A Case Report of Herlyn-Werner-Wunderlich Syndrome

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Abstract

Müllerian duct abnormalities (MDAs) are the most common congenital abnormalities of the genital tract in females and include a range of defects from minor anomalies, such as the bicornuate or septate uterus, to aplasia of the uterus. Herlyn-Werner-Wunderlich syndrome (HWWS) is a rare müllerian anomaly characterized by uterus didelphys with obstructed hemivagina and ipsilateral renal agenesis. The syndrome is usually associated with non-specific symptoms such as progressive pelvic pain after the menarche, dysmenorrhea, and palpable mass in the vagina caused by hematocolpos and hematometra. A 15-year-old single patient was admitted with abdominal pain and heaviness. On physical and ultrasonographic examination of the abdomen and rectum, she had a palpable tactile mass about 10 cm in diameter, heterogeneously attached to

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the right side of the uterine body through a base. The size and appearance of the left ovary were unremarkable, but the right ovary was not observed. On the right adnexa, a complex mass 46 mm in diameter was detected, indicating the presence of a serrated uterine fibroid or ovarian mass. The uterus was normal. On Abdominal MRI with and without contrast, renal agenesis and an 80 x 56 mm cystic lesion with several thin internal septa were found in the right adnexa. The rarity of Herlyn-Werner-Wunderlich syndrome (HWWS) results in complicated diagnostic and therapeutic procedures. Appropriate imaging techniques and correct interpretation are an attempt for faster diagnosis and treatment to avoid complications such as endometriosis, adhesions, and infertility caused by chronic infections. In young cases, due to the negative impact of multiple surgeries on fertility, making a timely decision and doing a proper surgery is suggested. By increasing the number of case reports in the future, the best diagnostic, and treatment methods will be more identified.

Keywords

- Herlyn-Werner-Wunderlich Syndrome
- Müllerian Ducts/abnormalities
- Kidney/abnormalities
- Vagina/abnormalities
- Uterus/abnormalities

Introduction

Müllerian duct abnormalities (MDAs) are the most common congenital abnormalities in females and include a multitude of defects ranging from minor anomalies, such as bicornuate or septate uterus; to major defects such as uterine aplasia.[1] The normal development of paramesonephric ducts (Mullerian ducts) occurs between the sixth and 22nd weeks of the embryonal age[2], and exit from normal structural changes lead to abnormal fusion or reabsorption of the Müllerian ducts. The precise incidence of uterine abnormalities is unknown, but it is estimated between 4.3% and 6.7%.[3-4] In some studies, it is reported in 1% of the general population and 25% of women with a history of infertility or abortion.[3-5]

Uterus didelphys is a type of MDAs where there is a complete duplication of uterine horns as well as duplication of the cervix, with no communication between them.[6] Its

prevalence is reported about 11% of all MDAs.[7]

The consequences and complications of this malformation include spontaneous recurrent pregnancy loss in the first trimester, infertility, endometriosis, intrauterine growth restriction (IUGR), preterm delivery, and abnormal fetal position.[7-8] However, the rate of these complications varies among different types of uterine anomalies.

Uterus didelphys may be asymptomatic in many cases, but some patients may have symptoms such as dysmenorrhea. Dyspareunia also may present with varying amount of longitudinal vaginal septum and vaginal obstruction. Rarely, genital cancers, hematocolpos/ hematometrocolpos, and renal abnormalities have been reported in association with a uterus didelphys. Despite some of these symptoms and complications, uterus didelphys may have no influence on fertility or pregnancy outcome in many women.

