DRAINAGE RELATED ULTRA SONOGRAPHY; ACUTE US TECHNIQUE IN CATEGORIZING PRIMARY MEGA URETER

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Abstract

Megaureter is a medical anomaly whereby the ureter is abnormally dilated. Regardless of the cause of megaureter (reflux or obstruction), megaureters are treated to prevent urinary tract infection and possible kidney damage. Sonographic characteristics and percutaneous catheter drainage of thigh abscesses in selected patients are described. In this study we try to evaluate and define the usefulness of DRUS in predicting the outcome of patient who presented with megaureter whom the vesicoureteral reflux has been ruled out. Relationship between DRUS findings and final outcome analyzed. For this purpose 284 patients (357 megaureters) for 15 years (2000-2015) with primary mega ureter are tested. Laboratory data such as routine complete blood count and urine analysis, creatinine level is obtained. Then statistical analysis was performed using the Social Sciences software. Results after treatment and placement of drainage shows that diameter of ureter can be decreased about 4.3±4.6 mm. Also, decrease in diameter of ureter observed in 72.8% of non-obstructing mega ureter while the same only observed in 27% obstructing mega ureter.

Keywords: Drainage related, sonography, US technique, categorizing primary, mega ureter.

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Introduction

Primary mega ureter has been defined as dilated ureter regarding to its normal value. Ureter diameter ≥ 7 mm is considered abnormal from prenatal period to children 12 years of old(1). Mega ureter is considered the second most common etiology of perinatal hydronephrosis after ureteropelvic junction obstruction (UPJO)(2).

It is generally classified into four categories:
1) refluxing non-obstructed;
2) refluxing obstructed;
3) non-refluxing obstructed;
4) non-refluxing non-obstructed(3).

While the first two categories generally treated and considered under the vesicoureteral reflux category and manage as such, the remaining two latter categories management and treatment remains controversial. While many of primary megaureter regress spontaneously(4, 5) some result in decrease renal function and ultimately need surgical management. Development of symptoms, decrease in renal function in subsequent follow up, increase in hydrenephrosis, and obstructed non refluxing megaureter are generally considered indication for surgical interventions(6).

Urological imaging has become the main stem for evaluation of patients with primary megaureter, ultrasonography, VCUG, renal scintigraphy, and newer imaging technique all use in combination to better manage and categorize patients.

Kajbaf et al introduces a novel technique with sonography, drainage related ultra sonography or DRUS, which potentially can discriminate with
high accuracy between non-refluxing obstructive and non-refluxing non-obstructive megaureter. Furthermore, it may be of use in determining the level of obstruction in former category\(^7,^8\). In this study, we try to evaluate and define the usefulness of DRUS in predicting the outcome of patients who presented with megaureter whom the vesicoureteral reflux has been ruled out.

**Materials and method**

284 patients (357 megaureters) from April 2000 to September 2015 with primary megaureter has enrolled in the study. Megaureter is considered when the ureter is dilated more than 7 mm (≥7 mm). Megaureter either suspected prenatally and confirmed in subsequent follow up by sonography or diagnosed antenatally incidentally or referred because of development of symptoms. Patients with established VUR diagnosed by VCUG, or those with past history of urological surgery were excluded. Those with transient hydronephrosis in whom the hydronephrosis is subsided following micturition also excluded from the study. DRUS or drainage-related ultrasound is performed as follows, urinary tract sonographic analysis with measurement of the anterior-posterior pelvic diameter (APPD) and ureteric diameters (UD), before and after a 3-h free bladder drainage, and regarded as drainage-related ultrasonography (DRUS).

All patients also undergone further testing with renal scintigraphy using technetium-99 m diethyleneetriamine pentaaceticacid (99mTc-DTPA) as a routine test for defining the obstructive versus non-obstructive nature of the megaureter. Prospectively participants consequently followed for 48 months whether they have undergone surgery or deterioration in renal functions is noted.

Relationship between DRUS findings and final outcome analyzed. Non-compliant patients, and those with incomplete data also excluded from the study. All Patients parents were provided with detailed description, and written consent was obtained from all parents or caregivers. All participants received care according to the 2008 World Medical Association Declaration of Helsinki. This study was approved by an appropriate institutional board review.

