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Case Report

Herlyn-Werner-Wunderlich syndrome: A case report in a young woman, with literature review^{☆,☆☆}

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ABSTRACT

Herlyn-Werner-Wunderlich syndrome is a rare complex congenital disorder, with combined Müllerian and mesonephric duct anomalies, presenting with uterus didelphys, unilateral blind hemivagina and ipsilateral renal agenesis. Hemivaginal obstruction usually leads to impairment of normal menstrual flow, resulting in symptoms after menarche, namely dysmenorrhea, pelvic pain or infertility. Age of presentation depends on the anatomical features of this anomaly. We report a case of a 21-year-old female presenting with few symptoms and incidental findings on transvaginal ultrasound, with typical findings of this disorder on magnetic resonance imaging, which remains the gold standard imaging technique for thorough assessment of Herlyn-Werner-Wunderlich syndrome, allowing for a correct diagnosis and adequate surgical management. Our case also highlights some unusual features, such as the presence of a blind ectopic ureter, with hematic content, and an incomplete septum within the obstructed hemivagina.

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Introduction

Herlyn-Werner-Wunderlich syndrome (HWWS) is a rare malformation of Müllerian and mesonephric origin, first described in 1922 [1–3]. The typical presentation is a triad of uterus didelphys, unilateral blind hemivagina and ipsilateral

renal agenesis, although anatomical variations have been described [1]. Patients with HWWS are usually asymptomatic until the onset of menarche, when dysmenorrhea, pelvic pain or infertility occurs [1–4]. In more serious cases, hemivaginal obstruction can lead to endometriosis, fallopian tube adhesions with hematosalpinx, pelvic inflammation or urinary obstruction [1,3,5].

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Even though ultrasound is usually the first imaging technique used, the imaging modality of choice for a precise diagnosis is magnetic resonance imaging (MRI), which allows for excellent anatomical depiction and sensitivity for hematometra and hematocolpos. The most common first imaging presentation is the presence of a cystic pelvic mass, corresponding to hematocolpos.

Vaginal septum excision is the preferred surgical treatment and should not be delayed, providing normalization of menstrual flow and symptom relief [2,3].

Case report

A 21-year-old, nulliparous, sexually active woman was referred to our hospital's Gynecology department to evaluate a cystic mass adjacent to the anterior wall of the vagina, seen on a computed tomography (CT) scan performed 1 month before elsewhere for unknown reasons. The patient was aware of having right kidney agenesis and uterus didelphys from birth (in utero diagnosis). Patient's menarche was at 14 years of age and she used a vaginal ring to regulate menstrual cycles and as a contraceptive, with no complaints. The patient referred mild dysmenorrhea, being otherwise asymptomatic. Specifically, she had no symptoms of urinary infection, hematuria or dyspareunia. Laboratory findings – complete blood count, kidney function and urine analysis – were normal, and a urine pregnancy test was negative.

Gynecological and physical examinations showed no significant changes. Transvaginal ultrasound was performed, identifying a cystic lesion adjacent to the anterior wall of the vagina. Uterus didelphys was also noted. The ovaries were unremarkable. Since the cystic mass was suspected to represent a urethral diverticulum, the patient was then referred to a Urologist, who ordered a pelvic MRI.

MRI was performed on a 3-Tesla magnet, using T1 and T2-weighted sequences, with and without fat suppression, before and after administration of intravenous paramagnetic contrast (Gadovist). The exam confirmed agenesis of the right kidney, the existence of two separate uterine bodies and two separate cervixes, thus confirming the presence of uterus didelphys. The two uterine bodies were widely splayed, with normal zonal anatomy and no abnormalities in the uterine cavities (Fig. 1). Ovaries were normal. Adjacent to the anterior wall of the vagina, two communicating cystic structures were identified, the superior one communicating with the right cervix. Both showed high-signal on T1-weighted sequences and the T2 “shading” sign, suggesting the presence of blood products (methemoglobin). These communicating cystic structures were thought to correspond to an obstructed hemivagina, partially septated (incomplete transverse septum), with hematocolpos, communicating with the right cervix (Fig. 2). In order to better understand the vaginal anatomy, particularly of the apparently collapsed left hemivagina, vaginal gel was administered, confirming the presence of an unobstructed posterior hemivagina, communicating with the left cervix (Fig. 3). Another fluid-filled tubular tortuous structure was identified on the right side of the obstructed hemivagina, communicating anteriorly with it,

presenting high signal on T1 sequences, representing a blind ectopic right ureter with reflux of hematic content from the right hematocolpos (Fig. 4).

