Which Imaging Method Must We Choose For A Complete Diagnosis Of Unilateral Renal Agenesis Associating Müllerian Duct Anomalies?

Oana M. Rizea¹ ², Andreea Scheau¹, Mihaela Buzoianu¹ ², Ioana G. Lupescu¹ ²

¹ Radiology and Medical Imaging Department, Fundeni Clinical Institute, Bucharest, Romania
² “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

Abstract

Introduction and Objectives. Our study’s objective is to discuss and illustrate cases of Müllerian duct anomalies (MDA) associated with unilateral renal agenesis (URA).

Material and Methods. We have reviewed our database for a period of seven years (between January 2013 and March 2020) using as key-point “renal agenesis” or “solitary kidney” looking for associated Müllerian duct anomalies. All the pediatric patients have been investigated by ultrasound as screening and follow-up method and one child has been investigated by ultrasound (US) and intravenous pyelography (IVP). All the adult patients have been investigated by sectional imaging methods, more CT urography than MRI exams.

Results. We have found a total number of 52 cases of URA (27 of them being female), but we selected only 8 female cases confirmed after imaging investigations with URA and MDA. Patients have been 13 to 39 years old with an average age of 25 years. URA have been located on the left side in 4 cases and on the right side in 4 cases. We excluded from our study the cases who had only one of the anomalies (only renal agenesis or only Müllerian duct anomalies) and also the cases associating to URA extra - Müllerian anomalies like vascular anomalies (inferior vena cava anomalies - azygos continuation), duplicated collecting system or ectopic ovary. MDA have been represented by didelphys uterus (5 cases, one uncertain - possible didelphys uterus, but CT scan was unable to provide a certain diagnosis), bicornuate uterus (2 cases) and indeterminate uterus (probably communicating unicornuate uterus with a rudimentary, hypoplastic left horn versus asymmetric septate uterus - 1 case). Another associated genital anomalies found in our patients have been endometriosis and leiomyofibroma (one case) and Gartner duct cyst (1 case). From our selected cases, two of them had some associated renal anomalies on the solitary kidney like pelviureteric junction obstruction (PUJO) with grade III hydronephrosis (HN) and a possible vesicoureteral reflux (VUR). Four of the patients have been diagnosed with Herlyn-Werner-Wunderlich syndrome.

Conclusions. Imaging investigations in patients with associated URA and MDA is essential for further prognostic of the disease. MDCT is an excellent diagnostic tool for associated congenital anomalies of kidney and urinary tract (CA-KUT) on solitary kidney but for associated genital anomalies, MRI is the gold standard method.

Keywords: renal agenesis, CAKUT, MDA, ultrasound, CT urography, MRI
Introduction

Renal agenesis is a pathologic condition consisting in absence of one or both kidney. Absence of both kidneys is incompatible with life having a general incidence of 0.1-0.3 of 1000 live births \([3]\). Unilateral renal agenesis (URA) is 4-20 times more common than bilateral renal agenesis \([3]\), the frequency of this anomaly varies according to the studies between 1/1000 and 1/3000 live births \([1,2,12]\). Most of the cases being asymptomatic.

In fetal life, the development of the kidney is induced by the ureteric bud. The absence of mesonephric ducts or the lack of interaction between the ureteric bud and metanephric blastema results in unilateral agenesis \([4,5,11,16]\). Sometimes the unique kidney and ureter can have an ectopic position \([8]\), can be affected by malformative urinary conditions like vesicoureteral reflux (VUR), duplicated collecting system (DCS), pelviureteric junction obstruction (PUJO), vesico-ureteric junction obstruction (VUJO) or can associate another urinary tract anomalies like contralateral blind ureteral remnant with/without ureterocele or ectopic insertion \([10]\) or posterior urethral valve (PUV) \([9]\), some of them increasing the risk of renal failure or the maternal risk during pregnancy \([18]\). Also, we can find associated malformative conditions outside the urinary tract, the most frequent being genital anomalies, especially Müllerian ducts anomalies (MDA). Furthermore, URA patients frequently have extra-renal anomalies such as cardiac, genital or gastrointestinal malformations \([4]\).

Müllerian duct anomalies have a frequency of 37 to 89% of female \([8]\) and represent a complex spectrum of genital anomalies caused by severe embryologic disruptions of Müllerian duct development. The most common MDA are uterine agenesis or different types of uterine duplications, double or absent vagina \([8]\) and usually does not include external genitalia and ovarian anomalies \([17]\). The complex process of Müllerian duct development include, in a simplified version, three steps: ductal development, ductal fusion, septal resorption \([17]\). Any perturbation of each of these steps will give birth to various uterine anomalies.

