Posterior urethral valves

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Introduction

Posterior urethral valves (PUV) are the commonest cause of bladder outlet obstruction in children. With improvement of primary health care and widespread use of ultrasonography during antenatal check-up, early diagnosis of PUV has increased. The first description of PUV was made in 1919 by Hugh Hampton Young[1]. PUV represents a spectrum of severity, ranging from disease incompatible with postnatal life to that which is minimal and not presenting until later in life. Management of PUV remains a clinical challenge requiring active management from infancy into adulthood to prevent progressive dysfunction and deterioration of both the upper and lower urinary tracts.

Pathophysiology

Aetiology appears to be multifactorial including a combination of teratogenic factors and gene mediated embryopathy. Young based his classification of PUV on their position in relation to the anatomy of the posterior urethra. In his classification, types 1 and 2 relate to the attachment of folds to the colliculus or verumontanum and their respective distal or proximal extension. Type 3 obstructions are diaphragmatic and usually seen distal and unattached to the verumontanum. During embryogenesis, the most caudal end of the mesonephric duct is absorbed into the primitive cloaca at the site of the future verumontanum in the posterior urethra. In healthy males, the remnants of this process are the posterior urethral folds called plicae colliculi. Abnormally high insertion and fusion of these primitive folds (type 1 PUV) are believed to be the origin of 95% of PUV. Most authors doubt the existence of type 2 obstructions. Type 3 is believed to originate from incomplete dissolution of the urogenital membrane.

Dewan et al studied the pristine uninstrumented posterior urethra of babies with PUV after suprapubic

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drainage. He believes that the 3 types of valves represent a single diaphragm-like structure with a central defect that can assume different appearances due to either an antenatal rupture or postnatal instrumentation. This protocol was subsequently followed on several babies and the concept of *congenital obstructing posterior urethral membrane* (COPUM) has been proposed by the same author[2].

Degree of obstruction caused by this abnormality varies considerably depending on configuration of the obstructive membrane within the urethra. Morbidity of PUV is not merely limited to transient urethral obstruction but also congenital obstruction of urinary tract at a critical time in organogenesis leading to profound and lifelong effect on kidney, ureteral and bladder function. Increased pressure and wall tension in valve leads to a thickened bladder with trabeculation easily seen in the micturating cystourethrogram (MCUG). Thickened bladder is due to increased collagen deposition and muscle hypertrophy within bladder wall. Hypertrophy and hyperplasia of detrusor muscle and increase in connective tissue decrease bladder compliance during filling. Bladder emptying occurs with high intravesical pressures that can be transmitted to ureters and kidneys. These patients are susceptible to incontinence, infection and progressive renal damage. Other changes in bladder include vesico-ureteral reflux (VUR), diverticulum formation and late detrusor atrophy. Ureters respond to outlet obstruction by changes similar to detrusor in microscopic structure and have visible changes of dilatation, elongation and tortuosity.

Early severe obstruction may result in renal dysplasia but this occurs in only 25% of valve kidneys submitted for biopsy. Pyelonephritis, reflux nephropathy and hyperfiltration may add to congenital damage, further reducing glomerular filtration rate (GFR) with hypotonic urine. Often the small capacity, functionally abnormal bladder is unable to handle this situation resulting in frequency, incontinence and persistent upper tract dilatation.

Less obvious functional deficiencies also occur in kidneys subjected to obstruction. Ability to conserve sodium, regulate acid-base metabolism and concentrate urine may be severely disturbed and complicate management of the newly diagnosed neonate. Disturbances in erythropoietin secretion and production of 1-alpha-hydroxylase are factors in development of anaemia and renal osteodystrophy. Exact cause of growth retardation seen in chronic renal failure is not known but azotaemia, acidosis, renal osteodystrophy and infection are incriminated

Clinical features

PUV are found in 1:2,500-4,000 child births[4]. Approximately 10-15% of children undergoing renal transplant have PUV as the cause of renal insufficiency and approximately one third of patients born with PUV progress to end stage renal disease (ESRD). Recent workers on PUV believe that much of the poor renal function in long-term evaluation is due to primary VUR and renal dysplasia rather than the hydronephrosis and hydroureteric changes with acquired pyelonephritis.