There were no signs of hematometra, hematosalpinx, ovarian anomalies or bladder malformations. No signs of endometriosis or pelvic adhesions or inflammation were identified. The left kidney was in its normal topography, with compensatory hypertrophy, presenting normal cortico-medullary structure. The left ureter also showed no remarkable findings.

Given the imaging findings – right renal agenesis, uterus didelphys and right hemivaginal obstruction –, the diagnosis of HWWS was made, in this case with extra features: right blind ectopic ureter with hematic content and an incomplete transverse septum within the obstructed right hemivagina.

The patient is awaiting follow-up urology and gynecology appointments and will be proposed for a vaginal septum excision by the surgical team.

Discussion

HWWS is a rare syndrome comprising Müllerian and mesonephric developmental anomalies, with a reported prevalence of around 2%-3% and an incidence of 1:200 to 1:600 in fertile women [5–8]. Its etiology is thought to be multifactorial, and its embryological pathogenesis is still a subject of debate, but it is believed that a defect in vertical or lateral fusion of mesonephric or paramesonephric ducts leads to this combination of uterine, vaginal and urinary tract malformations [3,7,9–11].

The most usual form of presentation is a triad of uterus didelphys, unilateral blind hemivagina and ipsilateral renal agenesis, although anatomical variations have been described [1,3,12]. It is also commonly described in the literature as OHVIRA, an acronym which stands for obstructed hemivagina and ipsilateral renal anomaly, with any kind of uterine anomaly other than uterine didelphys [3,7,12]. However, Zhang et al. [1] have also noted that HWWS can occur with bicornuate uterus and septate uterus, further explaining the interchangeability between both terms.

Despite its typical triad of uterine anomalies, HWWS is known to have a diverse and complex spectrum of presentations. Bicornuate and septate uterus, unilateral cervical obstruction and incomplete vaginal septum have all been described [1,4,13]. Furthermore, urinary tract anomalies may also vary, with dysplastic kidney, ureteral anomalies such as blind ectopic ureter with vaginal or cervical insertion, and paravaginal cervical cysts [1,9].

While the American Society for Reproductive Medicine (ASRM) lists HWWS under type III Müllerian duct anomaly (uterus didelphys) [14], the consensus between the European Society of Human Reproduction and Embryology (ESHRE) and the European Society for Gynecological Endoscopy (ESGE) states a classification as U3b/c (bicorporeal uterus / bicorporeal septate), C2 (double “normal” cervix), and V2 (longitudinal obstructing vaginal septum) [15]. Furthermore, Zhu et al. [13] have described a new classification for HWWS, based on the morphology and the degree of obstruction: classification 1 – completely obstructed hemivagina (1.1 – with blind hemi-



Fig. 1 – T2-weighted images showing two separate uterine bodies, widely splayed on axial view (A) and two cervixes on coronal view (B) - uterus didelphys – as well as agenesis of right kidney with compensatory hypertrophy of left kidney (C).

