recombinant interferon αA (Hoffmann-La Roche), receiving 9 MU daily intramuscularly for eight days followed by 3 MU daily for a week. At this stage the nodules on the chest wall were observed to be regressing. She developed malaise and headache, so during the third and fourth weeks of treatment the dose of interferon was reduced to 3 MU thrice weekly. By this time the nodules had completely regressed. After a week's break in treatment interferon 3 MU three times weekly was resumed for a further six weeks. The nodules had appeared again by week 9, and an excision biopsy of one showed epithelioid granulomas as before (figure). The assessable deposits of carcinoid tumour did not show any objective regression.6 Interferon was stopped after 11 weeks.

Comment

This patient's granulomas developed seven years after the implantation of the foreign material. The reason for their appearance at this time is unclear but may have been related to the withdrawal of chemotherapy. Histologically they had the appearance of allergic epithelioid granulomas. Their regression coincided with the administration of interferon in moderately high dose for the first 15 days of treatment. Their reappearance occurred after a break in treatment and the start of low dose, thrice weekly treatment, suggesting either a dose response relation or the development of resistance to interferon.

Interferons have a wide range of immunomodulatory functions,1 including inhibition of delayed hypersensitivity reactions4 and direct effects on the function of macrophages, such as enhancement of their motility and ability to phagocytose foreign particles.4 Allergic granulomas consist largely of epithelioid and giant cells, both of which arise from macrophages. This transformation may be mediated by lymphokines or other factors produced by lymphoid cells, which infiltrate granulomas to varying extents. Interferons may act either directly on macrophages or their derivatives or indirectly via the lymphocytes.

The interferon αA used in this study was produced by genetic engineering and is only one of a complex family of proteins whose functions are being elucidated. Granulomatous diseases such as sarcoidosis, Crohn's disease, and berylliosis may all be caused by a disturbed immune response to a foreign material or agent. This report suggests that there may be a role for interferons in the management of these diseases.

We thank Drs S De Garis and I Lenox-Smith of Hoffmann-La Roche for supplying the interferon.


(Accepted 24 April 1984)

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Donor ureteric calculus presenting as acute rejection in a renal transplant recipient

The morbidity that is associated with immunosuppressive treatment given for the rejection of a renal transplant makes the accurate identification and exclusion of non-immunological causes of deteriorating function essential. We report a case in which a ureteric calculus originating in the donor kidney (apparently unrecognised at transplantation) produced the clinical signs of acute rejection in the recipient.

Case report

A 24 year old man with end stage renal failure received a cadaveric renal transplant, which functioned immediately. During the first month after transplantation two episodes of deteriorating renal function (with normal isotope renograms and abdominal ultrasound) were diagnosed and treated as acute rejection. One month later he presented with deteriorating renal function and this time the transplanted kidney was enlarged. An abdominal ultrasound examination showed a dilated ureter and an intravenous urogram showed a calculus 0·6 cm in diameter in the lower ureter (see figure). Attempts to remove the calculus by Dormia extraction failed and the stone was removed by ureterolithotomy. The patient's recovery from the operation was uneventful, his renal function remained stable with a creatinine concentration of less than 200 μmol/l for a year, and the bone biochemistry remained normal throughout. The calculus contained calcium and phosphate.
The donor kidney came from a 36 year old woman who had died from a subarachnoid haemorrhage and who had not had any urinary problems. The recipient of the second kidney from this donor has had normal renal function and has shown no evidence of ureteric obstruction.

Intravenous urogram showing ureteric calculus originating in donor kidney.

Comment
Urological complications of renal transplantation are well recognised but, to our knowledge, this is the first case of ureteric obstruction resulting from a calculus in the donor kidney. The recipient's normal bone biochemistry and the time of presentation make it unlikely that the calculus arose de novo after surgery. Unless a calculus is particularly large it is unlikely to be recognised at retrieval surgery. Previous studies have emphasised the need for early detection in the management of the obstructed transplant ureter. The frequent use of an isotope renogram in preference to an intravenous urogram after transplantation may render early detection of such calculi more difficult.

