

Acute Allograft Renal Vein Thrombosis: A Case Report

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Abstract

Renal graft thrombosis is a serious and devastating complication of renal transplant that ultimately results in graft loss. It is associated with acute and hyper-acute rejections; however, the underlying cause in large proportion of patients remains unknown. We report a case of a young male who underwent live related kidney transplant but lost the graft on the operating table due to renal vein thrombosis (RVT).

Keywords: Kidney; Transplant; Graft; Loss; Thrombosis.

Introduction

Renal graft thrombosis accounts for one third of all early (within 90 days) graft failure in both adults and pediatric recipients.¹ The North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) reported that graft thrombosis was the major cause of graft failure in the first year in pediatric patients.² It usually occurs as early as 48 hours to first 10 days of transplant.³ However, thrombus formation may be delayed until after the first few weeks. It typically presents with sudden onset of oliguria or anuria, graft swelling and dysfunction. In case of venous thrombosis, flank pain and hematuria are also associated.²

Case Report

This is a 15-year-old boy who was diagnosed to have end-stage renal disease due to obstructive uropathy (vesico-uretric reflux with urethral stricture) three years ago. He was started on thrice-weekly haemodialysis in 2010 initially via tunneled catheter and later via arterio-venous fistula. His past medical history was significant for thrombosis of catheter followed by pulmonary embolism in 2010. Thrombophilia screen was not done at that time; as the hematologist's opinion was that of a catheter-related

provoked thrombosis for which he was treated with anti-coagulant for period of three months. He is not known to have hypertension and has no family history of thromboembolic disorders. He was referred to us for renal transplantation and he underwent live related renal transplant in April 2012. The donor was his father with low immunological risk. The patient's coagulation profile as well as his platelets count were both normal. Induction immune suppression included anti thymocyte globulin, methyprednisolone and mycophenolate mofetil in standard dosage. Unfortunately, after clamps removal, the graft turned pink for few minutes then immediately it became blue and dusky. He remained anuric and bruit was appreciated. Immediately, Doppler study was done and the venous flow could not be detected at the renal hilum; however, there was a normal venous flow more distally at anastomosis site. This was further evaluated with Magnetic Resonance (MR) renal angiogram and its delayed phase showed non-opacification of the renal vein at hilum and its intra-renal tributaries. Patchy cortical enhancement with focal area of non-enhancement was noted in the transplanted kidney.

He remained anuric; a graft biopsy was performed after 24 hours, which revealed vascular and glomerular thrombosis. C4d stain was negative making hyper-acute rejection less likely but not entirely excluded. We do not have the facility of testing for donor specific anti-bodies; however, the repeated cross match anti bodies screen was persistently negative. At this stage thrombophilia screen was performed, which revealed heterozygous for prothrombin G20210A mutation.

The patient got started on plasma exchange, intravenous immunoglobulins and anti thymocyte globulin though the above picture was not compatible with hyperacute rejection. Therapeutic anti-coagulation was tried as well but not thrombolysis in view of the fresh surgery. Lately graft nephrectomy was done.

Discussion

The exact cause of RVT in a large proportion of patients remains unknown; however, several risk factors have been identified and are related to recipients, donors, operative and immunosuppression. Recipient factors include young age,^{4,5} membranous nephropathy,⁶ peritoneal dialysis as mode of pre-transplant dialysis⁷ and hypercoagulable status⁸ including anti phospholipid anti bodies syndrome, anti-thrombin deficiency, mutation of factor V Leiden

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and prothrombin gene while the donor factors include female gender and old age. The operative risk factors of thrombosis risks are prolonged ischemia time, multiple graft vessels anastomosis,⁹ technical errors caused by vascular clamping. RVT can also be triggered by administration of monoclonal antibody like monoclonal antibody OKT3 that can induce procoagulant activity and risk is increased in patients treated with high dose of pulsed methylprednisolone, which may activate the tissue factor/factor VII pathway.¹⁰

Genetic causes of venous thrombosis due to deficiencies of anti thrombin, protein C and S are found in less than 1% of the population.¹¹ Even among patients with thrombosis, only a small percentage carries one of these defects. The most common genetic defect predisposing to thrombosis is FVL (factor V Leiden) with an overall prevalence in carriers of around 5%.¹² Factor V causes thrombosis because of the protein resistance to inactivation of protein C.¹³

The protein gene mutation, which this patient has, is considered the second most common cause of inherited thrombophilia in Caucasians. It was first described in 1996.¹⁴ The mutation is found in the 32 untranslated region of prothrombin gene at position 20210 (Gto A PT20210 A). It is found in about 3% of Caucasians with regional variation in prevalence ranging from 1 to 6%.¹⁵ Among patients with venous thrombosis enrolled in Leiden Thrombophilia Study, this mutation is present in 6%.¹⁶ It increases the risk of thrombosis about three folds, which appears to be mediated through elevated prothrombin levels.¹⁷

This patient was found to have the heterozygous form of the mutation i.e. only one gene is affected and this is more prevalent than the homozygous form, which has prevalence of 1% and a higher risk of thrombosis. Other tests showed FVL mutation negative, proteins S, C and antithrombin III were normal.

