

CASE REPORTS

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Successful pregnancies in an adolescent with Herlyn-Werner-Wunderlich (HWW) syndrome: a case report and literature review

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Abstract

Background: Müllerian anomaly is a congenital defect in the development of the female reproductive system that varies according to the stage of developmental failure resulting in agenesis, hypoplasia, or fusion defect in one or both Mullerian ducts; in such patients, it is expected to have higher pregnancy and delivery complications.

Case presentation: This case presentation of a 14-year-old adolescent girl with uterine didelphys, obstructed right hemi-vagina, and ipsilateral renal agenesis (Herlyn-Werner-Wunderlich syndrome, HWW) that was corrected surgically, then got married at the age of 16 with successful two consecutive term uncomplicated pregnancies of favorable maternal and fetal outcomes without a history of any miscarriage or recurrent collections.

Conclusions: Herlyn-Werner-Wunderlich syndrome is a rare case and represents a challenge to diagnose and treat especially in pediatrics and adolescents. Early recognition and treatment will help to improve outcome and reduce possible complications resulting from obstruction with retrograde menstruation and its consequences. Successful early management of our patient improved her quality of life by relieving her cyclical obstructive pain, preserve fertility, and normal sexual life.

Keywords: Herlyn-Werner-Wunderlich (HWW) syndrome, Mullerian anomaly, Pregnancy outcome, Renal agenesis, Obstructed hemi-vagina and renal anomaly (OHVIRA), Uterine didelphys

Background

Müllerian ducts are the embryological origin of the fallopian tubes, uterus, cervix, and upper two third of the vagina. Different anomalies can result from the disturbance of Müllerian duct development resulting in agenesis, hypoplasia, or fusion defect in one or both ducts [1]. Despite the availability of many classification systems, the American Society for Reproductive Medicine (ASRM) classification system is the most commonly used system and is based on uterine structure and its effect on fertility, stated that agenesis or hypoplasia (Mayer-Rokitansky-Kuster-Hausen Syndrome, MRKH) as class I, all types of

unicornuate communicating or non-communicating with or without cavity as class II, uterine didelphys class III, bicornuate uterus complete or partial as class IV, septate uterus complete or partial as class V, arcuate uterus class as class VI, and diethylstilbesterol-related anomaly as class VII. As ASRM does not accommodate all known anomalies, another system was developed by the European Society of Human Reproduction and Embryology (ESHRE) where it addresses the complexities and variations in these conditions more. Despite that, neither system can cover all possible anomaly varieties [1].

The accurate prevalence of congenital uterine anomalies is difficult to determine since many are asymptomatic. The reported prevalence varies one study describes a 5.5% prevalence of congenital uterine anomalies in an unselected population, 8.0% in infertile patients, 12.3% in patients with miscarriage history, and 24.5% in patients

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with miscarriage and infertility [2]. Patients with uterine anomalies have increased chances of spontaneous abortion, premature labor, cesarean section delivery, malpresentation, and decreased chance of live births compared to women with normal uterus. However, the outcome degree varies based upon the type and degree of uterine anomaly. But still, there are many cases that do not manifest any of these challenges [1, 3–5].

Herlyn-Werner-Wunderlich (HWW) syndrome is a very rare urogenital defect involving Wolffian structures and Müllerian ducts that are characterized by the triad of uterus didelphys, blocked hemi-vagina, and ipsilateral renal agenesis [6, 7]. In 1922, a combination of uterus didelphys and obstructed hemi-vagina was first reported by Purslow [8]. Purslow described this syndrome in a young woman who presented with gradually increasing pelvic pain and a pelvic mass with regular menstruation [9]. Then, Herlyn and Werner reported the triad in 1971, and Wunderlich reported it again in 1976. Obstructed hemi-vagina and ipsilateral renal anomaly (OHVIRA) syndrome is another name for HWW syndrome [10]. The didelphys uterus, which is linked to HWW, affects 1 in every 2000 to 1 in every 28,000 women, and it is associated with unilateral renal agenesis in 43% of instances. Unilateral renal agenesis affects 1 in every 1100 women, and 25–50% of those affected have genital anomalies [7]. A partial or complete vaginal septum is present in 75% of women with the didelphys uterus [6]. The most common presentation is dysmenorrhea, abdominal pain, and abdominal mass secondary to hematocolpos [11]. The exact causes, pathogenesis, and embryologic origin of HWW syndrome are unclear and remain a subject of discussion.

