Bench thrombolysis and “autotransplantation” as a rescue treatment for venous thrombosis after living-donor kidney transplantation

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Abstract

Background: Allograft venous thrombosis is a severe complication after kidney transplantation (KT). Early diagnosis and prompt treatment are crucial in preserving the survival of the allograft. In this study, we aimed to describe an emergent strategy for the management of acute allograft venous thrombosis.

Case presentation: A 4-year-old girl, weighing 13.5 kg, was diagnosed with bilateral congenital renal hypoplasia, urogenital sinus and anorectal malformation. The patient was referred to our department for living-donor KT. Her mother was eligible as a donor, presenting a body weight ratio of 1:4.5. Thrombosis of the inferior vena cava (ICV) was also identified, without any predisposing factor for thrombophilia. KT was performed by an extraperitoneal approach without complications. Venous anastomosis required a human vascular graft sutured to the ICV, and renal artery was anastomosed to the aorta. On postoperative day (POD) 8, acute abdominal pain and hematuria led to the diagnosis of an allograft venous thrombosis. An emergent laparotomy was required to explant the allograft, followed by bench surgery. The allograft was irrigated with thrombolytic agents and lactated Ringer’s solution and then after removing the venous vascular graft, it was reimplanted through vascular anastomosis with the ICV and aorta. The recovery of perfusion and function was good with diuresis since day 4 after re-surgery. At 2-year follow-up, the child presented normal allograft function with an estimated GFR of 65 ml/min/1.73 m².

Conclusion: According to our experience, explantation of the kidney allograft, followed by irrigation with thrombolytics in bench surgery, and reimplantation resulted in unexpected optimal outcomes in the case of allograft venous thrombosis.

KEYWORDS: kidney transplantation, pediatric, thrombolysis, thrombosis of the inferior vena cava, venous thrombosis

Abbreviations: DUS, Doppler ultrasonography; ESKD, end-stage kidney disease; ICV, inferior vena cava; KT, kidney transplantation; POD, postoperative day; RHD, renal hypoplasia.
1 | INTRODUCTION

Venous thrombosis of the kidney allograft affects up to 10% of the pediatric kidney transplantations (KTs) in the first postoperative days (PODs). This complication is one of the main causes leading to the loss of the allograft during the immediate postoperative period and might put the patient’s life at risk.

Several predisposing factors have been investigated, and children younger than 6 years or weighing less than 15 kg are at particular risk because of the smaller caliber of the vessel and the potential size mismatch between the donor and recipient. Moreover, it has been speculated that a hypercoagulable state and/or vascular anatomic variants might further account for the occurrence of allograft venous thrombosis. Renal vein thrombosis may also be triggered by kinking of the renal vein or stenosis of the venous anastomosis.

For these reasons, a preventive strategy using administration of anticoagulants after pediatric KT has been proposed in selected cases with controversial results. Despite the relevance of this event, no clinical, biochemical, or instrumental specific signs have been identified, and early diagnosis might be missed. A suspicion of allograft thrombosis requires urgent investigation because it might be potentially correctable, although a delay in the diagnosis or management will result in a graft loss.

Herein, we reported the acute management of a low-weight child who experienced an early kidney allograft venous thrombosis after a living-donor KT. In particular, we aimed to describe our emergent strategy that resulted in a complete rescue of the organ.

2 | CASE PRESENTATION

2.1 | Clinical history

A 4-year-old girl, weighing 13.5 kg, was referred to the Department of Women’s and Children’s Health of Padua University Hospital, Italy, for the pediatric KT program. The child was diagnosed with end-stage kidney disease (ESKD) due to congenital bilateral renal hypoplasia (RHD).

The girl was born at 38 weeks of gestational age without any antenatal finding. At birth, the clinical examination showed a complex perineal congenital malformation, consisting in urogenital sinus associated with anorectal malformation. During the first days of life, the girl presented ESKD. In order to set out the anatomy, a nuclear magnetic resonance was performed, detailing the complex malformation and pointing out a severe bilateral RHD.

