OPEN

Successful Kidney Transplantation in Children With a Compromised Inferior Vena Cava

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Background. Children with a compromised inferior vena cava (IVC) were previously considered unsuitable for kidney transplantation because of the technical difficulties and the increased risk of graft thrombosis secondary to inadequate renal venous outflow. **Methods.** We conducted a retrospective study of 11 transplants in 9 patients with end-stage renal disease and thrombosed IVCs who received adult kidney allografts between 2000 and 2015. The mean age at transplantation was 7.5 ± 3.5 years. A pretransplant diagnosis of the IVC thrombosis was made in 7 patients by magnetic resonance imaging and computerized tomography, whereas there were 2 instances of intraoperative discovery of the IVC thrombosis. **Results.** In the early cases, a kidney was placed intraperitoneally at the right iliac fossa with a venous anastomosis to the patent segment of the suprarenal IVC. After 2008, however, 6 adult-sized kidneys were subsequently placed in the left orthotopic position. Venous drainage was attained to the infrahepatic IVC (n = 3), left native renal vein (n = 2), and ascending lumbar vein (n = 1). Moreover, a venous bypass was created between the graft and the splenic vein in 2 children who showed high return pressure after the vessel was declamped. The mean glomerular filtration rate of the functioning 8 grafts 1 year posttransplant was 73.4 ± 20.4 mL/min per 1.73 m^2. Of note, 6 of the grafts have been functioning well, with a mean follow-up of 66 months. Both 1- and 5-year graft survival were 81.8%. **Conclusions.** Transplantation into the left orthotopic position and the revascularization methods are an effective set of surgical techniques that could potentially be adopted as safe and reliable transplant approaches in children with IVC thrombosis.

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I n recent years, advances relating to operative and postoperative management, as well as progress in postoperative immunosuppressant therapy have paved the way for transplantation in cases that would previously have been risky and contraindicated.[1] Vena cava thrombosis is a rare but serious complication in pediatric patients preparing for kidney transplantation. Congenital large vessel abnormalities,

previous surgery for the treatment of malignancy, and iatrogenic causes, such as the long-term placement of a catheter in the iliac vein, may lead to the complete obstruction of the inferior vena cava (IVC).[2]

Children can present operative challenges given the relatively large size of an adult kidney graft. Therefore, when an adult-sized kidney (ASK) is transplanted into a pediatric recipient, the largest diameter vein is selected to maximize venous drainage. Moreover, small children weighting 20 kg or less should undergo vascular anastomosis of the graft vessels to the distal aorta and IVC. If an ASK were transplanted into a child with IVC thrombosis with the graft vein anastomosed to the patent segment of peripheral vein (eg, iliac vein), impaired venous outflow might predispose the patient to venous hypertension, with the possibility of subsequent graft thrombosis. Therefore, children with absent or thrombosed IVCs were previously considered high-risk and unsuitable for kidney transplantation.[2-4]

However, Eneriz-Wiemer et al[2] have reported 6 renal transplants using a size-matched deceased donor (DD) allograft for children with a thrombosed IVC, showing satisfactory results. They preferred to use small DD kidney allografts so that renal outflow would not exceed the drainage capacity of the iliac or adjacent collateral veins.

Furthermore, several recent case reports in the literature have suggested that successful transplantation using an ASK may be achieved in this situation.[2,3,5,6] Potential sites can be considered for implantation based on the preoperative imaging and an intraoperative evaluation. A patent segment of

the IVC or iliac vein,[3-7] ovarian vein,[8,9] left renal vein, superior or inferior mesenteric vein (IMV), or portal vein have been used as the site for venous anastomosis.[10-12]

However, there have been no previous reports showing a universally agreed upon surgical approach for kidney transplantation in patients with IVC thrombosis. Therefore, the aim of this study was to examine the best possible approach for kidney transplantation in a child with IVC thrombosis.

