Prolonged Delayed Renal Graft Function Secondary to Venous Hypertension

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Abstract: The case of a 39-year-old highly sensitized woman who underwent second renal transplantation after being on warfarin because of a history of frequent thromboses of her left femoral arteriovenous graft (AVG) is reported here. The patient received a flow cytometric positive crossmatch kidney transplant from a deceased donor. Her posttransplant course was complicated by prolonged delayed graft function (DGF) lasting for 9 months. Antibody-mediated rejection occurred in the immediate postoperative period. This resolved after treatment, and resolution was confirmed by repeat biopsy. Despite this, she had persistent DGF and remained dialysis dependent. A computed tomography scan due to the development of perinephric hematoma after posttransplant biopsy demonstrated venous collateralization around the allograft. At 7 months posttransplant, a venogram during declotting of AVG revealed chronic thrombus in the inferior vena cava (IVC) above the level of native renal veins with a venous gradient of 26 mmHg. After declotting of the graft, iliac venoplasty, and subsequent IVC stent, her renal function continues to improve with a most recent creatinine of 1.4 mg/dL at 36 months posttransplant. Venous hypertension secondary to IVC thrombosis in presence of patent femoral AVG should be considered as a rare cause of prolonged DGF.

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CASE REPORT

This is a case of a 39-year-old African American woman with a history of end-stage renal disease secondary to focal segmental glomerulosclerosis. She received her first kidney transplant from a living unrelated donor in 2005, which eventually failed in 2010 because of recurrent focal segmental glomerulosclerosis, after which she went back on hemodialysis. Her transplanted kidney was removed because of ongoing chronic rejection and pain at the graft site. Her medical history was significant for a history of intradialytic hypotension requiring midodrine therapy and a right lower extremity deep vein thrombosis. She also had multiple failed hemodialysis accesses requiring multiple declotting procedures. In this
setting, despite a negative hypercoagulable work-up, she was placed on chronic warfarin therapy. At the time of transplant, she was being dialyzed via a left femoral thigh graft because there was no possibility of a dialysis access in upper extremity because of central vein stenosis. She underwent a second deceased-donor kidney transplant in November 2013 (panel reactive antibody = 88%) with an acceptable flow cytometric crossmatch per our institutional protocol. During the perioperative period, no anticoagulation with heparin was started given her negative hypercoagulable work-up. After a brief hiatus of 5 days, her warfarin was resumed on discharge. Her transplant was performed on the right side because she had a patent left femoral AV graft (AVG) hemodialysis access. It was felt that it is imperative to salvage the graft for possible need of dialysis in postoperative period. Her surgery was uneventful with a cold ischemia time of 18 hours and 52 minutes. The allograft was from a 29-year-old standard criteria brain-dead donor with normal anatomy.

Her immunosuppression included induction with rabbit antithymocyte globulin (Thymoglobulin, Genzyme, Boston, Mass) followed by maintenance tacrolimus, mycophenolate mofetil, and prednisone. She did require hemodialysis a day after her transplant because of hyperkalemia with marginal urine output. She also had asymptomatic hypotension that required reinitiation of midodrine. Her ultrasound showed patent renal transplant vessels without any abnormality. A transplant kidney biopsy done on postoperative day 7 showed early signs of antibody-mediated rejection (AMR) with microvascular inflammation. She was also noted to have class II donor-specific antibodies with a total mean fluorescence intensity of 16 000. Thus, plasmapheresis was initiated on discharge. Her transplant was performed on the right side because she had a patent left femoral AV graft (AVG). A repeat biopsy 1 month later demonstrated re-

After venoplasty, her urine output started to improve at 9 months after transplant. Another biopsy demonstrated complete resolution of AMR with mild acute tubular injury (Figure 1B). Thus, dialysis was discontinued. Subsequently, her creatinine trended down to a baseline of 1.7 mg/dL.

Later in the course at 34 months posttransplant, she was admitted to the hospital for increasing bilateral lower extremity edema. Recanalization of the suprarenal IVC via
balloon angioplasty with overlapping self-expanding stents resulted in clinical resolution of lower extremity swelling and improvement in abdominal wall collaterals (Figure 4). Her most recent creatinine 36 months posttransplant has further improved to 1.4 mg/dL with a glomerular filtration rate of 54 mL/min per 1.73 m² (Figure 5).

