Renal Transplantation: The Role of Pediatric Urologists in Management of the Urinary Tract to Maximize Good Outcomes

FROM THE GUEST EDITOR

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Transplantation is the best available management option for chronic renal replacement therapy in children and adolescents. It can dramatically change a child’s life, providing multiple benefits which clearly outweigh the possible complications and long-term risks. To optimize outcomes, appropriate preparation of the patient is paramount. Critical to ensuring this is the assessment of the urinary tract. Far from an innocent bystander, the native kidneys, ureters, bladder, urethra, sphincter mechanisms and interactions among these are often responsible for the child being in renal failure, and potential culprits in allograft deterioration after the transplant procedure. Therefore, pediatric urologists play a key role in the multidisciplinary team looking after these patients.

In this issue of Dialogues, we explore 3 important topics around renal transplantation. First, Catherine Chen and Craig Peters from Dallas provide an overview of how to prepare the lower urinary tract for transplantation. Important points are further emphasized with a pertinent case example. Then, Paul Bowlin from Kansas City reflects on the value and controversies surrounding removal of the native kidneys before or during the transplant procedure. Lastly, Frank Penna and Marty Koyle review options for lower urinary tract reconstruction, exploring the value of uretero-ureterostomy against ureteroneocystostomy based on their experience with these procedures in Toronto.

We sincerely hope that our readers will find these thoughtful offerings of value in their practice, and that we stimulate future generations of pediatric urologists to be heavily involved in renal transplantation.

FROM THE EDITOR

Elizabeth B. Yerkes, MD
Introduction

For any child undergoing evaluation for renal transplant, it is imperative for the urologist to adequately assess the urinary system to ensure that any urologic causes contributing to the renal failure be addressed prior to transplantation in order to prevent the same damage from occurring to the allograft. The main focus should be on ensuring a low-pressure urine storage system with adequate emptying and absence of infection through the fewest surgical procedures.

In cases of end stage renal disease (ESRD) due to non-urologic causes or in uncharacterized ESRD, a detailed history, renal ultrasonography and a post void urine residual volume by ultrasound may be adequate. However, when a urological etiology plays a contributing role to the renal failure, a voiding cystourethrogram (VCUG) becomes necessary to evaluate voiding function, urethral anatomy and reflux. Further evaluation with urodynamics should be completed if there is concern for significant bladder dysfunction. Oftentimes, these cases can be challenging because the underlying urologic pathology is multifaceted.

Congenital anomalies of the kidney and urinary tract account for up to 60% of chronic kidney disease in children, with obstructive uropathy as the single most common cause. Posterior urethral valves represent the most common etiology for obstructive uropathy in young boys. Patients with posterior urethral valves face an estimated 20-30% lifetime risk of ESRD. In situations of obstructive uropathy, a comprehensive bladder function evaluation is necessary.

Case Example

A 33w6d male born by normal spontaneous vaginal delivery had fetal sonograms showing persistent bilateral hydronephrosis and an enlarged bladder. His post-natal renal US demonstrated severe dilation of bilateral renal collecting systems with tortuous, dilated ureters. There was severe diffuse parenchymal thinning and increased echogenicity. (Figure 1 and 2).

A VCUG done at that time demonstrated bilateral grade 5 reflux and was equivocal for posterior urethral valves (Figure 3 and 4). The urinary system was decompressed by placement of a catheter and bilateral nephrostomy tubes. However, the infant had persistent renal failure and was started on peritoneal dialysis prior to discharge and remained on peritoneal dialysis.

At 2 months of life, he presented with bilateral large communicating hydroceles while still on peritoneal dialysis. He proceeded with bilateral hernia repair and given the equivocal findings of the prior VCUG, a cystoscopy was performed. He was noted to have type 1 posterior urethral valves, which were resected.

Post-procedure video urodynamics demonstrated a relatively small but smooth-walled bladder with significant bilateral reflux. Measured capacity was consistent with predicted bladder capacity for age; however, a sizable amount was refluxing up the severely dilated ureters. He did have intermittent leakage, although detrusor pressures remained low. During voiding, his urethra was normal.