MDA have been classified based on American Society for Reproductive Medicine, lateral fusion defects are the most common MDA and are more often associated with renal abnormalities \([15]\). Some pathological associations like unilateral renal agenesis, didelphys uterus and obstructed vagina vault are grouped as Herlyn-Werner-Wunderlich (HWW) syndrome or OHVIRA (obstructed hemivagina with ipsilateral renal agenesis) syndrome and the combination of congenital absence of the uterus and upper 2/3 vagina with normal ovaries and fallopian tubes is known as Mayer-Rokitansky-Küster-Hauser syndrome \([13]\).

A synthetic classification of MDA is presented in the Table 1.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Type</th>
<th>Malformation</th>
<th>Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early failure of the müllerian ducts development</td>
<td>I - Hypoplasia/agenesis uterus/vagina</td>
<td>absent/reduced dimension of the uterus and vagina</td>
<td>Mayer-Rokitansky-Küster-Hauser</td>
</tr>
<tr>
<td>Unilateral failure of müllerian ducts development with incomplete fusion of müllerian ducts</td>
<td>II - Unicornuate uterus</td>
<td>normal hemi-uterus, fallopian tube and cervix in one side, and abnormal structures on the other side - mostly a rudimentary horn, which may not communicate with the uterus</td>
<td>-</td>
</tr>
<tr>
<td>Absence of müllerian ducts fusion</td>
<td>III - Didelphys uterus</td>
<td>duplication of the reproductive structures - two uterus and two cervix, often associated with vaginal septum - double vagina</td>
<td>Herlyn-Werner-Wunderlich (OHVIRA)</td>
</tr>
<tr>
<td>Incomplete fusion of müllerian ducts</td>
<td>IV - Bicornuate</td>
<td>one uterus with an indented fundus, having various separation degrees of the uterine horns</td>
<td>-</td>
</tr>
<tr>
<td>Partial resorption of septum</td>
<td>V - Septate/subseptate uterus</td>
<td>one uterus with endometrial cavity divided by a total or partial septum</td>
<td>-</td>
</tr>
<tr>
<td>Almost complete resorption of septum</td>
<td>VI - arcuate uterus - minor form of septime uterus</td>
<td>one uterus with a mild indentation of the endometrium at the uterine fundus (sometimes considered as a normal variant)</td>
<td>-</td>
</tr>
</tbody>
</table>

*Table 1 - Müllerian duct anomalies classification* \([14,17]\)
voiding cystography (VC) is recommended for suspected VUR on solitary kidney in patients with associated UTI.

Intravenous pyelogram can be also use for junction obstructions (PUJO or VUJO) but, in the latest years, this method has been replaced by CT urography (CTU).

All the patients included in our study have been investigated through MDCT and/or MRI.

CT urography (CTU) have been performed in our patients to confirm URA and to evaluate associated reno-urinary anomalies. CT examination included one non-enhanced CT phase in order to evaluate lithiasis or blood collections and three contrast-enhanced phases (corticomedullary, nephrographic and excretory phases) for malformative conditions. In order to improve visualization of urinary pathways in excretory phase, we usually used a diuretic (Furosemid). Sometimes, urinary tract obstruction requires a delayed, full-bladder CECT phase.

Split-bolus CTU is an alternative, less radiant CT scan with a double injection of contrast medium and a single CECT phase which can replace classic CTU, especially in children.

Even if CTU is quite sufficient for superior urinary tract evaluation, in a limited number of cases, the inferior urinary tract and genital anomalies are assessed unsatisfactory or incomplete, in this cases MRI being the modality of choice. MRI remain indicated for uncertain cases, but the technique must be adapted by including thin slices and angled images, parallel and perpendicular to uterus in order to detect details of genital anatomy. MRI protocol must include T2 sequences (sagittal plane, coronal plane with fat saturation, thin sections in oblique-axial and oblique-coronal plane, long TE coronal plane), T1 sequences (axial plane with fat saturation or dual-echo, contrast enhanced phases with dynamic injection +/- delayed phase), DWI sequence. Contrast enhancement does not provide additional information for evaluating MDA and obstruction sites in HWW syndrome unless the patients had additional tumoral or infectious pathology.[13]

