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(Accepted 16 July 1986)

SHORT REPORTS

Thrombotic microangiopathy and acute renal failure associated with arteriography

Acute renal failure after administration of contrast media has been well documented. In the late 1950s a change from earlier contrast media to salts of diatrizoate was thought to have curtailed this problem, but a review in 1978 reported 75 well documented cases of acute renal failure after use of newer contrast media.¹ We report on a man with a well functioning renal transplant in whom thrombotic microangiopathy caused acute renal failure after aortofemoral angiography. This form of acute renal failure induced by a radiocontrast agent has not been recognised previously.

Case report

A 59 year old man with renal failure due to analgesic nephropathy started haemodialysis in 1973. In 1979 he underwent successful cadaveric renal transplantation, and the serum creatinine concentration remained normal (0.10-0.12 mmol/l (1.1-1.3 mg/100 ml)) for six years. In March 1985 he presented with severe bilateral intermittent claudication and underwent angiography before a left femoral-popliteal bypass operation. After angiography, in which he was given 70 ml of 65% meglumine diatrizoate intravenously, his renal function deteriorated acutely, the serum creatinine concentration rising from 0.12 to 0.22 mmol/l (1.3 to 2.4 mg/100 ml) and falling again to 0.11-0.12 mmol/l. His urine output remained normal during this episode.

He was readmitted in June for angiography on the right side because of worsening symptoms and distal ulceration. On admission creatinine concentration was 0.11 mmol/l (1.1 mg/100 ml). He was well hydrated on the day of angiography. The next day, however, the serum creatinine concentration rose to 0.27 mmol/l (3.0 mg/100 ml), and it continued to rise until the seventh day after angiography, when he required haemodialysis because of uraemic symptoms. Over the same period the haemoglobin concentration fell from 127 g/l to 86 g/l and the platelet count from $314 \times 10^9/l$ to $73 \times 10^9/l$. A blood film showed spherocytes and fragmented red blood cells. The bilirubin concentration peaked at 36 $\mu\text{mol/l}$ (2.1 mg/100 ml) (normal <19 $\mu\text{mol/l}$ (<1.1 mg/100 ml)). Urine output fell from 5950 ml on the day of angiography to 540 ml four days later (figure). Urine microscopy showed 10×10^9 glomerular red cells/l and numerous renal tubular epithelial cells. Renal biopsy on day 6 showed occlusion of many glomerular capillaries by fibrin thrombi, while others contained polymorphs. The appearances were those of thrombotic microangiopathy. Acute tubular necrosis and some mild features of chronic vascular rejection were also evident.

Plasma exchange with four litres of reconstituted plasma protein precipitate was begun as soon as the result of the biopsy was known and was continued daily for four days and then on alternate days for three weeks. The serum creatinine concentration fell rapidly to 0.14 mmol/l (1.5 mg/100 ml), and urine volumes returned to normal. In spite of the good initial response to plasma exchange renal function deteriorated gradually and three months later biopsy showed diffuse double contours in glomerular capillaries and continuing activity resembling chronic microangiopathy on electron microscopy.

Urine volume (—) and serum creatinine concentrations (----) after angiography.

Comment

The mechanism of acute renal failure after administration of contrast media was initially ascribed to acute tubular necrosis² or acute interstitial nephritis.³ To our knowledge we report a previously unrecognised mechanism of acute renal failure after arteriography—namely, thrombotic microangiopathy. The outlook for patients with acute renal failure resulting from thrombotic microangiopathy is poor without treatment.

Although thrombotic microangiopathy can result from acute graft rejection, this is unlikely to occur so long after transplantation. Fluid loading and high urine output, which are recommended to prevent acute renal failure after administration of contrast media, were not effective in this patient. Two mechanisms might have led to the diffuse thrombi in glomeruli in this case. In our view the most likely is that atheromatous emboli were dislodged into the renal artery during angiography. Atheromatous material has been shown to activate complement in vitro,⁴ and infusion of atheromatous material into the carotid artery in rats leads to diffuse fibrin thrombi in glomeruli. Alternatively, the activation of complement by contrast medium⁵ could have precipitated the thrombotic microangiopathy.

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(Accepted 11 July 1986)

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Availability of organs for transplantation: a three year study

The kidney transplant programme in Nottingham began 11 years ago. As the number of kidneys made available each year falls short of the number of patients added to the waiting list for transplantation we carried out a study to identify the number of potential donors. We also identified the number of other solid organs potentially available for transplantation and reasons for non-referral.

Method and results

The records of all deaths in the six intensive care units covered by the Nottingham renal transplant unit were examined, prospectively for the last six months of 1985 and retrospectively for the previous 42 months to the beginning of 1983. Any patient over 2 years old who was ventilated, diagnosed as brain stem dead before the ventilator was switched off, did not have appreciable sepsis or evidence of malignancy (except for primary cerebral malignancy), and had normal renal function was considered to be a potential kidney donor. From this group patients aged up to 55 with normal results of liver function tests and no history of liver disease or trauma were considered to be potential liver donors. Those patients aged up to 40 without cardiac disease or chest trauma were considered to be potential heart donors. During the prospective study reasons for non-referral of potential donors were actively sought.

