PUJ Obstruction in Infancy

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The contemporary approach to the diagnosis and management of pelvi-ureteric obstruction was heavily influenced by the practice and writings of Herbert Eckstein who, between 1978 and 1982 published a series of papers on this condition which laid the framework for future diagnostic and therapeutic advances. In reviewing a large personal experience, Mr. Eckstein championed the conservative and non-extirpative approach to management of PUJ obstruction in children and in addition defined the criteria for successful surgery [4,20]. This therapeutic approach was complemented by a significant report of the diagnosis of PUJ obstruction utilizing renal scintigraphy which showed the importance of analysis of individual kidney function and diuretic renogram washout kinetics in assessing and managing upper urinary tract dilation in young children [16]. Together these insights have continued to guide pediatric urological surgeons in the evolving management of this challenging patient population.

The contemporary approach to PUJ obstruction in infancy was jolted into existence with the introduction of fetal ultrasonography which converted a disease process whose clinical recognition was dependent on physical signs such as an abdominal mass or evidence of urinary tract infection into a diagnostic epidemic with an incidence approaching 1 in 500 births [1]. Suddenly a huge population of newborns existed with asymptomatic renal pelvic dilation. Large ultrasonographic studies such as Grignon's [6] which examined 34,592 fetuses identified 92 cases of hydronephrosis and recognized a rather unique behavior; about half of the cases of hydronephrosis were observed to improve spontaneously during fetal life and did not persist after birth.

Refinements in fetal and postnatal ultrasonographic techniques and careful longitudinal studies on the behavior of individual patients with hydronephrosis demonstrated that hydronephrosis in the fetus and newborn is unstable and not only has a high likelihood for spontaneous improvement but also for spontaneous deterioration [8,9].

Unstable perinatal hydronephrosis

There are a number of factors which contribute to the instability of perinatal hydronephrosis. First, hydronephrosis observed in utero may not be due to obstruction but rather may result from other conditions such as reflux or dysmorphism (i.e. prune belly syndrome). Second, obstruction may occur transiently during part of fetal development The ureter is normally a solid cord during part of its development [19]. Should ureteral cavitation not occur in a timely manner or if ureteral folds or valves persist, obstruction may occur temporarily. With an increase in luminal size or complete resolution of obstruction, hydronephrosis may persist postnatally or resolve in utero. Third, changes in fetal and newborn renal function may, depending on relative increases or decreases in urine output, cause an apparent increase or decrease in pelvic dilation. These volume changes are especially exaggerated at the end of the third trimester, when urinary output is exceptionally high, and then abruptly diminished at birth when urinary output decreases significantly. The added effects of body molding consequent to birth trauma may cause hydronephrosis to decrease or even disappear temporarily only to increase or reappear several days or weeks later. Had prior ultrasound examination not documented that fetal hydronephrosis was severe, these changes might produce the illusion that hydronephrosis was only minimal or absent at birth and progressed; when in fact the hydronephrosis might actually be unchanged or even improved compared to its fetal appearance.

Another important reason for instability in fetal-newborn hydronephrosis is that all PUJ obstructions

are not anatomically or functionally alike [14]. Some are caused by an intrinsic PUJ stenosis and produce a continuous fixed obstruction to urinary outflow so that for normal flow to occur across the PUJ there must be a continuous elevation in intrapelvic pressure. These obstructions are characterized by progressive hydronephrosis and renal deterioration. Other obstructions produce a variable restriction to urinary outflow being caused by extrinsic bands or kinks which become more tightly compressive as the pelvis enlarges. This produces a variable resistance to urinary outflow, which causes obstruction intermittently. Relatively high urinary flow rates as are present before birth tend to activate these obstructions and cause exaggeration of hydronephrosis. In contrast lower flow rates present at and after birth often fail to maintain pelvic dilation sufficient to cause PUJ compression which may allow the dilated pelvis to empty and decompress. Such differences in PUJ behavior can obviously cause diagnostic confusion.