Diagnosis is made before or at birth when a boy is evaluated for antenatal hydronephrosis. Before the era of prenatal sonography, PUV was discovered during evaluation of urinary tract infection (UTI), voiding dysfunction or renal failure. While rare, adult presentation of PUV has been described in case reports with symptoms varying from obstructive voiding to postejaculatory dysuria. In pre-sonography era, late presentation of PUV was considered a good prognostic sign suggestive of a lesser degree of obstruction.

History

- **Prenatal diagnosis**

In the developed world this anomaly is diagnosed in utero during second trimester based on a persistently dilated bladder, upper tract dilatation and oligohydramnios. Thomas reported that 10% of patients with prenatal hydronephrosis detected by ultrasound had PUV[5]. Dinneen et al demonstrated the sensitivity of antenatal ultrasound to be only 45% in detecting PUV in 45 patients who presented when younger than 6 months[6].

- **Delayed presentation**

UTI, primary diurnal enuresis in boys older than 5 years, secondary diurnal enuresis, voiding pain or dysfunction and decreased force of stream may indicate presence of PUV. It is stressed that one third of PUV kids may have a normal stream. PUV is sometimes discovered during evaluation of abdominal mass or renal failure.

- **Incidental diagnosis**

Hydronephrosis or proteinuria found on examination for unrelated conditions may be the first sign of PUV.

Physical examination

Most patients have normal findings on physical examination. When present, abnormal physical findings are the result of severe renal insufficiency.

Neonates may present with severe pulmonary distress due to underdevelopment of lung caused by oligohydramnios. An appropriate volume of amniotic fluid (produced by kidneys) is necessary for complete and proper branching of bronchial tree and alveoli. These patients will require ventilatory support with intubation, management of pneumothorax and occasionally extracorporeal membrane oxygenation. Such children have a mortality rate as high as 50% and those who survive have a high degree of renal insufficiency[7].

Physical findings can include the following:

- Small chest cavity
- Abdominal mass or ascites; 40% of neonatal ascites is due to obstructive uropathy. Severe electrolyte abnormalities may develop but bladder drainage is usually sufficient to stop extravasation, paracentesis being rarely required.
- Potter facies.
- Limb deformities.
- Indentation of knees and elbows due to compression within uterus.
- In older children physical findings can include poor growth, hypertension and lethargy. An intermittent or weak urinary stream is a non-reliable sign and only two third of patients with PUV have a poor stream.
- Palpable bladder.

Lab Studies

- Serum electrolytes, blood urea nitrogen (BUN), serum creatinine.

Neonatal serum levels of above are the same as the mother's. Monitoring serum levels a few days after birth will indicate true status of newborn renal function. Even normal newborn is susceptible to dehydration as kidney is unable to concentrate urine. Renal dysplasia, seen in PUV, may worsen this.

With gradual maturation of kidneys creatinine clearance normally improves. If significant renal dysplasia or damage has occurred, creatinine clearance fails to reach a normal level during first year of life.

Serum creatinine levels >0.8 mg/dL during first year of life have been demonstrated to be associated with poor long-term renal function.

Imaging Studies

Ultrasound Scan of kidneys, ureters and bladder (KUB)

Every child with antenatal hydronephrosis requires an ultrasound scan of KUB performed in the immediate postnatal period. As newborns have relative hypovolaemia during first few days of life, scan needs to be repeated if the neonatal scan is normal in a child with a diagnosis of antenatal hydronephrosis. Those with mild changes may be unrecognizable at birth having normal renal function and relatively free flow at micturition.

Micturating cystourethrography (Figures 1 and 2)

Key to work-up of any child with antenatal hydronephrosis is the MCUG. This is performed during voiding and under fluoroscopy with imaging of posterior urethra. Diagnosis of PUV is indicated by visualization of the valve leaflets. Other clues to diagnosis are a thickened trabeculated bladder, a dilated or elongated posterior urethra and a hypertrophied bladder neck. Diverticuli, VUR and reflux into the ejaculatory ducts, secondary to elevated bladder and urethral pressures, also may be present.

Figure 2

Figure 1

Renal scintigraphy

Isotope renography may be helpful. Tc-dimercapto-succinic acid (DMSA) or mercapto-acetyl triglycine (MAG-3) renal scintigraphy are cortical imaging studies providing information about relative renal function (each kidney relative to other) and intrarenal function (eg, photopenic areas within kidney indicate scarring or dysplasia). DTPA is useful to confirm obstruction at vesico-ureteric junction (VUJ.)