MATERIALS AND METHODS

A retrospective study of 11 transplants in 9 consecutive pediatric patients with end-stage renal disease and thrombosed IVCs who received adult kidney allografts at the Toho University and Tokyo Metropolitane Kiyose Children's Hospital between 2000 and 2015 was conducted. Doppler ultrasonography was used as the initial screening tool in patients before kidney transplantation. When IVC and/or iliac vein obstruction was suspected, a further preoperative vascular evaluation was performed using magnetic resonance imaging (MRI) and/or computed tomography (CT) in combination with venography. For each patient, the etiologies of end-stage renal disease and IVC thrombosis were determined, and the dialysis history and other patient characteristics at the time of transplantation, including age, height, and weight of each recipient, were obtained.

Posttransplant evaluation included an assessment of the renal vein drainage anatomy using MRI or CT performed at 3 months and 1 year after the transplant. Renal function was assessed based on serum creatinine and the glomerular filtration rate calculated by the Schwartz formula. Further, the hypertensive history for each patient was evaluated. The 1- and 5-year graft survivals were examined using a Kaplan-Meier curve.

RESULTS

Between 2000 and 2015, 9 patients (4 boys and 5 girls) with a compromised IVC received 11 adult kidney allografts (7 living donors [LD] and 4 DD kidneys, Table 1). The mean age at transplantation was 7.5 ± 3.5 years (range, 2.8-14.9 years). The weight at transplant ranged from 12.0 to 37.0 kg (median, 16.8 kg). The primary diseases of the recipients included hypo/dysplastic kidneys in 3 patients, diffuse mesangial sclerosis in 2 patients, and congenital

nephrotic syndrome, autosomal recessive polycystic kidney, Denys-Drash syndrome, and an immature teratoma in 1 patient each. Three patients had a history including the placement of femoral catheters. Moreover, 3 patients had a history of surgical treatment for malignancy. Patient 1 had a unilateral Wilms tumor and underwent nephrectomy with chemotherapy at the age of 1.6 years. Wilms' tumor-1 gene analysis showed heterozygous germline mutations in exon 9. Patient 8 was also diagnosed with hepatoblastoma at the age of 1.1 years and underwent an extended right hepatectomy after chemotherapy without relapse. Moreover, patient 6 had an immature teratoma, and the vena cava had been resected together with the huge tumor. In addition, 2 patients had lost their first graft soon after their transplantation because of graft thrombosis (patients 10 and 11). The subsequent imaging studies of the vasculature revealed complete obstruction of the IVC.

Seven patients had been managed with peritoneal dialysis, whereas 1 patient underwent hemodialysis before transplantation. A pretransplant diagnosis of IVC thrombosis was made in 7 patients using CT/MRI, and there were 2 instances of intraoperative discovery of an IVC thrombosis. No patients had any clinical symptoms of IVC thrombosis. The pretransplant hypercoagulable work-up was negative in all patients.

In the early recipients (patients 1, 2, 4, 6, 7) who received an adult kidney allograft (4 LD, 1 DD) before 2008, a vertical midline transperitoneal incision was made, and the graft was placed intraperitoneally at the right iliac fossa with renal arterial and venous anastomosis to the aorta and the patent segment of the suprarenal/infrahepatic IVC. These 5 patients showed good primary function, whereas patient 7 died of sudden heart failure after graft thrombosis at day 1 posttransplant. In addition, a graftectomy was performed on patient 2 at the day of surgery because of uncontrolled bleeding at the venous anastomosis site. This patient developed an intestinal perforation because of disseminated intravascular coagulation after heavy bleeding. She had been managed with hemodialysis until she received a second DD allograft 3.8 years after the first transplantation (patient 3). We speculated that the downward shifting of the graft due to liver enlargement may have caused this bleeding.

Therefore, the subsequent 6 children (patients 3, 5, 8, 9, 10, 11) received a kidney (3 LD, 3 DD) in the left orthotopic

TABLE 1.