The diagnosis of obstruction in newborn hydronephrosis

In addition to diagnostic difficulty related to the intermittent nature of hydronephrosis, tests for assessing obstruction in the newborn may be fraught with problems due to a potential for misinterpretation and inaccuracy that is unique in this age group. Not only can ultrasonography performed immediately after birth minimize or fail to confirm known hydronephrosis but subsequent changes in pelvic dilation may not truly represent changes in the degree of obstruction; rather they may simply reflect the stretchiness, high compliance, and disproportionately large size of the newborn renal pelvis, which readily expands yet produces insignificant increases in intrapelvic pressure.

The isotope washout pattern during diuretic renography is likewise a poor marker of obstruction because slow or no isotope washout from the renal pelvis does not define obstruction in this age group. In fact, because renal function is normally poor in the newborn, isotope washout after diuretic injection is normally delayed and the washout curve may assume a shape that is identical to a washout pattern that would be considered diagnostic for obstruction in an older patient. This phenomenon exists because the rate of washout depends on a variety of factors: the size of the renal pelvis, glomerular and tubular renal functions which determine the rate of presentation of isotope to the distal tubules and response to a diuretic, and the tightness of PUJ obstruction.

Consider a 2 kg newborn with a renal pelvis volume of 60 cc and a urine output of 7 cc/kg/hr. At this flow rate, it would take 5 to 6 hours to fill the renal pelvis and perhaps 12 to 20 hours to dilute isotope from a pelvis already filled. Consequently, not only does a prolonged isotope washout (T-half-time) not define obstruction in this age group, even a total failure of washout (infinite T-half-time) does not diagnose obstruction when renal function is poor, as often occurs in premature infants with immature kidneys.

The Whitaker test is likewise vulnerable to misinterpretation in the newborn because its interpretation and accuracy depend on having a fixed degree of obstruction at the PUJ. If the obstruction is not fixed, but variable and dependent on the degree of pelvic (over) filling, as occurs in many newborns, then the unphysiologically high flow rates during the test may cause abrupt and tight activation of an obstruction which would never exist and could never develop at normal, lower urinary flow rates. Thus in the newborn the Whitaker test can be predicted to over-diagnose obstruction whenever it causes an increase in PUJ resistance.

An evolving surgical approach to newborn hydronephrosis

When one balances the difficulties that exist in diagnosing obstruction in newborn hydronephrosis, against the goal of not allowing renal function to deteriorate while trying to determine if obstruction exists, it is not surprising that pediatric urologists initially approached newborn hydronephrosis with very early surgery [10]. The initial results from several centers were excellent [7,15,17,21]: improvement in hydronephrosis, increased renal function and renal growth. These results seemed to support an early operative strategy and reinforced the belief that obstruction existed and that surgical intervention was necessary.

Despite these apparent successes, surgeons who care for newborns with hydronephrosis did not lose

sight of the fact that in addition to problems related to instability of hydronephrosis and to difficulties in diagnosing obstruction there exists a unique therapeutic paradox in this age group: obstructed as well as nonobstructed kidneys will appear to benefit from pyeloplasty. This is so because in the very young patient, renal function will normally improve, unstable hydronephrosis will often decrease or improve spontaneously, and renal growth will occur in the hydronephrotic kidney whether or not obstruction exists. Consequently, successful results following pyeloplasty are not necessarily due solely to the surgery and unfortunately they do not prove, that obstruction actually existed or that surgery was necessary.

While this analysis raises concern that early surgical intervention may not be required for all newborns with hydronephrosis, it does not help solve the dilemma as to which subgroup(s) of infants with hydronephrosis do require an operation and which can be followed non-operatively without risk until hydronephrosis spontaneously improves. In order to approach these questions new information about newborn hydronephrosis is required. This includes: **1)** the natural history of unoperated hydronephrosis, **2)** the accuracy and optimal use of diagnostic tests for assessing obstruction, and **3)** reassurance that non-operative follow-up and management does not lead to deterioration of renal function.

