13. Pelvi-ureteric junction obstruction

George Vaos

Department of Paediatric Surgery, Alexandroupolis University Hospital, Democritus University of Thrace School of Medicine, 68100 Alexandroupolis, Greece

Introduction

Pelvi-ureteric junction (PUJ) obstruction is defined as a partial or total blockage to urinary outflow from the renal pelvis into the proximal ureter causing dilatation of the collecting system and potentially progressive renal damage, if left untreated [1].

The PUJ obstruction is the most common site of obstruction in the upper urinary tract of children. Before the advent of ultrasonography, the most common presenting symptom was intermittent flank or abdominal pain, reported in approximately 50% of older children. Other symptoms included urinary tract infection, hematuria, and palpable intra-abdominal masses. In infants, approximately 50% of intra-abdominal masses were of renal origin and 40% of them were associated with PUJ obstruction. Antenatal ultrasound and new imaging techniques have resulted in more frequent and earlier diagnosis of fetal and neonatal hydronephrosis and PUJ obstruction [2].

Optimal management of PUJ obstruction is difficult because of the degree of obstruction, functional variability, extent of renal damage and possibility for regeneration in growing kidneys. The outcome of PUJ obstruction is quite
satisfactory, if timely treated. Untreated unilateral PUJ obstruction may result in a nonfunctional, hydronephrotic kidney and renal insufficiency. Moreover, the outcome also depends on the coexistence of PUJ obstruction with other types of congenital anomalies, such as renal [vesico-ureteral reflux (VUR), duplication anomalies, horseshoe or pelvic kidney, megaureter, urethral valves or contralateral multicystic dysplastic kidney] or nonrenal (cardiac anomalies, skeletal dysplasias, hydrocephalus, or trisomy 21).

**Embryology**

The ureteric bud initiates its outgrowth from the mesonephric duct into the metanephric blastema in the fifth week of embryogenesis. The ureteric bud forms the epithelium (urothelium) of the renal pelvis and ureter, and the branches of the collecting system. Mesenchymal cells surrounding the ureteric bud form the cells of the lamina propria, smooth muscle and connective tissue of the renal pelvis and ureter. Inadequate canalization of the PUJ area may be the main embryological explanation of PUJ obstruction.

**Epidemiology**

PUJ obstruction is the most common pathologic cause of antenatally detected (44-65% of the cases) and neonatal hydronephrosis. The reported overall incidence of PUJ obstruction is 1 in 1000 to 1 in 2000 live births. The presenting symptoms, the male to female ratio, and the incidence of bilaterality differ according to age. In general, the peak incidence is in the first 6 months of life. Boys are affected with PUJ obstruction more commonly than the girls, especially in the neonatal period, when the ratio exceeds 2:1. The left side is more frequently affected, up to approximately 67%, than the right side. The reported rate of bilateral occurrence ranges from 10-40%. In duplication anomalies, the lower pole moiety is more likely to be obstructed, although both systems can be involved.

**Genetics**

Congenital PUJ obstruction appears sporadic with genetic heterogeneity. Linkage to the HLA area of chromosome 6 was confirmed in some families. Mutations in mouse or human genes are being identified in urinary tract anomalies. Teashirt 3 null mutant mice have congenital hydronephrosis without anatomical blockage in the PUJ. Moreover, a Teashirt 3 coding variant seems to be a risk factor for human congenital PUJ obstruction.
Etiology

The majority of PUJ obstruction is primary and congenital, although this condition may not be presented clinically until much later in life. The cause of congenital PUJ obstruction has not been clearly determined as yet [3], but it is generally accepted that there is an adynamic ureteral segment immediately below the PUJ which does not function properly.