Hyponatraemia induced by a combination of hydrochlorothiazide and triamterene

Hyponatraemia has become recognised as an adverse effect of treatment with diuretic drugs. The combination of hydrochlorothiazide and amiloride has been particularly blamed in several reports, and Brooks and Ritch suggested that amiloride might have a synergistic effect with the thiazide in producing the effect, although the mechanism of any such synergism is not clear. Potassium supplements are relatively ineffective in preventing hyponatraemia caused by diuretics, and this has given rise to a trend towards prescribing combinations of potassium wasting and potassium sparing diuretics. Whether this trend will lead to an increase in the incidence of hyponatraemia is of great interest. We report a case of hyponatraemia related to the use of a combination of hydrochlorothiazide and triamterene.

Case report
A 44 year old woman with epilepsy was admitted as an emergency in a confused and agitated state. She was receiving phenytoin 300 mg a day, sodium valproate 500 mg four times a day, and a combined preparation of hydrochlorothiazide 25 mg and triamterene 50 mg (Dyazide, one tablet daily). Diurepsam, piroxicam, and sex hormone replacement treatment had been stopped several weeks before admission. She had been taking diuretic drugs, including bendrofluazide and ciclosporin, regularly for several years for ankle swelling and shortness of breath. She had also received various non-steroidal anti-inflammatory agents and anticonvulsants but not carbamazepine. She experienced epileptic fits about once every month.

During the few days before admission she had become increasingly vage and confused. At the time of admission she was intermittently aggressive and unresponsive to verbal command and required parenteral sedation for management. Focal and postictal signs were absent, and there were no signs of cardiac failure or oedema. Blood pressure was 159/80 mm Hg supine with no postural change. On admission plasma concentrations were sodium 117 mmol(mEq)/l, chloride 74 mmol(mEq)/l, potassium 2.8 mmol(mEq)/l, bicarbonate 29 mmol(mEq)/l, and urea 5.4 mmol/l (324 mg/100 ml). Results of thyroid function tests and plasma cortisol concentration were normal. Plasma phenytoin concentration was at the lower end of the therapeutic range (11 mu/l (27-75 mu/l/100 ml)), and no sodium valproate was detectable in the plasma. A chest radiograph was clear.

Management consisted simply of restricting fluid to 500 ml a day and stopping the diuretic. She was fed normally. A 24 hour urine collection, started on the day after withdrawal of the diuretic, contained less than 2 mmol sodium and 18 mmol potassium and showed a creatinine clearance of 92 ml/min. Over the next three days her electrolyte abnormalities corrected and she became lucid and returned to normal both mentally and physically.

Comment
We are confident that this patient's presenting syndrome was hyponatraemia induced by the diuretic that she was taking. The mode of presentation and the clinical and biochemical findings were similar to those previously reported. The speed with which the effect was reversed and the results of our investigations excluded other causes of hyponatraemia and the syndrome of inappropriate secretion of antidiuretic hormone.

The main point of interest in this case is the drug treatment. The diuretic drugs taken previously by the patient had not caused appreciable electrolyte abnormalities but were not combinations of proximally and distally acting drugs. Thus the combination of triamterene and hydrochlorothiazide may well have been responsible for the profound electrolyte abnormality. This supposition is supported by one well documented case report of the occurrence of hyponatraemia related to this drug combination. On the other hand, Brooks and Ritch suggested that amiloride is specifically implicated.

The exact mechanism by which this adverse effect of diuretic treatment arises remains a source of debate. The most plausible explanation is that a minor degree of sodium depletion together with the drugs actions in the diluting segment of the nephron impair the capacity to excrete free water. Hyponatraemia also has been implicated in exacerbating the effect. Why, then, the addition of a potassium sparing diuretic should potentiate the problem remains a mystery.

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(Accepted 24 April 1984)

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