Urological disorders in children that progress to chronic renal failure

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Abstract

Unresolved obstruction of the developing renal tract can lead to irreversible damage to the developing kidneys and accounts for 25% of chronic renal failure seen in childhood. This article focuses on congenital and acquired causes of renal tract obstruction, including posterior urethral valves, pelvi–ureteric junction obstruction, prune belly syndrome, neuropathic bladder and renal tract calculi.

Keywords Kidney calculi; kidney failure; MRCP; neurogenic bladder; prune belly syndrome; ureteral obstruction; urethral obstruction

Key points

- Congenital obstruction of the urinary tract can lead to long-term bladder and kidney dysfunction, which evolves over time and requires regular surveillance
- Individuals with neuropathic bladders require early investigation and management to lessen the risk of kidney failure
- Nephrolithiasis requires investigation to identify causative factors, to lessen risk of further stone formation

Introduction

The urinary tract is vulnerable to anatomical malformations. If it becomes obstructed, increasing pressure from continuing glomerular filtration causes the system proximal to the obstruction to dilate. Dilatation of the collecting system transmits pressure to the proximal tubules and glomeruli, causing a decrease in renal perfusion with a reduction in glomerular filtration rate (GFR). Continuing pressure can lead to ischaemia of the tubules, stimulating an inflammatory cell infiltrate and, with time, irreversible damage. The recovery of the kidney depends upon the extent and duration of the obstruction. The kidney appears to be particularly sensitive to obstructive damage during the first 5 years of life.

In animals, obstruction during embryogenesis has been shown to decrease the number of nephrons formed and cause tubular epithelial cell apoptosis. Infants with antenatal obstruction can have fewer nephrons, but compensatory hyperfiltration of the remaining nephrons can give an initially normal GFR. Over time, however, GFR can decline, highlighting the need for long-term follow-up and, when appropriate, transition to adult services to minimize renal impairment.

Chronic renal failure can occur after progression of the clinical course in a number of urological abnormalities (Table 1); this article focuses on a few of these conditions in more detail.

Posterior urethral valves (PUVs)

PUVs are the most common urological cause of established renal failure in childhood. They are also the most common congenital cause of bladder outlet obstruction and account for 10% of newborn hydronephrosis. Their incidence is 1:5000 to 1:8000 male births. They are caused by membranous folds arising from the lumen of the prostatic urethra, but the aetiology in unknown. Prognosis has now improved owing to antenatal diagnosis being made in >50% of cases.[1]

Antenatal ultrasonography may show oligohydramnios, bilateral hydronephrosis, hydroureter, thick-walled bladder and a dilated posterior urethra. Postnatally, the infant can present with respiratory insufficiency, abdominal distension, failure to void in the first 24 hours, a palpable bladder and poor urinary stream; up to 10% die in the first year of life.[2] Later modes of presentation include recurrent urinary tract infection (UTI), straining to pass urine, palpable bladder and urinary incontinence. The diagnosis is confirmed if a voiding cystourethrogram (which must include urethral views) shows a thick-walled trabeculated bladder, elongated dilated posterior urethra and elevated bladder neck (Figure 1). There is a wide clinical and radiological spectrum of PUVs.

Relief of the obstruction is required to decompress the kidneys. This is achieved by urethral or suprapubic catheterization, or if this is not possible, a temporary vesicostomy or alternative urinary diversion can be formed. The definitive treatment is endoscopic ablation of the valves. Long-term follow-up through

Urological disorders that can lead to chronic renal failure

Congenital	• Posterior urethral valves • Ureterocoele • Vesico-ureteric junction obstruction • Pelvi–ureteric junction obstruction • Syringocele • Neuropathic bladder secondary to spinal cord abnormalities • Vesico-ureteric reflux • Prune belly syndrome
Acquired	• Renal tract stones • Tumours of the renal tract (Wilms' tumour, retroperitoneal tumour) • Urethral strictures • Neuropathic bladder (trauma, tumour, transverse myelitis, multiple sclerosis)

Table 1

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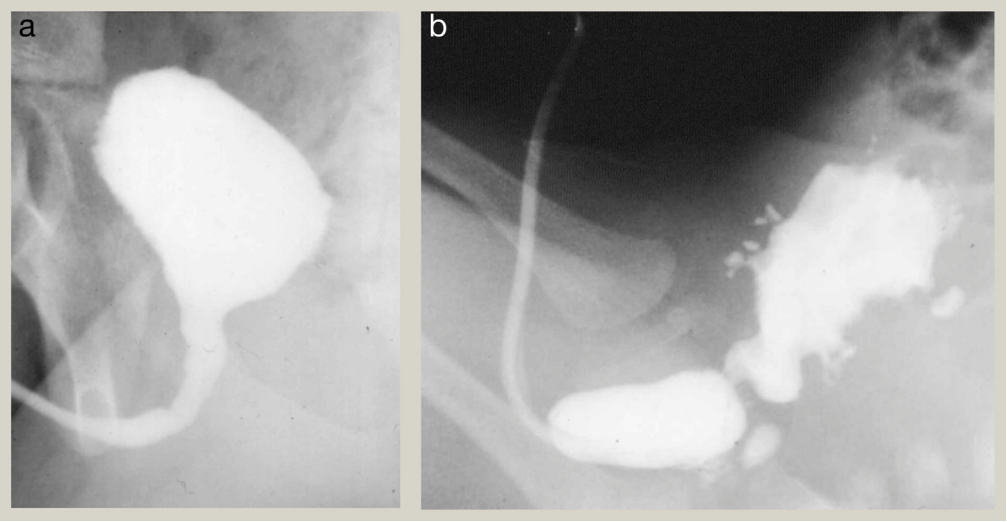

