Outcome of renal transplantation in Wiskott-Aldrich syndrome

Sir,

We were interested to read the recent article of Fischer et al. regarding the fatal outcome of a renal transplant in a patient with Wiskott-Aldrich syndrome [1]. In 1993, we reported the first case of renal transplantation in this condition [2], and would like to offer some comment and follow-up.

In the case reported, the recipient died 3 months after transplantation following a number of infective complications including CMV, bacterial sepsis, herpes zoster and Pneumocystis carinii pneumonia. Lymphoproliferative disease was also detected shortly before death. As the authors note, it is difficult to ignore the conclusion that the burden of immunosuppression given was excessive. In our patient, we avoided the use of antibody therapy. We also used a reduced dose of azathioprine (1 mg/kg rather than 2 mg/kg) and aimed for a lower trough cyclosporin level (100–150 ng/ml rather than 200–250 ng/ml).

In contrast to our experience, their patient (and a second patient reported in the French literature [3]) required treatment for rejection, including with anti-thymocyte globulin. It is instructive to note that the defects in cellular immunity that characterize this condition do not prevent rejection. However, given the predisposition of such patients to infection and lymphoproliferative disease, we would urge caution in the aggressive treatment of such events. It may be better to concede graft function than to risk over-immunosuppression. In particular, we would not have treated with pulses of methylprednisolone without biopsy proof of rejection.

What can we conclude? If such patients are to be transplanted successfully, it seems critical to reduce their overall immunosuppressive burden. Good tissue matching may be important in this respect; our patient received a 011 ABD mismatched kidney. Our patient had received no blood transfusions in the 10 years prior to his transplant, and at the time of transplantation had a 0% panel reactivity and negative FACS analysis, indicating minimal immunological activation. It may also have been relevant that the donor organs were in good condition with a short cold ischaemic time, and that there was immediate graft function. Avoidance of a CMV positive donor may in future be appropriate.

One last word of caution. Despite an uncomplicated post-transplant course, our patient died at home 35 months after transplantation, from an unknown cause. He was aged 49. Post-mortem examination showed severe triple vessel coronary artery disease and it is presumed that the cause of death was cardiac. No evidence of malignancy was detected. While graft function was excellent (creatinine 99 μmol/l at the time of death), it remains to be seen whether the long-term prognosis of transplantation in Wiskott-Aldrich syndrome is sufficient to justify initial enthusiasm, and this will need to be borne in mind when considering future candidates for transplantation and the appropriateness of organ allocation.

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Reply

SIR,

We thank Dr Andrews and Dr Koffman for their comments on our case report of renal transplantation in a patient with Wiskott-Aldrich syndrome (WAS) [1] and completely agree with their recommendations to reduce the dose of immunosuppressive drugs, and especially to avoid the use of antithymocyte globulin should a rejection episode occur. As pulses of methylprednisolone were well tolerated in the case described by Meisels et al. [2] the cautious use of steroids for treatment of a well documented rejection episode is probably acceptable. We also agree with Dr Andrews and Dr Koffman’s recommendations to minimize the risk of acute rejection by carefully selecting a donor with good HLA matching and a short cold ischaemia time. Our patient received a one-haplotype-matched kidney from his father and despite the defect in cellular immunity associated with WAS he developed rapidly aggressive rejection episodes. We were very interested to receive follow-up information about the first WAS renal transplant recipient reported in the literature [3] who died at age 49, nearly 3 years after transplantation, of presumed cardiac cause (severe triple vessel coronary artery disease), with a perfectly functioning graft function than to risk over-immunosuppression. It may be better to concede graft function than to risk over-immunosuppression. In particular, we would not have treated with pulses of methylprednisolone without biopsy proof of rejection.

What can we conclude? If such patients are to be transplanted successfully, it seems critical to reduce their overall immunosuppressive burden. Good tissue matching may be important in this respect; our patient received a 011 ABD mismatched kidney. Our patient had received no blood transfusions in the 10 years prior to his transplant, and at the time of transplantation had a 0% panel reactivity and negative FACS analysis, indicating minimal immunological activation. It may also have been relevant that the donor organs were in good condition with a short cold ischaemic time, and that there was immediate graft function. Avoidance of a CMV positive donor may in future be appropriate.

