Herlyn-Werner-Wunderlich syndrome: a challenging diagnosis
Síndrome de Herlyn-Werner-Wunderlich: um diagnóstico desafiante

Sara Dias Leite1, Maria Inês Raposo2, Mariana Teves1, Ana Furtado Lima1, Joana Sampaio2
Hospital Divino Espírito Santo

Abstract
Herlyn-Werner-Wunderlich syndrome (HWW) is a rare congenital anomaly of the female urogenital tract, characterized by the triad of bicorporeal uterus, obstructed hemivagina and ipsilateral renal agenesis. The most common symptoms are pelvic pain, dysmenorrhea and an abdominal mass. Prompt surgical treatment is advisable. If not immediately possible, medical treatment should be initiated to induce amenorrhea. We describe a case of HWW with chronic pelvic pain and mild dysmenorrhea. The ultrasound revealed uterine duplication and a retro-uterine mass contiguous to the cervix. Magnetic resonance imaging (MRI) confirmed a genital tract anomaly. The patient was medicated with continuous oral estroprogestative and was proposed to surgery.

Keywords: Uterine anomalies; Dysmenorrhea; Pelvic pain; Unilateral renal agenesis.

Resumo
O Síndrome de Herlyn-Werner-Wunderlich (HWW) é uma anomalia congênita rara do trato urogenital feminino, caracterizada pela tríade de útero bicorporal, hemivagina obstruída e agenesia renal ipsilateral. Os sintomas mais comuns são a dor pélvica, dismenorreia e presença de massa abdominal. É recomendado o tratamento cirúrgico atempado. No caso de impossibilidade, deve ser iniciado tratamento médico para indução da amenorreia. Descreve-se um caso de HWW em doente com dor pélvica crónica e dismenorreia ligeira. Ecograficamente constatada duplicação uterina e a presença de uma massa retro-uterina contígua ao colo uterino. A ressonância magnética confirmou a presença de malformação uterina. A doente foi medicada com estroprogestativo oral contínuo e proposta para cirurgia.

Palavras-chave: Anomalias uterinas; Dismenorreia; Dor pélvica; Agenesia renal unilateral.

INTRODUCTION
Congenital malformations of the female genital tract are deviations from normal anatomy resulting from Mullerian ducts anomalies (MDA), with a prevalence of 4-7%1.

1. Interno de Formação Específica, Department of Gynecology and Obstetrics, Hospital Divino Espírito Santo, Ponta Delgada.
2. Assistente Hospitalar, Department of Gynecology and Obstetrics, Hospital Divino Espírito Santo, Ponta Delgada.
3. Assistente Hospitalar Graduado, Department of Gynecology and Obstetrics, Hospital Divino Espírito Santo, Ponta Delgada.

Renal tract anomalies are associated with MDA in as many as 30% of the cases. The close relation between the urinary and reproductive systems during embryogenesis may explain this association2.

HWW is a complex and rare type of congenital anomaly of the genital tract consisting of bicorporeal uterus, obstructed hemivagina and ipsilateral renal agenesis.

The etiology of HWW is unclear, but it appears to be caused by the abnormal development of Mullerian and Wolff ducts3. It occurs in 0.1-3.8% of the population4.
HWW is usually diagnosed after menarche in a patient with nonspecific symptoms, such as progressive pelvic pain, dysmenorrhea and palpable mass due to associated hematocolpos or hematometra, secondary to retained menstrual flow in the obstructed vagina.

Diagnosis is difficult, once it is a rare condition and can present with general and multiple symptoms. The presence of regular menstruation, the improvement of pain with anti-inflammatory drugs and the elimination of menses with contraception pills make HWW a defiant diagnosis, only possible under high clinical suspicion.

In order to achieve a correct diagnosis, a detailed anamnesis is of the utmost importance, complemented with physical examination and ultrasound assessment to outline possible genital tract abnormalities. Although laparoscopy is considered the gold standard for the evaluation of the female reproductive tract anomaly, MRI provides detailed information of the pelvic anatomy and it is a valuable technique to obtain an accurate MDA classification.