**Data acquisition**

Laboratory data such as routine complete blood count and urine analysis, creatinine level is obtained. Routine US examination for evaluation of urinary track was performed. Further sonography following micturition for excluding transient hydronephrosis also were performed. Sonographic exams were done by an experienced pediatric radiologist using a US unit (Siemens model Ultrasound, Siemens Medical Solutions, USA) equipped with a linear array transducer with 4-9 MHz or a curved array transducer with a 1- to 4-MHz emission frequency (based on the child’s age).

Diuretic renography using TC 99-DTPA and furosemide was performed and obstruction labeled as delayed wash out of the substance more than 20 minutes from renal system.

VCUG also was done to exclude vesicoureteral reflux. For minimizing of the procedure VCUG has been done following DRUS procedure if possible, since for two would take only one time catheterization. Further specific testing was done as needed. Final categorical diagnosis was made by an experienced pediatric urologist with some consultation with pediatrician and the experienced pediatric radiologist. Surgical decision was also made by the same pediatrics’ urologist.

**Drainage related ultrasonography (DRUS)**

DRUS was performed with a multistep approach there were no restriction on food or fluid. Unlike renal scintigraphy no diuretic agent was given. At the beginning routine sonography was performed. Renal parenchyma diameter, as stated previously cortex and medulla combined, was measured. Pelvic diameter, and also ureter diameter at its widest diameter measured. General appearance if bladder also were noted. Ultra sonography was repeated after micturition to exclude transient hydronephrosis. A single 6f-8f (straight) Nelaton catheter was inserted for 3-hour drainage.

Then the urinary bag is secured to patient’s body. Infant was kept on their mothers lap while toddlers were allowed to walk around. Initial hydro ureter measurements were used to categorize hydro ureter into three category; grade I as 7 ≤ D1 < 10, grade II: 10 ≤ D1 ≤ 15 and grade III: D1 > 15.

After the catheterization above mentioned measurement were repeated and recorded as D2. the change in diameter is measured (D1-D2), to overcome size variability due to age, body habitus it was reasonable to use a ratio for better comparing the result (D1-D2)/D1 and is regarded as D ratio. All the examination was done by a single pediatric radiologist using a US unit (Siemens model Ultrasound...
Ultrasound, Siemens Medical Solutions, USA) equipped with a linear array transducer with 4-9 MHz or a curved array transducer with a 1- to 4-MHz emission frequency (based on the child’s age). VCUG was performed at the beginning of the study before the DRUS procedure.

All participants received a prophylactic dose of antibiotics (cephalexin, 15 mg/kg/night) before catheterization as the routine of our center to avoid urosepsis.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences software (SPSS, version 16; Chicago, Illinois, USA).

Categorical variables were compared using the Chi-square test. Continuous variables were expressed as mean ± SD and compared using the Student t test. The Kolmogorov-Smirnov test was used to assess the normality of continuous variables. Diameters measured by US were expressed in millimeters.

The receiver operating characteristic (ROC) curve was drawn to determine the cutoff value for the D ratio to discriminate between obstructive and non-obstructive cases of non-refluxing hydro ureter. The area under the curve, the positive predictive value (PPV), the negative predictive value (NPV), and the sensitivity and specificity of the test were determined.

Result

Of 284 patients (357 mega ureters) was referred for primary mega ureter evaluation, 223 of them were male while 61 of them were female. Male to female ratio was 3.65. 73 of them had bilateral megaureter (26% of total). While 152 patients had left sided mega ureter and 59 of them had right sided. ratio of left to right sided mega ureter was 2.6 seven percent (7%) of patients had contralateral dysplastic or absent kidney. Median age of patients was 2.2 years (in the range of 1 month to 8 years). Median parenchymal thickness 10.16 cm (±1.4) for right kidney and 11.01 cm (±.66) for left kidney. Mean ureteral diameter before drainage was 11.20 mm (±57) (table 1, fig 1, 2).

After placement of drainage there were decrease of 4.3±4.6 mm in diameter of ureter. Decrease in diameter of ureter observed in 161/221 (72.8%) of non-obstructing mega ureter while the same only observed in 36/136 (27%) obstructing mega ureter. There was also a decrease of AP pelvic diameter in 40 patients with mean of 8.2(±5). The D ratio that was defined as D1-D2/D1 was calculated for each measurement and area under ROC curve was calculated for differentiating between obstructing versus non obstructing mega ureter. The cut of point of 18 % was able to differentiate between these two by sensitivity, specificity, PPV, and NPV of 82, 85, 94, and 80 %, respectively (fig. 3).