Patient characteristics

Case	Sex	Original disease	History of surgery	Placement of HD catheter	Age at dialysis, y	Age at RTx, y	Body weigh, kg	Donor
1	F	DDS	nephrectomy for lt. Wilms tumor	yes	1.6 (PD)	7.4	13	LD
2	F	DMS	no	yes	0.8 (PD)	2.8	12	LD
3 (2-2)					2.8 (HD)	6.4	19.5	DD
4	M	Hypo/dys	no	no	None	4.7	14.3	LD
5 (4-2)					None	14.9	37	DD
6	M	Teratoma	removal of tumor with IVC	no	0.6 (PD)	4.5	14.7	DD
7	M	DMS	no	yes	1.7 (PD)	6.8	18.6	LD
8	M	Hypo/dys	Hepatectomy for hepatoblastoma	no	10.0 (PD)	10.3	22.9	LD
9	F	CNS	no	no	1.0 (PD)	9	16.8	LD
10	F	Hypo/dys	Graftectomy due to thrombosis	no	0.5 (PD)	4.9	14	DD
11	F	ARPKD	Graftectomy due to thrombosis	no	0.1 (PD)	11.3	21.2	LD

DDS, Denys-Drash syndrome; DMS, diffuse mesangial sclerosis; Hypo/dys, hypoplastic/dysplastic kidney; CNS, congenital nephrotic syndrome; ARPKD, autosomal recessive polycystic kidney; PD, peritoneal dialysis; HD, hemodialysis.
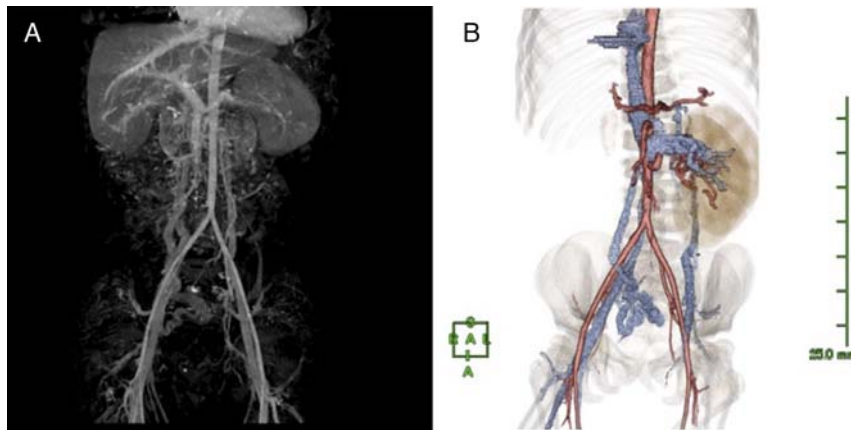
FIGURE 1. A, An MRI image showing complete obstruction of the infrarenal vena cava with an enlarged ascending lumbar vein (patient 10). B, An image of a 3D-CT performed 4 months after transplantation. The graft vein was pulled through between the superior mesenteric artery and aorta and was anastomosed to infrahepatic inferior vena cava.

position. The surgery proceeded transperitoneally from an anterior transverse incision into the left upper abdomen. In 3 recipients (patients 5, 10, 11), the graft vein was pulled through between the SMA and aorta and was anastomosed to the infrahepatic IVC. The renal artery was anastomosed to the aorta. The left renal vein of the decease donor was long enough to anastomose to the contralateral infrahepatic IVC (patient 10) (Figures 1A and B). When the right kidney was used, a vena cava extension was performed to elongate the graft vein using the donor's vena cava (patient 5). In a patient (patient 11) who received a LD kidney allograft, venous anastomosis required an interposition using a 7-cm segment of the donor's gonadal vein and great saphenous vein between the renal vein and infrahepatic IVC. In patient 3, who lost the first kidney because of a surgical complication, it was difficult to approach the infrahepatic IVC owing to intestinal adhesions. Therefore, the graft vein was anastomosed to the left native renal vein after nephrectomy.

The most technically troublesome cases were 8 and 9, who both demonstrated complete obstruction of the IVC below the diaphragm; they had no patent segment of IVC for venous reconstruction of the graft. In these cases, MR venography as well as CT 3D reconstruction (3D-CT) showed that the infrahepatic IVC was completely obstructed to below the branch of the iliac vein. The collateral circulation consisted of the azygos vein passing from the left common iliac vein to the ascending lumbar vein. Additionally, an expansion of the vertebral venous plexus was detected (Figure 2A).