HWW can lead to several complications. Acute complications include infections such as pyohematocolpos, pyosalpinx or peritonitis. In patients with a complete obstructed vaginal septum, menstrual regurgitation occurs leading to long-term complications such as chronic pelvic pain, endometriosis and pelvic adhesions. There is also an increased risk of abortion and infertility.

Surgery is the first-line treatment, being the most effective in relieving pain and maintaining fertility. When not immediately possible, it is important to achieve menstrual suppression with hormonal treatment to prevent further accumulation of blood.

CASE DESCRIPTION

A 14-year-old female with no sexual life presented with a history of mild abdominopelvic pain, which increased during menstrual cycles. Gynecologic history include menarche at 13 years of age, with regular menses. In 2018, in other institution, the patient performed a pelvic ultrasound that raised the suspicion of a bicorporeal uterus with hematocolpos. The MRI performed promptly after confirmed only the hypothesis of a bicorporeal uterus, excluding other associated genital malformations, showing an adnexal hemorrhagic cyst of 61 mm compatible with endometrioma. A laparoscopic cistectomy was performed, with no clinical reports presented at the appointment.

The abdominal examination was normal and the gynecologic exam was not possible to perform.

A transabdominal ultrasound showed two independent uterine structures, with both endometrial cavities in the virtual status, with a liquid homogeneous collection of 50x55 mm, well delimited, retro-uterine, apparently contiguous to the cervix (Figure 1).

A diagnosis of genital tract anomaly was raised with a bicorporeal uterus with obstructed hemivagina and hematocolpos. The patient was medicated with continuous oral contraceptive pill to induce amenorrhea and a MRI was requested.

Due to the COVID-19 pandemic this exam was postponed several months and the patient was checked regularly by telemedicine, with no clinical worsening.

MRI confirmed two individualized uterine horns with a deep and divergent septum, cervical duplication, two external cervical os and a complete vaginal septum. The right hemivagina was dilated with fluid accumulation exhibiting a hyperintense signal on T1-weighted images and highly hypointense on T2-weighted images, compatible with chronic and cyclic accumulation of blood, referred to hematocolpos. The left hemivagina was collapsed with a recent small amount of blood. (Figures 2-4).

A previous renal ultrasound revealed right renal agenesis.

The patient is waiting to be transferred to a tertiary center to receive surgical treatment.

The authors have parental and patient’s consent to publication.

DISCUSSION

We present a case of HWW, characterized by the triad of bicorporeal uterus, obstructed hemivagina and ipsilateral renal agenesis.

Congenital malformations of the female genital tract are a miscellaneous group of deviations from normal anatomy with consequences for health and reproduction,
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most common renal tract anomaly associated is renal agenesis5-7.

HWW is a very rare congenital anomaly of the female genital tract first described in 1976, characterized by the triad of bicorporeal uterus, blind hemivagina and ipsilateral renal agenesis4.

The exact etiology and pathogenesis of HWW is still unknown. One of the hypotheses is to represent an anomaly of the Mullerian (paramesonephric) and Wolffian (mesonephric) ducts development. The Wolffian ducts not only origin the kidneys, but are also inducers for the proper fusion of the Mullerian ducts8-10.

There may be an abnormal development of the caudal portion of the Wolffian ducts, leading to its absence on one of the sides. On the side where the Wolffian duct is absent, the Mullerian duct is displaced laterally and cannot fuse or contact with the urogenital sinus centrally. The contralateral Mullerian duct originates a

Renal tract anomalies are associated with congenital malformations of the female genital tract in up to 30% of cases due to the embryologic relationship between the paramesonephric and mesonephric ducts5. The

FIGURE 1. Ultrasound scan with a retro-uterine collection of 50x55 mm contiguous to the cervix.

FIGURE 2. MRI scan showing two separate uteri with divergent apices.