Primary PUJ obstruction

Intrinsic

Improper innervation with diminished synaptic vesicles and decreased factors involved in neural development (nerve growth factor, protein gene product, S-100 protein and synaptophysin) have been found in the resected specimens of PUJ. The transforming growth factor may be involved in the abnormal smooth musculature in the obstructed renal pelvis. Light microscopy [3] demonstrates that PUJ obstruction is secondary to disorientation or absence of smooth muscle fibers at PUJ, and decrease of nerve terminals and nerves at the stenotic segment. Absent muscle fibers are replaced by excessive collagen forming a stenotic fibrosis. These findings may lead to an inelastic conduit that impedes the transport of urine and blocks the downward transmission of ureteral peristalsis. Furthermore, electron microscopy shows disruption of the intracellular junctions which are necessary to co-ordinate the transmission of peristaltic waves. Altered expression of interstitial Cajal cells, mediating neurotransmission, in resected specimens of obstructed PUJ may also be the cause of failure of transmission of ureteral peristalsis across the PUJ.

Further rare causes of intrinsic obstruction are ureteral polyps, ureteric papilloma and persisting fetal folds in the proximal segment of the ureter.

Extrinsic

Obstructions secondary to various kinks, angulations and aberrant vessels are commonly encountered at operations in cases of hydronephrosis. Do these findings represent the primary pathology or are secondary to a less overt functional or anatomical lesion in the upper ureter? In 40% of cases aberrant, accessory lower pole renal vessels (arteries and/or veins) are crossing the upper 1 or 2 cm of the ureter causing mechanical obstruction which increases as the distended pelvis drops into the gap between the upper and lower hilar vessels. These vessels are usually directed at the lower limit of the hilum rather the lower pole. Compression by the inferior vena cava, horseshoe or pelvic kidney, duplication anomalies and other rotational anomalies also can cause
PUJ obstruction. Cases of so-called high inserted ureter into the antero-medial aspect of the renal pelvis, exist but it is suggested to be an effect rather than a cause of obstruction because intrinsic ureteric hypoplasia may present with this high-insertion variant. In the early stages spontaneous resolution of the obstruction may occur when the urine excretion rate returns to normal but obstruction becomes persistent when adhesions form later. Moreover, an external tumor may also cause obstruction by compressing the ureter.

Secondary PUJ obstruction

Secondary PUJ obstruction can be caused by previous surgical intervention for other diseases such as impacted stones or failed repair of a primary PUJ obstruction. In massive VUR, that rapidly distends the upper urinary tracts, the ureter may become very tortuous and link on itself producing a secondary PUJ obstruction. However, this condition is transient and pelvic dilatation does not occur at normal rates of urine flow. Similar secondary obstruction at the PUJ may be found with megaureter and with hydroureter secondary to lower urinary tract obstruction.

Pathophysiology

Urine flow occurs when renal pelvic pressure exceeds upper ureteral pressure. Pelvic pressure is determined by the functional capacity of glomerulus and collecting system, the urine volume and flow, the compliance of renal pelvis and the degree of PUJ obstruction. The pressure gradient is raised by the hydrostatic force of the pelvic urine, but principally by the peristaltic contractions triggered by pacemaker cells and progressed across the PUJ and down the ureter, while preventing reflux.

Pathophysiology of congenital PUJ obstruction remains still unclear. The absence of an anatomical obstruction in the ureter in combination with an abnormal smooth muscle and neural arrangement at the PUJ, have resulted in the meaning of “functional” obstruction. The compliance of the collecting system at first attempts to avoid increased pressure by accommodating the filtered urine through dilatation. The pressure within the renal pelvis in patients with PUJ obstruction is usually in the normal range assessed during surgery. However, persisting urine flow blockage results in hypertrophy of the renal pelvis and rising pressure within the collecting system. The most considerable functional change in the hydronephrotic kidney is the impaired ability to concentrate the urine. This is probably due to loss of the papillae, which are compressed and undergo ischemic necrosis, and subsequent damage of Henle’s loop and, therefore, interference with the countercurrent mechanism in the medulla. Significant PUJ obstruction
eventually results in tubular dilatation, sclerosis of glomeruli, inflammatory infiltrate predominantly of mononuclear cells in both the medulla and cortex, and fibrosis. These renal histological changes are well documented in PUJ obstruction and are more severe in cases of differential function of less than 35%. In general, PUJ obstruction in early gestation affects renal growth and differentiation, producing small dysplastic kidneys. Later, it results in a dilated collecting system preceding functional and histological changes.

