Teaching Point
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Papillary necrosis following segmental renal infarction: an unusual cause of early renal allograft dysfunction

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Case

A 29-year-old man with end-stage renal failure secondary to autosomal dominant polycystic kidney disease underwent preemptive cadaveric renal transplantation from a 21-year-old male donor. His past medical history was unremarkable, except for mild hypertension controlled with a combination of atenolol and nifedipine, but with no history of diabetes mellitus, urinary tract infection or analgesic abuse. Cold ischaemia time was 14 h and re-warm time was 58 min. The renal graft had two arteries which were each sewn to the external iliac artery in an end-to-side fashion. The surgical procedure was complicated by an 800 ml haemorrhage with transient systemic haemodynamic collapse, immediately after arterial declamping, due to bleeding from small vessels in the renal hilum. The haemodynamic condition rapidly improved after meticulous haemostasis and vigorous fluid repletion with isotonic saline and albumin. Pre- and post-operative bleeding time, thrombin time and activated partial thromboplastin time were normal.

Initial immunosuppressive treatment included antithymocyte globulins, prednisolone, mycophenolate mofetil, and ciclosporine A introduced on post-transplantation (PT) day 4. Immediate progress was satisfactory, as the serum creatinine dropped from 5.2 to 2.1 mg/dl on PT day 5, and physical examination was unremarkable. However, on PT day 8, serum creatinine rose to 3.3 mg/dl while the trough level of ciclosporine A was 145 ng/ml. Colour flow Doppler ultrasound revealed complete thrombosis of the upper polar artery and Mag3 technetium scintigraphy confirmed a perfusion defect at the upper pole of the graft, consistent with segmental polar infarction. A biopsy of the allograft lower pole showed mild ischemic glomerular and tubular lesions with no evidence of tubulitis or vascular rejection. The double J stent was removed on PT day 23 and serum creatinine stabilized at 2.7 mg/dl.

On PT day 39, serum creatinine increased to 3.5 mg/dl and diuresis was maintained at 2.2 l/day. Urine cultures remained sterile, blood glucose was 5 mmol/1 and blood pressure was 130/80 mmHg. Doppler ultrasound and renal tomodensitometry showed urinary tract dilatation which extended from the ureterovesical anastomosis to the renal pelvis. Cystoscopy revealed white material protruding through the ureteral meatus (Figure 1A). An attempt to remove this material endoscopically was unsuccessful. A percutaneous nephrostomy was performed (Figure 1B), followed by ureteroscalic reimplantation which allowed the removal of the obstructive material and led to rapid improvement of allograft function and resolution of ureterohydronephrosis. Histological analysis of this material revealed a necrotic papilla (Figure 2).

One year after transplantation serum creatinine was 2.2 mg/dl with slight microscopic haematuria and proteinuria of 0.4 g/day. Ultrasound and CT scans revealed moderate residual dilatation of the graft ureter and calyceal cavities, with two opacities within the pyeloureteral cavities consistent with persistent calcified necrotic papillae.
Discussion

Early allograft dysfunction, a frequent complication in kidney transplant recipients, is associated with increased morbidity and may compromise long-term graft survival. The main causes of postoperative long-term transplant failure include post-ischemic acute tubular necrosis, atheroemboli and thrombosis, acute rejection,

Fig. 1. (A) Obstructive material protruding through the ureteric meatus. (B) Upper urinary tract dilatation secondary to obstruction of the ureterovesical junction.

Fig. 2. Ischaemic necrosis of papilla with no evidence of inflammatory reaction (haematoxylin and eosin, original magnification ×400).
ciclosporine A toxicity and infection [1]. Although the incidence of urinary obstruction has fallen dramatically since the use of double J stents [2], obstructive renal failure may also occur in the post-operative period, secondary to stenosis or oedema at the anastomosis between ureter and bladder, twisted ureter, uretero-necrosis or ureteric compression by hematoma or lymphocele [3].

