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

Tiago Tuna, José Estevão-Costa, Carla Ramalho, and Ana Catarina Fragoso

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.

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 $65 \times 25 \times 22$ 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 normally implanted normal right cervix, compatible with uterus didelphys. Cystoscopy was also performed, showing a normally implanted cervix. An incision was made in this wall with massive cautery, 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

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<td>ARK, PCM, uterus didelphys</td>
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<td>Prenatal US, suspicion of pelvic kidney</td>
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<td>ALK, PCM, uterus didelphys</td>
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<td>—</td>
<td>ALK, PCM, double uterus</td>
<td>Double uterus and blind hemivagina with hydrocolpos</td>
<td>Not described</td>
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<td>Present case</td>
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<td>ARK, PCM</td>
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<th>Case</th>
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<td>Angotti et al(^9)</td>
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<td>ARK, PCM, vaginal septum</td>
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<td>Intermitten lower abdominal pain and distension</td>
<td>ARK, PCM</td>
<td>ARK, uterus didelphys, double vagina, hydrocolpos</td>
<td>—</td>
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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%. 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 Wolfian 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.

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. 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. Obstructed hemivagina and renal agenesis in patients with uterus didelphys seems more likely to occur on the right side.

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

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. 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.

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. 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. 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.

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). 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). 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.

REFERENCES