The natural history of untreated newborn hydronephrosis

Beginning about five years ago, we began to follow nonoperatively all newborns with primary unilateral pelviureteric hydronephrosis regardless of the degree of dilation, the shape of the diuretic renogram washout curve or the initial degree of functional impairment. Surgical treatment was initiated only for children whose kidneys developed evidence of deterioration. In 1992, preliminary experience with 45 newborns indicated that renal deterioration occurred rarely in this population, and that even the most severely hydronephrotic, functionally impaired kidneys had good potential for improvement [11]. Long term observations on the natural history of these children corroborated these initial observations.

Our patient population now includes 104 infants with prenatally detected primary pelviureteric hydronephrosis suspected of being caused by PUJ obstruction [12]. Surgical intervention was performed only if a reduction (>10%) in isotopically determined differential glomerular filtration rate (GFR) occurred in the hydronephrotic kidney or if there was clear cut ultrasonographic progression of hydronephrosis. Of these 104 patients, only seven (7 %) have required pyeloplasty during the past five years with a mean follow up of nearly 2 years. When the patients were subdivided according to their initial differential renal function, the degree of renal functional impairment did not influence outcome. 88 patients had a nearly normal (>40%) contribution to total GFR by the affected kidney of whom only six or 7 % required pyeloplasty. The remaining 16 patients all had low initial differential renal function (<40%); only one (6 %) required pyeloplasty. Notably, pyeloplasty returned renal function to predeterioration levels in all kidneys.

The group of 16 patients who presented initially with poorly functioning severely hydronephrotic kidneys serves to illustrate and characterize the unique clinical issues in this age group. Ultrasonography was used to assess hydronephrosis and all patients had severe hydronephrosis. During follow up, hydronephrosis actually disappeared in six kidneys, improved in six, remained stable in three, and deteriorated in one. Measurement of opposite kidney length showed no evidence of compensatory enlargement in 15 of the 16 patients.

During follow up, differential renal function showed a rapid increase in all but one kidney. Starting with initial differential function percentages that ranged from 7-40 %, and averaged 26 %, 14 kidneys reached final differential renal function in excess of 40 %. Diuretic renography showed a washout pattern that was initially obstructed in 15 of 16 kidneys; in 11 cases the T 1/2 time was infinite (a flat curve with no diuretic response) and in four it was between 20-40 minutes. The T 1/2 time was equivocal at 17 minutes in one patient. During follow up, the slope of the washout curve improved in 15 of 16 kidneys, and actually became nonobstructed in six (T 1/2 time <15 minutes).

This longer term follow up confirms our initial observations and the ongoing protocols of others [2,3,5,18]. Unilateral neonatal hydronephrosis appears to be a relatively benign condition. During five years

of follow up there was no appreciable risk to the patients, and the risk to the kidney of developing clinical evidence of obstruction defined as deterioration of renal function or progressive hydronephrosis and requiring surgical repair was only 7 %. Furthermore, watchful waiting and appropriately timed surgery was not associated with permanent loss of renal function in any kidney; all operated kidneys returned to or exceeded their predeterioration levels of renal function.

In addition to providing needed information on the natural history of newborn hydronephrosis, the above information indicates that potential flaws exist whenever one attempts to diagnose obstruction in this age group. First it is clear that in the newborn, the presence of severe primary unilateral hydronephrosis, even when associated with a profound reduction in differential renal function, does not define obstruction, nor suggest that surgery is required. Second, traditional diagnostic tests and criteria for assessing obstruction in older children or adults are fraught with inaccuracy when applied to this population; this includes the degree of hydronephrosis, the level of initial functional impairment, and especially the diuretic renogram washout pattern which actually misdiagnosed obstruction in 15 of 16 poorly functioning kidneys. It is therefore suggested that since these tests and measurements have no prognostic validity, they should no longer be used to base decisions for operative intervention.