Herlyn-Werner-Wunderlich syndrome (HWWS) is a rare MDA characterized by uterus didelphys with obstructed hemivagina and ipsilateral renal agenesis.[9] The actual incidence of the syndrome is estimated to be 0.1% to 3.8%.[10-11] It is usually associated with non-specific symptoms such as progressive pelvic pain after the menarche, dysmenorrhea and palpable mass in the vagina caused by hematocolpos and hematometra.[10] Invasive diagnostic modalities such as hysteroscopy, hysterosalpingography and Laparoscopy / laparotomy are frequently used for certain diagnosis. Although the first non-invasive diagnostic method is 2D and 3D ultrasound (US), it is not suitable for correct diagnosis because of its incapability to distinguish different types of anomalies. MRI is a non-invasive diagnostic method with high reliability that can also detect urinary tract anomalies simultaneously.[12-13] Some of these abnormalities are usually treated by removing the obstructions by surgery.[14]

Case presentation

A 15-year-old virgin female patient was admitted with an abdominal pain and a feeling of heaviness, and had a palpable soft pelvic mass measuring about 10 cm in diameter on abdominal and rectal examination. A transabdominal Ultrasound of the pelvic was then performed and found a 67mm round mass with heterogeneous echoes attached to the right side of uterine

corpus via a pedicle, which hypothesized a pedunculated uterine fibroid. The left ovary was normal in size and appearance, but the right ovary was not seen. On the right adnexa, a 46 mm diameter complex mass was presented which suggested a pedunculated uterine fibroid or an ovarian mass. The uterus was normal. Due to the patient's virginity and incapability of performing a transvaginal sonography (TVS), we performed MRI for the next evaluation. In abdominal MRI with and without contrast, renal agenesis and an 80×56mm cystic mass lesion with multiple thin inner septa at the right adnexa was found.

Past medical history indicated two surgical procedures with same complaint at the age of 12 and 14 years. Menarche was at the age of 11 years and a year later, at age 12, she had been admitted following a severe dysmenorrhea episode. At that time, the transabdominal ultrasound had found a complex anomaly in the urogenital system, the right kidney was not observed. It demonstrated a uterus measuring 48x21x30mm and an appearance of blood within the uterine cavity. The Cervix and vagina had been reported to be normal. In addition, it had been reported a cystic structure (86 mm in diameter) with echogenic fluid inside (blood) at right side of the uterine (hematometra). Also, hematosalpinx (35mm) had been observed at right lower quadrant. The ultrasound findings had suggested two separate uteruses and vaginas, that the left side had a normal function, but an imperforated hymen had led to hematometra and hematosalpinx at the right side. Thus, the patient had undergone the first surgical operation on the basis of the physical examination and ultrasound findings at age 12 to remove the accumulated blood in the uterine cavity (hematometra) and hematosalpinx. Histopathological evaluation of the resected surgical specimen had shown tubular glands lined with pseudostratified columnar cells along with a dense stroma with hemorrhagic spots as well as a normal myometrium. She was using low-dose oral contraceptive pills for two years after the first surgery. She was consuming 80 days of continuous active pills followed by a pill-free interval of ten days and had menses during these pill-free intervals. She had regular menstruation cycles during these two years. Two years after the first surgery (at age 14), the abdominal and pelvic MRI evaluation had indicated uterus didelphys with hematometra, obstruction in the right

hemivagina, fluid in the endometrial cavity of the right uterine horn as well as hematocolpos in the right fallopian tube. Thus, she underwent the second surgical operation with just an incision and drainage of the fluid. Eight months after the second surgery, MRI was repeated due to continuing abdominal pain that indicated fluid accumulation on the right side and myometrium atrophy in favor of hematocolpos in the right uterine horn, and no obvious changes in comparison with the previous MRI were shown. After that, the patient had been treated with cyclic medroxyprogesterone (10 mg /day for the first ten days of each month) for eight months just before referral to our center. In our center, after evaluating the patient's medical records and performing physical examinations and imaging studies, the patient underwent a trans-rectal ultrasound assessment, and tumor markers were measured. The results of tumor markers were normal (ALP: 4.19, CA125: 23.24, HE4: 90ml). The ultrasound report showed a uterus with dimensions of 40x25 mm extended into the vagina with an echogenic cystic lesion along the right side of the uterus with dimensions of 101x76x51mm and an internal septum. The uterine tissue was observed at the top of the mentioned lesion, and its lumen was connected to the lesion. Moreover, this uterine tissue was extended to the main uterus. These findings were in favor of a complete bicornuate uterus with an obstructed right horn. So, the patient was a candidate for resection of the uterus horn **Figure 1.**

After a midline incision and opening of the abdomen, the right uterine horn was detected and it was completely removed from the distal vagina. In the middle part, the remnant of endometrial tissue was destroyed by cautery because of the impossibility of complete resection from the main uterus **Figure 2.**

The patient was discharged with a good general condition after two days.