<table>
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<td>Lt: 10.34±.6</td>
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<td>Ureteral diameter</td>
<td>12.5±6.1</td>
<td>12.06±3.4</td>
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</table>

Table 1: ?????????

Figure 1: DRSU in a boy secondary nonrefluxing, non obstructive hydroureter that well hydrated before procedure similar to all other participant. a Start of DRUS with a unilateral right nonobstructed. b At the end of DRUS with dramatic decrease, more than 40%, in nonobstructed ureter diameter.

Figure 2: D1 in bilateral hydroureteronephrosis of a girl with ureterovesical junction obstruction was 15.8 mm on the left side and 16.9 mm on the right side, and a the end of DRUS, D2 was not changed. RU right ureter. LU left ureter; After Cath, at end of DRUS when D2 was measured.
Megaureter is defined as a presence of enlarged ureter with or without associated upper collecting system dilation. Primary megaureter (PM) is idiopathic functional or anatomical abnormality of ureterovesical junction (UVJ) and categorized due to presence or absence of reflux and obstruction\(^9\,10\). The refluxing megaureter mostly treated by anti-reflux therapy but the management of non-refluxing group remains contentious. Discussion about the patients presenting with reflux is out of the content of this text.

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The management, therapeutic approach and outcome are different in the obstructive and non-obstructive PM. The rate of spontaneous resolution of primary non-refluxing megaureter and its management plan varies between the different literatures. Multiple imaging tools could be used in order to follow-up these patients. Recently physicians likely prefer to monitor them with ultrasound and functional nuclear renal scans\(^5\,11\,12\,13\).

Diuretic renography and intravenous urography (IVP) are mostly utilized for the detection of obstruction\(^14\,15\). Diuretic renography remains the main imaging tool for diagnosis of obstructed uropathy but IVP is suggested as an alternative in some studies\(^14\). The child is exposed to ionizing radiation by diuretic urography and this modality has high rate of false-positive and indeterminate findings\(^16\).

Mithusami et al. proposed the usage of MRU in evaluation of morphological details of obstructive uropathy but nephrogenic systemic fibrosis is the adverse outcome of gadolinium administration particularly in patients with chronic kidney injury\(^14\).

CTU is the other probable technique for determination of anatomical information but it has the radiation exposure risk mostly for the infants\(^17\).

Color Doppler sonography also could be differentiate between obstructive and non-obstructive megaureter but it has higher cost than the ultrasound and its ability to determine the obstruction mostly limited to the proximal ureter\(^18\). Kajbaf et al. suggested that the patients could be precisely classified to non-refluxing non-obstructive and non-refluxing obstructive hydroureter by a novel ultrasonography technique (DRUS). This method improves urine outflow and reduce bladder pressure in non-obstructing hydroureter. It also could relieve the obstruction and progress the bladder function in obstructing hydroureter. It has the ability to discriminate upper from lower urinary tract obstruction. In this method, a formula was designed as \(((D1-D2)/D1) \times 100\). The largest ureter’s diameter immediately after the insertion of bladder catheter and \(D2\) was the same value after 3h of catheterization. The cut off value was set as 22\%, which had the highest sensitivity and specificity to distinguish obstructive from non-obstructive megaureter (sensitivity: 78.5\% and specificity: 83.4\%)\(^10\).

In this study we evaluated 284 patients with 357 megaureters during 48 months follow-up and concluded that DRUS could discriminate the types of megaureter and helps the surgeon in determination of treatment plan. By setting a cutoff value of 18\% in this study, obstructive and non-obstructive megaureter could be differentiated with sensitivity, specificity, PPV and NPV of 85\%, 94\%, 80\% and 85\% respectively which affirms the previous study results.

In our study, the primary megaureter was more commonly seen in male (male to female ratio was 3.65) which affirmed the other studies’ results\(^4\,9\,13\,19\). Its prevalence was higher in the left side. Aksnes et al. evaluated 17 primary megaureter between January 1997 and April of 2001. Ten of them were the left and 7 were the right sided\(^13\). Melini et al. also reported that the left ureter is 1.6-4.5 times more frequently involved. In this study, the prevalence of bilateral involvement was 25\%(9). In our study, it evaluated about 26\%.

