Spontaneous resolution of primary obstructed megaureter: Myth or reality?

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Abstract. Objective: Controversy surrounds the optimal management of primary non refluxing megaureter because of lack of clear guidelines regarding observational or surgical intervention. By this study we are trying to establish does spontaneous resolution really exist? Methods: We retrospectively analyzed our data from January 2005 to December 2010. Diagnostic modalities include ultrasonography (USG), micturating cystourethrogram, renal scintigraphy, plasma rennin activity and glomerular filtration rate (GFR). Megaureter was defined as ureteric dimension more than 7 mm on USG in the retrovesical region with unknown etiology. Obstructive megaureter was defined as those which had a ureteric dilatation, obstructive pattern of clearance on renal dynamic scans, absence of vesical dysfunction or urethral obstruction. Cases with split renal function <10%, falling GFR and differential renal function from baseline were straight away reimplemented while those with preserved renal function and who were asymptomatic were followed up using serial USG and renal scintigraphy at 6 months intervals. Results: Twenty six children were diagnosed as primary obstructive megaureter. Mean follow up period was 45.5 months (range 26 to 60 months). Obstruction resolved spontaneously in 11 out of 26 ureters after a mean follow up period of 39.1 months. Nine out of the 26 required surgery after a mean follow up period of 45.8 months. Conclusion: Because spontaneous resolution of obstructive megaureter is observed within several months to years, expectant approach with long term follow up and prophylactic antibiotics should be considered as a safe modality of treatment with close watch on renal function and drainage pattern.

Key words: Primary obstructed megaureter; secondary megaureter; reimplantation; spontaneous resolution

Introduction

Developmental abnormalities of the ureter encompass a wide range of disorders. Anomalies of the ureter are one of the common causes of morbidity in children. Primary obstructed megaureter (POM) is an uncommon disease, most commonly caused by adynamic juxtavesical segment of the ureter that fails to effectively propagate the urine. Management of this entity still remains controversial. Spontaneous resolution of congenital megaureter other than primary obstructed megaureter has been reported in literature, but the resolution of POM has not been reported yet.

By this study we are trying to establish does spontaneous resolution of POM really exist?

Materials and Methods

We retrospectively analyzed our data from January 2005 to December 2010. Mean age of presentation was 2.8 years (range 1.6 – 5 years). There were 133 cases of megaureters. Out of them primary megaureters were 53. Out of these 53, 26 were obstructive megaureters. Megaureter was defined as ureteric dimension more than 7 mm on ultrasound scan in the retrovesical region with unknown etiology. Obstructive megaureter was defined as those which had a ureteric dilatation, obstructive pattern of clearance on renal dynamic scans, absence of vesical dysfunction or urethral obstruction. Diagnostic investigations include ultrasonography (USG), micturating cystourethrogram (MCU), renal scintigraphy i.e. diethylene triamine pentaacetic acid (DTPA) scan and dimercapto succinic acid (DMSA) scan, glomerular filtration rate (GFR), plasma rennin activity (PRA). We used 99m technetium diethylene triamine pentaacetic acid for a modified, well tempered diuretic renography, along with calculation of split renal function (SRF) and GFR. Children were considered to have delayed drainage if the drainage t1/2 was more than 20 minutes of presentation. Using t1/2 after peak serum concentration, clearance was considered good, equivocal and poor when t1/2 was less than 10 minutes, 10 to
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20 minutes and more than 20 minutes, respectively. The PRA was measured by radioimmunoassay using a commercially available kit. Increase in PRA was expressed as percent increase from the initial values. Normal laboratory is 4 to 8 ng/ml per hour at age 1 to 12 months, 1 to 9 ng/ml per hour at 1 to 3 years, 1 to 5 ng/ml per hour at 3 to 6 years. Cases with an obvious poor renal function (<10% SRF) were straight away reimplemented while those with preserved renal function and who were asymptomatic were followed up using serial USG (6 months interval) and renal scintigraphy (12 months) intervals. These cases, which were followed up were kept on chemoprophylaxis till the age of 5 years. The average follow up period was 45.5 months (range 24 – 60 months). Surgical intervention (ureteric reimplantation) was done when there was fall in differential renal function, fall in GFR, recurrent UTI, breakthrough UTI and appearance of new scars on DMSA scan. Asymptomatic and stable renal function patients after 5 years of age were followed up clinically and using USG every 2 yearly.

All cases of POM with a minimum follow up of 24 months were included in the study. Cases with vesicoureteral reflux, urinary tract duplication, ectopic ureter, bladder or urethral pathology, bladder outlet obstruction, ureterocele, abnormal bladder dynamics on urodynamic study and incomplete data were excluded from the study.