A left kidney bigger than the normal dimensions (143x47mm) and abcsence of the right kidney were observed by ultrasound after the surgery (compensatory renal hypertrophy). The uterus with dimensions of 83x40x20mm and normal echo was also reported. Uterus was leaning toward the left side and a normal endometrial thickness (5 mm) and echo pattern was indicated. Indeed, there was no space-occupying lesion in the uterine cavity. During five years of follow-up, the patient had no abdominal pelvic mass and had a regular menstruation.

TVS: Transvaginal Sonography

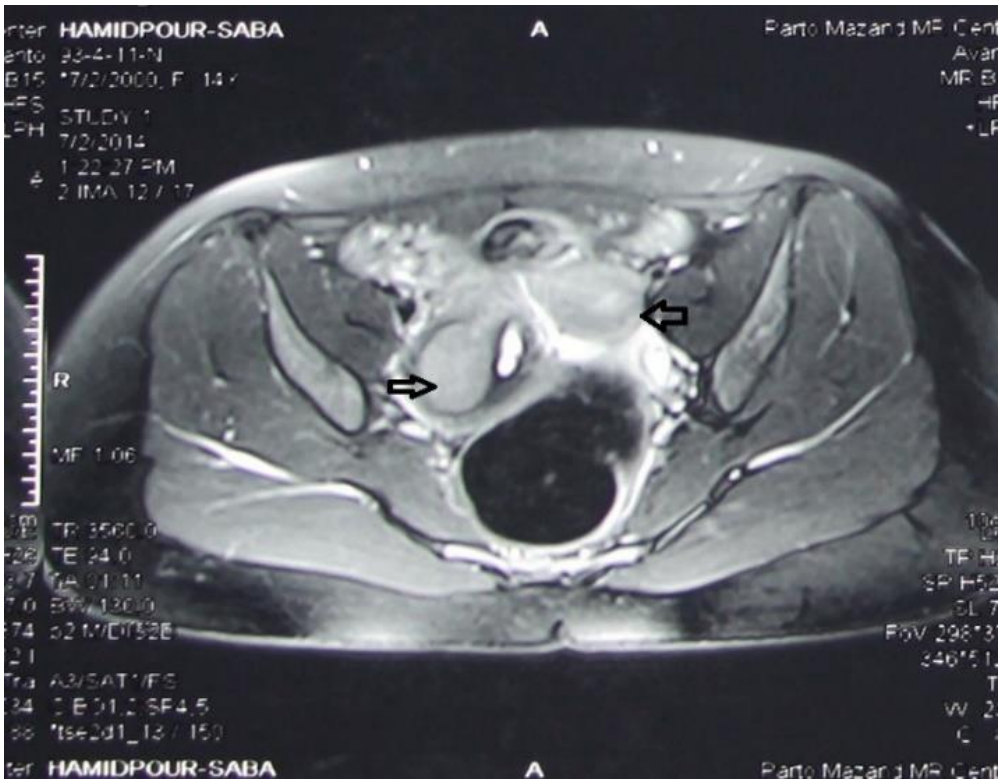

Figure 1: MRI image shows a complete bicornuate uterus with a septum before the third surgery (uterine horn resection).