In our study, we detected 7\% of contralateral dysplastic or agenetic kidney. Cozzi et al. evaluated 26 infants with 38 primary non-refluxing megaureter between January 1981 and December 1991. They found two contralateral kidney agenesis\(^19\).
Melini et al. expressed that in 10-15% of primary non-refluxing megaureter, the contralateral kidney is either absent or dysplastic (10). Surgical therapy was traditionally a treatment of choice in most cases of obstructive megaureter. The number of patients who are discovered prenatally is dramatically increased by the usage of modern radiologic techniques which is mostly by screening ultrasonography (US) (11, 13) so the percentage of symptomatic children has been declined (12, 19).

Garcia-Aparicio et al. evaluated 13 patients with primary obstructive megaureters (POM) from 2008 to 2010. The indications for surgery were set as combination of clinical, US and renographic findings. Recurrent febrile UTI, increase in hydronephrosis or parenchymal thinning in US, differential renal function (DRF) less than 40% or more than 10% reduction in renogram were defined as surgical indications. They declared that the majority of these patients did not need surgery but high pressure balloon dilation of the UVJ is an effective surgical approach but long term follow-up mostly with US is recommended (13).

Gimpel et al. investigated the complication and long term outcome of 49 children with 56 POM. Therapeutic approach was determined by 2001 German guidelines so just 23% of patients were surgically treated. They measured the rate of spontaneous regression of obstructive megaureter in 4-year follow-up about 50% that mostly was in association with sonographic retrovesical ureteric diameter and renography results (5).

Hemal et al. analyzed 55 adults with the mean age of 30 years old with primary obstructive megaureter from 1989 to 2001. They proposed that most of these patients were symptomatic and complications such as reduced renal function and stone formation were commonly detected. Surgical intervention was required almost exclusively (20).

Multiple studies suggested to follow-up the selected non-obstructing primary megaureter with normal renal function. Keating et al. in 1989 evaluated 23 prenatally diagnoses megaureters and non-operative management was chosen for the 20 cases based on the result of DTPA renography. Fifteen cases showed decrease in the size of ureter and no clinical deterioration reported (21).

Shukla et al. evaluated a total of 57 megaureters in the 40 patients. Four infants underwent surgery due to decrease in renal function which was detected by renography. In the other patients who were followed by radiological imaging for a mean of 7 years without surgical intervention, complete resolution in 52.5% megaureters at a mean of 2.9 years and improved or stable megaureter in 47.5% of them were detected (10).

By detection of megaureter etiology, the urologist could choose the best treatment. In spite of presence of vast diagnostic modalities, US is mostly utilize as an initial step. In this study with catheterization and diameter measurement of ureters as part of DRUS procedure, valuable findings regarding the site of pathology were evaluated.

Although most of obstructive and non-obstructive primary megaureters are managed conservatively (5, 13, 16), reduction in renal function in renography, severe hydronephrosis (grades IV and V) and a ureter diameter of more than 15 mm were considered as surgical indications (21) which the two later could be simply identified by DRUS. This modality is fully available even in developing countries and is safe, cost-effective and inexpensive. Being radiation free makes this modality so suitable for evaluation of neonates and children who are frequently presenting with megaureter. This modality is portable and could be used almost everywhere. In addition, it is repetitive, highly sensitive and does not need for contrast agent. Due to capability of DRUS to accurately classification of megaureter to obstructive and non-obstructive, the authors suggest to apply this imaging modality as a screening before performing diuretic renography. However, for enforcement of this hypothesis, more studies are demanded.

Differentiation between primary and secondary forms of obstructive megaureter could not be adequately achieved by DRUS and although this study has investigated more patients in comparison to previous one (13), further studies are requested.

The limitation of this study was that it was taken about 3 hours and the infants who were mostly our clients, bothered somehow from this time consuming procedure. DRUS is an operator dependence technique but with better standardization, we could overwhelm to this probable problem. In obtaining the diameter measurement, the imprecision might have arisen because of nonexistence of a computerized program. Because of tortuosity of the ureter, we might have some varieties in the place of diameter measurement.

Furthermore, more investigations are mandatory in order to be possible to utilize the DRUS in the routine clinical practice.
References