Urodynamic studies

Urodynamic evaluation provides information about bladder storage and emptying. The term "valve bladder" is used to describe patients with PUV and a fibrotic noncompliant bladder. These patients are at risk of developing hydroureteronephrosis, progressive renal deterioration, recurrent infections and urinary incontinence persisting in school-aged children. Patients with PUV require periodic urodynamic testing throughout childhood because bladder compliance may deteriorate over time.

Cystoscopy

This serves both diagnostic and therapeutic functions in these infants. Appropriate infant-sized cystoscopes (<8 F), available in most centres, including Lady Ridgeway Hospital (LRH), have improved the management remarkably. Confirmation with

cystoscopy is required in every child in whom PUV is suggested after MCUG. In some, the filling defect observed on MCUG, may represent only external sphincter contraction during voiding. In others valve leaflets are confirmed.

Antenatal diagnosis and management

Antenatal diagnosis and assessment has improved understanding of the natural history of PUV from inception to postnatal life. More babies receive medical and surgical care in early neonatal life than ever before. However, it is not yet clear whether it reduces incidence of ESRF secondary to PUV. The exact form and role of fetal intervention remains to be defined. It is certain that open fetal surgery has no role today

When bladder obstruction is suspected in first trimester, commonest cause, confirmed on post-mortem examination, has been fibro-urethral stenosis. Majority have an associated chromosomal anomaly and multiple congenital anomalies and prognosis is very poor[8].

Bladder obstruction, suspected in second trimester, is almost always due to PUV in a male baby. If it is demonstrated that a baby has PUV and during period of observation there is definite fall in volume of amniotic fluid and deterioration of renal function, based on fetal urine aspiration, intervention would be appropriate. Options for intervention include vesico-amniotic shunt, fetal cystoscopic ablation of valves and termination of pregnancy.

If diagnosis of PUV is made late (third trimester) in pregnancy without decreasing amniotic fluid, best course of action is for nature to take its course as this period is towards the end of renal structural development

Antenatal diagnosis has certainly allowed early institution of postnatal treatment of PUV preventing perinatal morbidity[9]. However there is no convincing evidence that late antenatal relief of obstruction is actually beneficial in improving outcome in terms of renal function and bladder dynamics.

Management

Medical management of PUV relates to treatment of secondary effects of the valves. Adequate care involves a team approach that includes a neonatologist, general paediatrician, paediatric urologist and paediatric nephrologist.

Short-term goals involve treating pulmonary distress, immediate relief of urethral obstruction (placement of 5F feeding tube), and fluid and electrolyte management. In children who survive the pulmonary distress, long-term issues include treatment of bladder dysfunction and renal insufficiency.

Renal treatment

Newborn period: A minority of patients present with bilateral renal dysplasia at birth. In the past, if patients did not die from associated pulmonary insufficiency, they succumbed to progressive renal insufficiency. With recent advances in peritoneal dialysis, some children may be treated successfully from birth. If growth is adequate, renal transplantation is often possible after first year of life.

Delayed renal insufficiency: About one third of patients with PUV progress to ESRD and the need for dialysis or transplantation. Progression of ESRD is accelerated at the time of puberty due to increased metabolic workload placed on the kidneys. Growth in these children may be significantly below the accepted norm for child's age. Adequate caloric intake and protein nutrition are key to growth but also may accelerate rise in serum creatinine. Renal dysfunction can be accelerated by recurrent infections and elevated bladder pressures. Treatment of lower urinary tract may influence progression of upper tract disease.

Bladder management

While awaiting MCUG, place a 5F or 8F urethral catheter to allow for bladder drainage. Catheterization may be difficult or even impossible due to thickness of valves or dilation of posterior urethra with a hypertrophied bladder neck. Surgical relief of obstruction has the primary aim of providing low pressure drainage and preventing infection that can cause sudden and extensive additional damage. The 3 surgical choices are primary valve ablation, vesicostomy and high upper tract cutaneous diversion

Primary valve ablation: Ideal treatment involves transurethral incision of PUV during first few days of life. Multiple techniques have been described for ablating valves. Disruption of obstructing membrane by blind passage of a valve hook is now of only historical interest. This was widely practised at LRH some time back without screening as appropriate cystoscopes were not available. In most centres valves are disrupted under direct vision by cystoscopy using an endoscopic loop, bugbee electro-cauterization or laser fulguration. Perform this in

least traumatic fashion to avoid secondary urethral stricture or injury to urethral sphincter mechanism. Some surgeons prefer to leave a catheter in place for 2-3 days after the procedure. Urethral damage leading to stricture formation is apt to occur when an instrument is forced or is passed through a urethra that has been softened by an indwelling catheter. Catheterization for retention of urine following resection of valves is apt to dislodge patches of swollen mucosa leading to subsequent stricture. It is therefore important to perform primary valve ablation in those patients whose bladders will be expected to empty efficiently. Valve resection with subsequent vesicostomy may also lead to stricture due to healing in apposition of resected valves in the dry urethra. Timing of postoperative MCUG varies ranging from several days to several months:

Vesicostomy: When urethral size precludes safe valve ablation, vesicostomy can be performed as a temporary solution until urethral growth has been adequate to allow transurethral incision. Generally an 18-20F stoma is created approximately midway between pubis and umbilicus in midline. Vesicostomy is indicated for the premature, low birth weight baby and those with massive unilateral or bilateral reflux. In premature infants and low birth weight (<2.5 kg) boys urethra size will preclude early valve resection. If cystogram reveals one or more large diverticuli or when one or both ureters, through massive reflux, act like large diverticulae, then primary valve resection should not be selected. Vesicostomy and high diversion have no beneficial effect on ultimate renal function except in preventing further damage from unrelieved obstruction or recurrent infection[10,11].

Supravesical urinary diversion procedures (eg, cutaneous ureterostomies) generally do not offer better upper tract drainage than standard vesicostomy and theoretically may increase bladder dysfunction. Valve ablation must be accomplished at the same time that ureterostomies and vesicostomies are closed.

Follow up

PUV is a lifelong disorder that can have a profound effect on entire urinary tract. As such, patients need periodic long-term urologic follow-up care. While the paediatric surgeon keeps focusing on the urinary tract of the child, overall care of child must stay with a paediatric nephrologist. This ensures adequate nutritional support, medications to treat hypertension and other subtle features of azotaemia, and regular estimation of GFR.

Delayed bladder management

Abnormal bladder dynamics may remain in a large majority of babies despite adequate endoscopic relief of bladder outlet obstruction due to PUV. This raised bladder pressure leads to impairment of urinary drainage across VUJ in a dilated tortuous ureter further worsening the poor renal reserve. Poor renal reserve, compromised by dilatation, dysplastic changes and secondary pyelonephritis, produces large volume of hypotonic urine. Often the small capacity functionally abnormal bladder is unable to handle this situation resulting in frequency, incontinence and persistent upper tract dilatation.

The Valve Bladder

3 patterns of dysfunction are seen in older children treated for PUV viz. myogenic failure of bladder, detrusor hyperreflexia and bladder hypertonia with small capacity[12]. Myogenic failure can be treated by intermittent catheterization. Hyperreflexia and hypertonia may respond to anticholinergic medication with or without intermittent catheterization.

Correct management of bladder function depends on adequate bladder evaluation with urodynamic studies: Chronic changes that can lead to elevated intravesical pressures may occur in bladder of patients with PUV. This leads to upper tract changes, urinary incontinence, and recurrent UTI. These patients may need periodic urodynamic studies to determine bladder capacity, compliance and postvoid residual urine volumes.

Upper tract changes: Patients may have baseline renal dysplasia. Elevated bladder pressures and recurrent UTI may further compromise renal function. Obtain periodic renal sonography and serum creatinine levels. Severity of renal and bladder dysfunction determines the frequency of these studies.

Urinary incontinence: Approximately one third of patients with PUV have problems with diurnal enuresis when older than 5 years. Diurnal enuresis may be caused by bladder changes that lead to elevated storage pressures and poor emptying. Rarely, sphincteric dysfunction, secondary to valve ablation, can be present. Treatment includes anticholinergic medication, intermittent catheterization and, in some patients, bladder augmentation.

During urodynamic evaluation, high voiding pressure and low flow rates must raise the question of residual valve, urethral stricture or bladder neck hypertrophy. All 3 need evaluation on check cystoscopy and endoscopic treatment

Lowering bladder pressure, improving bladder compliance and minimizing postvoid residual urine volume contribute to attainment of urinary continence. Early institution of anticholinergics, with or without clean intermittent catheterisation, should lead to improvement in residual symptoms and persistent upper tract dilatation.

Anticholinergics are used to improve bladder capacity and compliance in patient with elevated detrusor pressures leading to hydronephrosis, UTI, or incontinence. Oxybutynin chloride is inexpensive, effective and the first-line anticholinergic. By inhibiting muscarinic action of acetylcholine on smooth muscle it exerts antispasmodic effect on bladder muscle.