The objective of this case study is to report a rare Müllerian anomaly of Herlyn-Werner-Wunderlich (HWW) syndrome case who had successful early diagnosis and surgical treatment with improved quality of life by relieving her cyclical obstructive pain, preserving fertility with successful two consecutive term uncomplicated pregnancies of favorable maternal and fetal outcome without a history of any miscarriage, and normal sexual life.

Case presentation

A 14-year-old girl was referred to our University Hospital, in January 2017, complaining of severe lower abdominal pain a few months after menarche at 12 years of age; the pain was initially cyclic and then become chronic, increasing in severity, relieved by analgesics, radiating to back associate with right pelvi-abdominal mass and oligomenorrhea. She had no fever, nausea, vomiting, abdominal distension, or changes in bowel habits. There was no history of burning micturition or vaginal discharge. She gave a history of uterine

anomalies diagnosed in another hospital 1 year back (uterine didelphys with hematometrocolopus on the right side with right renal agenesis based on CT scan and ultrasound). She had an exploratory laparotomy at that time, June 2016, and aspiration of the collected blood in the right hemi-uterus was done as written in here report. The pain was relieved for a few months after surgery but started again with more severe intensity and was progressively increasing with lower abdominal distension.

On examination, she had normal secondary sexual characteristics with normal external genitalia, intact hymen. Lower transverse abdominal scar is seen, palpable pelviabdominal mass, tender, soft and globular.

Radiological studies in our hospital (U/S, CT) show uterine didelphys with a normal size left hemi-uterus of 6.8×2.3 cm and endometrial lining of 0.9 cm, and right hemi-uterus bulky of 11.6×3.5 cm with dilated upper vagina down to urethral level filled with blood (hematocolpus) (Figs. 1 and 2), both ovaries were normal—absent right kidney (Fig. 2B). The rest of the examination was normal, so she was diagnosed with Herlyn-Werner-Wunderlich (HWW) syndrome which is an obstructed hemi-vagina and ipsilateral renal agenesis. Hormonal profile and chromosomal analysis (46 xx) were done in the previous hospital during her initial presentation as a routine test for all cases of anomalies to exclude any other undiagnosed conditions and were normal.

In March 2017, she was taken under general anesthesia for surgical treatment. The examination showed normal external genitalia and intact hymen. Hysteroscopy after doing two cuts in the hymen at 5 and 7 o'clock (parents' permission and consent taken) showed normal vaginal length and mucosa with a large bulge on the right upper side, with left cervix pushed to the left upper vaginal fornix. The left uterine cavity was small with normal endometrial lining and tubal Ostia seen. A small needle was inserted in the right vaginal bulge to confirm the presence of chocolate materials, and then, the septum between the two vaginas was removed by a harmonic scalpel (Fig. 3A, B). The postoperative period was uneventful and discharged from the second day postoperative in good condition. Follow-up after 3 weeks with ultrasound shows an empty uterus, and she had no complaints. She continued to have a regular period with no pain and no recollection, both uteri empty. Six months later, hysteroscopy was done, showing the vagina, both cervix, and uterine cavities (Fig. 3C, D); repair of the hymen was done. She got married at the age of 16 years. She had two successful pregnancies over the last 3 years with no complications; both were in the right hemi-uterus which was obstructed before. She had two healthy boys (the first baby is 3.1 kg and the second boy is 2.8kg).