Despite these shortcomings, the best way to follow newborn hydronephrosis at the present time is by a combination of renography to monitor individual renal function and ultrasonography to monitor hydronephrosis. This will allow obstruction, should it develop, to be recognized sufficiently early to treat it before irreversible renal injury occurs. This approach does require relatively frequent serial measurements. Reassuringly, obstruction can be safely excluded in most hydronephrotic newborn kidneys, if renal function and/or hydronephrosis show progressive improvement.

A contemporary approach to diagnosis and management

Because of the combination of diagnostic inaccuracy, the low risk of developing obstructive injury and the fact that many newborn kidneys with hydronephrosis spontaneously improve rapidly, it appears safe to follow neonatal unilateral hydronephrosis nonoperatively provided follow up is sufficiently close. This requires that ultrasonography and renography be readily available for early and frequent use during the first year of life. In order to take full diagnostic advantage of the normally occurring rapid rate of increase in renal function in infancy, it is important to perform the first renogram within two weeks of birth. This will allow depressed levels of differential renal function to be identified so subsequent examinations can confirm singificant improvement. We recommend that the timing of subsequent renographic studies be based on the initial degree of differential renal function in the hydronephrotic kidney [12]. If there is less than 20 % function in the affected kidney, a follow up renogram is performed in two weeks; if function is between 20-30 %, follow up is in one month; for 30-40 % function, follow up is in two months; and if function is greater than 40 %, a three month follow up renogram is obtained. In addition, follow up ultrasound examinations should be timed at least halfway between serial renograms.

The findings in these studies definitely do not suggest that surgery for neonatal PUJ obstruction is unnecessary or ineffective or should be delayed. When obstruction is diagnosed, immediate surgery for obstructed newborn hydronephrosis will markedly improve renal function and hydronephrosis, and will prevent permanent renal injury. But operating on dilated kidneys whose function can be shown to progressively and predictably improve because of a fear that dilation equals obstruction or that deterioration **may** occur in the future is both illogical and unlikely to be predictably beneficial. Hopefully in the future, by focusing more on the unique behavior and features of the newborn kidney, additional diagnostic tests and criteria will be able to be designed to further improve diagnostic accuracy and allow appropriate surgical intervention to be rendered in a timely fashion.

One specific area where observations on the unique behavior of the newborn kidney may enhance the ability to diagnose obstruction is in the area of compensatory renal growth. A recent preliminary study in infants with unilateral hydronephrosis indicated an overly responsive autoregulation and counterbalance between the two

kidneys [13]. This was reflected in the ability of the normal newborn kidney to rapidly change its rate of growth in response to functional changes in the opposite kidney. These compensatory changes in growth velocity in the normal kidney were determined primarily by whether or not an obstruction, sufficient to cause deterioration in renal function, existed in the opposite hydronephrotic kidney. In cases where renal function transiently decreased in the obstructed hydronephrotic kidney, the normal kidney was observed to be stimulated to increase its function and growth rate; as expected it became larger than normal for age and demonstrated compensatory hypertrophy. The opposite compensatory response was shown to occur when a non-obstructed hydronephrosis with initially poor renal function developed spontaneous improvement and rapidly increased its function. In this setting the normal kidney was stimulated to decrease its percent of differential function and to actually slow its growth rate.

Based on these observations, this unique behavior of the normal newborn kidney which rapidly changes its growth velocity in response to changes in function in the opposite hydronephrotic kidney may be used to develop a diagnostic test and a set of diagnostic criteria to help confirm or exclude a diagnosis of obstruction. The application of this test involves developing and using a renal growth chart to plot serial measurements of the length of the kidney contralateral to a hydronephrosis just as one would plot serial measurements of height and weight on a child's individual growth chart. The resulting graphical representation of changes in renal length is then compared to a graphic representation of renal lengths for normal children to determine if the contralateral kidney is growing faster or slower than normal. This information provided the needed anatomic corroboration of changes in renal function in the hydronephrotic kidney and served to help validate or exclude a diagnosis of obstruction. The development of and the initial experience with a renal growth chart has been encouraging.

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