All cases were divided into 3 groups. Group 1 were those with a ureteric diameter of <10mm, Group 2 had ureteric diameter between 10-20 mm and Group 3 had diameter > 30 mm. The diameter was measured with USG at retrovesical region. All the surgeries were performed by single experienced surgeon. Cohen's cross trigonal ureteric reimplantation was done as surgical procedure. The results were analyzed.

Results

Twenty six children (17 male, 66.6%) were diagnosed as primary obstructive megaureter including five with bilateral involvement, therefore comprising a total of 31 ureteric units. Twenty one (80.7%) out of twenty six unilateral obstructed megaureters were left sided. There were 7 cases in group 1, 9 in group 2 and 10 in group 3.

Mean ureteric diameter in group 1 was 8.4 mm (range 7-9 mm) and 4 (57.1%) of these resolved completely over a mean time duration of 29.1 months (range 26-34 months) (Fig. 1). Two (30%) underwent ureteric reimplantation due to fall in differential renal function after a mean follow up period 42.7 months. One developed a single episode of UTI which responded to conservative management and on last follow up child was asymptomatic with dilated ureter and preserved renal function.

Mean ureteric diameter in group 2 was 15.7 mm (range 12-19 mm) and 3 (33.3%) resolved completely over a mean time duration of 39.6 months (range 30-58 months) (Fig. 1). Four (44.4%) required surgical intervention for multiple episodes of UTI and falling differential function. Two (22.2%) are asymptomatic and renal function remain unchanged in both of them.

Mean ureteric diameter in group 3 was 25.8 mm (range 21-34 mm) and 4 (40%) resolved completely over a mean time duration of 54.1 months (range 36-60 months) (Fig. 1). Three (30%) required surgical intervention after a mean follow up period of 51.1 months because of multiple episode of febrile UTI and appearance of new scars on DMSA scan. Two (20%) developed pyonephrosis requiring external drainage by percutaneous nephrostomy. Both responded to conservative management. In both of them renal function improved over a period of time. One (10%) developed culture proven UTI, sensitive to nitrofurantoin and after a full course of antibiotic child was asymptomatic with preserved renal function on last follow up.

Out of 26 obstructed megaureters, 11 (42.3%) resolved spontaneously over a mean follow up period of 39.1 months. Nine (34.6%) out of 26 required surgical intervention because of deterioration in renal function which was evident by falling GFR and fall in differential renal function from baseline as shown in figure 2. Outcome of children surgically treated and followed up nonoperatively were shown in table 1. In nonoperated patients SRF, PRA, GFR were preserved, diameter of ureter was decreased and drainage pattern of ureters improved and became nonobstructive.

![Fig 1. Status of cases at last follow up](image)
Discussion

After ureteropelvic junction obstruction, obstructive megaureter is the second most common cause of obstructive uropathy of the ureter in children. Primary nonrefluxing megaureter represents 23% of all prenatal hydrohephrosis. They are more common in males and on the left side and in 25% are bilateral.\[2\] Megaureters in general and obstructive category in particular is prone to recurrent UTI, renal damage, arterial hypertension and renal insufficiency. Spontaneous resolution of primary non refluxing megaureter is a well-known event. Rates of and time until reduction, as well as outcome predictors, are still a matter of debate. Historically in 1971 Cussen and later in 1986 Hellstrom et al showed in their study that in children normal diameter of ureter rarely exceeds 5 mm.\[14\] Smith et al in 1977 gave a classification of megaureters which was later modified by King in 1980.\[5,6\] Etiopathogenesis of POM still remains unknown. Universally accepted hypothesis is functional obstruction at the vesicoureteric junction largely due to the presence of adynamic ureteric segment. Various authors had reviewed the histology of this adynamic distal ureter and concluded that atrophy of longitudinal muscle fibre and abnormal orientation of circular fibre are the main causative factors.\[7-10\] Nicotina et al tried to stabilise the role of transforming growth factor (TGF-β) with level of TGF may correlate with the spontaneous resolution in the first 2 years of life.\[10\]

In the present era with the frequent use of USG in obstetric practice, POM are usually diagnosed antenatally and the incidence of prenatal diagnosis has increased from 10% to 23% as shown by Brown et al.\[11\] Post natal presentations of POM are either asymptomatic or as recurrent febrile UTI. For Diagnosis, USG is the initial investigating modality. In POM USG will show the dilated ureter from the renal pelvis to its entry into the bladder. The ureter is visualized behind the bladder as it terminates with a large, bulbous ending changing abruptly to the thin aperistaltic segment. USG is a good tool for follow up because it can precisely measure the dimension of the retrovesical ureter and pelvis. The USG should be followed by the MCU. MCU not only help in differentiating between relaxing or nonrefluxing megaureter but also helps in diagnosing the secondary megaureter. Once the diagnosis is confirmed next investigation to be done is renal functional assessment by renal scintigraphy, GFR, PRA. Renal scintigraphy should be done after 4 weeks of life.