The table gives details of donation of kidneys and potential donors. During the three years there was an average of 35 potential donors. On the assumption that each potential donor would give two kidneys this equates with an average of 50 kidneys/million population/year. Only 25 kidneys/million/year were offered.

In addition to the 105 patients who were brain stem dead and suitable for kidney donation there were two children aged under 2 (several units do not use kidneys from children of that age). One 8 year old liver donor had unsuitable kidneys. Ninety of these patients were potential liver donors (21/million/year) and 71 potential heart donors (17/million/year). Five livers and 14 hearts (two heart-lung combinations) were retrieved.

During the retrospective study the reason for non-referral could not be determined accurately, but in the prospective study two patients were not referred by medical staff and in seven cases the relatives refused donation (table).

Comment

In 1975, from a survey in Nottingham, 43 kidneys/million population were considered to be potentially available but only 37% were transplanted.¹ At present 40 kidneys/million population is the number of transplants needed each year in the United Kingdom. We have shown that 50 kidneys/

million/year are suitable for transplantation in our district but 50% were not referred for retrieval.

We also identified 17 potential heart and 21 potential liver donors/million/year, but the use of these organs is governed by day to day needs of the recipients and compatibility of blood groups, size, and facilities at the various units.

The stated policy of the intensive care units studied is to refer patients who are brain stem dead for consideration as organ donors. The fact that seven of 15 potential donors were lost in the last six months of the study because relatives refused to agree to donation is alarming. Before this study there was no strict policy regarding who should ask relatives. It is now recommended that the senior medical staff in the intensive care unit should do so. We consider that whoever asks must be well informed and motivated towards transplantation because the way in which the relatives are approached is as important as ensuring that all relatives are asked. The nursing staff caring for the patients have the closest contact with relatives; thus they also should be well informed and may be able to introduce the subject of organ donation. These points should be remembered if required request becomes law.

Intensive care units participating in the study were those at Queen's Medical Centre (adult and paediatric), Nottingham City Hospital, Derby Royal Infirmary, Derby City Hospital, and Mansfield General Hospital.

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(Accepted 28 July 1986)

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Nifedipine in the treatment of chilblains

Perniosis, or chilblains, consists of inflammatory lesions of the skin, usually arising on acral sites as a result of an abnormal reaction to cold.¹ Often, but not invariably, they are associated with acrocyanosis or erythrocyanosis and only rarely with Raynaud's phenomenon. The lesions usually develop in early winter and present as itchy and painful erythematous purplish swellings. They may resolve spontaneously in two to three weeks, but in severely affected patients chilblains may be present throughout the winter and summer and may blister or ulcerate.² Their aetiology is unknown but the gross pathology shows vasoconstriction of the subcutaneous arteries and larger arterioles associated with a vasodilatation of the superficial minute vessels.³ Histopathologically there is dermal oedema, an intense perivascular mononuclear cell infiltrate, thrombosis of vessels in late cases, and spread of the inflammatory process into the subcutaneous fat.⁴

The treatment of chilblains is unsatisfactory. As the slow calcium channel antagonist nifedipine has been shown to be one of the most useful treatments for primary and secondary Raynaud's phenomenon⁵ we decided to study whether it might also be beneficial in the treatment of another cold related disorder: idiopathic perniosis. We therefore undertook a double blind, placebo controlled, randomised crossover study of nifedipine in the treatment of perniosis during the winter of 1985-6.

Patients, methods, and results

Ten otherwise healthy patients who had suffered from severe idiopathic perniosis for a minimum of five months each year for the previous three years were selected for the study. Patients were enrolled as soon as lesions had developed and all gave their signed informed consent before the study began. The study consisted of two periods of six weeks of treatment with either nifedipine retard 20 mg or identical placebo tablets taken three times daily. Nifedipine retard was prescribed because it gives a stable blood concentration throughout the 24 hours, which probably minimises the incidence of side effects. The dose of 60 mg daily was chosen because in an earlier pilot study this dose resulted in a good therapeutic response and few side effects. Patients were assessed clinically every two weeks throughout the study, and at each visit lesions were photographed. In addition, patients kept a daily diary of any change in the clinical appearance, degree of irritation, and pain and soreness of the lesions assessed on a three point scale: better, same, or worse. The duration of established lesions and the appearance of new lesions were also recorded.

In seven of 10 patients treated with nifedipine the established lesions resolved within seven to 10 days, and no patient developed new chilblains while taking the

Numbers of patients diagnosed as brain stem dead and numbers of kidney donors used

	1983	1984	1985	
			Jan-June	July-Dec
Donors used	16	21	10	6
Donation refused:				
By relatives	1		4	7
By coroner		1		
Donation not offered	19	14	4	2
Total potential donors	36	36	33	
Potential kidneys/million population	51	51	47	