Figure 2:

Discussion

Uterus didelphys is a rare malformation among the MDAs and includes only 5% of these abnormalities.[15] Most of the information is based on case reports or small series and the number of studies in this area is scarce due to the small number of cases in the general population. Many women with uterus didelphys may be asymptomatic; however, some may present with symptoms such as dysmenorrhea or dyspareunia and also vaginal septum or vaginal obstruction. This obstruction may lead to hematocolpos/hematometrocolpos resulting in a concurrent chronic abdominal pain. Rarely, reproductive system cancers, endometriosis, and kidney abnormalities has been reported associated with this malformation.[2-16-17] Uterus didelphys is one of the clinical presentations of HWW syndrome which is also known as obstructed hemivagina and ipsilateral renal anomaly (OHVIRA). This syndrome is a rare congenital malformation of the genitourinary system involving Müllerian ducts and Wolffian structures and has three presentations of uterus didelphys, obstructed hemivagina and ipsilateral renal agenesis.[18] The true incidence of the

syndrome has been estimated to be 0.1% to 3.8%.[10-11] It may lead to hematocolpos/hematometrocolpos on the site of obstructed hemivagina and consequently may develop inflammation which is associated with lower abdominal pain in patients.[19] Most cases of the disease present after the first menstruation with an acute severe lower abdominal pain and/or a mass protruding from entrance of the vagina.[19-20] Sudden and severe vaginal pain is also one of the rare reported presentations.[21] Long-term complications of the syndrome include endometriosis caused by the backflow of menstrual blood and obstetric complications such as repeated pregnancy loss, preterm labor, and abnormal fetal presentations due to uterine malformation.[22] The ultrasound evaluation followed by MRI of the pelvis helps final diagnosis.[2-19] It has been shown that MRI is the gold standard imaging technique for Müllerian abnomalies with an accuracy of 100%.[22] However, laparoscopy is the best way for diagnosis because of its benefits for treatment and diagnosis of the disease, including drainage of hematocolpos/hematometrocolpos, removal of the vaginal septum, and marsupialization.[23] Treatment is usually through surgical resection of vaginal septum, which helps to relieve the obstruction.[14] Also, surgical treatments reduce the risk of pelvic endometriosis, which is a consequence of menstrual blood backflow.[23] Delay in diagnosis or misdiagnosis can lead to complications such as endometriosis and infertility.[24] The optimal treatment is full excision and marsupialization of the obstructing vaginal septum so that both uteri can drain through the patent vagina.[25] Our patient had been presented with symptoms of severe dysmenorrhea a year after the menarche. In the primary ultrasound of patient's urogenital systems, a complex anomaly and no evidence of the right kidney had been observed. The findings of ultrasound and MRI were suggestive for two separate uterus and vagina (uterus didelphys, bicornis), in which the left system was normal but at the right side an imperforated hymen with a transverse vaginal septum had led to hematocolpos/hematometrocolpos. Two open abdominal surgical procedures had been carried out to relief the patient's symptoms, discharge the accumulated blood, and open the blood path in the right uterine horn. However, since both previous surgical methods were ineffective in symptoms relief, we decided for surgical

resection of the right uterine horn in a medical joint committee.

Conclusion

The rarity of HWWS results in complicated diagnostic and therapeutic procedures. Although it is a very rare disease, it is necessary that all physicians, especially emergency physicians, take this syndrome into account in a postmenarcheal girl with sudden lower abdominal pain, after ruling out the other causes[2-19] Appropriate imaging techniques and correct interpretation is an attempt for faster diagnosis and treatment to avoid complications such as endometriosis and adhesions caused by chronic infections, and infertility. In such cases with low age, due to the lack of a kidney and also negative impact of multiple surgeries on fertility, it is better the first decision to be made as a group in a medical joint commission. By increasing the number of case reports in the future, the etiology, best diagnostic and treatment methods will be more identified.

Ethical Consideration

Written consent for participation was obtained from the parent or guardian of the participant in the study**.** This study was approved by the Shahid Beheshti University of Medical Sciences by ethical committee (IR.SBMU.RETECH.REC.1400.130).

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Conflict of interests

There is no conflict of interest

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