Secondary bladder surgery

Augmentation cystoplasty: Indications for bladder augmentation include inadequately low bladder storage volumes and high bladder pressures despite anticholinergic medication and clean intermittent catheterization. Before undertaking augmentation procedure, seriously consider need for lifelong intermittent catheterization and risk of bladder ruptures; electrolyte disturbances may be worsened by placement of intestinal mucosa in contact with urine; mucus production can be a source of catheter blockage and may be a nidus for stone formation and there is a risk of neoplasia.

Continent appendico-vesicostomy: In children with PUV, institution of intermittent catheterization through a sensate urethra can be difficult. This procedure involves placement of a non-refluxing tubular conduit for catheterization between bladder and skin to provide an alternative channel for catheterization. The stoma often can be hidden in the umbilicus to provide acceptable cosmesis. Appendix, ureter, and tubularized bowel can be used for formation of this channel.

Diet: Dietary restrictions depend on renal status. Avoiding progression of renal deterioration, while supporting growth, requires careful regulation of protein intake, which is best managed under the care of a paediatric nephrologist. In the absence of renal insufficiency, no modification of diet is needed.

Renal insufficiency

Historically, of those patients with adequate pulmonary function, approximately 25% died of renal insufficiency in first year of life, 25% died later in childhood and 50% survived to adulthood with varying degrees of renal function. Today, with advent of better techniques in treatment of paediatric renal insufficiency, most children can be expected to survive. The goal of treatment is to preserve the maximal obtainable renal function for each patient. This entails aggressive treatment of infections and bladder dysfunction.

Vesicoureteral reflux (VUR)

VUR is found in 50% of patients with PUV and half of that resolves with ablation of valves. VUR in most children is believed to be due to an insufficient intravesical ureter. When associated with PUV, reflux is generally secondary to elevated intravesical pressures. Therefore treatment of VUR in patients with PUV involves treatment of intravesical pressures through anticholinergics, timed voiding, double voiding, intermittent catheterization and at times, bladder augmentation.

Urinary tract infections

Recurrent UTIs are common in patients with PUV due to elevated intravesical pressures that predispose patients to infection, possibly by altering urothelial blood flow, elevated postvoid residual urine volumes, leading to stasis of urine and dilated upper urinary tracts, with or without VUR

UTI management involves

1. Lowering bladder pressures (anticholinergic medication).

2. Lowering postvoid residual urine volume (via clean intermittent catheterization).

3. Administering prophylactic antibiotics.

Patients with a history of recurrent UTI may benefit from antibiotic prophylaxis, especially in presence of VUR. Ideal antibiotic for urinary prophylaxis should be safe, effective and inexpensive with no adverse effects. Prophylactic dosage is usually one quarter of therapeutic dose administered once daily. Too high a dose increases adverse effects (e.g. gastrointestinal upset) and may alter faecal flora. More appropriate antibiotics in children include trimethoprim (TMP), sulfamethoxazole, amoxycillin or nitrofurantoin.

Prognosis

Prognosis of children with PUV is improving continually. Early in utero diagnosis, severe upper tract dilatation on antenatal examination, oligohydramnios, corticomedullary differentiation and fetal urine chemistry (urine sodium >100 meq/1) arc all associated with poor prognosis[13].

Bilateral severe VUR and persistence of wetting beyond 5 years have been found to be poor prognostic factors. Unilateral massive reflux in VURD syndrome (valves, unilateral reflux and renal dysplasia) was thought to be a good prognostic factor with its presumed role as a pop-off valve. But this has been questioned[14]. Prompt resolution of bladder obstruction, aggressive treatment of bladder dysfunction and improved surgical techniques have lowered neonatal mortality to less than 3%.

Long-term prognosis[15] involves:

1. Renal function impairment in 30 to 50% leading to hyperdiuresis, low GFR and acidosis. Improved dialysis and transplantation techniques have significantly improved not only mortality rate for these children but also their quality of life.

2. Impairment of bladder urodynamics in 75% with abnormal urine storage, abnormal micturition and VUR.

3. Bladder and renal failures leading to incontinence and recurrent UTI. Medical and surgical management can achieve urinary continence in nearly all patients.

4. Abnormal bladder outlet leading to incontinence and abnormal ejaculation.

Renal impairment leads to anorexia, nutritional and growth failure and loss of libido as well.

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