Figure 1 (**a**) Micturating cystogram showing a normal bladder and urethra. (**b**) Micturating cystogram showing a dilated proximal urethra and trabeculated bladder secondary to posterior urethral valves.

adolescence and adulthood is required as renal function can deteriorate at any time; this is caused by of glomerular and tubular injury from the obstruction and/or renal hypoplasia and dysplasia resulting from either pressure during development or abnormal embryonic development.

In the long term, 50–70% of patients develop renal impairment, with up to 17–30% progressing to end-stage renal failure in childhood. Satisfactory kidney transplant outcomes are achieved with aggressive bladder management. Bladder dysfunction is common and can change over time, leading to further deterioration in kidney function and urinary incontinence (19–81%). Polyuria is present in 75% of cases because medullary damage impairs urinary concentrating capacity. The factors predicting poor outcome are early presentation, plasma creatinine >75 micromol/litre after initial catheterization, proteinuria and daytime incontinence at 5 years of age.

Regular surveillance is required to preserve renal function by preventing urinary infections, ensuring compliant urinary storage with the use of bladder training (regular timed voiding and double voiding), anticholinergics, clean intermittent catheterization, bladder augmentation and Mitrofanoff appendicovesicostomy formation (continent urinary diversion using the appendix reimplanted into the bladder wall) as required. Proteinuria is an indicator of hyperfiltration and glomerular damage, and heralds a decline in renal function. The use of angiotensin-converting enzyme inhibitors is beneficial in the management of proteinuria.

Pelvi–ureteric junction (PUJ) obstruction

This is the most common cause of antenatal hydronephrosis, found in 1:1500 live births. It results from impaired urine flow from the renal pelvis to the proximal ureter caused by a dysfunctional, adynamic segment at the PUJ (75% of cases), crossing vessels, peripelvic fibrosis or an anatomical variant (horseshoe or duplex kidney). The left side is involved more commonly than the right (60:40), but obstruction is bilateral in 10–40% of cases, and is more common in males (M:F, 3:1). PUJ presents on antenatal scan or, in older children, with recurrent infection, pain, abdominal mass, haematuria and renal nephrolithiasis.

Investigations are aimed at distinguishing between an obstructive hydronephrosis, which can lead to progressive deterioration in renal function, and non-obstructive hydronephrosis. In two-thirds of children, PUJ obstruction resolves spontaneously, leaving one-third at risk of kidney damage while under surveillance. Predictive urinary biomarkers remain under investigation. Renal ultrasonography is currently used to assess renal pelvis dilatation, and a MAG3 scan to assess differential function of the kidneys and drainage.

Surgical repair is likely to be necessary to relieve obstructed kidneys, when increasing hydronephrosis is observed or significant hydronephrosis >3 cm and either declining function or symptoms or both. Pyeloplasty is performed with excision of the diseased segment, the redundant pelvis is trimmed and a JJ-stent is inserted temporarily, allowing urine to flow from the renal pelvis to the bladder.

Prune belly syndrome (Eagle–Barrett syndrome, triad syndrome)

This congenital abnormality is characterized by a triad of urinary tract abnormalities (dysplastic kidneys, grossly dilated ureters, enlarged thickened bladder), abdominal muscle deficiency and bilateral cryptorchidism. The pathogenic mechanisms underlying the condition are not clear but are likely to include urethral obstruction and a mesodermal developmental defect.[3] Approximately 84% of patients have abnormalities in another system, with up to 27% dying in infancy from cardiopulmonary complications. The incidence is 1:35,000 to 1:50,000 births, 97% of cases are male and around one-third are diagnosed antenatally. Postnatally, the neonate's abdomen has a wrinkled or lax appearance with a palpable urinary tract and cryptorchidism. Prune belly syndrome leads to the development of renal failure in around 25–40% of cases secondary to renal dysplasia, recurrent

UTIs, ureteric obstruction, vesico-ureteric reflux and/or bladder dysfunction.