Discussion

This case represents one of the more complex situations for bladder evaluation in a patient with ESRD. While video urodynamics demonstrate a glimpse of bladder anatomy (size, smooth walled), it is very difficult to assess the true long-term potential for bladder compliance and capacity in the setting of significant reflux.

There are several different approaches to prepare this child’s bladder for renal transplantation, with the focus of ensuring an adequate bladder capacity with good compliance as well as effective bladder (continued on next page)
Preparing the Pediatric Bladder (continued from previous page)

emptying. For this to occur, the severe ureteral reflux needs to be addressed and the bladder allowed to cycle. This can be achieved by ureterostomy or either unilateral or bilateral reimplants. Another option would be to use one of the distal ureters as a catheterizable channel with an extravasal flap mechanism and a trans-ureteroureterostomy into a reimplanted ureter.

Renal preservation, if possible, will allow continued fluid volume clearance for as long as possible and also preserves the ureters for possible use in ureterocystoplasty or a catheterizable channel. Enterocystoplasty may even be necessary if repeat urodynamics after reflux resolution and bladder cycling demonstrate a persistently low volume bladder with poor compliance. Parental and patient treatment compliance is critical and may help guide surgical management.

Assessing bladder function and emptying

In general, functional assessment of the bladder with urodynamics is crucial in cases of ESRD secondary to obstructive uropathy, neurogenic uropathy, persistent voiding dysfunction, hydronephrosis or recurrent urinary tract infections. The goal is to establish adequate bladder capacity (predicted bladder capacity for age) and good compliance (bladder pressures <30 cm H2O at capacity) in order to prevent damage to the renal transplant.

Studies of posterior valves patients have demonstrated that in the subset of patients with persistent hydroureteronephrosis after valve ablation there is a decrease in bladder compliance that contributes to the persistent dilation5-7. Furthermore, posterior valve patients with bladder dysfunction have a 56% graft failure rate compared to 27% graft failure rate in posterior valve patients without bladder dysfunction6. Over time, bladder dysfunction may change from hypertonicity to hypotonicity; thus, it is key to identify and monitor those with bladder dysfunction7.

The initial management of bladder hypertonicity should be with anticholinergics, using bladder augmentation as second-line. Oftentimes clean intermittent catheterization will need to be initiated if the child is unable to empty on his own sufficiently. If unable to catheterize per urethra, a catheterizable channel should be created.

Urethral function

Delineating urethral anatomy is particularly important in ensuring that the urethra is not a contributing factor to the ESRD. There needs to be a high index of suspicion for urethral pathology in cases of obstructive uropathy, as not all urethral valves are obvious on imaging as demonstrated in the case example. Post valve ablation urethral imaging should be obtained to ensure adequate ablation.

Reflux

Vesicoureteral reflux can be seen as an isolated etiology for ESRD or it can occur in addition to other urological pathologies, such as in the case example. Vesicoureteral reflux is seen in up to 70% of patients with posterior urethral valves as a consequence of pressure transmission from a dysfunctional bladder4.

In cases of isolated vesicoureteral reflux, the grade of reflux as well as compounding clinical picture guides the need for surgical intervention. Close observation can be a safe option in cases of low grade reflux with normal bladder capacity and no history of infection. However, intervention for reflux is warranted if recurrent urinary tract infections are present.

When high grade reflux is present, there are concerns regarding incomplete emptying because of residual urine. This can become a risk for urinary tract infections, especially in the setting of immunosuppression. Furthermore, it is difficult to adequately assess bladder dysfunction in the setting of high grade reflux, as the ureters may act as a pop-off valve for high bladder pressures. In this situation, one approach is to correct the reflux and re-evaluate bladder function in order to better understand bladder capacity and compliance. This approach must be considered relative to the need to maintain the native kidneys, as nephrectomy may also be an option.

Figure 3: VCUG. Severe bilateral grade 5 reflux.

Figure 4: VCUG. Urethra equivocal for posterior urethral valves.

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Spare parts preservation

Unless surgically indicated, native kidney preservation is advantageous to excrete excess water while on dialysis or in cases of graft failure. When a nephrectomy is indicated, preserving the ureter should be considered as the ureters can be potentially used for urinary reconstruction in the future as a continent catheterizable channel or ureteral bladder augment.