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Comments of a frustrated Batavian friend having unsuccessfully practised Yoga to solve the Nephroquiz

Although I do not consider myself a beginner, I was unable to solve the Nephroquiz ‘Out of the Blue’ in the issue of last September. I have studied Figure 1 for quite a long time. Most puzzling to me was the question of whether the extremity presented was the right leg of a supine patient or the left arm of a prone patient. In either case the two severely cyanotic fingertips in the picture most probably belonged to a second individual who was also seriously ill. When I tried to simulate the position of the fingers by lying on my back or on my stomach, the only thing I accomplished was that I almost twisted first my left and subsequently my right arm.

In addition to this acrobatic exercise the presented case raised another question, which is usually the first that I ask in such instances: ‘Who examined the urinary sediment?’ First, there is a failure to report on the morphology of the erythrocytes. I can imagine that the authors left this out to make their question not too easy. But I certainly refuse to believe that there were no erythrocyte casts present. In such a case of active IgA nephropathy the absence of erythrocyte casts must be considered as highly unusual. Such a result is most often caused by the failure of the examiner to screen the sediment carefully at low magnification (<×100). We have shown in a blinded, controlled study of 107 patients with proven causes of either glomerular or non-glomerular haematuria that, in the patients with glomerular haematuria, erythrocyte casts can be detected in 83% of the cases [1]. Especially the presence of dysmorphic erythrocytes should be a reason for a thorough screening of the entire sediment. This may take some time (up to 10 min), but the examiner is often rewarded by the detection of one or two characteristic erythrocyte casts.

We have recently proposed a very simple procedure to fix the urinary sediment [2]. It will enable the beginner to save the sediment for later consultation of a more experienced ‘uroscopist’.

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A case of early-onset pre-eclampsia associated with IgA nephropathy

Sir,

A 31-year-old healthy Japanese woman presented to an obstetrician in September 1996 with amenorrhoea and was found to be pregnant (7th week of gestation). In November 1996 (16th week of gestation), she weighed 56 kg, which represented a gain of 2 kg over her normal weight. Pretibial oedema was noted. During the 19th week of gestation, she weighed 70 kg and anasarca was noted. She consulted another obstetrician who noted a positive test for proteinuria and haematuria, hypoproteinaemia and hypoalbuminaemia, and hypertension. She was transferred to our hospital with a diagnosis of severe pre-eclampsia. On admission, the serum creatinine (s-Cr) was 141 μmol/l (normal range in pregnant women; 35–71 μmol/l), blood urea nitrogen (BUN) 5.3 mmol/l, uric acid 9.55 mg/dl (normal; 3.0–6.0), total protein (TP) 44 g/l and albumin 18 g/l in blood chemistry. Her urine gave a +++ test for proteinuria and haematuria (RBC 5–10/high-power field), but was negative for glycosuria. The 24-h urinary protein (UP) was 5.5 g. To determine the aetiology of the hypertension, a plasma renin and aldosterone, and thyroid function tests were all within normal limits.

She was treated with antihypertensive agents, but blood pressure was not controlled. During the 20th week of gestation, she decided to discontinue the pregnancy and the fetus was aborted. Her blood pressure returned within the normal range rapidly, and 2 weeks later she did not require any antihypertensive agents. Three weeks later, blood chemistry revealed that a TP of 54 g/l, albumin of 28 g/l, s-Cr of 76 μmol/l, and BUN of 2.5 mmol/l, and urinary tests revealed a UP of 0.7 g/day.

A renal biopsy was performed 3 weeks after the abortion. The specimen revealed segmental sclerosis, visceral epithelial caps, a double-contour appearance, swelling of the endothelium, adhesions, and mesangial deposits. In an immunofluorescence (IF) study, staining for antibodies against IgA, IgG, and C3 was positive in the mesangial area, while staining for IgM, C1q, C4, and fibrinogen was negative. Electron-microscopy revealed fusion of foot processes, swelling of endothelial cells, matrix widening, and mesangial dense deposits without mesangial proliferation (Figure 1). These results were consistent with IgA nephropathy and nephropathy of pre-eclampsia.

Pre-eclampsia is thought to produce renal alterations such as endothelial swelling and ballooning of the glomeruli, similar to focal glomerulosclerosis. In the present case the onset of proteinuria, generalized oedema, and hypertension occurred during the 18th week of gestation, and the hypertension and oedema disappeared 2 weeks after delivery. The pathological findings in renal biopsy are characteristic of the nephropathy of pre-eclampsia, while that mesangial deposits and IF findings are characteristic of IgA nephropathy. These results show that IgA nephropathy and nephropathy of pre-eclampsia coexisted in this patient. There is no evidence,