Results

From a total number of 27 female cases of renal agenesis, we have selected only the cases with URA and MDA confirmed through imaging investigations (8 cases). We excluded from our study the cases who had only one of the anomalies (only URA or only MDA) and also the cases who associates to URA extra-genital anomalies. For example, we have excluded three adult cases of URA that have associated renal ectopia and inferior vena cava anomaly-azygos continuation type (1 case), duplicated collecting system (one case) and ectopic ovary (the last case). The other cases were little girls and prepubertal age girls discovered at US with URA, but in the absence of estrogenic stimulation, the dimensions of internal genital organs is too small to allow a proper characterization, this group requiring imaging investigation (pelvic MRI) after pubertal development of internal genitalia. All the children had been evaluated by US (most of them by US only), but not all the adults has been evaluated by ultrasound prior to cross-sectional imaging. However, one of the children has been explored by voiding cystography (VC) for a suspected VUR followed by surgery and another two children have been investigated by intravenous pyelography (IVP) for the investigation of hydronephrosis, then confirmed as PUJO. In one adult case, a VUR has been suspected on CTU in the presence of acute pyelonephritis and thickness of the ureter, but the patient did not undergo a VC for a certain diagnosis. Even if ectopic/malrotated kidney, duplicated collecting system and ureterocele are another urinary tract anomalies associated to renal agenesis, we have not found any cases, the reason being the reduced number of cases.

The 8 selected cases were adolescents or child-bearing age females, with ages between 13 and 39 years old (average age 25 years). The location of the agenesis has been equally distributed, 4 cases on the left side and 4 cases on the right side. All cases have been investigated by sectional imaging, 6 cases at CT and 5 cases on MRI (one MRI exam was unsuccessful, two of them having both CT and MRI exams. The uterine anomalies found have been didelphys uterus (5 cases, one uncertain-possible didelphys uterus, but CT scan was unable to provide a certain diagnosis), bicornuate uterus (2 cases) and indeterminate uterus (probably communicating unicorne uterus with a rudimentary, hypoplastic left horn versus asymmetric septate uterus - 1 case). Three cases with renal agenesis, didelphys uterus and vaginal obstruction can be classified as Herlyn-Werner-Wunderlich syndrome (HWW syndrome). The remaining case associating renal agenesis, didelphys uterus and Gardner duct cyst can be considered also as an HWW variant (atypical form). Three cases of HWW had complication consisting in hematometra and hematocolpos, one of the cases associating also hematosalpinx. One of the cases had a retrovesical nodule suggestive for endometriosis. The group with confirmed MDA had also associated urinary pathology consisting in PUJO (1 case) and possible VUR with secondary acute pyelonephritis (1 case).

All the associated pathology is presented in the table below (Table 2) and the most interesting cases are presented in the following pages.
### Clinical studies

#### Table 2 - URA and MDA

<table>
<thead>
<tr>
<th>Case</th>
<th>Urinary tract anomalies</th>
<th>Mullerian duct anomalies</th>
<th>Complications / Other anomalies</th>
<th>Syndrome</th>
<th>Imaging investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>Renal agenesis</td>
<td>Didelphys uterus</td>
<td>Crohn disease</td>
<td>Herlyn-Werner-Wunderlich</td>
<td>CECT, MRI</td>
</tr>
<tr>
<td>Case 2</td>
<td>Renal agenesis</td>
<td>Didelphys uterus</td>
<td>Hematocolpos</td>
<td>Herlyn-Werner-Wunderlich</td>
<td>US, MRI</td>
</tr>
<tr>
<td>Case 3</td>
<td>Renal agenesis</td>
<td>Didelphys uterus</td>
<td>Hematocolpos</td>
<td>Herlyn-Werner-Wunderlich</td>
<td>CECT, unsuccessful MRI</td>
</tr>
<tr>
<td>Case 4</td>
<td>Renal agenesis</td>
<td>Didelphys uterus</td>
<td>Hematocolpos</td>
<td>Herlyn-Werner-Wunderlich</td>
<td>MRI</td>
</tr>
<tr>
<td>Case 5</td>
<td>Renal agenesis PUJO (grade III HN)</td>
<td>Probably didelphys uterus (uncertain at CTU)</td>
<td>-</td>
<td>-</td>
<td>US, CECT</td>
</tr>
<tr>
<td>Case 6</td>
<td>Renal agenesis Possible VUR</td>
<td>Bicornuate uterus</td>
<td>Acute pyelonephritis</td>
<td>-</td>
<td>CECT</td>
</tr>
<tr>
<td>Case 7</td>
<td>Renal agenesis</td>
<td>Bicornuate uterus</td>
<td>-</td>
<td>-</td>
<td>CECT</td>
</tr>
<tr>
<td>Case 8</td>
<td>Renal agenesis</td>
<td>Undeterminate uterus (asymmetrical, probably communicating unicorneate uterus)</td>
<td>Endometrioma Bartholin gland cyst Leyomiofibroma</td>
<td>-</td>
<td>CECT, MRI</td>
</tr>
</tbody>
</table>