Clinical presentation and physical examination

Antenatal ultrasound allows PUJ obstruction to be identified before becoming symptomatic. However, although most PUJ obstructions are detected on prenatal US, some still present in infants and older children [4]. The clinical symptomatology of PUJ obstruction presents a broad spectrum depending on the age of the patient. In infants, a palpable abdominal mass is often the presenting feature. Failure to thrive, unexplained fever and recurrent urinary tract infections may also occur. In severe cases, infants may present with symptoms of sepsis. Older children, most often present with intermittent loin or abdominal pain, reflecting acute distension of the renal pelvis. The pain can be associated with nausea and vomiting and frequently is suggestive of a gastrointestinal disturbance. Hematuria and hypertension are less common presentations. Hematuria may be due to rupture of stretched vessels in the dilated collecting system, while a possible explanation for hypertension may be stretching of the renal artery by dilated renal pelvis. Children with untreated bilateral PUJ obstruction may present symptoms of renal insufficiency.

Attention should be paid to infants with associated congenital anomalies, occurring in approximately 50% of patients with PUJ obstruction. Associated anomalies include VATER (Vertebral defects, imperforate Anus, Tracheo-Esophageal fistula, Renal dysplasia) syndrome, esophageal atresia, contralateral multicystic kidney, horseshoe kidney, ureteric hypoplasia, vesicoureteral junction obstruction (VUJ), ipsilateral VUR, duplication anomalies and congenital heart disease.

Diagnosis

Laboratory studies

Urine microbiology

Whenever a urinary tract infection complicating a PUJ obstruction is suspected, urine should be sent for microscopy, culture and sensitivity. Red or white blood cells and proteinuria may be found in complicated cases.
**Urine biochemistry**

In patients with a normal contralateral kidney, serum electrolytes, bicarbonate, urea and creatinine usually suffice. However, in bilateral cases measurement of the glomerular filtration rate may be required.

**Urine biomarkers**

Urine reliable biomarkers for PUJ obstruction are being researched [5].

a. N-acetyl-β-glucosaminidase-a tubular lysosomal enzyme found in the urine of children with different renal diseases-urine concentration increases in PUJ obstruction and decreases with the recovery from the obstruction.

b. Urinary concentration of β₂-microglobulin, normally resorbed from the tubular lumen, increases when disruption of proximal tubules occurs. An increase in urinary levels of β₂-microglobulin may indicate tubular dysfunction because of the obstructive effect.

c. Other biomarkers. Abnormal levels of growth factors [epidermal growth factor (EGF), transforming growth factor-beta-1 (TGF-b1), platelet-derived growth factor (PDGF), monocyte chemotactic peptide-1(MCP-1), endothelin-1(ET-1)], cytokines and vasoactive substances have been identified in urine of children with PUJ obstruction and obstructive uropathies. However, further studies are necessary to determine the importance of biomarkers in clinical practice.

**Imaging studies**

**Prenatal**

Prenatal ultrasound (US) can show a renal pelvis dilatation between 16 and 20 weeks of gestation. Following fetal hydronephrosis with US is also important to monitor possible development of the dilatation during pregnancy. A prognostic limit for the anterior-posterior diameter (10-11mm) of the renal pelvis has been determined. Generally, renal pelvis dilatation below this limit may no longer be detected or require treatment postnatally. A meta-analysis on antenatal hydronephrosis showed that 98% of children with anterior-posterior pelvic diameter below 12mm stabilized, resolved or improved. When renal pelvis dilatation exceeds this limit and remains postnatally, the diagnosis of PUJ obstruction requiring surgery is frequently made.
Postnatal

Postnatal systematic imaging investigations of PUJ obstruction are important in order to detect increasing renal-pelvis calyceal system dilatation and/or reduced differential renal function requiring surgical treatment [6]. When the prenatal diagnosis of PUJ obstruction or other entities causing hydrenephrosis is made, the neonate should undergo US examination on the 2nd and 3rd day of life, although bilateral hydrenephrosis may require more rapid assessment. About 20% of antenatal hydrenephrosis are not identified on postnatal US. The diagnosis of PUJ obstruction can be suspected when an US shows a central lucency—the renal pelvis—surrounded by dilated calyces without ureteric dilatation and a normal bladder. Doppler ultrasound may show lower pole crossing vessels.