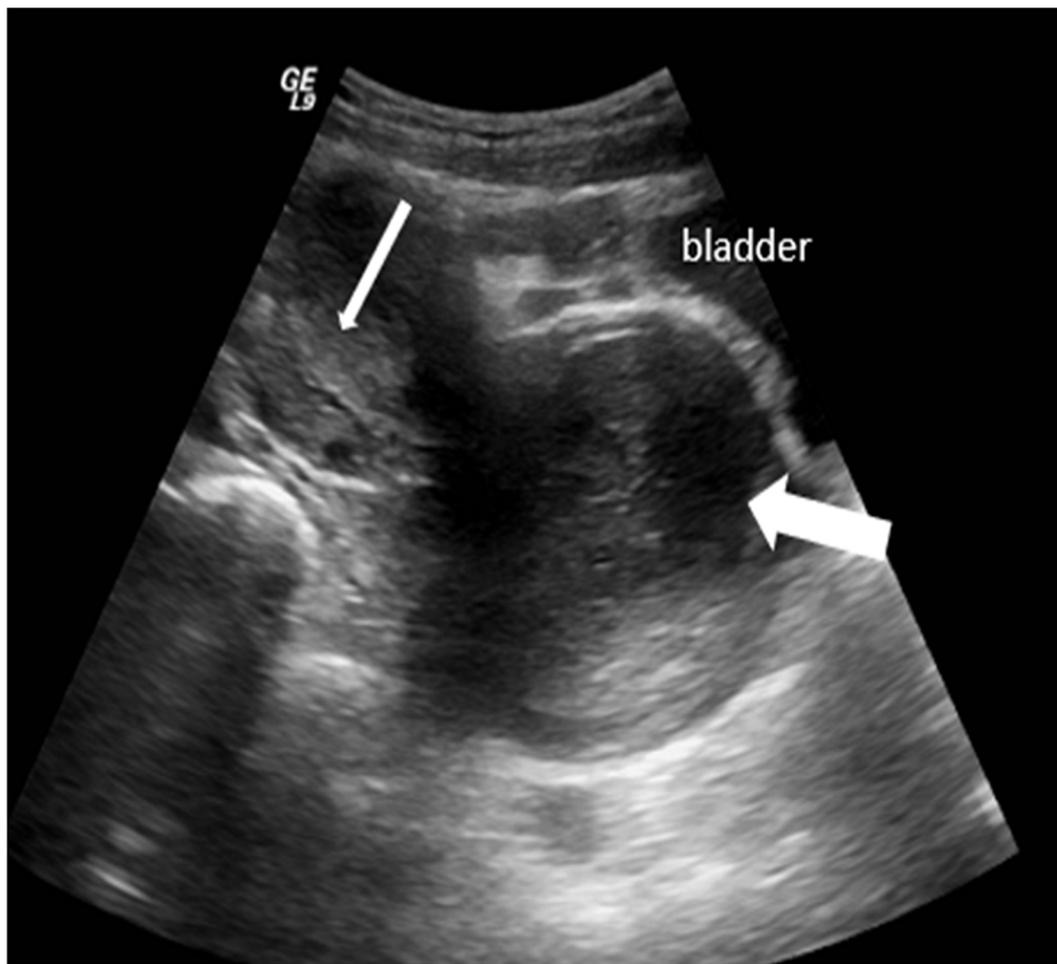


Fig. 1 Ultrasound at first presentation of the patient showing right hematocolpos of obstructed right hemi-vagina (thick arrow) with an empty cavity of the right hemi-uterus (thin arrow) after drainage of the hematometra in another hospital previously

Both deliveries were by elective lower segment cesarean section early term at first pregnancy at 38 weeks, second at 37 weeks (Figs. 4 and 5). She did not experience any complications in both pregnancies and no miscarriage since marriage.

Discussion

Herlyn-Werner-Wunderlich (HWW) syndrome is a rare form of Mullerian Duct Anomalies (MDA) with the prevalence of 2–3% and incidence of 1 in 200 to 1 in 600 among fertile women [8, 12]. Uterine didelphys accounts for 11% of MDA while aplasia/hypoplasia of the proximal vagina and uterus make up approximately 5–10% of MDA [12]. The didelphys uterus is a complete duplication of the uterine horns and cervix and septate vagina in 75% of the cases [13]. It is rare and accounts for about 8% of congenital anomalies of the female reproductive

tract [14]. An estimated 45% of cases of uterine didelphys associated with unilateral renal agenesis [12]. While maldevelopment (aplasia, hypoplasia, poor fusion, or failed resorption) of paramesonephric ducts is linked to MDA pathogenesis, the near proximity of mesonephric ducts that give rise to the kidney and ureter is hypothesized to cause genital tract defects that frequently accompany MDA [8].

Patients with MDA should be counseled appropriately to reassure them that pregnancy is possible and to relieve their psychological stress [1]. The fertility of didelphys uterus patients has been shown to be better than those with other Mullerian duct abnormalities but still less than women with normal uterine anatomy [15]. For didelphys uterus, vaginal delivery can be considered but cesarean delivery is better [14, 15]. In comparison to a normal uterus, patients with the didelphys