Patients 8 and 9 received living donor kidney allografts from their mothers. The reconstruction of the renal-transplanted vein started with the end-to-side anastomosis of the graft vein to the left native renal vein (patient 8) or enlarged ascending lumber vein (patient 9). Moreover, as it seemed that the venous return pressure had become too high soon after the vessel was declamped, a venous bypass was created using the donor's ovarian vein, between the graft vein and the splenic vein after splenectomy. The aim of this bypass was reducing the venous return pressure of the transplant (Figure 2B). Such double venous drainage worked very well; blood flow appeared normal upon resuming blood circulation, and no excess swelling of the transplanted kidney was observed.

In most cases, urinary drainage was accomplished with ureteroneocystotomy by using an extravesical approach (Lich-Gregoir technique). In 4 of the 6 patients who underwent orthotopic kidney transplantation through the left anterior transverse approach, a new small lower abdominal
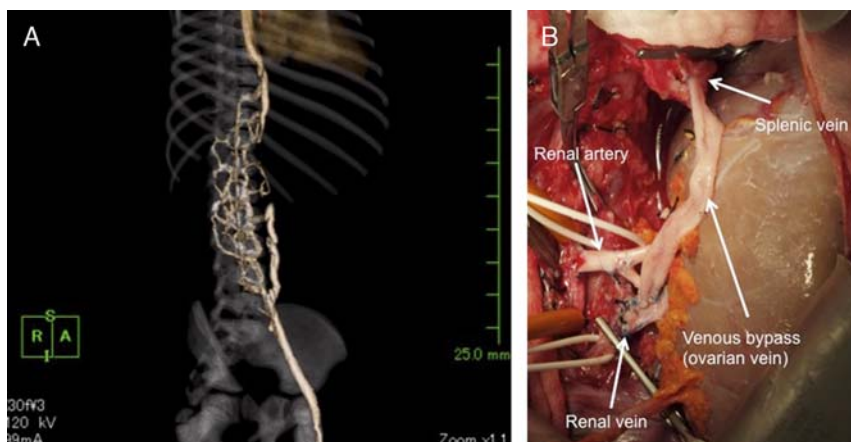
FIGURE 2. A, An image of a 3D-CT in combination with venography showing complete obstruction of the inferior vena cava with an enlarged ascending lumbar vein and gonadal vein (patient 9). An expansion of the vertebral venous plexus was also detected. B, A graft was placed in the left orthotopic position with a graft venous anastomosis to the ascending lumbar vein. Moreover, a venous bypass was created between the graft vein and the splenic vein.

TABLE 2.

Renal allograft function and long-term graft outcome

Case	Serum creatinine, mg/dL		CCr, mL/min per 1.73 m^2	Graft outcome	
	3 mo	1 y	1 y	Graft survival	Months
1	0.56	0.7	77	Graft loss	100
2	ND			Graft loss	0
3 (2-2)	0.65	0.78	72.2	Graft survival	123
4	0.54	0.58	107.7	Graft loss	122
5 (4-2)	1.55	1.76	56.5	Graft survival	31
6	0.98	0.92	64.2	Graft survival	138
7	ND			Death	0
8	0.84	1.27	55.4	Graft survival	67
9	0.57	0.84	71.6	Graft survival	49
10	0.62	0.61	94.2	Graft survival	17
11	0.37	ND	ND	Graft survival	3

CCr, creatinine clearance.

transverse incision was made suprapubically, and an extravesical reimplantation of the ureter was performed. However, in 2 patients (patients 7, 10) whose ureter did not reach the bladder, an anastomosis with the native ipsilateral ureter was made.

The immunosuppression regime consisted of basiliximab upon induction of anesthesia with a further dose of basiliximab on day 4. Tacrolimus or cyclosporine, mycophenolate mofetil, and steroids were used for maintenance of immunosuppression. In addition, dipyridamole (5 mg/kg) and ticlopidine hydrochloride (5 mg/kg) were administered starting 3 days posttransplantation to prevent platelet aggregation.