In the case reported here, allograft dysfunction was related to upper urinary tract obstruction by a necrotic papilla, following post-operative arterial thrombosis with upper pole infarction. Renal papillary necrosis (RPN) is the consequence of focal or diffuse ischaemic necrosis of the renal medulla, most commonly caused by pyelonephritis, urinary tract obstruction, diabetes mellitus, analgesic abuse, sickle cell haemoglobinopathies or vascular inflammatory diseases such as calyceal arteritis or necrotizing angiitis. However, RPN appears to be a rare cause of upper urinary tract obstruction by itself [4].

RPN has been described rarely in renal transplant recipients. It is usually a rather late complication, diagnosed an average of 28 months after transplantation [5] (Table 1), but, as in this case, may also occur in the early post-operative period [6–8]. Papillary necrosis in the renal allograft may be due to the usual causes of medullary necrosis [5,8,9], and is sometimes discovered fortuitously after the elimination of one or more necrotic papillae in the urine [5,6,10]. However, in most of the previously reported cases, RPN in renal transplant patients was associated with the dramatic features of acute allograft rejection [5–7,10]. In this situation RPN may add to immunological injury and contribute to allograft loss. It has been hypothesized that in renal allograft rejection, vasculitis with lymphocytic and monocytic infiltration could lead to obliteration of the vessels supplying the papillae, resulting in papillary ischaemia and necrosis [4]. Interestingly, in the present case, none of the conditions usually associated with RPN were found. RPN was discovered only 7 weeks after the procedure, when acute obstructive allograft failure with severe hydronephrosis led to diagnostic endoscopic and surgical exploration. Acute rejection was definitively ruled out by renal histological examination and it appears clear that RPN was a consequence of upper polar artery thrombosis and partial polar infarction. In contrast with most of the previous reports, RPN was not associated with graft loss. Renal function rapidly improved and remained stable after successful surgical treatment of the upper urinary tract obstruction.

Due to the frequency of arterial complications in the peri- and post-operative period, it is conceivable that the frequency of RPN in renal transplantation is underestimated. This case suggests that RPN should be considered in transplanted patients who develop acute upper urinary obstruction after arterial thrombosis or embolism.

### Table 1. Main clinical features of renal transplant patients with papillary necrosis

<table>
<thead>
<tr>
<th>Author (ref.)</th>
<th>Number of cases</th>
<th>Sex/age (yr)</th>
<th>Clinical presentation</th>
<th>Time of diagnosis post-transplantation</th>
<th>Associated conditions</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kneipshield et al. (9)</td>
<td>1</td>
<td>Female/31</td>
<td>Oliguria, graft failure</td>
<td>9 mo</td>
<td>Systemic Candida albicans infection</td>
<td>Graft failure Death</td>
</tr>
<tr>
<td>Edmonson et al. (10)</td>
<td>1</td>
<td>Male/22</td>
<td>Passing tissue</td>
<td>14 mo</td>
<td>Acute rejection</td>
<td>Stable chronic renal failure Nephrectomy</td>
</tr>
<tr>
<td>Withworth et al. (6)</td>
<td>2</td>
<td>Male/26</td>
<td>Passing tissue</td>
<td>7 d</td>
<td>Acute vascular rejection</td>
<td>Nephrectomy</td>
</tr>
<tr>
<td>Tuma et al. (7)</td>
<td>1</td>
<td>Female/14</td>
<td>Initial graft failure</td>
<td>25 d*</td>
<td>Acute vascular rejection</td>
<td>Death</td>
</tr>
<tr>
<td>Stefanov et al. (8)</td>
<td>1</td>
<td>NA/32</td>
<td>Abdominal pain</td>
<td>10 d</td>
<td>Urinary tract obstruction by haematoma</td>
<td>Nephrectomy</td>
</tr>
</tbody>
</table>

Abbreviations: NA–not available, UTI–urinary tract infection

* diagnosis was made on post-mortem pathological examination.

Teaching points

1. RPN is a rare complication of renal transplantation, but its frequency is probably underestimated.
2. Although it has been mainly described in the context of severe acute allograft rejection, RPN may occur in the absence of immunological complications and is not always associated with graft loss.
3. The diagnosis of RPN should be suspected in patients with obstructive allograft failure following arterial thrombosis or embolism.
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References


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