A voiding cystourethrogram (VCUG) is recommended for all neonates suspected of obstruction to exclude VUR and other lower urinary tract causes of hydrenephrosis such as posterior urethral valves. If renal US shows hydrenephrosis without VUR on VCUG, a diuretic renal scan should be performed to evaluate relative renal function and to determine the extent of obstruction.

Functionally significant obstruction is often diagnosed and quantified with diuretic renal scintigraphy [7]. The most common radionuclides are DTPA (99mTc-diethylenetriaminopenta-acetic acid), MAG-3 (99mTc-mercaptoacetyltriglycine) and DMSA (Dimercaptosuccinic acid). DTPA has a low renal extraction rate and therefore it is not recommended for young children whose kidney is still immature with renal clearance progressively increasing, until about the age of 2 years. MAG-3 is thus preferred in this case. Diuretic renal scanning with MAG-3 is the most popular imaging modality in PUJ obstruction. Diuretic scintigraphy produces two significant results: (1) It allows estimation of the percentage of total renal effort contributed by each kidney [Differential renal function (DRF)]. The DRF is best estimated between 1 and 2 minutes, and ranges from 45 to 55%. DRF of less than 40% is most commonly associated with obstruction. Therefore, DRF is important in determining the indication for surgical intervention especially in asymptomatic patients, and in selecting the appropriate surgical technique (pyeloplasty or nephrectomy), (2) it calculates the time it takes for half of the radionuclide to wash out of the kidney after administration of diuretic (t½). A flat or rising washout curve after diuretic with t½ of more than 20 minutes is usually associated with obstructed systems (Fig. 1). However, the definition of impaired drainage has been strongly debated. Recent studies in neonates with antenatally diagnosed hydrenephrosis suggest that an increased half-time alone may not necessarily indicate clinically significant PUJ obstruction. Diuretic
scintigraphy is also used to evaluate outcomes after surgical intervention. Although significant obstruction leads to decreased renal function, supranormal DRF of the affected kidney in PUJ obstruction may be found on a renal scan. It has been suggested that an increase in single nephron filtration or nephron volume causes this paradoxical increase of renal function. DMSA provides the most accurate DRF and it is the examination of choice for renal parenchymal anomalies. In cases of impaired overall renal function, DMSA is recommended instead of MAG-3. Furthermore, if DRF is about 15%, DMSA can assist to decide between pyeloplasty and nephrectomy.

**Intravenous pyelography** (IVP) provides excellent renal anatomy and especially facilitates operative planning while delayed films best demonstrate the exact point of obstruction (Fig. 2). However, the low glomerular filtration rate in infants impedes adequate visualization of the collecting system and precludes the use of IVP. Nowadays, diuretic scintigraphy has taken the place of IVP in evaluating children with a hydronephrotic kidney.

**Computed tomography** scan provides information about the dilatation of the kidney and the collecting system, and may be used to estimate the DRF by calculating the cortical thickness. Vessels of 1mm diameter may be identified in the PUJ area.
The dynamic magnetic resonance urography (MRU) with gadolinium-DTPA can show details of renal vasculature and lower pole crossing vessels, renal cortical and pelvic morphology and ureter anatomy. Moreover, as general anesthesia is generally necessary for MRU in young children under 6 years of age, this modality is mostly used for complex anomalies of the urinary tract.

In equivocal cases, antegrade pyelography allows examination of the flow of contrast through the PUJ after puncture of the collecting system. Whitaker performed pressure-flow studies following percutaneous puncture of the renal pelvis and instillation of saline at a constant rate. However, results obtained do not offer conclusive evidence of obstruction as defined by others.

Retrograde ureteropyelography, through cystoscopy, is occasionally used to elucidate uterine anatomy. It may differentiate between PUJ and VUJ anomalies if this was equivocal on pre-operative imaging studies or identify an additional VUJ anomaly before pyeloplasty.