Table 1. Outcome in surgically treated children versus children followed up nonoperatively

<table>
<thead>
<tr>
<th>Patient types</th>
<th>SRF (%)</th>
<th>PRA (ng/ml/hr)</th>
<th>GFR (ml/min/1.73 m²)</th>
<th>UD (mm)</th>
<th>Drainage Pattern</th>
<th>Follow up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operated (9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial (mean)</td>
<td>37.25</td>
<td>14.2</td>
<td>76.3</td>
<td>19.8</td>
<td>Obs</td>
<td>45.8</td>
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<td>Final (mean)</td>
<td>43.75</td>
<td>7.4</td>
<td>83.6</td>
<td>4.1</td>
<td>Nonobs</td>
<td></td>
</tr>
<tr>
<td>SR (11)</td>
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<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Initial (mean)</td>
<td>44.8</td>
<td>7.1</td>
<td>81.5</td>
<td>9.5</td>
<td>Obs</td>
<td>39.1</td>
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<tr>
<td>Final (mean)</td>
<td>49.7</td>
<td>5.3</td>
<td>87.2</td>
<td>4.7</td>
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<tr>
<td>Nonoperated (6)</td>
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<td></td>
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<tr>
<td>Initial (mean)</td>
<td>41.4</td>
<td>8.4</td>
<td>78.2</td>
<td>11.6</td>
<td>Obs</td>
<td>42.7</td>
</tr>
<tr>
<td>Final (mean)</td>
<td>47.8</td>
<td>6.9</td>
<td>82.5</td>
<td>11.3</td>
<td>Nonobs</td>
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</tr>
</tbody>
</table>


Arrow indicates “point in time” of surgery due to deterioration in parameters

Fig.2. Temporal relationship between drainage pattern and GFR in children demonstrating indications for surgery during follow up
with Foley’s catheter in bladder.

In our study group, cases which presented with poor renal function and an obstructive drainage pattern and were symptomatic were implanted without delay. All cases underwent Cohen’s cross trigonal ureteric reimplantation by a single experienced surgeon. Renal parameters, follow up period are shown in the table 1. Cases with preserved renal function were observed with 6 monthly USG and yearly RDS (renal dynamic scan) and PRA. Drainage pattern, t1/2, differential renal functions were observed. Records were maintained and compared with previous studies at every follow up visit. Chemoprophylaxis was given till 5 years of age in all cases which were managed by observational therapy. Concept of spontaneous resolution and watchful nonsurgical management strategy was started by Keating et al in 1989. In their series of 23 antenatal diagnosed cases, non operative management was successful in 20 megaureters. [12] Rickwood et al presented the similar findings in their series of 38 Cases. [13] Since then various other authors have published their work with reported spontaneous rate of 34 to 88%.[14,15] Most recently McLellan et al reported spontaneous resolution in POM correlating the severity of hydronephrosis and duration of spontaneous resolution. [16] In a series of 42 cases by Stehr et al [17] only 11.9% were subjected to surgical intervention over a period of 48 months, a finding firmly supported by Merlini et al. [2] In our study group spontaneous resolution rate was seen in 11 (42.3%) cases.

The cause of spontaneous resolution is not proven in the literature we propose that this may probably be due to the differential growth of the intramural part of the ureter with age leading to the remodelling of the ureteric orifice and resolution of obstructive megaureter. Endpoint Criteria which considered by various authors for converting from observation to surgical intervention was fall in renal function at the onset or follow up. In our study group we have observed that cases with ureteric diameter > 2 cm with a rat tail appearance on USG does not respond to conservative treatment irrespective of duration of observation, a fact which can be appreciated from the facts that in 19 POM in which ureteric diameter was more than 1cm, 7 (36.8%) cases required reimplantation. Debates are still on regarding the end point of observational therapy as a line of demarcation between reversible and irreversible renal damage does not exist. Parameters of early marker of renal damage are still under investigations. Till the modern technology comes out with new biomarkers of renal damage we have to rely on differential renal function, drainage pattern, t½, drainage curve, ureteric anatomy and symptoms to decide regarding observation or surgical management. What we recommend is well tempered renography after proper hydration to be done to tide over the false interpretation of obstructed patterns in cases of poorly functioning kidneys.

Conclusion

Because spontaneous resolution of obstructive megaureter is observed within several months to years, expectant approach with long term follow up and prophylactic antibiotics should be considered as a modality of treatment with a close watch on renal function and drainage pattern.

References