**DISCUSSION**

DGF is common after kidney transplantation and can happen in up to 60% of patients. DGF can be related to various donor and recipient characteristics, cold and warm ischemia time, and various perioperative factors. Although vascular thrombosis can present acutely, chronic venous outflow obstruction has not been described as a cause of DGF.

In this report, we describe the first case of prolonged DGF secondary to renal venous hypertension caused by a previously unknown suprarenal IVC thrombosis with concomitant hyperdynamic flow secondary to patent left femoral AVG. Our patient had a complicated posttransplant course with early rejection. Although this likely contributed to her DGF, she continued to remain anuric despite serial normal allograft biopsies, suggesting an alternative additive etiology. Subsequent imaging procedures and venograms revealed that she had IVC thrombosis. In addition, we performed venous pressure measurements that confirmed a second cause of venous hypertension. She had a left femoral artery–to–femoral vein graft that likely contributed to retrograde flow in the right femoral vein because of the presence of suprarenal IVC thrombosis. Our theory of venous hypertension was again confirmed by the drop in the infrarenal IVC pressure from 34 to 27 mmHg with subsequent reduction in the right atrial to infrarenal IVC gradient from 26 to 19 mmHg (right atrial pressure, 8 mmHg) after the balloon occlusion of the...
patent AVG. We hypothesize that these findings lead to the development of multiple collaterals originating from the right femoral vein. Corrective action through iliac venoplasty and development of collaterals likely resulted in improved allograft outflow and subsequent recovery of graft function.

IVC thrombosis in the absence of an identifiable hypercoagulation disorder is very rare. Surveillance for IVC thrombosis is recommended in pediatric population with significant risk of anatomical problems or risk factors for thrombosis. Nevertheless, no such guidelines exist for adults with end-stage kidney disease. Our patient had multiple reasons that put her at risk of the development of IVC thrombosis. She had a long-standing history of intradialytic hypotension that required the use of midodrine. Intradialytic hypotension is a known cause of vascular access thrombosis. She also had multiple catheters placed that might have contributed to the development of IVC thrombosis due to chronic traumatic injury. Although the acuity of IVC thrombosis in our patient is difficult to determine, it is possible that her IVC thrombosis evolved during the perioperative period when she was significantly more hypotensive and off anticoagulation.

Several lessons can be learned from our experience. We chose to hold anticoagulation in the immediate perioperative setting to minimize the risk of bleeding. In the absence of a known hypercoagulable disorder this was felt to be a safe approach. Similarly, we held anticoagulation when our patient was receiving plasmapheresis. In retrospect, it is likely that her IVC thrombus could have been related to the lack of bridging with heparin during the times when she was off warfarin. Secondly, development of subcutaneous collaterals on imaging in our patient should have triggered an early investigation for venous outflow obstruction with a contrast venogram.

As per our institution protocol, the patient received a noncontrast CT of her abdomen and pelvis to assess calcifications in the iliac vasculature. A contrasted study was not performed. The possibility of venous outflow obstruction was not considered in the presence of a functioning left femoral AV access and absence of collaterals over the abdomen. In retrospect, given her history of multiple AV access thromboses, ongoing therapy with warfarin, and previous procedures with a femoral access, a pretransplant CT with intravenous contrast should have been performed to assess her vasculature. In fact, this is our current institutional protocol at the current time. With the application of this protocol, we have diagnosed 1 patient with IVC thrombosis and another patient with high-grade IVC stenosis. One patient's transplant was drained into the portal system as previously described in the literature. The second patient underwent serial IVC venoplasties before her transplant. Both these patients have good allograft function at the time of the writing of this article.
We conclude that renal transplant venous hypertension is a very rare but important cause of DGF. It should be considered in the differential diagnosis of DGF among patients with risk factors including intradialytic hypotension, history of multiple thromboses, and normal-appearing kidney transplant histology. We also propose that a careful assessment of vascular anatomy should be performed in patients with lower extremity dialysis grafts particularly those with a history of thrombosis. In the event of a known IVC thrombosis, alternate venous drainage should be considered prospectively to prevent DGF and chronic vascular complications.

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