All children showed good primary renal function, but 2 grafts were lost due to surgical complications, as mentioned above. The mean glomerular filtration rate of the functioning 8 grafts 1 year posttransplant was 73.4 ± 20.4 mL/min per 1.73 m^2 (Table 2). An additional 2 patients lost their first graft at 8.4 and 10.3 years posttransplant because of chronic rejection. One patient (patient 1) returned to dialysis and the other (patient 5) has preemptively received a second kidney allograft from a DD. Of note, 6 grafts have been functioning well with a mean follow-up of 66 months (range, 3-135 months) (Table 2). Both 1- and 5-year graft survivals were 81.8%.

DISCUSSION

A compromised vena cava is a rare but serious complication in a child preparing to undergo for kidney transplantation. In the current study, patients 10 and 11 developed IVC thrombosis from their previous kidney transplantations. The precise reasons for the IVC blockade in the other patients were not known, although a collapsed and fibrotic IVC was confirmed during the operation. Patients 1, 2, 7, and 9 developed nephrotic syndrome in their early life, which is known to be associated with a hypercoagulable state, and IVC thrombosis is well recognized in this condition.[2,3] In addition, a previous abdominal surgery (patients 1, 6, and 8) is a further risk factor.

A detailed imaging study of the vasculature is an essential part of the pretransplant evaluation, especially for children with the risk of having a compromised IVC, history of femoral vein catheter placement, or intra-abdominal processes for the treatment of malignancy. First, an ultrasound can provide reliable information on the vascular anatomy of the iliac vein and IVC, even in infants and young children. Whenever IVC and/or iliac vein obstruction is suspected, further preoperative vascular evaluation is important for safe and successful renal transplantation. Computed tomography and magnetic resonance angiography with 3D reconstruction is an accurate, reliable, noninvasive tool for evaluating the iliocaval axis of children scheduled for transplantation.[5,12] These examinations can provide a detailed picture of the vascular anatomy and help define appropriate alternative vascular anastomosis sites in the presence of IVC and/or iliac vein thrombosis.

In our experience, a 3D-CT in combination with venography was quite useful to assess the collateral circulation, especially in cases with a complete obstruction or anomalies of the intrahepatic IVC. In addition, the total amount of contrast media can be saved, as opposed to that in contrast-enhanced CT.

Children with an absent or thrombosed IVC were previously considered unsuitable for kidney transplantation because of the technical difficulties and the increased risk of graft thrombosis secondary to inadequate renal venous outflow.

Several previous studies have shown that when the iliac veins are patent irrespective of a thrombosed IVC, the iliac system can be used if the venous pressure is below 25 mm Hg.[12,13] However, anastomosing an ASK distal to the thrombosed IVC of a pediatric patient is not recommended because impaired venous outflow would predispose the patient to venous hypertension, with the possibility of subsequent graft thrombosis.[4,6] Moreover, inadequate venous drainage of the graft could compromise long-term renal function.[6,14] Generally, the largest diameter vein should be selected to maximize venous drainage in a child who receives an ASK. In our experience, the infrahepatic thrombus-free segment of the IVC is the preferable site for the renal vein anastomosis when both the iliac veins and/or distal IVC are unsuitable. In addition, according to the review by Salvatierra et al,[15] the site of the donor's renal vein anastomosis in pediatric recipients was mainly the patent segment of the IVC.

In this study, 8 of the 11 transplants were performed with a renal venous anastomosis to the patent suprarenal/infrahepatic segment of the IVC. However, it should be noted

that the maximum length of graft vein was sometimes not adequate for venous anastomosis to the infrahepatic IVC, especially when a live donor kidney allograft was used. Moreover, the liver may restrict the graft position when an ASK is placed at the right iliac fossa of small children, which might be associated with an increased risk of post-transplant vascular complications. In our experience, 2 of the early 5 recipients whose graft was placed at the right iliac fossa with a renal arterial and venous anastomosis onto the aorta and patent segment of the IVC lost their graft because of thrombosis or uncontrolled bleeding at the site of venous anastomosis. We speculated that the downward shifting of the graft by an enlarged liver might have caused such a tragic complication.

