal hyperplasia, or occasionally morphologically normal adrenal glands. The usual management of Conn’s tumours is surgical excision or maintenance treatment with spironolactone. Large doses of this drug may be needed, however, in combination with other antihypertensive agents and this may produce untoward side effects. We describe a patient whose Conn’s tumour was treated by superselective catheterisation and venous infarction.

Case report

A 55 year old woman with an eight year history of hypertension had been found to be hypokalaemic two years previously, the lowest potassium concentration (1.7 mmol/L) being recorded when she was not taking spironolactone. Her medical management was complicated by severe side effects of her drugs. Laboratory investigations suggested a diagnosis of primary aldosteronism. A left adrenal aldosterone producing adenoma was confirmed by computed tomography, 35S cholesterol scintiscanning, and venous sampling. She was thought to be a poor surgical risk and was referred to the Hammersmith Hospital for percutaneous tumour ablation. Under local anaesthesia, using the Seldinger technique, a catheter (French 7) was directed from the right femoral vein into the left adrenal vein. The adenoma was clearly visualised (figure). A coaxial catheter (French 3) was inserted through the larger catheter, manipulated into the tumour vein (figure), and a mixture of 0.5 ml absolute alcohol and 0.5 ml contrast medium (iodohexol) injected into the tumour. The sclerosant mixture filled the venous network of the tumour and rapidly abolished flow in the opacified vessels.

After the procedure the patient experienced a little discomfort in her left loin, which was controlled with mild analgesics, and a fever of 38°C subsided after three days without antibiotics. Labetalol and hydralazine were withdrawn and her blood pressure remained well controlled. She was discharged home taking spironolactone (200 mg daily) only, which was stopped six weeks later. Computed tomography showed a reduction in tumour size and a 35Se cholesterol scintiscan showed normal uptake on the right but no uptake on the left gland. Blood pressure and plasma aldosterone and plasma and urine electrolyte concentrations remained normal when she had stopped all drugs. Twelve months after tumour ablation the patient remained normokalaemic without spironolactone and had needed only a small dose of a ß adrenoceptor antagonist (candesartan 40 mg twice daily) to control her blood pressure.

Comment

Conn’s tumours are usually hypovascular; this and the fact that the adrenal gland receives its arterial supply from at least three different sources mean that it is not feasible to embolise these tumours by the arterial route, the approach normally employed for tumour embolisa-
Cyclosporin A nephrotoxicity related to changes in haemoglobin concentration

Cyclosporin A is increasingly being used for patients undergoing bone marrow and solid organ grafting. Also preliminary results show that cyclosporin A may be of benefit in some autoimmune diseases, including primary biliary cirrhosis.1 Of the side effects of cyclosporin A, nephrotoxicity is the most common; this is largely dose dependent and reversible,2 and with careful monitoring of cyclosporin concentrations in blood or plasma the frequency of the complication may be reduced. We describe four patients with primary biliary cirrhosis receiving cyclosporin A in whom the development of nephrotoxicity was unexpected and shown to be related to a fall in haemoglobin concentration associated with a rise in plasma cyclosporin values.

Case histories

The four patients (two women; age range 56-63) had primary biliary cirrhosis at the cirrhotic stage diagnosed by liver biopsy. Serum bilirubin concentrations ranged from 25 to 98 μmol/l (1.5 to 5.7 mg/100 ml) (median 60 μmol/l (3.5 mg/100 ml); upper limit of normal 15 μmol/l (0.9 mg/100 ml)). All four were participating in a pilot study to determine a therapeutic and non-toxic dose of cyclosporin before a formal double blind, prospective controlled trial. The patients had normal renal function on admission to the study, as evidenced by normal serum creatinine and urea concentrations and creatinine clearance.

Cyclosporin A (3 or 4 mg/kg/day) had been administered at a constant dose for at least three months before the occurrence of complications, and during this time the serum creatinine concentration had remained below 100 μmol/l (1.1 mg/100 ml). Trough plasma concentrations of cyclosporin A, as measured by radioimmunoassay, were maintained in the therapeutic range below 200 μg/l—a concentration that is effective in correcting the in vitro suppressor cell abnormalities of patients with primary biliary cirrhosis,3 although a little lower than that currently aimed at in prevention of graft rejection.

Subsequently, in association with a fall in haemoglobin concentration, there was a rise in serum creatinine and trough plasma cyclosporin A values (figure). In two cases falls in haemoglobin of 5-6 g/dl and 2-6 g/dl were due to gastrointestinal haemorrhage, from varices and gastric erosions respectively. In the other two the haemoglobin concentration fell by 0-8 g/dl and 2-3 g/dl and the blood film showed a macrocytosis, which after investigation was attributed to chronic liver disease and myxoedema. In the two patients with blood loss the dose of cyclosporin A was maintained and correction of the anaemia by blood transfusion and iron supplements was accompanied by a return of serum creatinine and plasma cyclosporin A to previous values. In the other two the dose of cyclosporin A was reduced, with a concomitant fall in serum creatinine concentration. In all patients serum lipoprotein concentrations remained stable and normal throughout.

Comment

Cyclosporin A is extensively metabolised by the liver before being excreted into the bile and then undergoes enterohepatic circulation, though results obtained to date at a dose of 5 mg/kg/day in patients with primary biliary cirrhosis show the pharmacokinetics and metabolism of cyclosporin to be similar to those in normal subjects (Robson et al, unpublished data). In the blood cyclosporin A is bound predominantly to red cells (50%) and to a less extent leucocytes (20%); the remaining 30-40% of the drug is in the plasma, mostly bound to lipoproteins.4 In our patients we postulate that the rise in