Conclusion

Allograft thrombosis generally causes irreversible damage and treatment options are usually disappointing. Few cases were reported in which the grafts were salvaged by early intra-arterial injection of anti fibrinolytic agents.¹⁸ We do believe that thrombophilia screening is mandatory in all patients with history of venous thromboembolism prior to transplant whether considered provoked or unprovoked. Screening should be also done for those with positive family history. Therapy with heparin for the above group in the pre-transplant period has been proved to be beneficial in preventing RVT.¹⁹

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References

1. Irish A. Renal allograft thrombosis: can thrombophilia explain the inexplicable? *Nephrol Dial Transplant* 1999 Oct;14(10):2297-2303.
2. Ponticelli C, Moia M, Montagnino G. Renal allograft thrombosis. *Nephrol Dial Transplant* 2009 May;24(5):1388-1393.
3. Balachandra S, Tejani A. Recurrent vascular thrombosis in an adolescent transplant recipient. *J Am Soc Nephrol* 1997 Sep;8(9):1477-1481.
4. Penny MJ, Nankivell BJ, Disney AP, Byth K, Chapman JR. Renal graft thrombosis. A survey of 134 consecutive cases. *Transplantation* 1994 Sep;58(5):565-569.
5. Harmon WE, Stablein D, Alexander SR, Tejani A. Graft thrombosis in pediatric renal transplant recipients. A report of the North American Pediatric Renal Transplant Cooperative Study. *Transplantation* 1991 Feb;51(2):406-412.
6. Dodhia N, Rodby RA, Jensik SC, Korbet SM. Renal transplant arterial thrombosis: association with cyclosporine. *Am J Kidney Dis* 1991 May;17(5):532-536.
7. Murphy BG, Hill CM, Middleton D, Doherty CC, Brown JH, Nelson WE, et al. Increased renal allograft thrombosis in CAPD patients. *Nephrol Dial Transplant* 1994;9(8):1166-1169.
8. Friedmann GS, Meier-Kriesche HU, Kaplan B, Mathis AS, Bonomini L, Shah N, et al. Hypercoagulable states in renal transplant candidates: impact of anticoagulation upon incidence of renal allograft thrombosis. *Transplantation* 2001 Sep;72(6):1073-1078.
9. Rigotti P, Flechner SM, Van Buren CT, Payne WT, Kahan BD. Increased incidence of renal allograft thrombosis under cyclosporine immunosuppression. *Int Surg* 1986 Jan-Mar;71(1):38-41.
10. Abramowicz D, Pradier O, Marchant A, Florquin S, De Pauw L, Vereerstraeten P, et al. Induction of thromboses within renal grafts by high-dose prophylactic OKT3. *Lancet* 1992 Mar;339(8796):777-778.
11. Tait RC, Walker ID, Reitsma PH, Islam SI, McCall E, Poort SR, et al. Prevalence of protein C deficiency in the healthy population. *Thromb Haemost* 1995 Jan;73(1):87-93.
12. Tait RC, Walker ID, Perry DJ, Islam SI, Daly ME, McCall E, et al. Prevalence of antithrombin deficiency in the healthy population. *Br J Haematol* 1994 May;87(1):106-112.
13. Rosendaal FR. Risk factors for venous thrombotic disease. *Thromb Haemost* 1999 Aug;82(2):610-619.
14. Bertina RM, Koeleman BP, Koster T, Rosendaal FR, Dirven RJ, de Ronde H, et al. Mutation in blood coagulation factor V associated with resistance to activated protein C. *Nature* 1994 May;369(6475):64-67.
15. Rees DC, Cox M, Clegg JB. World distribution of factor V Leiden. *Lancet* 1995 Oct;346(8983):1133-1134.
16. Dahlbäck B, Carlsson M, Svensson PJ. Familial thrombophilia due to a previously unrecognized mechanism characterized by poor anticoagulant response to activated protein C: prediction of a cofactor to activated protein C. *Proc Natl Acad Sci U S A* 1993 Feb;90(3):1004-1008.
17. Poort SR, Rosendaal FR, Reitsma PH, Bertina RM. A common genetic variation in the 3' untranslated region of the prothrombin gene is associated with elevated plasma prothrombin levels and an increase in venous thrombosis. *Blood* 1996 Nov;88(10):3698-3703.
18. Rouvière O, Berger P, Béziat C, Garnier JL, Lefrançois N, Martin X, et al. Acute thrombosis of renal transplant artery: graft salvage by means of intra-arterial fibrinolysis. *Transplantation* 2002 Feb;73(3):403-409.
19. Rerolle JP, Antoine C, Raynaud A, Beyssen B, Julia P, Duboust A, et al. Successful endoluminal thrombo-aspiration of renal graft venous thrombosis. *Transpl Int* 2000;13(1):82-86.