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Salvaging of severely ruptured living-related renal allograft secondary to acute antibody mediated rejection

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ABSTRACT

INTRODUCTION: Spontaneous renal allograft rupture (RAR) is a serious and potentially life-threatening complication of kidney transplantation. Debate on the management of RAR has focused on graft nephrectomy versus salvaging in cases where: the allograft rupture site is surgically manageable; the bleeding can be controlled; and/or leaving the renal allograft in situ does not compromise patient survival.
PRESENTATION OF CASE: A 45-year-old, living-related, female, kidney allograft recipient experienced RAR on the fourth day post transplantation. Surgical exploration showed 12 cm laceration along the convex border of the graft. Histologically the graft demonstrated mild acute kidney injury and linear deposition of C4d along the cortical peritubular capillaries; morphological features for violent humoral or cellular rejection were not identified. The graft was surgically salvaged with excellent clinical and biochemical improvement.
DISCUSSION: Observations arising from this case are: (1) RAR caused by rejection is still encountered in clinical practice despite effective immunosuppressive management; (2) the severity of the histopathological features of rejection does not necessarily correlate with the extent of graft rupture; and (3) salvaging the graft should be attempted whenever possible as current immunosuppression and advances in surgical techniques may have an impact on long-term graft function and survival, differing from those previously published.
CONCLUSION: With modern immunosuppression therapy and proven surgical procedures, the efficacy of salvaged renal grafts and graft survival rates may improve substantially.

1. Introduction

Renal allograft rupture (RAR) is rare yet recognized potential complication of renal transplantation. It typically occurs in the first few weeks after transplantation, and it is associated with graft tenderness, hematoma and/or hypotension. The majority of graft ruptures are immunologically-mediated and caused by acute rejection.[1,2] Current immunosuppressive medication regimens contribute to a decreased incidence of allograft rupture.[3–5] Recognition and prompt management of allograft rupture is important due to its likely devastating clinical course and outcome. Usually, nephrectomy is a necessary treatment measure, but conservative surgical intervention has also been successfully attempted to preserve the renal allograft.[3,6–9] We report the clinical presentation of

severely ruptured renal allograft secondary to antibody-mediated rejection, and discuss the surgical and medical management, as well as the follow up and clinical outcome.

2. Case report

A 42 year old woman, known case of end stage kidney disease, due to chronic hypertensive nephropathy, and chronic anemia, received a living-related kidney transplant from her 21 year old son. Immunologically, pre-transplant T-cell cross match by complement dependent Cytotoxic (CDC) was negative, flow cytometric crossmatching (FXM) was negative, and HLA studies showed favorable mismatch 0,1,1 for A, B, DR. Her anti-HLA (PRA) antibody profile was negative by Luminescence, and post transplant PRA became positive for class I, negative for class II, and revealed the following specificity: Class I positive, B7 = 4500MFI, with donor specific antibodies. The transplantation was uneventful and the graft's vein and artery were anastomosed to the recipient's external iliac vein and artery respectively. Intraoperative urine production was

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Fig. 1. Laceration along the convexity of the renal allograft, extending from the upper to lower pole of the kidney.

Fig. 2. Biopsies from the ruptured graft showing mild kidney injury and interstitial oedema, and minimal interstitial inflammation (H&E ×400).