Recent data have suggested that prenatal intervention with a vesico-amniotic shunt in selective cases can improve outcome, but numbers were small.[3] There are no established guidelines for treatment. Approaches range from comprehensive corrective surgery to an approach dictated by individual patient need, directed at preserving renal function by preventing UTIs and providing adequate bladder drainage with the use of timed voiding, clean intermittent catheterization or formation of a Mitrofanoff channel to allow catheterization as required. Early orchidopexy in the first year of life is recommended. There is a high complication rate with surgery.

Neuropathic bladder

There are many causes of a neuropathic bladder, which can be primary (open or closed spina bifida, sacral agenesis, anorectal malformations) or secondary (trauma, spinal tumours, transverse myelitis, multiple sclerosis). The early identification of cases at risk of kidney damage with appropriate investigation of the bladder and early management has led to a marked reduction in progression to established renal failure. All primary cases, including those with 'open spina' bifida prenatal closure, should be followed from early infancy. The child can present antenatally or after birth with overt spinal problems, incontinence or associated bowel problems.

Pre- and post-micturition ultrasound scans, video-urodynamics (VUD) and baseline assessment of renal function (GFR, DMSA scan) are usually indicated. VUD is used to identify children with 'dangerous bladders', most of whom fall into two groups. The first have decreased bladder compliance and static or fixed distal sphincters acting as an obstruction to urine outflow, exposing the kidneys to continuous high pressure. The second group comprises children with normal bladder compliance, neurogenic detrusor overactivity and detrusor sphincter dyssynergia; this leads to the bladder and sphincter contracting simultaneously, with a resultant increase in intravesical pressure.

Raised intravesical pressure is potentially dangerous to the kidneys and is the primary concern in managing children with neuropathic bladders. Neurogenic detrusor overactivity can be treated with anticholinergics. Detrusor sphincter dyssynergia and fixed distal sphincter is managed with clean intermittent catheterization, if acceptable to the patient, or by formation of a Mitrofanoff appendico-vesicostomy. A vesicostomy can be formed in infants where catheterization is not possible. Reduced bladder wall compliance can be treated with anticholinergics, intravesical botulinum A toxin or surgery in the form of bladder augmentation, such as the 'clam cystoplasty'. In the presence of vesico-ureteric reflux, the use of prophylactic antibiotics should be considered.

All children with a neuropathic bladder require follow-up with regular renal tract ultrasonography and VUD as bladder function can change over time. Renal function requires regular review by monitoring blood pressure and early morning urine for protein.[4]

Renal tract calculi

The urinary tract can become obstructed by calculi. Renal stones are most commonly formed after infection (60–80%) and the chance of stone formation increases if there is urinary stasis as a result of congenital or acquired structural abnormalities.[5] Metabolic abnormalities are not uncommon and tend to continue in adult life. A full metabolic work-up is warranted, with blood and urine investigations to attempt to identify the cause and start medical management to prevent further stone formation. Bladder calculi occur with increased frequency in children with augmented bladders. The treatment of calculi depends on the underlying cause, but any stone causing urinary tract obstruction is a urological emergency.

Calculi in the renal pelvis can be treated with extracorporeal shock-wave lithotripsy, or percutaneous nephrolithotomy for larger stones. Distal ureteral stones can be removed by ureteroscopy. Percutaneous nephrostomy is useful in anuric renal failure secondary to bilateral obstruction or obstruction of a solitary kidney, to relieve the obstruction before a definitive procedure is undertaken. ◆

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online here.

Question 1

A male infant presented with a urinary tract infection and poor urinary stream. On clinical examination, he had normal male genitalia and a palpable bladder. Antibiotics were commenced.

Investigations

- Creatinine 150 micromol/litre (60–110)
- Ultrasonography showed bilateral hydronephrosis and a thickened bladder wall

What is the most appropriate next step?

A Perform a micturating cystourethrogram
B Endoscopic ablation of posterior urethral valves
C Referral for a MAG3 scan to assess any obstruction of urine flow from kidney to the bladder
D Placement of a urethral/suprapubic catheter
E Commencement of dialysis

Question 2

A 3-year-old girl presented with anuria and loin pain.

Investigation

- Ultrasonography showed a single kidney with hydronephrosis >4 cm, with a large stone in the proximal ureter

What is the most appropriate next step?

A Complete a metabolic urine and blood screen to identify the cause
B Urgent urology team involvement to consider percutaneous nephrostomy
C Urinalysis to exclude a urinary tract infection
D Refer for a MAG3 scan
E Take a family history

Question 3

A 15-year-old girl presented with recurrent urinary tract infections and secondary-onset daytime urinary incontinence. She had a history of transverse myelitis.

Investigations

- Ultrasonography showed a thickened bladder wall and significant post-void residual volume of 200 ml

Which of the following is the best investigation to perform next?

A Video-urodynamics
B MAG3 scan
C Glomerular filtration rate
D MRI of the spinal cord
E DMSA scan