**Treatment**

The challenge in the management of congenital PUJ obstruction is to identify which ones will result in renal deterioration, if left untreated, from those which will improve or resolve spontaneously over time. There is no single diagnostic test that can distinguish accurately the obstructive from the non-obstructive cases and thus avoiding unnecessary surgery and its complications.
Conservative treatment

When the diagnosis of a PUJ obstruction has been made, aim is focused on maintaining sterile urine and assessing the degree of hydronephrosis and renal function. Prophylactic antibiotic therapy is recommended because any urinary tract infection (UTI) seriously increases the chance of parenchymal damage [8]. However, no studies have proved that it prevents UTI’s. Asymptomatic infants with unilateral PUJ obstruction can be close observed [9]. A prospective study showed that less than 25% of the observed infants progressed to surgical treatment. Furthermore, stable or decreasing pelvic dilatation, measured with repeated US’s, and stable or improving differential function of the affected kidney, measured with radioisotope studies, may be kept under regular observation [10]. If UTI’s occur or the US shows an increase in the renal pelvis dilatation, a new series of imaging examinations should be carried out. Although conservative treatment allows the surgeon to avoid risks associated with surgical intervention, there is a certain number of patients with renal damage that could have been prevented by early pyeloplasty.

Surgical treatment

The aims of surgical treatment are to improve renal drainage, improve or correct the hydronephrosis, and prevent renal deterioration. Therefore, surgery is advocated by most in the case of significantly impaired renal drainage or poor renal growth. The accepted criteria for surgical intervention include moderate pelvic dilatation (>20mm) with calyceal dilatation, bilateral moderate to severe pelvic dilatation, t½ of more than 20 minutes and differential function less than 40% in unilateral hydronephrosis. Surgical treatment is also indicated in patients with pain, hematuria, secondary renal stone formation, recurrent UTI’s despite prophylactic antibiotic therapy, and hypertension. However, it is difficult to determine the indication of surgical management because US and diuretic scintigraphy are inaccurate and occasionally misleading to assess hydronephrosis. Moreover, some cases of hydronephrosis identified by imaging studies may not be obstructive, and therefore, benign. These data led to a conservative approach even with severe pelvic dilatation. However, spontaneous resolution of hydronephrosis is not as benign as described, since 15-30% of patients with asymptomatic neonatal hydronephrosis show progressive ipsilateral renal deterioration. Early surgical intervention is recommended by some who argue that the youngest of kidneys achieve maximal benefit in terms of drainage and renal function by relieving the obstruction.

In children, the procedure of choice is a dismembered pyeloplasty, as described by Anderson and Hynes. The pyeloplasty can be performed through
an anterior extraperitoneal approach or a flank dorsal lumbotomy. This repair allows removal of the fibrotic and stenotic PUJ segment and formation of a funnel-shaped anastomosis to connect the renal pelvis and the ureter. If lower pole crossing vessels are present, anastomosis is fashioned anterior to the vasculature. A meta-analysis showed 95% success rate of pyeloplasty for treating PUJ obstruction with or without stenting.

**Transperitoneal laparoscopic dismembered pyeloplasty** [11], a technically demanding procedure, is increasingly used to perform pyeloplasty in children. The main disadvantage is the long learning curve. However, given significant experience with laparoscopic suturing, laparoscopic pyeloplasty will be as effective as the standard open pyeloplasty with decreased morbidity, shorter hospital stay, and quick recovery [12]. This technique is not recommended in smaller infants because of space constraints. A small intrarenal pelvis is also a relative contraindication to laparoscopic pyeloplasty as the renal dissection would be unfeasible. One-trocar-assisted pyeloplasty [13] is an innovative technique which is effective and applicable to the entire ranges of ages, but more experience is required. Laparoscopic transposition of lower pole crossing vessels in pure PUJ obstruction has been described in children as an alternative to open dismembered pyeloplasty [14].

A **retroperitoneoscopic dismembered pyeloplasty** [15] has been advocated by some as offering better exposure and less postoperative complications. The reporting of this pyeloplasty in infants and older children is limited and long-term results are expected.

**Robotic-assisted laparoscopic pyeloplasty** is another approach being explored for treating PUJ obstruction. Robotic systems enhance visualization and manipulation but they are very expensive, require larger ports and a robot-trained team. In short-term studies, efficacy and safety are comparable to open surgery. However, long-term follow-up will provide information about the efficacy of this procedure.