Ongoing follow-up post transplant

A multi-disciplinary team including urology, nephrology and transplant surgery is critical to ensure the overall success of the renal allograft. Over time, bladder function can change, putting increased risk on the renal allograft. Re-evaluation of bladder function is critical in cases of increased hydronephrosis, worsening of graft function, and urinary tract infections. Toilet training is also a critical time to ensure development of healthy voiding habits.

Conclusion

Understanding urologic etiologies of ESRD and a high index of suspicion is key to identifying bladder dysfunction and optimizing bladder management in anticipation of renal transplantation. Communication with the family, patient, and multi-disciplinary team improves compliance as well as early detection of bladder function changes that can potentially cause damage to the allograft.

References

The Role of Native Nephrectomy in Children with End-Stage Renal Disease

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The role of renal transplantation for children is well defined as the treatment of choice for children with end-stage renal disease (ESRD). Both living related and deceased donor transplants can be successfully performed across a wide range of pediatric patients with various nephrologic and/or urologic issues. The management of the native kidney(s) however is much more debated. Numerous variables exist in the decision-making process for how to manage the native kidney(s) including: indication(s) for nephrectomy, removal of one or both renal units, and timing of removal.

Native nephrectomy, done either pre-transplant or at the time of transplant, can be done for a variety of indications including: polyuria, proteinuria, hypertension, chronic infection, hydronephrosis, renal cystic disease, hematuria, large renal size, or malignancy. For most of these indications however there is no universally agreed upon degree of severity that makes the indication for nephrectomy absolute. Classically, native nephrectomy in the presence of focal segmental glomerulosclerosis (FSGS) has been felt to reduce the risk of disease recurrence, although this too is debated.1

The support for native nephrectomy has historically been much greater than it is today.2 This trend is multifactorial but certainly relates to advances in the treatment of hypertension, urinary tract infection, anemia, stones, as well as advances in the delivery of dialysis. Malignant indications, primarily bilateral Wilms’ tumor not amenable to neoplastic ligation as a means of deriving the benefits of native nephrectomy with less potential morbidity.3,4 As technology continues to allow greater research collaboration it will hopefully be easier to define the best role for native nephrectomy in the pediatric ESRD population to maximize successful outcomes in this complex cohort of patients.

The arguments against native nephrectomy pertain to the lack of impact on the offending condition, effects of being anephric, potential need for the native ureter, as well the potential morbidity of the procedure itself. Native nephrectomy is effective in the management of polyuria but comes at the potential expense of anuria. In the post-transplant period polyuria can complicate fluid management and is often cited as a risk for thrombotic complications with the graft, although the latter issue has been contended.5 It is also generally effective in managing severe proteinuria, although this can recur in select cases.6,7 It can be effective in managing refractory hypertension but it is difficult to predict who is likely to benefit.8 In some patients with ESRD the native kidneys can still be useful with fluid management and regulation of hematopoesis.9 Removal of the native kidneys requires additional regulation of fluids and anemia. Additionally, in cases of a failed transplant, the native kidneys can resume some of the fluid management duties while awaiting repeat transplantation.10 Complications rates related to the ureter have been reported to be as high as 20%.7 Some of these complications can be salvaged with the transplant ureter but others can only be managed using additional tissue, such as a native ureter. While rare, studies have noted the potential for life threatening complications with native nephrectomy.8

When felt to be indicated, the timing of native nephrectomy needs to be considered. Pre-transplant nephrectomy can help make the patient a more suitable transplant candidate when it successfully addresses the indication. It also allows the procedure to be done in a controlled setting separate from the transplant itself. When done via a retroperitoneal approach it preserves the peritoneal space for use with peritoneal dialysis. Staged nephrectomy can also be performed, which has the advantage of preserving one renal unit for a period of time prior to transplant. This can alleviate some of the issues associated with being anephric. Nephrectomy can also be performed at the time of transplant. This consolidates the operations but adds additional time and complexity to the operation overall.

Currently the role and timing of native nephrectomy in the pediatric ESRD population remains debated with the only absolute indication being malignancy or malignant predisposition syndromes. Management of severe proteinuria and refractory hypertension are relatively strong indications for native nephrectomy but only apply in relatively few cases.2 Several studies have proposed the idea of native ureteral ligation as a means of deriving the benefits of native nephrectomy with less potential morbidity.9,10 As technology continues to allow greater research collaboration it will hopefully be easier to define the best role for native nephrectomy in the pediatric ESRD population to maximize successful outcomes in this complex cohort of patients.