Therefore, since 2008, the graft has been placed at the left orthotopic position in 6 recipients through a transperitoneal approach. The orthotopic positioning of the kidney was previously described by Gil-Vernet et al.[16] Martinez-Urrutia et al[6] also reported successful left orthotopic kidney transplantation in 3 children with a previous IVC thrombosis. In this way, direct access can be gained to the infrahepatic IVC and aorta, or the recipient's splenic vessels may be used. The weakness of this technique is that the length of the graft vein is sometimes too short to anastomose at the contralateral patent segment of the IVC when the graft is placed at this position.

In a recipient who received a left kidney from an adult DD, the renal vein was long enough to anastomose directly to the infrahepatic IVC. Moreover, vena cava extensions could be performed to elongate the graft vein by using the donor vena cava when the right kidney from the DD was used. In both cases, an end-to-side anastomosis of the renal artery to the aorta was performed. If an ASK from an LD is transplanted in this manner, venous interposition would be needed between the renal vein and infrahepatic IVC. In our experience, venous interposition was created using a good segment of the donor's gonadal vein and great saphenous vein.

Furthermore, the most technically serious cases were those with complete obstruction of the intraabdominal IVC, because they had no patent segment of IVC for venous reconstruction of the graft.

Several investigators have recommended the use of the portal system for renal allograft revascularization in the setting. Drainage of the renal vein into the portal vein, superior mesenteric vein, and IMV has been described.[8-12] Anastomosis of the renal vein to the IMV may be technically simpler owing to the anatomic situation of this vein, which is accessible in the peritoneal cavity and has a relatively long course.[6] On the contrary, the small caliber of this vein may pose an excessive risk of thrombosis. Furthermore, a higher risk of graft rotation has been suggested because of its accessibility and long course.[11]

Previous studies have shown that collateral circulation in cases with IVC blockages is mainly mediated by "the deep route" through the ascending lumbar vein to the hemiazygos and azygos veins.[17,18] In 2 cases (patients 8 and 9), as indicated in the diagnostic images, the collateral circulation was mainly through this route. Moreover, on the left side, pelvic venous blood flowed into the renal vein through the left gonadal vein.[19] Because a connection between the left renal vein and the left ascending lumbar vein can potentially exist, even if some pathological change blocks the stem of the left renal

vein, it is possible that the blood in the left renal vein may flow backward through the ascending lumbar vein and pass through the azygos vein, from the hemiazygos vein to the superior vena cava. Furthermore, backflow from the renal vein can flow back into the right atrium through the left inferior phrenic vein.

In this setting, therefore, we recently prefer to use this deep route for renal allograft revascularization. Three recipients, including 2 children with complete obstruction of the infrahepatic IVC (patients 8 and 9), underwent kidney transplantation at the left orthotopic position with venous anastomosis to the left renal vein or ascending lumber vein. Furthermore, we showed that in cases in which the drainage vein may not be sufficient, an additional venous bypass using a donor ovarian vein between the graft vein and splenic vein could be a treatment option for reducing venous pressure. In addition, if it is not possible for the ureter to reach the bladder, the recipient's urinary tract may be used by ureteroureterostomy.

In conclusion, thorough recipient assessment along with careful and thoughtful examination of options to determine, the best approach for transplantation is absolutely essential. Venous drainage into the patent segment of the IVC is an initial option when both the iliac veins and/or distal IVC are unsuitable. Transplantation in the left orthotopic position and the revascularization methods mentioned above are an effective set of surgical techniques that could potentially be adopted as a safe and reliable transplant approach in a child with IVC thrombosis. Another option for the venous anastomosed site is the "deep route" (left ascending lumbar vein or left renal vein) for a pediatric recipient with serious blood vessel anomalies, such as complete obstruction of the intra-abdominal IVC.

We showed several important techniques for venous extension when the length of the graft vein was too short to anastomose. Furthermore, we showed that in cases in which the drainage vein may not be sufficient, an additional venous bypass using a donor ovarian vein between the graft vein and splenic vein could be used as a treatment option for reducing venous pressure. These techniques might also be beneficial in similar clinical situations.

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