Renal allograft rupture is associated with rejection or acute tubular necrosis, but not with renal vein thrombosis

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Abstract

Background. Whereas rejection was reported to be the most common cause of renal allograft rupture (RAR) in the pre-cyclosporin era, renal vein thrombosis (RVT) is purported to be the main cause of RAR in patients taking cyclosporin. The extremely low incidence of RVT in our series (0.11%) prompted us to analyse our collective with regard to RAR.

Method. Between 1974 and 1999, 1811 renal transplants were performed. Patients with RAR, defined as a tear of the renal capsule and parenchyma, were identified and possible underlying factors studied.

Results. RAR was diagnosed in nine male and five female recipients (0.8%) with a median age of 36 years. Immunosuppression consisted of azathioprine and prednisolone in seven patients and of cyclosporin-based therapy in the seven others. At exploration five grafts were removed immediately: three because of irreversible rejection, one because of deep wound infection, and one with a twisted renal vein. Six of the nine salvaged kidneys have been functioning after a mean observation time of 45 months. In the pre-cyclosporin era RAR was associated with acute rejection in five out of seven cases as compared with only three of the seven on cyclosporin treatment. Core biopsies might have been the cause in three cases.

Conclusion. RAR is a rare complication after renal transplantation. Acute rejection still represents the most frequent cause of RAR in the cyclosporin era.

Keywords: Cyclosporin; renal allograft rupture; acute tubular necrosis

Introduction

As first reported in 1968 [1], spontaneous renal allograft rupture (RAR) is a rare but potentially life-threatening complication following kidney transplantation associated with high rate of graft loss [2–4]. Its incidence has been reported to range from 0.3 to 9.6% of all transplants. The majority of RAR has been described to occur in the first 3 weeks after surgery. In the pre-cyclosporin era acute rejection was the most common cause, whereas under cyclosporin-based immunosuppression renal vein thrombosis has been reported to be the main cause of RAR [4]. Since the incidence of renal vein thrombosis was extremely low in our series (0.11%), we were interested in the factors potentially involved in RAR in our patients.

Patients and methods

Between March 1974 and May 1999, 1811 renal transplants were performed at Innsbruck University Hospital. Of these 1730 were from cadaver donors, 71 from living-related and 10 from living-unrelated (spouses in all cases) donors. Until 1980, prophylactic immunosuppression consisted of azathioprine and high-dose steroids. Acute rejection episodes were treated with $3 \times 1 \text{g}$ methylprednisolone, later on with $3 \times 500 \text{mg}$ methylprednisolone and anti-thymocyte globulin (ATG) for steroid-resistant rejection. From 1980, more and more patients were treated with cyclosporin, either alone or in combination, with low-dose steroids. Most of the patients in the early 1980s were enrolled in prospective trials [5,6]. Since 1984 most patients have received triple-drug therapy with cyclosporin, azathioprine and steroids. Patients at immunological risk (more than 80% panel-reactive HLA antibodies, loss of a previous transplant from irreversible acute rejection) received induction therapy with ATG. In the late 1980s some patients received various monoclonal antibodies and from 1995 on tacrolimus (FK506) (in controlled trials). The surgical procedure was carried out in a standardized manner. The graft vein was anastomosed end-to-side to the external iliac vein with a 5/0 or 6/0 Prolene running suture, or sometimes, in re-transplants or for reasons of size to the common iliac vein. In cadaveric kidneys the right renal vein was usually extended with the attached vena cava. The renal artery was anastomosed with an aortic patch end-to-side to the external iliac artery. In some live donor transplants, the artery was anastomosed end-to-end with the internal iliac artery, which was also done in cases of en-bloc transplantation of paediatric kidneys. The ureteroneocystostomy was performed using a modified Leadbetter–Politano technique in most patients.
RAR was defined as a tear of the renal capsule as well as the renal parenchyma associated with haemorrhage and was confirmed by exploration in all instances. Various donor, procurement as well as recipient characteristics were compared between patients who developed RAR and the entire patient population with the use of the t-test, Z-test or Mann–Whitney U-rank sum test, as required. A logistic regression model was fitted to evaluate whether cold ischaemia, acute tubular necrosis, acute rejection, age of the recipient and CMV infection are independent risk factors. P-values <0.05 were considered statistically significant.