observed, and a urine output in the rate of 2 ml/kg/h was evident in the first hour post surgery. The induction immunosuppression regimen, consisting of prednisone, basiliximab and mycophenolate mofetil was initiated. Within the following 24 h, her urine output dropped to 915 ml/day, and calcineurin inhibitors were not administrated due to deteriorating graft function and low urine output. Graft Doppler Ultrasound revealed a well-vascularized graft with no evidence of a vascular thrombo-embolic event. A renal scan demonstrated features suggestive of acute kidney injury. On the second day post surgery, the patient became anuric and was started on anti-thymocyte globulin. The following day, the patient developed volume overload and respiratory distress, which necessitated a session of hemodialysis. On the fourth day post surgery, the patient developed graft pain and became tachycardic and hypotensive. Abdominal ultrasound revealed a 20 cm peri-graft and retroperitoneal hematoma at the upper pole of the renal graft. The patient was immediately taken to the operating room wherein exploration of the renal graft through the old transplant scar was performed. After evacuation of the hematoma, a laceration measuring 12 cm in length and extending along the convex border from the upper to lower pole of the kidney was identified causing evisceration of at least 1.5 cm in depth and exposing the kidney parenchyma, and was associated with active oozing (Fig. 1). The graft vessels were patent and there was no bleeding from the vascular sites of anastomosis. The ruptured graft was surgically salvaged; the bleeding was controlled using argon beam coagulator; TachoSil™ was applied in the laceration; BioGlue™ surgical adhesive was injected over the ruptured graft, and pressure control was applied for 15 minutes using wet gauze. After ensuring bleeding control, graft biopsies using an 18-guage needle gun were obtained from the upper pole, and an abdominal drain was placed before the abdominal closure. The urine output improved to 0.7 ml/kg/h in the same day of re-exploration.

Histological examination showed morphological features consistent with mild acute antibody-mediated (humoral) allograft rejection. The glomeruli showed mild transplant glomerulitis in the form of mononuclear inflammatory cells infiltrating the glomerular capillaries. No glomerular proliferative features or microthrombi were identified. The renal tubules exhibited mild acute tubular epithelial cell degenerative and regenerative changes/acute kidney injury in the form of dilatation of the renal tubules, simplification of the renal tubular epithelial cells, and nuclear reactive changes and mitoses (Fig. 2). No viral cytopathic effect was identified. The interstitium was mildly edematous but no interstitial hemorrhage was
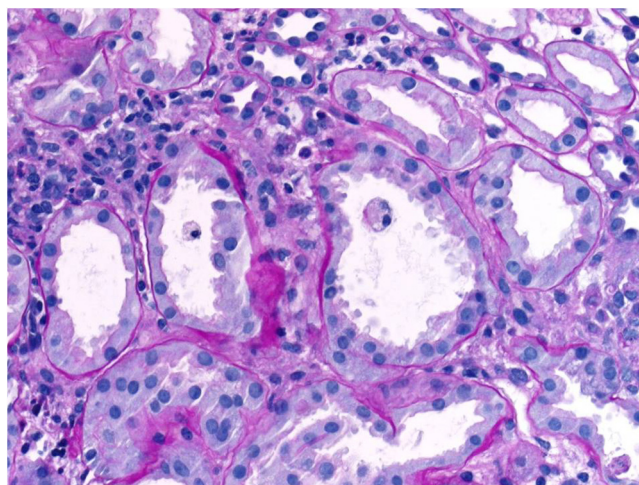
noted. Focal minimal interstitial inflammation involving less than 10% of the renal cortical tissue was noted. There was no lympho-cytic tubulitis or endarteritis. Dilatation of the cortical peritubular capillaries and moderate capillaritis (ptc2), of which the inflammatory cells are predominantly mononuclear, were seen. Neither arteriolar hyalinosis nor arterial sclerosis was noted; nor thrombi in the interstitial blood vessels. Immunohistochemical staining for C4d (dilution 1:40, polyclonal Abcam, Cambridge, UK) showed diffuse yet strong linear staining in the peritubular capillaries (C4d 3+) in the renal cortex and medulla (Fig. 3).