Afterward, the girl underwent a placement of a peritoneal dialysis catheter. In the next years, several episodes of catheter-related peritoneal infections were encountered, requiring a switching in the dialysis modality. It is relevant to underline that the insertion of a venous line for hemodialysis in the right femoral vein failed because of the presence of thrombosis.

At our center, the patient underwent a complete diagnostic workup. Living donation was offered, and her mother resulted eligible, even if a considerable size mismatch between the donor and recipient was reported, presenting a body weight ratio of 1:4.5.

As to the vascular anatomy, the clinical history and Doppler ultrasonography raised the suspicion of thrombosis of the inferior vena cava (ICV). Therefore, a phlebography was performed, showing no blood flow from the retro-hepatic ICV to the right common iliac vein (see Figure 1). The left iliac venous axis was patent. The bilateral iliac arterial axis and aorta were patent as well. A thrombophilia evaluation resulted negative; however, prophylaxis with daily low-molecular weight heparin was prescribed in order to avoid a further extension of the thrombosis.

For these reasons, the use of a human vascular graft was considered in order to reach the patent tract of the ICV, which was close to the liver, after having placed the kidney allograft in the right iliac fossa. Indeed, the main concern consisted in a predictable insufficient length of the donor’s vein to allow a tension-free anastomosis.

To complete the pretransplant evaluation, a detailed perineal examination and cystoscopy were performed, confirming the diagnosis of urogenital sinus without a bladder of adequate capacity. For this
reason, the feasibility of the vesical-ureteral reimplantation during KT was excluded, and ureterocutaneostomy was indicated.

2.2 | Kidney transplantation

According to the protocol of our institution, immunosuppression was induced with basiliximab and methylprednisolone. The extraperitoneal approach was chosen. The right iliac venous axis and the ICV were identified. These vessels appeared fibrotic. The ICV presented a normal caliber just before its retro-hepatic tract. A human vascular graft from the organ bank was prepared and sutured in an end-to-side fashion to the ICV.

The donor’s kidney did not present any anatomic variants, and the bench surgery did not require any further procedure. The allograft was implanted in the right flank in an orthotopic position, rather than in the right iliac fossa, as previously planned (see Figure 2). The renal artery was sutured to the aorta in an end-to-side fashion, and the vein was sutured to the vascular graft in an end-to-end fashion. The warm ischemia time was 55 min. Thereafter, the ureterocutaneostomy was performed, and a 6-Fr ureteral stent was inserted.

At the end of the vascular anastomosis, a continuous intravenous infusion of unfractioned heparin was started until reaching the maximum dose of 15 UI/kg/h. The target was 1.5-2 times prolongation of pretransplant aPTT. Unfractioned heparin was stopped on POD 7, after having reached a normal kidney allograft function.

After the KT, the immunosuppression was continued with methylprednisolone, mycophenolate mofetil, and cyclosporine. The function of the allograft presented a rapid recovery and the Doppler ultrasonographic (DUS) monitoring found good allograft perfusion with normalization of intraparenchymal resistive indices from POD 3, while the child was still on intravenous heparin.

2.3 | Management of the allograft venous thrombosis

On POD 8, the child showed acute abdominal pain, decreased urinary output with hematuria, and blood loss from the retroperitoneal drain. A DUS was promptly performed without identifying blood flow in the renal vein, and the renal artery presented diastolic reverse flow. These findings confirmed the diagnosis of allograft venous thrombosis, and an emergent laparotomy was indicated. Before surgery, a single bolus of intravenous urokinase (50 000 IU) was administered.

At the operating table, the kidney appeared congested and surrounded by a hematoma. The allograft was explanted and prepared
for bench surgery. The venous graft was removed, and several intramural blood clots were found inside the lumen. Then, the allograft was irrigated with 1500 ml of lactated Ringers’ solution, 100 000 IU of urokinase, and finally, 50 mg of alteplase in order to wash out blood clots from the parenchyma. Afterward, the allograft was reimplanted. The renal vein was directly anastomosed to the ICV in an end-to-side fashion, and the renal artery was re-anastomosed to the aorta in an end-to-side fashion (see Figure 3). The removal of the vascular clamps took place 95 min after the explantation. Finally, the ureterocutaneostomy was refashioned without complications. The allograft presented a vital aspect showing a good recovery of the parenchymal perfusion.

