# SHORT REPORTS

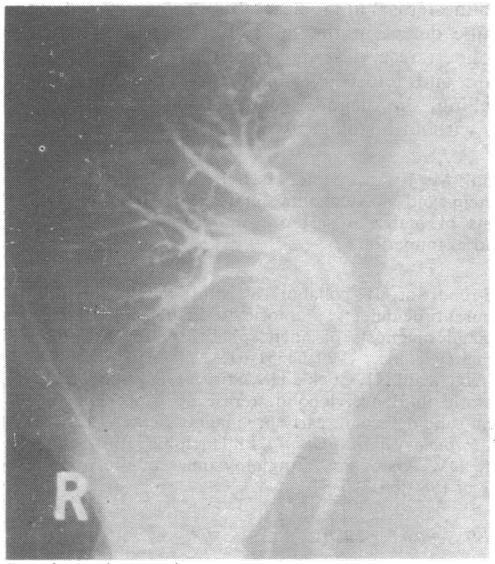
## Rejection of renal transplants: a further cause of intrarenal aneurysms

Aneurysms of the intrarenal arteries may occur in arteriosclerosis,[1] diffuse vasculitis,[2] mycotic disease,[3] secondary to drugs,[4] in neurofibromatosis,[5] and in the presence of mass lesions of the kidney. Rarely, renal aneurysms are congenital. Pseudoaneurysms may occur in renal trauma. We describe two patients in whom multiple intrarenal aneurysms developed in association with rejection of renal transplants.

### Case reports

*Case 1*—A 40-year-old woman with chronic glomerulonephritis presented in October 1978 with end-stage renal failure. Maintenance haemodialysis was instituted, and in September 1979 she was given a cadaveric transplant (immunosuppressive treatment: azathioprine 125 mg in the morning, prednisone 20 mg daily) with immediate return of renal function. Ten days later, however, rejection occurred, and renal biopsy showed distinct cellular changes. She was treated with a booster dose of prednisone (300 mg daily, decreasing over 10 days). Arteriography disclosed multiple small intrarenal aneurysms with pruning of the peripheral vessels (figure). She was given a further dose of prednisone for persistent rejection, and three weeks later the transplant was removed. Histological examination showed severe vascular rejection with aneurysm formation and areas of infarction. The donor's other kidney, which was transplanted into another patient in our unit, was normal arteriographically.

*Case 2*—A 25-year-old man presented in February 1971 with advanced renal disease due to reflux nephropathy and associated pyelonephritis. Maintenance haemodialysis was begun in May 1974 and in May 1979 he received a cadaveric transplant (immunosuppressive treatment: azathioprine 150 mg and prednisone 20 mg daily). Dialysis was continued for 15 days after the operation for acute tubular necrosis. A clinical rejection episode three weeks after operation was treated with prednisone 300 mg, decreasing over 10 days. Serum creatinine concentration remained high at 415 μmol/l (4·7 mg/100 ml). Arteriography disclosed pruning of the peripheral vessels with small intrarenal aneurysms. Renal biopsy showed distinct cellular rejection with a moderate vascular component. A further booster dose of prednisone was begun, and serum creatinine concentration fell to 130 μmol/l (1·5 mg/100 ml). He was discharged and remained well 13 months after the operation.




Renal arteriogram in case 1.

### Comment

The pathological changes of rejection may be cellular or vascular, depending on cellular and humoral immunity. We use selective renal arteriography to determine the patency of the anastomosis and renal artery, and occasionally to diagnose rejection.

Arteriography of the donor's other kidney in case 1 excluded the possibility of congenital or diffuse vasculitis in the donor. We could not examine the twin graft in case 2 as the recipient was not in our unit. Neither donor had been treated with drugs. Repeated blood cultures showed no evidence of septicaemia, and culture of the transplant removed in case 1 was sterile. The histopathological features in case 1 showed progression of rejection from the time of the initial biopsy to nephrectomy. The biopsy features in case 2 resembled those in case 1, with inflammation of the vessel wall, suggesting that weakness of the wall was the reason for the radiological appearances.

We thank Professor G D Doyle for his advice.

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[2] Herschman A, Blum R, Lee YC. Angiographic findings in polyarteritis nodosa. *Radiology* 1970;**94**:147.
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[4] Halpern M, Citron PB. Necrotizing angiitis associated with drug abuse. *AJR* 1971;**111**:663.
[5] Salyer WR, Salyer DC. The vascular lesions of neurofibromatosis. *Angiology* 1974;**25**:510.

