Case Report

Is trauma associated with acute rejection of a renal transplant?

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Introduction

Acute renal allograft rejection due to injury, usually as a result of ischaemia, is a well-recognized feature. The injury usually takes place during the actual transplantation procedure. We report a case of acute rejection of a renal allograft after an episode of blunt trauma outwith the early transplant period.

Case

A 33-year-old male renal transplant recipient was admitted to the renal unit with a rapid deterioration in his renal function. His previous medical history included insulin-dependent diabetes mellitus, diagnosed at the age of 11. He had suffered from several diabetic complications including proliferative diabetic retinopathy, presumed diabetic nephropathy, hypertension and hyperlipidaemia. At the age of 29, he reached end-stage renal failure and was commenced on haemodialysis. He remained on dialysis for 5 months before receiving a transplant kidney (0:0:0 mismatch with a cold ischaemic time of 13 h 44 min). The post-operative recovery was completely unremarkable with no episodes of rejection. He was discharged on the 10th post-operative day with a serum creatinine of 160 μmol/l on an immunosuppressive regimen of cyclosporin A, azathioprine and prednisolone in combination with aspirin and a calcium channel antagonist. Subsequent progress was uneventful and he maintained good graft function with a serum creatinine in the range of 150 μmol/l to 190 μmol/l and cyclosporin A trough concentrations of 140 ng/ml to 220 ng/ml.

Thirty-four months after the transplant, the patient was kicked in the right iliac fossa overlying the transplant kidney. His occupation involved caring for young adults with mental and behavioural difficulties. The kick delivered by one of these male adults, managed to propel our transplant patient about 5 m, giving an indication of the force involved.

The patient began to develop symptoms of increasing tenderness of his graft followed by general malaise and nausea within 3 days of the event. He reported to his general practitioner who checked his electrolytes and found the serum creatinine concentration to be 571 μmol/l, nine days after the event. The renal unit was contacted and he was admitted the next day. The serum creatinine on admission was 562 μmol/l, with bicarbonate and potassium concentrations being 16.4 mmol/l and 5.4 mmol/l respectively. Serum trough cyclosporin A concentration was 150 ng/ml and the blood glucose was 12.8 mmol/l. Full blood count was within normal range and urine analysis revealed 1+ of glucose only. There were no red blood cells, casts or white blood cells on urine microscopy. Urine culture was negative. The urinary albumin/creatinine ratio was 5.4 mg/mmol. A renal ultrasound was performed which showed an enlarged allograft kidney measuring 13 cm but with no evidence of obstruction and normal doppler flows. The following morning the patient underwent graft biopsy, which was reported as follows: ‘Renal cortex contains at least 4 glomeruli which show no significant abnormality. There is a moderate diffuse lymphocytic tubulitis. No vasculitis is identified, however there is diffuse interstitial haemorrhage. The appearances are those of cellular rejection. Whilst the interstitial haemorrhage could be due to trauma, there is a very strong possibility that this is due to vascular rejection, not seen in this material.’

These changes are seen in Figure 1.

The patient was treated with three intravenous pulsed doses of 500 mg of methylprednisolone. The dose of cyclosporin A was increased from 300 mg daily to 400 mg daily. He was discharged on an increased dose of oral prednisolone, in addition to the cyclosporin and azathioprine. The patient’s creatinine improved from a peak of 623 μmol/l and eventually reached a plateau of 318 μmol/l, 21 days post discharge. Unfortunately, the patient’s renal function slowly declined and eventually he commenced haemodialysis 3 months later. The course of events is demonstrated in Figure 2.

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Discussion

Most studies on the immunology of rejection have focused on the specific recognition of the antigens of the allograft and the subsequent anti-allograft response [1].

Several authors have postulated that allograft injury is a possible means of immune recognition and thereby triggering acute rejection. Inflammation is the natural response to injury. Responses include activation of complement, the coagulation pathways, activation of the endothelium to express adhesion molecules and production of cytokines and chemokines. These responses may promote the traffic of dendritic cells in the allograft which then migrate to the recipient's lymph nodes and spleen where naïve T cells may be sensitized [2]. Ischaemic injury induces the release of TNF-α and other cytokines which then induce expression of costimulatory molecules. By inducing such costimulatory signals, the response to injury changes the interaction between antigen and the T cell receptor into an activating rather than a tolerogenic response [3].

Unconventional T cells include those with both natural killer cell activity and CD4 on their cell surfaces, or have T cell receptors consisting of gamma delta chains instead of alpha beta chains [3]. These unconventional T cells are activated by injured renal cells and may be important in regulating the differentiation of CD4 T-cells and therefore resulting in the rejection process.

Conclusion

In the hypothesis that recognition of injury initiates rejection, Lu et al. [3] refers to the injury sustained during the actual transplantation process. We have extrapolated this to explain the episode of acute rejection in our patient following direct trauma to the renal allograft.

We believe this to be the first reported case of rejection in a kidney allograft precipitated by blunt trauma. It may be important to warn potential transplant recipients about the dangers of trauma and recommend avoiding susceptibility through sport or occupation.

References


Received for publication: 26.3.01
Accepted in revised form: 25.7.01