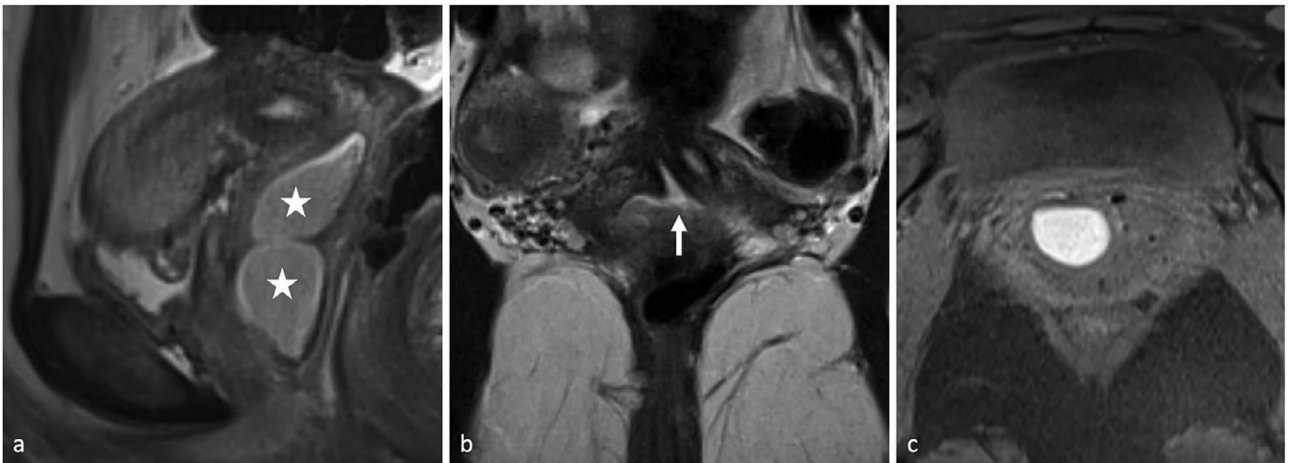


Fig. 2 – T2-weighted images revealing two cystic lesions on the anterior aspect of the vagina (stars) on sagittal view, corresponding to the obstructed anterior hemivagina, with an incomplete transverse septum inside (A), communicating with the right uterine cervix on coronal view (arrow) (B); T1-weighted axial image with fat-suppression showing high signal of the anterior hemivagina, concurring with hematocolpos (C).

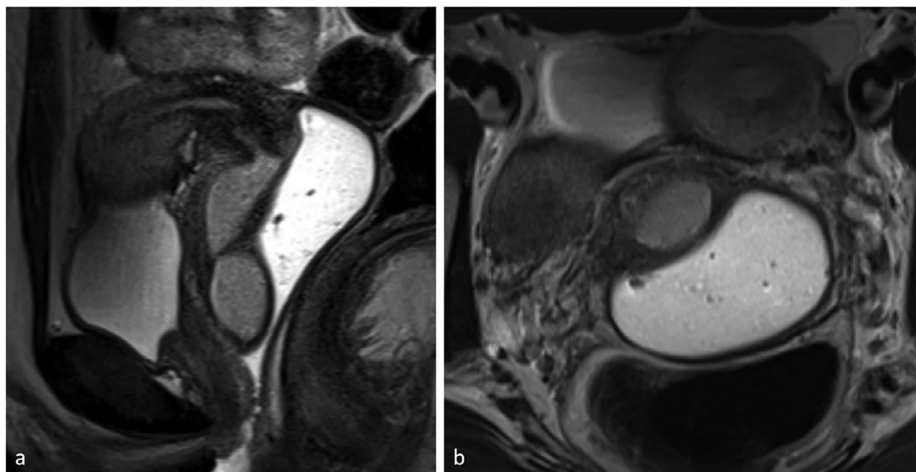


Fig. 3 – T2-weighted sagittal (A) and axial (B) images after administration of vaginal gel, delineating the abnormal anatomy: the obstructed anterior hemivagina, with T2 “shading,” and the unobstructed posterior hemivagina, distended with gel.

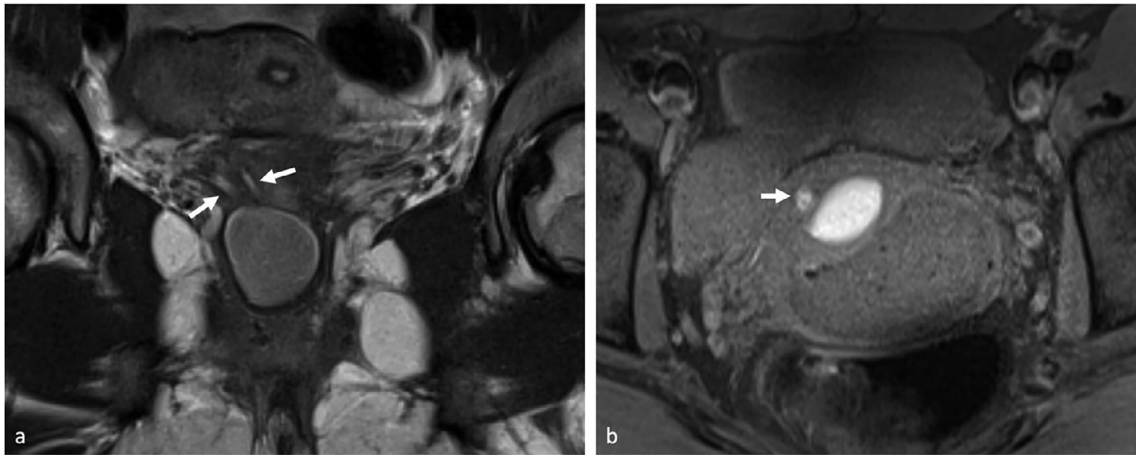


Fig. 4 – T2-weighted coronal image showing a small kinked tubular structure (arrows) adjacent to the obstructed hemivagina, corresponding to a blind right ectopic ureter (A); T1-weighted axial image with fat suppression shows the high T1 signal of the ureter (arrow), due to hematic reflux from hematocolpos.

vagina; 1.2 – cervicovaginal atresia without communicating uteri); classification 2 – incompletely obstructed hemivagina (2.1 – partial resorption of the vaginal septum; 2.2 – with communicating uteri).

