Uterine didelphys with concomitant renal anomalies in both mother and fetus

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ARTICLE INFO
Article history:
Received 12 June 2016
Received in revised form
26 August 2016
Accepted 26 August 2016

Key words:
Uterine didelphys
Fetal Müllerian anomaly
Renal agenesis
Multicystic kidneys

ABSTRACT
Uterine didelphys results from impaired fusion of the paired Müllerian ducts. The incidence of uterine anomalies is believed to be 0.5–2.0% of reproductive-age women, with didelphic uterus accounting for approximately 10%. Uterine didelphys is associated with renal agenesis in approximately 25% of cases.

We present a case of didelphys uterus with a left solitary kidney in a mother whose female fetus also demonstrated uterine didelphys with right multicystic dysplastic kidney. This report highlights the significant contribution and complimentary role of fetal MRI in identifying fetal anomalies.

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A didelphys uterus is characterized by failure of the Müllerian ducts to fuse, leading to separate uterine cavities, two cervices, and two vaginas. Because of the close association and interrelated development between the two tracts, Müllerian duct abnormalities are often associated with Wolffian duct abnormalities resulting in congenital anomalies of the kidney and urinary tract (CAKUT). The incidence of uterine anomalies is believed to be 0.5–2.0% of reproductive-age women, with didelphic uterus accounting for approximately 10% [1]. Uterine didelphys is associated with renal agenesis in approximately 25% of cases [2].

Didelphic uteri can be associated with a longitudinal vaginal septum and a blind hemivagina in 15–30% of cases [3], which is referred to as Herlyn-Werner-Wunderlich syndrome. These cases are all associated with obstructed hemivagina due to either unilateral obstructed longitudinal septum, or a unilateral oblique vaginal septum and ipsilateral renal anomaly, highlighting that anomalies of the urogenital tract are related to malformations in the Wolffian duct [4]. Renal abnormalities are additionally seen in 15–30% of non obstructed uterine didelphys, as in our case. Systematic literature review suggests right-sided renal abnormalities occur twice as often as left-sided anomalies, though no clear rationale has been established [2]. Through experimental and observational studies it has been established that the Müllerian duct requires a functional Wolffian duct to guide its attachment to the vaginal plate [5]. In our case, the cranial structures of the Müllerian duct formed normally producing two fallopian tubes. However, as the Müllerian tube travels caudally, it follows and then crosses the Wolffian duct. If there is an abnormality in the Wolffian duct, then the renal and the reproductive structure formation may be disrupted [6].

1. Case presentation

A 31-year-old, G2P0010 female presented at 25 weeks gestation to the Colorado Fetal Care Center (CFCC) for consultation regarding a fetal genitourinary anomaly detected on routine prenatal ultrasound (US). The 20-week US could not identify the right kidney and...
raised concern for unilateral renal agenesis on the right. On follow-up, the ultrasound demonstrated a low-lying, enlarged, and echogenic right kidney. The left kidney was enlarged but with normal echo texture. This case was compounded by the fact that oligohydramnios, bilateral clubfeet, and bilateral multicystic dysplastic kidneys resulting in Potter sequence complicated the mother’s first pregnancy. A later microarray revealed trisomy 16. Moreover, on prenatal US the mother was found to have uterine didelphys, which led to a renal US demonstrating an absent right kidney with compensatory hypertrophy of the left kidney. Given the prior fetal history and current renal concerns, further evaluation of the current pregnancy was sought at the CFCC.

Upon referral, repeat US confirmed the previous findings, including a low-lying, echogenic right kidney (Fig. 1). Fetal magnetic resonance imaging (MRI) was obtained and confirmed maternal didelphys uterus and an absent right kidney (Fig. 2). The fetal right kidney was ectopic; specifically it was low-lying with transverse orientation with mild hydronephrosis and diffuse microcysts, consistent with multicystic dysplastic kidney. The left kidney and pelvis were duplicated, but no dilated or abnormal ureter was seen (Fig. 3). Additionally, the fetal MRI demonstrated fetal uterine didelphys (Fig. 4).

Genetic consultation revealed that the maternal family history was otherwise negative for known congenital anomalies of the kidney and urinary tract (CAKUT). The amniotic fluid index was normal and fetal lung development appeared normal. The mother was counseled on the pregnancy risks associated with uterine didelphys, including preterm birth and the potential for fetal malpresentation. With regards to the neonatal course, she was counseled for anticipated normal outcome of the fetus in the setting of duplex renal pelvis but not ureteral duplication. However it was discussed that complete duplication of the left ureter remained

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**Fig. 1.** Coronal fetal ultrasound image demonstrating normal left kidney with low-lying echogenic right kidney.

**Fig. 2.** Coronal single shot fast spin echo (SSFSE) of the maternal abdomen demonstrating absent right kidney and mild compensatory hypertrophy of a normal left kidney (LK).

**Fig. 3.** Coronal SSFSE of the fetus demonstrating duplicated but otherwise normal left kidney (LK) with partially duplicated renal pelvis. There is diffuse cystic dysplasia of the right kidney (RK).

**Fig. 4.** Axial SSFSE of the fetal pelvis demonstrating small amount of fluid in separate uterine horns (arrows). An inferior image (not shown) demonstrated small amount of fluid in separate vaginal canals.
a possibility for which postnatal renal US, voiding cystourethrogram (VCUG), and renal function panel could further evaluate. Finally, the patient was counseled that this pregnancy appeared unrelated to the previous pregnancy that presented with bilateral multicystic dysplastic kidneys, oligohydramnios and Potter sequence as a result of trisomy 16. Additionally, the recurrence risk for trisomy 16 is expected to be less than 1%.

2. Discussion

The mother in our case has a didelphys uterus with either right-sided renal agenesis or complete involution of the right kidney. The fetus was shown to have uterine didelphys with ectopic, malrotated, and mildly hydronephrotic kidney with diffuse microcystic dysplasia. The finding of a maternal–fetal matching phenotype suggests a possible inheritance pattern or genetic cause rather than teratogenic or maternal influences during organogenesis, which have been postulated [2]. Familial recurrence of didelphys uterus has rarely been reported in the literature [7,8]. Copy number variants have been reported in a few women with uterine didelphys [9,10]. Women with uterine didelphys and 22q11.2 micro deletions have been reported. A female with developmental delay, uterine didelphys, duplicated cervix, absent left kidney, and obstructed hemivagina has been reported with a 22q11.2 micro deletion detected by fluorescence in situ hybridization [10]. A second case of uterine didelphys in the setting of an atypical distal 22q11.2 micro deletion detected by fluorescence in situ hybridization has also been reported, though with additional complications including left diaphragmatic eventration, and multiple ventricular septal defects [11]. A third patient with the triad of uterine didelphys, obstructed hemivagina, and ipsilateral renal agenesis also had developmental delay, seizures, and a 16p11.2 micro deletion [11]. Thus, chromosomal microarray analysis may be considered. In our case, a standard karyotype was reported as normal prior to presentation, and a microarray was not pursued.

Finally, it is important to note the role of fetal MRI in this case. While fetal MRI is not indicated in the routine assessment of the fetal urinary and reproductive tract, when abnormalities are identified by ultrasound, fetal MRI is a welcome adjunctive study to further accurately delineate the genitourinary anatomy. In this case, the details of fetal microcystic dysplasia to the parenchyma of the entire right kidney, duplication of the left renal pelvis and didelphys uterus were added to anomalies found on ultrasound.

3. Conclusion

To our knowledge, diagnosis of uterine didelphys in a 25-week fetus has not been previously described, but it is now possible with the level of detail provided by fetal MRI. The maternal–fetal matching phenotype may suggest a possible inheritance pattern or genetic cause, rather than teratogenic or maternal influences.

References