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## Nifedipine and beta-blocker drugs

Nifedipine, a calcium antagonist, is used in treating angina pectoris. It has a negative inotropic effect and may therefore theoretically precipitate heart failure, though this has not been reported[1] apart from a case of pulmonary oedema.[2] I report the cases of two patients who developed heart failure when nifedipine was given in addition to a beta-blocker drug.

### Case reports

*Case 1*—A 72-year-old man with angina pectoris was given alprenolol 200 mg twice daily in March 1978. He had no evidence of valvular heart disease and had never had signs of congestive heart failure. A chest radiograph was normal and his resting electrocardiogram showed ST-segment depression in several leads. In May 1980 he complained of increasing angina. He had no abnormal clinical signs and his chest radiograph and electrocardiogram were unchanged. He was put on nifedipine 10 mg three times daily. After 16 days he was admitted with dyspnoea. His jugular venous pressure was raised (7 cm at angle of 45°), his apex beat was 1 cm to the left of the midclavicular line at the fifth intercostal space (ICS), his ventricular rate was unchanged (60/min, regular), and he had bilateral basal crepitations and severe pitting oedema of both legs. His electrocardiogram was unchanged. Nifedipine was discontinued, he was kept on the same dose of alprenolol, and he was treated with frusemide. His chest was clinically clear and the oedema disappeared three days later. He was discharged on alprenolol 200 mg twice daily, frusemide 40 mg daily, and potassium supplements. When I saw him one week later he had no signs of heart failure, and frusemide was discontinued. He had no signs of heart failure after 40 days' follow-up.

*Case 2*—A 58-year-old man had severe angina pectoris. He had no abnormal clinical signs, his chest radiograph was normal, and he had a positive exercise electrocardiogram (ST-segment depression 2 mm, duration 0·10 s). He had been taking alprenolol for several months. As he had not appreciably improved his private doctor stopped the alprenolol and put him on propranolol 40 mg three times daily and nifedipine 10 mg three times daily. Six days later he complained of dyspnoea on exertion and oedema of his legs, which gradually worsened over the next two weeks. He was kept on propranolol, and nifedipine was discontinued. His dyspnoea improved

and the oedema disappeared within four days. One month later he was again given, by another doctor, nifedipine 10 mg three times daily and three days later he again developed dyspnoea and oedema of his legs. When I saw him one week later he had signs of congestive heart failure. His jugular venous pressure was raised (5 cm at angle 45°), the apex beat was 1 cm to the left of the midclavicular line at the fifth intercostal space, his ventricular rate was regular at 68/min, and he had bilateral fine basal crepitations and moderate pitting oedema of his legs. His resting electrocardiogram was unchanged. He was treated with frusemide, and propranolol and nifedipine were discontinued. After four days he had no signs of heart failure. After one week he was put on metoprolol 300 mg daily. After 30 days' follow-up he had no signs of heart failure.

### Comment

Side effects of nifedipine are rare. They are more common at the beginning of treatment. They include headache, facial flush, a sensation of heat, dizziness, nausea, and tiredness. Very rarely, oedema of the lower extremities may occur, as with other vasodilator drugs. The patients reported on here developed heart failure after nifedipine was added to a beta-blocker. When nifedipine was discontinued there were no signs of heart failure, although both patients were kept on the beta-blocker. After the second patient was restarted on nifedipine heart failure recurred.

When nifedipine is given with beta-blocker drugs it should be with caution.

[1] Anonymous. Drug treatment of chronic stable angina pectoris. *Br Med J* 1978;i:462-3.
[2] Gilmer DJ, Kark P. Pulmonary oedema precipitated by nifedipine. *Br Med J* 1980;**280**:1420-1.

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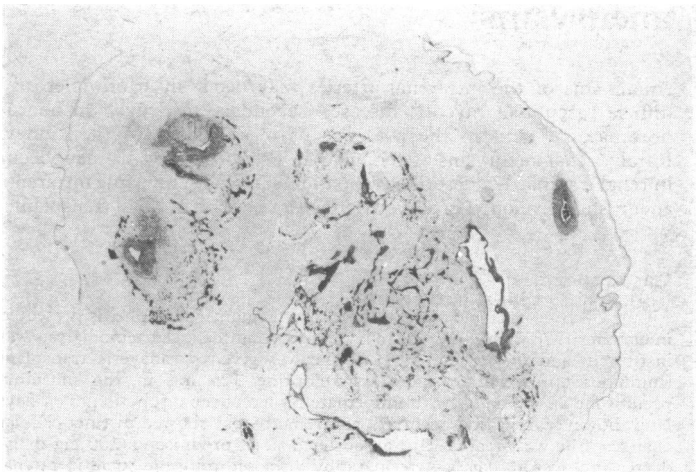
# Haemangioma of the cord: further cause of raised maternal serum and liquor alpha-fetoprotein

We report a cause of raised maternal serum and liquor α-fetoprotein concentrations which has not, so far as we know, been previously described.