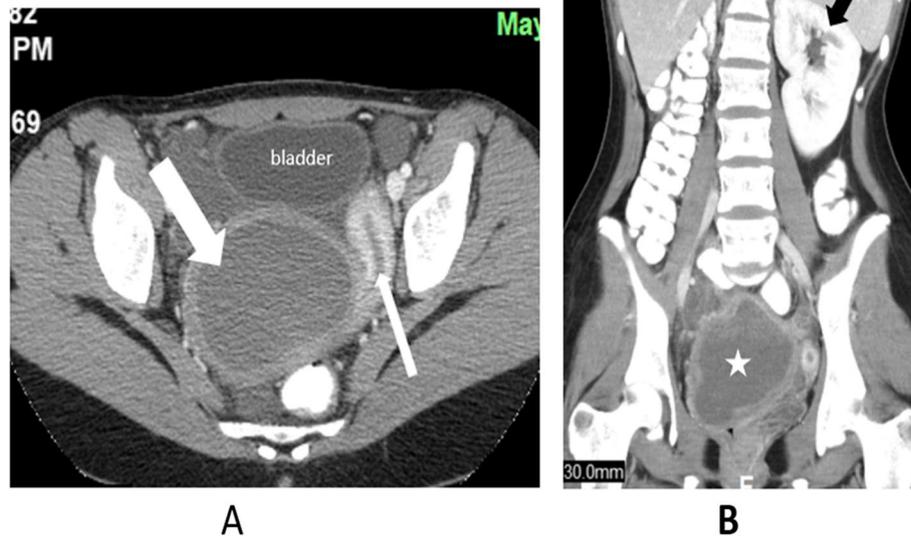


Fig. 2 CT scan showed **A** distended obstructed right hemi-vagina (hematocolpos wide arrow), right hemi-uterus (thin arrow), and **B** absent right kidney and compensatory hypertrophy of left kidney (black arrow) and hematocolpos (star)

uterus have term delivery rates of ~45%. Those patients have a higher rate of poor obstetrics outcomes as spontaneous abortions 32%, preterm birth 28% [3, 4], intrauterine growth restriction, malpresentation, preterm labor, and delivery [16, 17]. It is thought that these complications occur due to impaired ability to distend and decreased cavity size and abnormality in endometrial, myometrial, and cervical function. Patients with uterus didelphys belong to a high-risk group and need close prenatal care and follow-up [18]. Malpresentation and dystocia from obstruction of the pelvic inlet by non-pregnant uterine cavity are two of the major reasons for a high rate of cesarean sections of patients with uterus didelphys [14, 18, 19]. Although pregnancy with uterus didelphys is most commonly occurs unilaterally, there are documented cases of twin pregnancies occurring [18]. Cervical incompetence is not commonly occurred with didelphys uterus so cervical cerclage is not routinely recommended unless there is evidence of cervical incompetence or dilation either by clinical examination or ultrasonography during the early second trimester [15]. In didelphys uterus with obstructed hemi-vagina, ipsilateral urinary tract anomalies such as renal agenesis or pelvic kidney are common in around 15–30%, the right side, as in our current case, is usually affected twice as often as the left side [20, 21]. The triad of didelphys uterus, obstructed hemi-vagina, and ipsilateral renal agenesis occurs as a part of a very rare syndrome called

Herlyn-Werner-Wunderlich (HWW) syndrome, also known as obstructed hemi-vagina and ipsilateral renal anomaly (OHVIRA); this syndromic triad is fulfilled in our patient [1, 15, 22].

Most patients of the didelphys uterus are asymptomatic, but in obstructive anomalies, they presented after menarche with cyclic or chronic pelvic pain and variable-sized pelvic abdominal mass in the vagina or pelvis due to hematocolpos only or hemato-metro-colpos with retrograde menstruation which if neglected increase risk of endometriosis and tubal damage [15, 23]. Didelphys with a septate vagina can cause dyspareunia, abnormal bleeding [13], and infertility depending upon the defects involved [24].

Diagnosis of Mullerian anomaly can be made using ultrasound as the first line of radiological modality. Its sensitivity, specificity, positive, and negative predictive values for detecting Mullerian duct anomalies all have been found to be 100% and correlated with the external uterine configuration in 91.6% of cases compared with laparoscopy. Conventional (2D) US is not able to determine the external contour of the uterus compared to (3D) US and MRI. Also, the US is none invasive and less expensive than HSG and can serve in the office to diagnose and classify Mullerian duct anomaly, which rarely requires MRI to make a definitive diagnosis [24, 25]. MRI of the pelvis is the most accurate modality to characterize and classify genital tract anomalies and associated pelvic findings [12]. Characteristic findings on MRI