Accordingly the patient was started on tacrolimus (1 mg twice daily) and intravenous immunoglobulin (IVIG) infusion (0.5/mg/kg/day) in addition to induction immunosuppressive regimen and ATG (total dose 7 mg/kg). On the first post re-exploration day, the urine output reached 1.7 ml/kg/h. A total of six doses of IVIG were administrated and the patient received five sessions of plasmapheresis (one session every other day starting on the fifth day post re-exploration). Anti-B7 after treatment dropped to 3000MFI. The clinical course was complicated on post operative day (POD) 11 by a positive urine culture for *Enterococcus faecium*, which was treated by linezolid (600 mg every 12 h for 14 days); the patient was treated also by meropenem (1 g every 12 h) on POD
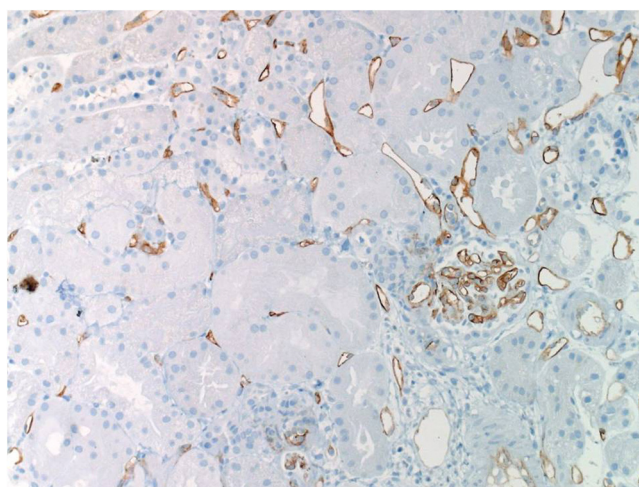

Fig. 3. Immunohistochemical staining for C4d showing diffuse linear, and strong circumferential, staining in the cortical and medullary peritubular capillaries consistent with acute antibody-mediated rejection (C4d IHC ×200).

20 with Extended-Spectrum Beta-Lactamases due to positive urine and blood cultures for *Escherichia coli* and *Klebsiella carbapenem*. The patient improved clinically and biochemically and was discharged on POD 31 with a urine output of 1.5 l/day and serum creatinine 54 μmol/l. Her immunosuppression status was maintained with prednisone, myocophenolate mofetil and tacrolimus (serum level 6.3 at the time of discharge).

3. Discussion

Non-traumatic spontaneous renal allograft rupture is a potentially serious complication of kidney transplantation[6,10–12] and defined as a superficial or deep tear of the renal capsule as well as renal parenchyma. It typically occurs within three weeks after transplantation.[2] The prevalence of RAR ranges from 0.3% to 3%,[6] The most frequent cause of RAR is acute graft rejection.[1] Other major factors contributing to RAR include ischemic acute kidney injury; damaged hilar lymphatic channels; renal vein thrombosis; and ureteral obstruction with subsequent hydronephrosis.[2,6–8] In contrast, renal allograft biopsy rarely causes RAR.[12] The pathological mechanisms contributing to the pathogenesis of RAR are not understood, and may vary between cases. Cortical and capsular ischemia resulting from interstitial edema and cellular inflammatory cell infiltration, in the setting of immunologically-mediated graft rejection, is considered a major cause of RAR by exerting capsular tension, tearing and eventually rupture. This may occur several years after transplantation. We previously reported a case of combined acute cellular and antibody-mediated rejection-associated, spontaneous RAR, 63 months post transplantation in a patient, two months after abrupt cessation of immunosuppressive medications;[13] despite the presence of severe chronic interstitial fibrosis and tubular atrophy (IF/TA) in the biopsy, severe rejection resulted in ARA. Due to the increased risk of ischemic acute kidney injury in renal grafts from non-heart-beating donors, recipients of this type of graft are at a greater risk of developing graft rupture. The presence of focal areas of cortical necrosis might predispose a graft to rupture. Another risk factor of RAR is high peak PRA, likely due to more vigorous immunological responsiveness.[6] The age of the recipient, cold ischemia, preservation conditions, and cytomegalovirus infection were not found to be risk factors.[1]