### Case report

The patient was a 28-year-old gravida 2 Iraqi. Her first pregnancy resulted in the delivery of a normal female infant at term, birth weight 3200 g. The marriage was non-consanguineous and there was no family history of fetal malformation. The maternal serum α-fetoprotein concentration at 16 weeks' gestation was raised at 65 μg/ml (2 × median). At 19 weeks' gestation it was 165 μg/ml (3 × median), so an amniocentesis, yielding clear liquor, was performed 24 hours later. The liquor α-fetoprotein concentration of 61 μg/ml was 4·6 × median. (In the UK collaborative study[1] only 0·15% of clear fluids from pregnancies with normal outcomes had amniotic α-fetoprotein concentrations at 19-21 weeks above four times the median and none exceeded 4·1 × median.) The qualitative amniotic fluid acetylcholinesterase test by gel electrophoresis[2] was negative, showing only one band. Ultrasound examination at 19 weeks showed a single, viable fetus with an anterior placenta. The liquor volume was within normal limits and the gestational age was confirmed. Although further ultrasound examination of the fetus showed no abnormality of the neural tube, neck, anterior abdominal wall, or kidneys, the patient and her husband were counselled that the raised liquor α-fetoprotein concentration indicated a high risk of fetal malformation. Both agreed to have the pregnancy terminated, and this was done with extra-amniotic prostaglandin.

A female fetus (karyotype 46 XX) was delivered weighing 362 g and measuring crown-heel 26·4 cm and crown-rump 18·0 cm. No malformation could be detected either externally or on gross dissection of the cranium, spine, thorax, and abdomen. Histological examination of all the major organs, including kidneys, showed no abnormality. The placenta weighed 133 g and was grossly and microscopically normal. The umbilical cord contained three vessels and was approximately 0·7 cm diameter throughout except for the placental extremity, which displayed a rounded swelling 1·5 cm across contiguous with the placental amnion. Histological examination of this showed the presence of a capillary haemangioma within the Wharton's jelly. A minority of the vascular spaces were thrombosed and appeared to communicate with vessels in the placenta rather than with those in the cord (figure).



Cross section of umbilical cord swelling showing numerous irregular vascular spaces within Wharton's jelly × 8·7 (original magnification).

### Comment

Vascular hamartomatous tumours of the umbilical cord are rare. Fox[3] reviewed 15 cases of cord haemangioma and Fortune and Ostor[4] recently reviewed 12 cases, preferring the term angiomyxomas of the cord. In common with placental haemangiomata, they are probably often overlooked without a specific search. The present case is important in that the tumour may account for high serum and liquor α-fetoprotein concentrations in an apparently normal pregnancy.

Although amniotic fluid α-fetoprotein concentration is in most cases a reliable indicator of a fetus with an open neural tube defect, several other conditions may also cause raised concentrations—for example, exomphalos, Finnish-type nephrotic syndrome, and Turner's syndrome. Careful examination of the fetus by ultrasound and the acetylcholinesterase gel technique may help differentiate these conditions. Raised α-fetoprotein concentration with normal acetylcholinesterase in a clear fluid indicates a lesion other than neural tube defect in the fetus, but the false-negative rate of the acetylcholinesterase test is uncertain. Nevertheless, while both ultrasound and fetoscopy might theoretically detect an umbilical cord swelling, the diagnosis of haemangioma cannot be made with certainty without histological examination.

We thank Ms J Tracey and Ms S J Fennell for estimations of amniotic α-fetoprotein and acetylcholinesterase, Drs I Laing and P Astley for estimations of maternal serum α-fetoprotein, and Dr M Gowland for ultrasound examination.

[1] Second report of UK collaborative study on alpha-fetoprotein in relation to neural tube defects: amniotic fluid alpha-fetoprotein measurement in antenatal diagnosis of anencephaly and open spina bifida in early pregnancy. *Lancet* 1979;ii:651-61.
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