When PUJ obstruction is associated with other congenital anomalies, more severe anomalies should be treated first. If PUJ and VUJ obstruction coexist, PUJ obstruction should be treated first because distal ureteric obstruction is not severe.

**Endopyelotomy** may be performed through an antegrade or retrograde approach. The obstructed portion is incised and dilated. The incision is followed by prolonged ureteral stenting (4-8 weeks). Before the incision of a PUJ obstruction, careful evaluation of adjacent ureteral vasculature is recommended to avoid intraoperative hemorrhage. In general, long lateral incision is the only safe option, as the anterior surface of the renal pelvis has a lower pole vessel in 65% of cases, while the posterior surface is in contact with a vessel in 6% of cases. Endopyelotomy may be used in older children after
failed open pyeloplasty. Success rates for primary PUJ obstruction are approximately 85%. Repeat incision, open or laparoscopic pyeloplasty are recommended after failed endopyelotomy.

**Percutaneous nephrostomy**, as a preliminary to definitive surgery, may be useful in assessing functional recovery in a poorly functioning, severely dilated kidney. Acute presentation with pyonephrosis requires prompt temporary diversion of the pelvic urine for 3-4 weeks, relieving the kidney which is infected and painful because of the hydronephrosis. Nephrostomy is performed percutaneously under general anesthesia, with ultrasonographic guidance.

**Ureterocalycostomy** may be considered in the rare case of failed open pyeloplasty when intrarenal pelvis and extensive hilar scarring are present. Renal parenchyma overlying a lower-pole renal calyx is resected, so that the ureter can be anastomosed to this calyx.

**Nephrectomy** is indicated for infants with severe pelvic dilatation and a very low DRF (<10%) in the presence of a normal contralateral kidney. This can be performed with open, laparoscopic or retroperitoneoscopic approach. Thorough diagnostic examination to determine that the kidney is functionally worthless should be performed prior to nephrectomy.

**Postoperative outcome**

The overall success rate with the Anderson-Hynes dismembered pyeloplasty is quite satisfactory; most studies report a success rate of 90-95%. Moreover, the overall re-operative rate is quite low, occurring in approximately 5% of cases.

Infection and bleeding are rare following pyeloplasty. The common early complications are urinary extravasation and failure of drainage through anastomosis with resultant backflow of urine. Intraoperative insertion of a drain can prevent the leakage or backflow of urine. Pain and fever following pyeloplasty may indicate urine leakage or obstructed anastomosis. This is diagnosed on US and managed by insertion of a JJ stent or nephrostomy. Urinary extravasation usually stops spontaneously within approximately 2 weeks. In 80% of cases, obstructed anastomosis opens approximately within 3 months of surgery and significant improvement in hydronephrosis could be found until 6 months following surgery. Persistent obstruction may be caused by a flap-valve or stricture formation at the anastomosis. In some cases, previously undiagnosed co-existing VUJ obstruction may be found after pyeloplasty using ureteropyelography. Dilatation or stenting of the stenotic area can be used but some children will require a new pyeloplasty or ureteric reimplantation. The reoperation rate for anastomotic stricture following pyeloplasty is low, occurring in 2-5% of cases.
Success of the pyeloplasty is not the complete reduction of the renal pelvis dilatation but the free flow urine, stable or improved DRF and resolution of symptoms. Follow-up investigation should include US and MAG-3. Patients may be discharged from postoperative follow-up, if these imaging studies show that hydronephrosis is decreased and DRF is stable or improved [16]. Pain and UTI’s should prompt a repeat investigation in the future.

Conclusions

Early prenatal detection of congenital PUJ obstruction would make possible a timely diagnosis and treatment postnatally. However, predictive diagnostic methods do not exist and repeated measurements of DRF are still imprecise. In general, given timely diagnosis and appropriate treatment, it is feasible to maintain kidney function without further complications. However, in very severe cases complete loss of the renal function and serious complications may occur despite timely treatment. Until an accurate diagnostic method will be discovered, the changing nature of kidney function and development requires serial examinations in order to detect PUJ obstruction.

References