FIGURE 3. MRI scan with two separate cervices.

FIGURE 4. MRI scan with hematocolpos.
normal vagina and the displaced Mullerian duct coalesces into a blind sac, forming an obstructed hemivagina.  

Although symptoms can vary widely, the most common presentation is with pelvic pain, dysmenorrhea and a pelvic mass secondary to hematocolpos. Our patient had the first two symptoms. The pelvic mass was not identified, probably because a gynecological exam was not possible to perform due to the patient’s age and absence of sexual life. In order to perform a correct diagnosis a high clinic suspicion and a thorough examination are extremely important. 

In the presented case, ultrasound allowed the correct diagnosis by showing urovaginal duplication and hematocolpos, confirmed in greater detail by MRI, with no need to proceed with diagnostic laparoscopy. 

In 2013 the European Society of Human Reproduction and Embryology (ESHRE) and the European Society for Gynaecological Endoscopy (ESGE) have established a new classification of female genital tract congenital anomalies based on anatomy. According to this, our case is classified as U3bC2V2 anomaly (complete bicornoreal uterus with double “normal” cervix and a longitudinal obstructing vaginal septum). 

In 2015, after the biggest review of HWW, including 79 patients, Zhu et al. suggested a classification of this syndrome based on the presence of a complete or incomplete vaginal septum, advocating that clinical manifestations of the two groups are distinctively different. 

Once a diagnosis of MDA is made, it is imperative to investigate the urinary tract and vice versa. In our case, right renal agenesis was confirmed. Patients with HWW have renal agenesis ipsilateral to the blind vagina. In the current literature, there is a 100% incidence of ipsilateral renal agenesis among patients with uterus didelphys and unilaterally obstructed hemivagina. Jail Tong et al. also described all 70 patients with ipsilateral renal agenesis. 

The lateral distribution of obstructed hemivagina and renal agenesis have right side prevalence, as it was in our case. Jiali Tong et al. reported right renal agenesis in 60% of the patients. 

HWW is usually not diagnosed until puberty, shortly after menarche. The majority of the reported cases are in post-pubertal adolescents or adults. In the presented case, the patient was diagnosed one year after menarche. Although the presentation of this anomaly is very rare in prepubertal ages, Pansini et al. described a 5-month-old infant with HWW and Yogendra Sanghvi et al. a 4-year-old girl. 

Definitive treatment is septectomy, to permit drainage of the blood deposited in the obstructed vagina. When not drained, retrograde blood flow impairs tubal function and leads to endometriosis and other complications like infections, which can result in pelvic adhesions and affect fertility. 

A timely diagnosis with prompt treatment is extremely important to prevent unintended consequences. If treatment is delayed, complications may develop, such as hematometra, pyometra, hematosalpinx, pyosalpinx, endometriosis, pelvic adhesions or diminished fertility. 

The prognosis of HWW is good when diagnosed and treated promptly. In the absence of complications, 87% of patients achieve a successful pregnancy. 

Our case was even more challenging due to the installation of the COVID-19 pandemic, that made our national hospitals cancel elective and non-urgent activities, delaying the realization of a MRI to confirm the diagnosis and the possibility to transfer the patient to a tertiary center to perform surgery. 

The COVID-19 pandemic affected our daily clinical care, placing a tremendous weight on public hospitals, leading to deferred care for important non-COVID-19 conditions.

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CONTRIBUTIONS
Sara Dias Leite – Writing of the article
Maria Inês Raposo – Critical review of the intellectual content
Mariana Teves – Contributions to conception and design, data collection or analysis, and interpretation of data
Ana Furtado Lima – Critical review of the intellectual content and final approval of the version to be published
Joana Sampiao – Critical review of the intellectual content and final approval of the version to be published

CONFLICTS OF INTEREST
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ENDERECO PARA CORRESPONDÊNCIA
Sara Dias Leite
E-mail: saradiasleite@hotmail.com

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