While most of the reported RAR cases due to immunological causative factors, were associated with significant degree of cellular or humoral rejection,[9,14] the association between the severity of histopathological features of allograft rejection and the incidence of RAR is still not clear. In the present report, histological examination of core biopsies from the renal graft, obtained from areas distant from the rupture wound, demonstrated only mild interstitial edema and insignificant interstitial inflammation, along with mild tubular manifestations of acute kidney injury; yet the extent of graft rupture was remarkably severe and evident as a deep hemifracture of the kidney. This is consistent with the observations of Dryburgh et al. [15], describing eight ruptured grafts, which were grossly tensely edematous; however, histological examination did not suggest violent cellular or humoral rejection. This, as previously postulated, might suggest that mild histological findings such as interstitial edema, insignificant interstitial inflammation and glomerulitis reflect early changes before the development of the more recognizable characteristics of severe rejection;[15] or less likely, reflect the heterogeneity of the rejection severity in the graft. In addition, in cases of acute humoral rejection, such as the one reported herein, mechanisms other than circulating preformed antibodies either contribute to, or entirely predispose RAR.[14]

Clinically, RAR is most commonly characterized by a sudden onset of abdominal pain, graft tenderness and swelling, and decreased hematocrit with hemorrhagic shock.[5] These clinical
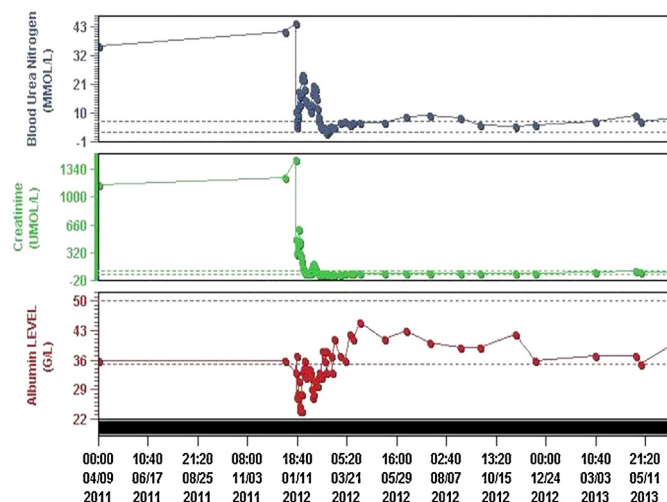

Fig. 4. The patient's blood urea nitrogen, serum creatinine and serum albumin, pre- and post-transplantation (time related graph).

features are commonly associated with oliguria, and occasionally with gross hematuria and fever. The life-threatening nature of RAR mandates immediate recognition of the entity and prompt intervention. The treatment of ruptured renal graft always hinges upon whether or not to perform graft nephrectomy. The usual course of management in RAR is urgent exploratory operation to control bleeding, to perform nephrectomy if indicated, and to evacuate the hematoma in order to reduce the possibility of secondary infection.[14] Empirical evidence in the literature suggests that ruptured renal grafts are salvageable by conservative surgical repair of the rupture with good success rates,[7,16] despite the risk of rerupture.[17] The salvage rates vary between 40 and 100%,[1] with variable post salvage complications and long-term performance of ruptured grafts. Our patient developed severe rupture and damage of the graft, but with prompt surgical intervention, the graft was salvaged, with a serum creatinine of 58 μmol/l 19 months after surgery (Fig. 4). This supports the trend toward graft salvaging in patients with a stable clinical condition, in cases where allograft rupture site is surgically manageable, and the bleeding can be effectively controlled, also when RAR does not compromise patient survival.

In summary, RAR secondary to acute rejection may be encountered in clinical practice despite the era of potent pre- and post-transplant immunosuppressive therapy. The degree of histopathological features of acute rejection may not necessarily reflect the extent and gross severity of graft rupture. This is because causative factors other than immunologically mediated graft injury may contribute to the pathogenesis of RAR. Prompt surgical intervention to control bleeding, to evacuate the hematoma, and to perform graft nephrectomy (or salvaging) whenever possible is essential. With modern immunosuppression therapy and proven surgical procedures, the efficacy of salvaged renal grafts and graft survival rates may improve substantially.