2.4 | Outcomes

During the first three PODs, infusion of dopamine together with blood transfusions was required to maintain hemodynamic stability. On POD 4, continuous intravenous infusion of heparin was restarted and continued for 2 weeks, maintaining the aPTT within 1.2–1.5 times the normal range. DUS showed no sign of thrombosis in the abdominal vessels; therefore, intravenous heparin was discontinued, and oral warfarin was started to obtain INR values within the range of 2–3.

DUS monitoring showed a gradual improvement of the allograft perfusion. As to the function of the allograft, the recovery was slow but complete, and the diuresis was present since POD 4.

A 99mTc-MAG3 diuretic renography was performed 1 year after KT, showing an inhomogeneous cortical uptake with good urine drainage, as shown in Figure 4.

At the last follow-up at 2 years after transplantation, the girl is growing well, and she is still on oral warfarin. Her serum creatinine is 59 µmol/l, with an estimated glomerular filtration rate of 65 ml/min/1.73 m². Protocol transplant biopsies performed at 6, 12, and 24 months after transplantation were normal (Banff 1, class I). After 2 years since KT, a computerized tomography angiography was performed, finding patency of the ICV from the right atrium until the origin of the native right renal vein and also the complete patency of the allograft anastomosis, as shown in Figure 5. No further progression of the thrombosis was reported. Then, the discontinuation of warfarin was considered. Further surgical interventions will be required for the treatment of the complex urogenital and anorectal malformation.
3 | DISCUSSION

Kidney transplantation is the gold standard for the treatment of ESKD in children. However, in this case, the intervention represented a surgical challenge for several reasons. First, patient's young age and low body weight are recognized as risk factors for complications after KT. Second, size mismatch between the donor and recipient might increase the occurrence of vascular events. Then, the complex urogenital and anorectal malformation needed a careful diagnostic workup before the KT. Finally, the presence of thrombosis in the ICV made allograft implantation and vascular anastomosis more difficult and required the insertion of a vascular graft, which itself represents a prothrombotic factor.

Nevertheless, thrombosis of the ICV did not represent a contraindication for pediatric KT, but several series reported a higher rate of adverse events. Taking into account all these reasons, in our case, anticoagulation with LMWH was preventively prescribed at the pretransplant evaluation in order to avoid further extension of thrombosis. Continuous infusion of unfractioned heparin was also started in the immediate posttransplant period.

Despite this, posttransplant graft thrombosis was heralded by the onset of sudden anuria, hematuria, and tenderness and severe pain over the graft region. Treatment of graft thrombosis is generally disappointing, and a prompt management is mandatory. Systemic thrombolysis has been already proposed for the treatment of vascular events after KT, but this procedure might not be completely effective in solving blood clots. Conversely, higher doses in the early postoperative period might put the patient at risk of severe bleeding.

In our case, explanation of the allograft was followed by “autotransplantation,” as previously performed for renovascular, ureteral, and malignant pathologies. This staged procedure allowed a complete thrombectomy and a local irrigation with thrombolytic agents in higher doses. In the first instance, urokinase was used, but the washing solution flowing out of the allograft was still not clean. Therefore, alteplase, a safe alternative to urokinase, was chosen. Finally, the irrigation with the washing solution was continued after the administration of thrombolytics in order to completely remove all the blood clots and the residual infusion of thrombolytics.

In conclusion, a careful diagnostic workup is essential for children with risk factors for vascular events. In our case, a continuous monitoring in the postoperative period allowed an early diagnosis of thrombosis and, consequently, a prompt treatment. According to our experience, explanation of the allograft, followed by bench thrombolysis and “autotransplantation,” might be considered a safe and effective treatment for venous thrombosis of the kidney allograft in children.

CONFLICT OF INTEREST
The authors declare no conflicts of interest.

AUTHORS’ CONTRIBUTIONS
FG and FDC participated in the design of the study. FG, MP, and EV collected the data. FG and MC wrote the first draft of the manuscript. FDC, FFL, DT, MP, CT, MC, EV, and PG reviewed and commented on the manuscript. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT
The data underlying this article will be shared on reasonable request to the corresponding author.

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