#### Fig. 1: 30 yo girl with pelvic pain - Herlyn-Werner-Wunderlich syndrome (right renal agenesis, didelphys uterus, vaginal obstruction with hematocolpos and hematometra); MRI exam a. Cor T2 WI - right renal agenesis; b. Oblique-Cor T2 - two separate uterine cavities without blood content (white arrows); c. Oblique-axial T2 WI showing two separate uterine cavities (white arrows) with two cervix, the right cervix distended by hematometra (white asterisk); d. Sag T1 WI - subacute blood collection (hypersignal T1) inside the right cervix and vagina (black asterisk); e. Cor T2 WI - double cervix and double vagina complicated with right hematometra and hematocolpos; dilated blind ureter on the right side (white arrow); f. Axial T2 - aberrant right ureter with ectopic insertion into the vagina and stenosis (white arrow); right hematocolpos (white asterisk)
Fig. 2: 25 yo female - Left renal agenesis, didelphys uterus with Gartner duct cyst (HWW variant); MRI exam a. Left renal agenesis with slightly hypertrophic right kidney but without associated renal anomalies; b. Oblique - axial T2 WI - two normal uterine cavities without hematometra (white arrows); c. Oblique-Coronal T2 WI - separate uterine cavities (white arrows) and elongated, fluid collection between bladder and vagina suggestive for Gartner duct cyst (black asterisk); d. Axial T1 fs WI after contrast enhancement - two separate cervix (black arrows) without pathological collections inside; e Sag T2 WI - Gartner duct cyst (black asterisk) adjacent to the anterior vaginal wall, above pubic symphisis; f. Axial T2 WI at the level of bladder and vagina - normal right vagina (white arrow) and Gartner duct cyst (black asterisk)
Discussions

URA is a CAKUT requiring a careful imaging investigation, but we must admit not all agenesis are true renal agenesis, some of them being pseudo-agenesis represented by involuted form of multicystic dysplastic kidney (MDK) or ectopic kidney. The typical aspect on US is compensatory hypertrophy of the solitary kidney, sometimes associating minimal or mild pelvicalyceal dilatation. Genital female anomalies associated to solitary kidney are difficult to detect on US in childhood because genital system is insufficiently developed, except for the neonatal period. In childhood, US is useful in detecting urologic anomalies, but children must be follow-up during adolescence and early adulthood. If pelvic US does not confirm normal anatomy of the reproductive organs, an MRI must be performed after pubertal development of internal genitalia. In MDA, US (abdominal US in adolescence or transvaginal US in adulthood) is helpful in detecting endocavitary hypoechoic (or hyperechoic if fresh) blood collections located inside the uterus or cervix known as hematometra or hematocolpos.

CTU is indicated for a certain diagnosis of URA, for associated urological anomalies and its complications like lithiasis or acute pyelonephritis. CTU sensitivity in detecting all MDA is limited, especially in vaginal anomalies, in one of our cases the CTU was inconclusive regarding associated MDA, but it was quite sufficient for renal anomalies (PUJO).

MRI is the gold standard method for genital anomalies because it is a non-invasive, non-radiating, multi-planar method and allows excellent differentiation of pelvic structures and can characterize the entire genital system.

In our patients, the most frequent MDA have been type III-didelphys uterus and type II-bicornuate uterus, similar to the medical literature. In three cases we have detected complication like hematometra or hematocolpos explained by congenital vaginal obstruction. Endometriosis is a well-known associated pathology, considered as a possible and expected consequence of retrograde menstruation.

Gardner duct cyst is a mesonephric remnant located within the anterolateral vaginal walls. It is considered as a blind, atretic vagina or a distended as pseudoureterocele-type ectopic ureter. Our patient with Gardner duct cyst has associated also renal agenesis and didelphys uterus (HWW syndrome), but the unusual aspect of the case is the presence of an inflammatory chronic bowel disease (Crohn disease), an unknown pathological association, which can be consider a random association.

The investigation algorithm in URA and MDA is presented below (Table 3).

Conclusions

The association between URA and MDA is relatively frequent because Müllerian system and kidney have similar embryological defects since the Wolffian and Müllerian ducts develop in close anatomical relationship. Imaging investigations in patients with URA and associated urologic and genital anomalies is essential for further prognostic of the disease.

US remain the best screening and follow-up method, especially in children. CT urography is an appropriate diagnostic tool for the cases associated with other CAKUT, but for associated internal genitalia anomalies, MRI is the best imaging choice being able to delineate accurately the precise anatomy of the reproductive system.
References