References
Uretero-ureterostomy: A Viable Primary Alternative in Pediatric Renal Transplantation

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The traditional method of establishing urinary continuity in renal transplantation is by way of uretero-neocystostomy (UNC), with reimplantation of the transplant ureter directly into the bladder1. In adults, there is controversy as to whether UNC should be performed in a non-refluxing manner, but in children, creation of an anti-refluxing mechanism is conventional. Techniques that instead utilize the native anti-reflux mechanism may carry additional benefit, particularly in children, to prevent graft loss, given the childhood predilection to symptomatic vesicoureteral reflux and pre-existing bladder pathology.1 In children, there are certain instances, however, where UNC may not be the ideal primary approach in selected cases, particularly in the presence of a “challenging” bladder (valve bladder or augmented bladder), when the donor ureter might be compromised or is too short, or in children that have had long-term anuria.

Donor-to-recipient uretero-ureterostomy (U-U) has been described as an alternative method of establishing urinary continuity in renal transplantation in adults, for both primary and secondary indications.2 U-U and pyeloureterostomy to the recipient native ureter may be advantageous when the donor transplant ureter is too short or after failed primary UNC resulted in anastomotic stricture, urinary leak and/or ureteral necrosis of the allograft.2-4 There are distinct benefits of performing U-U primarily, including a lower risk of urine leak or strictures by minimizing anastomotic tension and ischemia, as well as preservation of a non-refluxing system with an orthotopic ureteral orifice, thereby minimizing the risk of developing symptomatic vesicoureteral reflux, while facilitating subsequent endourological procedures, which can be performed more readily through a native ureteral orifice. Figure 1 demonstrates clinical scenarios where U-U would be or would have been beneficial. Another inherent advantage of performing U-U is that it obviates the need to reposition the retractor for proper exposure of the bladder, opening the bladder if performing intravesical reimplants or inadvertently entering the bladder during an extravesical UNC.

For these reasons, we have proposed that U-U would be viable as a primary method for urinary diversion during renal transplantation in children, rather than reserving it only for secondary indications, in the selected patients noted previously. At our institution, we have performed primary U-U in 23 children during renal transplantation, using both deceased- and living donor allografts, with excellent long-term outcomes and with minimal complications: two patients developed a urine leak warranting further intervention.5 Figure 2 demonstrates the indications for primary U-U in our single-institution series from 2004-2015. The procedure is versatile and can be applied to unique patient populations including children with pre-existing urinary conduits.6-7

The surgical technique entails spatulation of the donor kidney ureter, a longitudinal ureterotomy in the recipient ureter after minimal dissection and mobilization, followed by antegrade stent placement and a running end-to-side anastomosis with absorbable suture. For select cases (usually when right kidney is placed in right iliac fossa), we have even placed the allograft in an upside-down orientation to assure that the collecting system is the most anterior structure, while facilitating

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Uretero-Ureterostomy (continued from previous page)

This is our preferred approach in select patients with a complex urological history where avoidance of surgery on the bladder is preferred, and as a salvage procedure in secondary case where the donor ureter is compromised and the recipient ureter is healthy and available.

U-U remains an excellent technique for the salvage procedure where exposure and dissection through dense scar tissue can be a challenge, especially if a complication arises months after the transplant. In cases of ureteral stenosis that cannot be remedied percutaneously or endourologically and when symptomatic vesicoureteral reflux fails an injection of dextranomer/hyaluronic acid copolymer (Deflux), U-U provides an alternative. This achieves the ultimate goal of prolonging the life of the allograft by providing unobstructed urinary drainage while minimizing the risk of complications, including urinary tract infection. Certainly, there are inherent limitations, as it should not be utilized in patients with a recent history of symptomatic vesicoureteral reflux.

We believe that the technique is safe and efficacious as an alternative to UNC for primary repairs in children. This is our preferred approach in select patients with a complex urological history where avoidance of surgery on the bladder is preferred, and as a salvage procedure in secondary case where the donor ureter is compromised and the recipient ureter is healthy and available.

References: