Herlyn-Werner-Wunderlich Syndrome: Report of a Prenatally Recognised Case and Review of the Literature

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Herlyn-Werner-Wunderlich syndrome, defined by the triad of uterus didelphys, obstructed hemivagina and ipsilateral renal agenesis, is a rare Mullerian malformation, usually diagnosed after menarche, when symptoms related to hematocolpos arise. Rarely, this malformation is diagnosed in the neonatal period, normally following prenatal diagnosis of renal agenesis. Herein, a case recognized on prenatal imagiology that underwent surgery on the fourth day of life is reported. The records of prepubertal cases were also collected, addressing the clinical and imagiological features. In the presence of a solitary kidney and/or a pelvic mass on prenatal ultrasound, Herlyn-Werner-Wunderlich syndrome should be considered, enabling neonatal treatment. UROLOGY 125: 205–209, 2018. © 2018 Elsevier Inc.

The Herlyn-Werner-Wunderlich syndrome (HWWS), defined by the triad of uterus didelphys, obstructed hemivagina, and ipsilateral renal agenesis, is a rare complex Mullerian anomaly with associated mesonephric malformation.[1]

As in other Mullerian anomalies, patients with HWWS are usually asymptomatic until menarche. The retention of menses in the obstructed hemivagina leads to hematocolpos and to progressive and/or recurrent abdomino-pelvic pain and development of a pelvic mass.[2] Even after menarche, the diagnosis may be delayed for several months because of the normal appearance of external genitalia and the patency of 1 hemivagina.[1]

Rarely, HWWS may present clinical manifestations in the prepubertal girl or even in the prenatal and neonatal period. Early and accurate diagnosis and treatment are of the utmost importance to avoid complications and maintain the reproductive potential of the patients.[3]

Most evidence available on HWWS comes from case reports, the majority of them concerning postpubertal girls. Only a few cases are reported in prepubertal girls and even less in newborns. In the present report, we describe a case of prenatal presentation with neonatal management, and review the prepubertal records of HWWS published in the last decade.

CASE REPORT

A female newborn was delivered at 38 weeks and 5 days of gestation by an eutocic and unremarkable delivery. Prenatal ultrasound at the 36th week showed an absent right kidney and a cystic lesion in the pelvis (**Fig. 1A**). Fetal magnetic resonance imaging, 1 week later, confirmed right renal agenesis and a left kidney with pelvicalyceal dilation (10 mm). A cystic lesion measuring 65 × 25 × 22 mm was shown behind the bladder, suggesting hydrocolpos, although an anorectal malformation was not excluded (**Fig. 1B**).

Soon after birth, the abdomen was soft and painless, with no masses or organomegaly. Meconium and white vaginal secretions were present in the diaper. Perineal inspection showed a normal anus, a normally placed urethral meatus and a bulging in the location of the vaginal introitus, which increased with Credé maneuver (**Fig. 2**). A perforated hymen was present and, at the left side of the bulging, another orifice was visible allowing the introduction of a catheter with drainage of vaginal discharge. This raised the suspicion of a septated/duplicated vagina with an obstructed right hemivagina. The remaining physical examination was unremarkable.

In the fourth day of life, vaginoscopy was conducted under general anesthesia, using a 9,5Fr cystoscope through the left vaginal orifice. A normal cervix was identified and the right vaginal wall (vaginal septum) was protruding medially. An incision was made in this wall with massive drainage of white secretions. Right vaginoscopy was then performed through the incision, with identification of a normal right cervix, compatible with uterus didelphys. Cystoscopy was also performed, showing a normally implanted left ureter and absence of the right ureteric orifice.

Then, vaginal septotomy was done, first with electrocautery, and afterwards with an 11Fr resectoscope in the upper part of the septum. The incision edges were sutured

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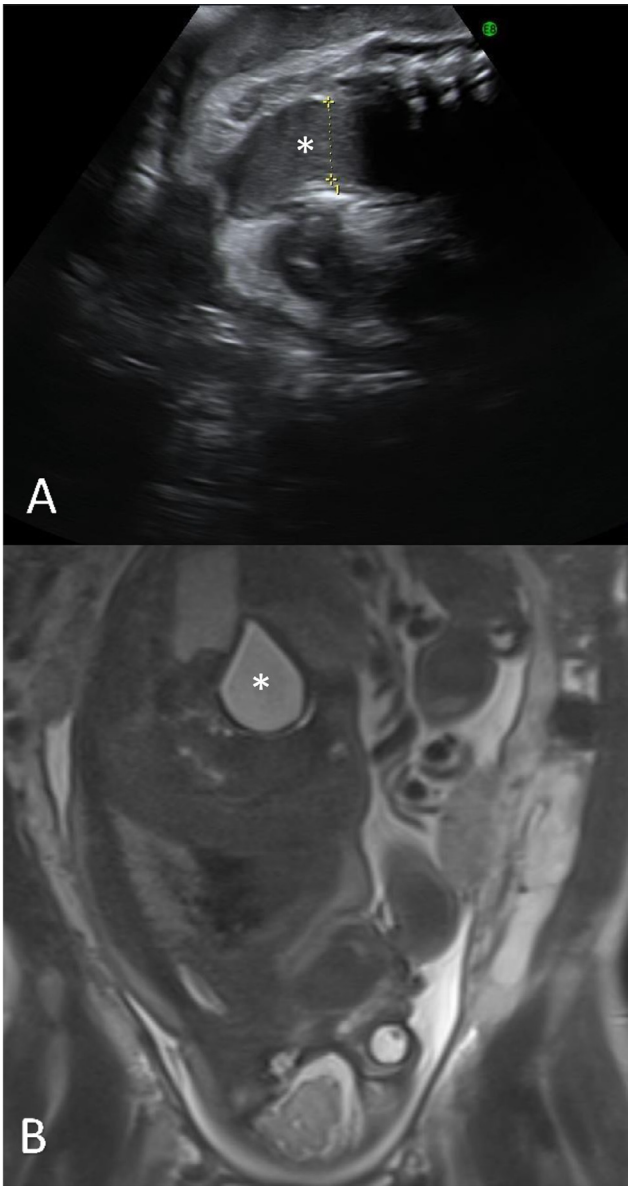

Figure 1. Prenatal imagiology showing pelvic, retrovesical cystic mass (asterisk): (**A**) Ultrasound; (**B**) MRI. (Color version available online.)

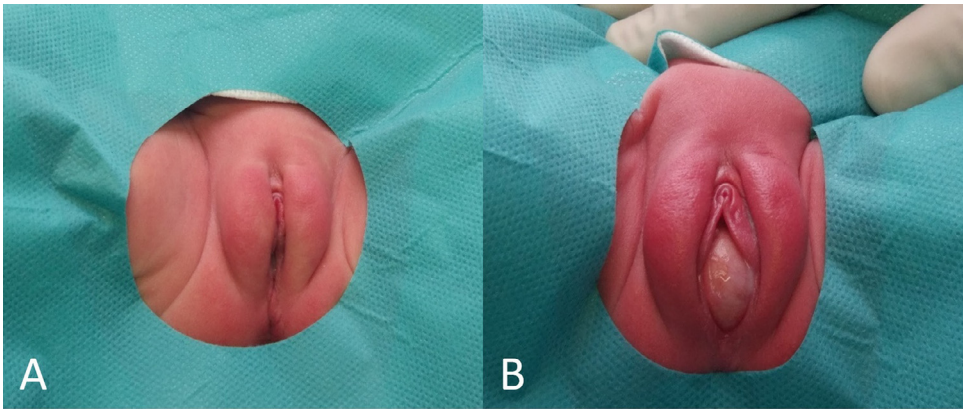

Figure 2. External genitalia: (**A**) Apparent normal genitalia; (**B**) Vestibular bulging with Credé's maneuver. (Color version available online.)

Table 1. Prepubertal HWWS.ARK, absent right kidney; ALK, absent left kidney; HWWS, Herlyn-Werner-Wunderlich syndrome; PCM, pelvic cystic mass

A—Neonatal Cases

Case	Prenatal Findings	Clinical Presentation	US	MRI	Treatment	Age at Time of Surgery
Wu et al[8]	ARK	Vestibular bulging mass	ARK, PCM	ARK, PCM, uterus didelphys	Simple incision and drainage	5 d
Vivier et al[14]	Prenatal US, suspicion of pelvic kidney	—	ALK, PCM, uterus didelphys	ALK, PCM, uterus didelphys	Trans-hymenal vaginal septotomy	1 mo
Han et al[15]	ALK, PCM	—	ALK, PCM, double uterus	Double uterus and blind hemivagina with hydrocolpos	Not described	—
Present case	ARK, PCM	Vestibular bulging mass	ARK, PCM	ARK, PCM, left pelvicalyceal dilation	Trans-hymenal vaginal septotomy	4 d

B—Nonneonatal Cases

Case	Age (y)	Clinical Presentation	US	MRI	Colposcopy	Treatment
Angotti et al[9]	3	Abdominal pain, dysuria and palpable abdominal mass. Vaginal bulging	ARK, PCM	ARK, PCM, vaginal spetum	Double cervix (visible after septum resection)	Transhymenal resection of vaginal septum
Roth et al[12]	3	Painless abdominal mass	Solitary kidney and dilated uterus	—	Bulging lateral wall; double cervix after septum resection	Transhymenal resection of vaginal septum
Sanghvi et al[6]	4	Abdominal pain, dysuria and palpable abdominal mass	ARK, PCM	—	Bulging of the right wall	Pfannenstiel laparotomy revealing uterus didelphys and hydrocolpos; open septotomy
Fernández-Ibieta et al[13]	6	Intermitent lower abdominal pain and distension	ARK, PCM	ARK, uterus didelphys, double vagina, hydrocolpos	—	Transhymenal resection of vaginal septum

with 5-0 polyglactin910 and a vaseline petrolatum gauze was left inside the vagina. On the first postoperative day, the gauze was removed and the parents were instructed to flush the vagina daily with normal saline. The newborn was discharged on the second postoperative day and examined a week later, showing a permeable vagina.

After 1 year of follow-up, the child is well, with a permeable vagina and symptomless. Ultrasonography showed resolution of the pelvicalyceal dilation.

DISCUSSION

Developmental abnormalities of the female genital tract involve a wide variety of disorders of the fallopian tubes, uterus and vagina, and have a reported mean prevalence of approximately 7%.[4] They occur from maldevelopment of the Mullerian or paramesonephric ducts and can be associated with reproductive issues. The development of Mullerian ducts is embryologically interlinked to the development of Wolffian or mesonephric ducts, explaining the frequent association of renal and urologic abnormalities and Mullerian malformations. Absent kidney is the most common of these concurrent anomalies, being present in up to 30% of cases.[5]

In 1971, Herlyn and Werner reported a case of renal agenesis with blind hemivagina and a Gartner duct cyst. Later, in 1976, Wunderlich described the association of renal aplasia, bicornuate uterus with simple vagina, and isolated hematocervix.[6] Since the 80s, the term HWWS has been applied to the triad of uterus didelphys, obstructed hemivagina and ipsilateral renal agenesis.

The incidence of HWWS is not known. It is estimated that 6% of patients with uterine duplication have an obstructed hemivagina, and that renal agenesis is found in 63%-81% of uterine duplications and in 92%-100% of obstructed hemivaginas.[7] Obstructed hemivagina and renal agenesis in patients with uterus didelphys seems more likely to occur on the right side.[7]

Patients with HWWS usually present within 1 year after menarche with hematometrocolpos on the side of the obstructed hemivagina, producing abdominal pain, dysmenorrhea, and abdominal mass.[8,9]

Although uncommon, this malformation can be diagnosed in the neonatal period prior to any clinical manifestation, normally following prenatal diagnosis of renal agenesis. Hydrocolpos can also be detected in the neonatal or even in the prenatal period, being reported as early as the 25th week of gestation.[9] The most common finding in the neonatal period is a soft vulvar mass. However, the perineal examination is difficult at this age, making the differential diagnosis with imperforate hymen not straightforward.[10]

Ultrasound may be sufficient to make a correct diagnosis but magnetic resonance imaging remains the preferred imaging method for investigation of mullerian duct anomalies particularly in pediatric patients.[11]

Obstructive reproductive tract anomalies, such as HWWS, comprise a higher risk of hematosalpinx, endometriosis, and pelvic inflammatory disease, potentially threatening the fertility of these patients.[11] If treated, fertility is generally not jeopardized but the spontaneous abortion rate is high, reaching 40% in some series. The preferred treatment consists in the excision of the obstructing vaginal septum.[1]

The available literature on HWWS is scarce and derived mainly from descriptions of clinical cases. The neonatal approach of this syndrome is even less reported. We conducted a literature review in PubMed database including reports of HWWS in prepubertal girls published in the last decade. Reports of other similar malformations, often designed as obstructed hemivagina and ipsilateral renal anomaly, were excluded.

We identified 4 case reports in the nonneonatal prepubertal population, aging between 3 and 6 years (**Table 1**).[6,9,12,13] The majority presented with abdominal pain and a palpable mass. Our search returned 3 case reports of newborn patients with diagnosis of HWWS (**Table 1**).[8,14,15] All had abnormal prenatal ultrasound, but only one had a vestibular mass.

In our case, prenatal detection of right renal agenesis and pelvic cystic mass led to the suspicion of a Mullerian anomaly, although other diagnosis such as anorectal malformation was considered. Imperforate hymen was excluded during the first physical examination due to the finding of a perforated hymen with permeable vaginal introitus despite the vestibular bulging. Physical exam and vaginoscopy allowed the diagnosis of an obstructed hemivagina and immediate treatment.

CONCLUSION

Our clinical case shows that prenatal suspicion and careful physical examination at birth allows early diagnosis and management of HWWS, which relates to better outcomes and avoidance of potential lifelong complications. The presence of renal agenesis in the prenatal ultrasound, especially when associated with a cystic pelvic mass, should raise the clinician awareness of complex urogenital malformations such as HWWS.

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