Results

RAR was diagnosed in 14 (0.8%) of the 1811 renal transplant recipients (Table 1). Between 1974 and 1981 the incidence was as high as 2.8% and decreased to about 0.7% after 1982. The average age of the nine male and five female patients was 36 (22–57) years. Eleven of the 14 transplants were first transplants, for three patients it was their second graft. The underlying kidney diseases were glomerulonephritis in eight patients and pyelonephritis in four. The two remaining patients suffered from nephroangiosclerosis. The demographics of the 14 cadaveric donors, nine of which were male, show a mean age of 28 (0.5–69) years. For organ preservation HTK solution was used in one, UW in five and EuroCollins in eight cases.

Prophylactic immunosuppression consisted of azathioprine and prednisolone in seven patients, and of cyclosporin, azathioprine and prednisolone in the remaining seven patients. RAR occurred on day 11 (3–21), post-transplant. Clinical presentation was similar in all patients: sudden pain and swelling over the graft with a drop in haematocrit and in blood pressure accompanied by oliguria. When RAR was suspected, diagnosis was confirmed in most but not all patients by ultrasound examination. At emergency exploration, a huge haematoma surrounding the convexity of the graft was found in 13 patients. In one patient the haematoma was ruptured into the abdominal cavity. Most of the RAR had occurred along the convex border of the graft, others at either renal pole. In one patient who had received two paediatric kidneys en-bloc, twisting of the left renal vein occurred as a result of poor placement of the graft. This outflow problem appeared to be the cause of the RAR. In all other grafts, vessels were found to be patent. Five grafts were removed immediately; three because of irreversible concomitant rejection, one because of deep wound infection, and the one with the twisted renal vein. In the remaining nine grafts, haemostasis was achieved with careful suturing, and/or the use of haemostyptic material as well as infrared or laser coagulation and fibrin glue. In two cases with deep extended scars, repair was achieved by wrapping the graft with a mesh of absorbable material. In one case RAR occurred on day 6 and was repaired successfully. A second RAR, however, on day 39 prompted nephrectomy. All patients survived RAR. Six of the nine repaired kidneys are currently functioning after a mean observation time of 45 (1–111) months. Figure 1 depicts the possible aetiologies. In the pre-cyclosporin era RAR was associated with acute rejection in five out of seven cases, whereas under cyclosporin only three of seven RAR were caused by rejection. Cyclosporin levels of these three patients on the day of or the day before RAR were 213, 91, and 188 ng/ml. Core biopsies seem to have been the cause of RAR in three cases, since all of them occurred within 6 h following biopsy. When comparing the incidence of cold ischaemia, acute tubular necrosis, acute rejection, age of the recipient and CMV infection between patients with and without RAR, only acute tubular necrosis and rejection were found to be significantly different between the two

Table 1. The demographics of the 14 cases with renal allograft rupture

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Year of TX</th>
<th>Prophylactic immunosuppression</th>
<th>Day of rupture postop.</th>
<th>Graft lost</th>
<th>Putative cause of rupture</th>
<th>Result of biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.R.</td>
<td>44</td>
<td>M</td>
<td>1992</td>
<td>Aza./Cort</td>
<td>17</td>
<td>No</td>
<td>Biopsy</td>
<td>ATN</td>
</tr>
<tr>
<td>C.W.</td>
<td>26</td>
<td>F</td>
<td>1980</td>
<td>Aza./Cort</td>
<td>21</td>
<td>Yes</td>
<td>ATN</td>
<td>–</td>
</tr>
<tr>
<td>C.G.</td>
<td>57</td>
<td>M</td>
<td>1994</td>
<td>CsA./Aza./Cort</td>
<td>6</td>
<td>No</td>
<td>Biopsy</td>
<td>ATN</td>
</tr>
<tr>
<td>D.D.</td>
<td>37</td>
<td>M</td>
<td>1991</td>
<td>CsA./Aza./Cort</td>
<td>6</td>
<td>Yes</td>
<td>Rej.</td>
<td>–</td>
</tr>
<tr>
<td>E.R.</td>
<td>23</td>
<td>M</td>
<td>1993</td>
<td>CsA./Aza./Cort</td>
<td>9</td>
<td>Yes</td>
<td>Rej.</td>
<td>–</td>
</tr>
<tr>
<td>F.F.</td>
<td>41</td>
<td>M</td>
<td>1983</td>
<td>Aza./Cort</td>
<td>8</td>
<td>No</td>
<td>Rej.</td>
<td>Rej.</td>
</tr>
<tr>
<td>P.J.</td>
<td>30</td>
<td>M</td>
<td>1980</td>
<td>Aza./Cort</td>
<td>13</td>
<td>Yes</td>
<td>Rej.</td>
<td>–</td>
</tr>
<tr>
<td>S.E.</td>
<td>48</td>
<td>M</td>
<td>1989</td>
<td>CsA./Aza./Cort</td>
<td>4</td>
<td>No</td>
<td>Biopsy</td>
<td>ATN</td>
</tr>
<tr>
<td>S.G.</td>
<td>45</td>
<td>M</td>
<td>1992</td>
<td>CsA./Aza./Cort</td>
<td>10</td>
<td>No</td>
<td>ATN</td>
<td>–</td>
</tr>
</tbody>
</table>

Age, gender, the year of transplantation (TX), the prophylactic immunosuppression (CsA, cyclosporin A; Aza, azathioprine; Cort, cortisone), the postoperative time-point of the rupture, graft loss, the putative cause of the rupture (ATN, acute tubular necrosis, Rej., rejection) and the biopsy results are listed. M, male; F, female.
Fig. 1. Graft ruptures show temporal associations with acute rejection, closed-needle biopsies and acute tubular necrosis. Of our 14 patients who underwent renal allograft rupture, seven received conventional prophylactic immunosuppression with azathioprine + cortisone (Aza/Cort). The other seven patients were treated with cyclosporine-based triple therapy.

cohorts and may therefore be considered a possible risk factors of RAR (Fig. 2).

Discussion

In a series of 885 consecutive renal transplants, performed in Oxford between 1975 and 1990 renal vein thrombosis (RVT) with consequent RAR was observed in eight cases (0.9%), all of which were receiving cyclosporin-based triple drug therapy as prophylactic immunosuppression [4]. In another series of 75 consecutive renal transplants in Riyadh, RAR was encountered in three male patients; two of these cases were associated with steroid-resistant rejection and one with RVT [7]. Our experience does not confirm the association of RAR with venous thrombosis since the incidence of venous thrombosis in our series was 0.11% in contrast to 0.8% for RAR. Furthermore, RAR was associated with renal vein thrombosis in only one out of seven patients with RAR taking cyclosporin, azathioprine and prednisolone for immunosuppression. In the remaining seven patients with RAR immunosuppression consisted of azathioprine and prednisolone, and no renal vein thrombosis was seen.

Our data revealed an association between RAR and rejection as well as ATN. Cold ischaemia, preservation conditions, age of the recipient and CMV infection were not found to be risk factors. In a similar analysis of 12 patients sustaining RAR in a series of 331 consecutive renal transplants recipient age, the white-to-black donor-recipient race mismatch and the need for dialysis were identified as risk factors [8]. A recent case report concludes that renal allograft rupture results from interstitial edema due to acute tubular necrosis [9].

In most but not all of our RAR patients ultrasound was a valuable aid in establishing the diagnosis. Soler et al. found in six out of 18 cases of RAR a disruption of the white linear echo of the graft capsule [10].

Transplant nephrectomy is a definite treatment for RAR, but some authors argue that transplant nephrectomy is justified only in patients who would otherwise die [11]. The salvage rate varies between 40 and 100% and was 64% in our series, which would indicate that it is well worth trying to salvage spontaneously ruptured renal allografts [2–4].

References

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