The usual clinical presentation of HWWS occurs after the onset of menarche, with cyclical dysmenorrhea, dyspareunia, mucopurulent vaginal discharge, pelvic pain, pelvic mass or even acute abdomen [1–3,6,7,11]. The mean age of onset of symptoms reported by Tong et al. [16] was 17 years of age. With late onset disease, due to longstanding vaginal obstruction, infertility, pelvic adhesions and endometriosis ensue [1]. The degree of obstruction also determines the severity and age of presentation, with incomplete vaginal septum causing a late onset disease [3,12], whereas complete obstruction more likely presents with hematocolpos and hematometra, as well as endometriosis and infertility in more serious and chronic cases, due to retrograde menstrual flow to the peritoneal cavity [1–4,9,11]. Use of contraceptives, anti-inflammatory drugs and normal menstrual absorption between menses are also important reasons for delayed symptoms and diagnosis [3,11].

Ultrasound is usually the first imaging study used for diagnosing HWWS, due to being widely available, convenient and radiation-free, especially in younger patients [1,3,5]. However, MRI is the imaging modality of choice, due to its optimal tissue contrast and large field of view, allowing for a broad understanding of the anatomical changes happening in Müllerian anomalies [1,4,5,8]. MRI can provide detailed information regarding uterovaginal morphology, the nature of the fluids within the cavities and can accurately assess potential complications such as endometriosis or pelvic adhesions [2,5,9,17], providing useful insight for the correct management and surgical treatment [3].

Vaginal septum excision, with a laparoscopic or endoscopic technique, is the treatment of choice, providing an adequate drainage for hematometrocolpos, with symptomatic relief and, in many cases, viable pregnancy [2–4,17].

Also, the level of obstruction determines the type of surgical approach, since less common obstructions, like an obstructed hemicervix require a different approach [1]. Some authors consider laparoscopy the gold standard for both diagnosis and surgical treatment, although it could be argued that it should be reserved for cases in which the diagnosis is not clear after imaging exams [2,3,11]. Hemihysterectomy should be avoided, since the reported incidence of pregnancy in both uterine cavities is the same [10,11].

Our case presents the classic triad of HWWS - uterus didelphys, unilateral blind hemivagina and ipsilateral renal agenesis – with the extra feature of a blind ectopic right ureter with reflux of hematic content from the right hematocolpos (Fig. 5). To our knowledge, few cases of HWWS with associated blind ectopic ureter have been described in the literature. This feature is probably due to maldevelopment of mesonephric duct, which is responsible for the embryogenesis of the ureteric bud [1,9]. The late diagnosis at 21 years of age could be due to various factors. First, the use of a vaginal ring suppresses the cyclical occurrence of hematocolpos, with attenuated symptoms, as described by Vescovo et al. [11]. Second, normal absorption of hematocolpos between menses should not be underestimated, as stated by Dias et al. [3]. Finally, Zhang et al. [1] have pointed out that MRI might be insensitive for identifying small communications between the obstructed and the unobstructed hemivaginas, which could explain small drainage of hematocolpos in our case. Another unusual feature of our case is the presence of an extra partial transverse septum diving the obstructed vagina in two communicating cavities of hematocolpos, which, to our knowledge, has not been described in the literature. The fact that our patient had known renal agenesis and uterus didelphys from birth should also have prompted a clinical suspicion of eventual development of HWWS, thus emphasizing the importance of awareness for this congenital anomaly.



Fig. 5 – Illustration of our case of HWWS: uterus didelphys, unilateral blind right hemivagina and ipsilateral renal agenesis. The right hemivagina presents an inner incomplete transverse septum. An ectopic right ureter with reflux of hematic content is also seen.

Conclusion

HWWS is a rare congenital anomaly with clinical implications and a relatively simple surgical management if diagnosed within the right timing. MRI plays an important role in diagnosis, providing adequate anatomical assessment for surgical planning. Understanding the intertwining nature of Müllerian and mesonephric anomalies is key for the detection of more cases of HWWS. Early diagnosis allows for symptomatic relief and reduces the rate of complications such as endometriosis, pelvic adhesions or infertility.

Patient consent

The authors obtained written informed from the patient for publication of this case report.

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