Conflict of interest

None.

Ethical approval

Part of the manuscript was presented in an abstract form in the 16th Congress of the European Society for Organ Transplantation, Vienna, Austria, September 2013.

Author contributions

Dr. M Al Marasatani: Performed the surgical interventional and clinical management, wrote the clinical part of the manuscript and reviewed the manuscript.

Dr. K O Alsaad: Wrote the discussion part of the manuscript, reviewed the histopathology, captured images for publication, and performed the proof-reading of the manuscript.

Dr. N Aloudah: Performed the gross, histopathological and immunohistochemical examinations, and analysis of the material.

Dr. M Hamshow and Dr. B Hegab: Participated in the clinical management, data collection and follow up.

References

1. Hochleitner BW, Kafka R, Spechtenhauser B, et al. Renal allograft rupture is associated with rejection or acute necrosis, but not with renal vein thrombosis. *Nephrol Dial Transplant* 2001;**16**:124–7.
2. Szenohradszky P, Smehak G, Szederkenyi E, et al. Renal allograft rupture: a clinicopathological study of 37 nephrectomy cases in a series of 628 consecutive renal transplants. *Transplant Proc* 1999;**31**:2107–11.
3. Guleria S, Khazanchi RK, Dinda AK, et al. Spontaneous renal allograft rupture: is graft nephrectomy an option? *Transplant Proc* 2002;**35**:339.
4. Vallejo HJ, Rodriguez Luna JM, Fernandez FA, et al. Rupture of the graft in kidney transplant. Our caseload. *Acta Urol Esp* 1989;**13**:252–5.
5. Oesterwitz H, Strobelt V, May G, et al. Spontaneous kidney transplant rupture—effect of immunosuppressive therapy on incidence of rupture. *Z Urol Nephrol* 1990;**83**:157–63.
6. Shahrokh H, Rasouli H, Zargar MA, et al. Spontaneous kidney allograft rupture. *Transplant Proc* 2005;**37**:3079–80.
7. Sanchez de la Nieta MD, Sanches-Fructuoso AI, Alcazar R, et al. Higher graft salvage rate in renal allograft rupture associated with acute tubular necrosis. *Transplant Proc* 2004;**36**:3016–8.
8. Busi N, Capocasale E, Mazzoni MP, et al. Spontaneous renal allograft rupture without acute rejection. *Acta Biomed* 2004;**75**:131–3.
9. Odocha O, Callender CO, Pinn-Wiggins VW. Spontaneous rupture of the renal allograft. *J Natl Med Assoc* 1991;**83**:171–4.
10. Chan YH, Wong KM, Lee KC, et al. Spontaneous renal allograft rupture attributed to acute tubular necrosis. *Am J Kidney Dis* 1999;**34**:355–8.
11. Salaman JR, Calne RY, Pena J, et al. Surgical aspects of clinical renal transplantation. *Brit J Surg* 1969;**56**:413–7.
12. Nikonenko AS, Zavgorodnii SN, Kovalev AA, et al. Surgical strategies in spontaneous rupture of renal allograft. *Klin Khir* 2002;**1**:37–9.
13. Askandarani S, Aloudah N, Al Enazi H, et al. Late renal allograft rupture associated with cessation of immunosuppression following graft failure. *Case Rep Transplant* 2011;**2011**:512893.
14. Homan EP, Cheigh JS, Kim SJ, et al. Renal allograft fracture: clinicopathological study of 21 cases. *Ann Surg* 1977;**186**:700–3.
15. Dryburgh P, Porter KA, Krom RA, et al. Should the ruptured renal allograft be removed? *Arch Surg* 1979;**114**:850–2.
16. Finely DS, Roberts JP. Frequent salvage of ruptured renal allografts: a large single center experience. *Clin Transplant* 2003;**17**:126–9.
17. Lord RS, Effeney DJ, Hayes JM, et al. Renal allograft rupture: cause, clinical features and management. *Ann Surg* 1972;**177**:268–73.