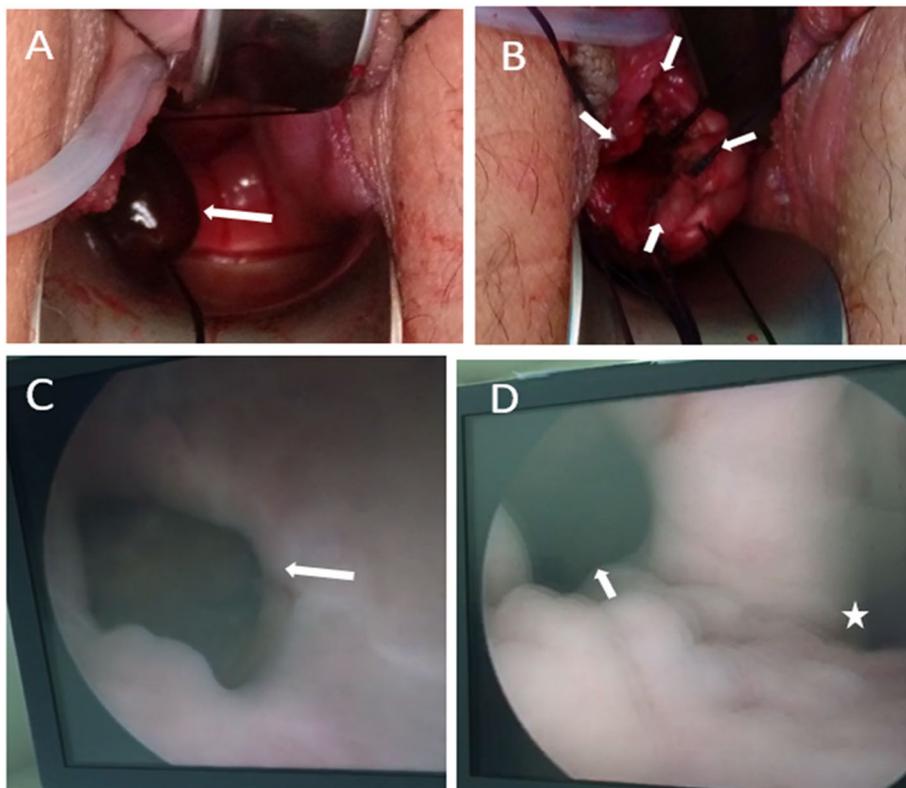


Fig. 3 Intraoperative views showed **A** intraoperative resection of vaginal septum with the chocolate materials coming-out from obstructed right hemi-vagina (arrow), **B** sutured edges of the opened right hemi-vagina (4 arrows), **C** colposcopic view showing the healed edges of the opened right hemi-vagina 3 months post-operative, and **D** colposcopic view of right hemi-vagina (arrow) and left hemi-vagina (star)

include complete duplication of uterine and endocervical cavities (didelphys uterus). Typically, a cystic structure is seen distal to and communicating with one of the endocervical canals, representing obstructed hemi-vagina. The obstructed vagina usually contains

the blood or proteinaceous fluid that appears bright on T1-weighted images. A fluid-fluid level may be seen. Other findings including hematometrosis and or hematosalpinx may be seen as bright T1 intensity filling the cavities of the uterus or fallopian tubes. Mullerian

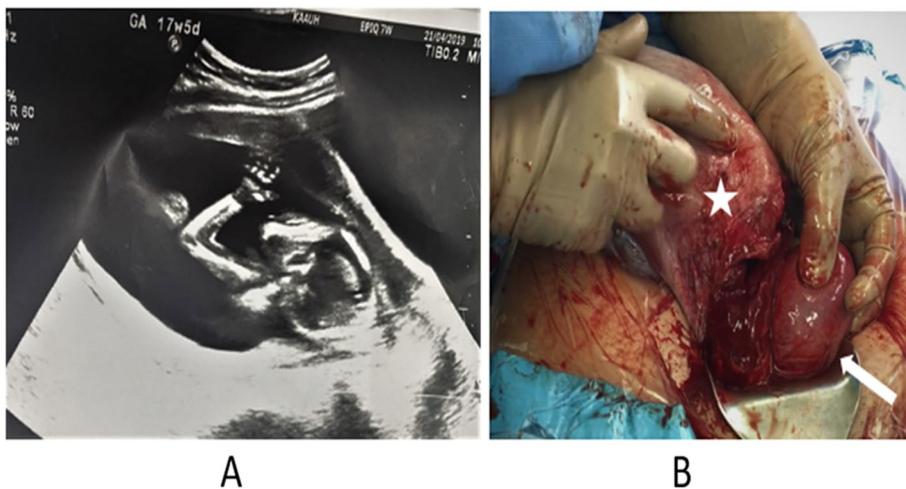


Fig. 4 The first pregnancy at 2019 showed **A** ultrasound during pregnancy and **B** lower segment CS in the right hemi-uterus which was obstructed before (star) and left hemi-uterus (arrow)

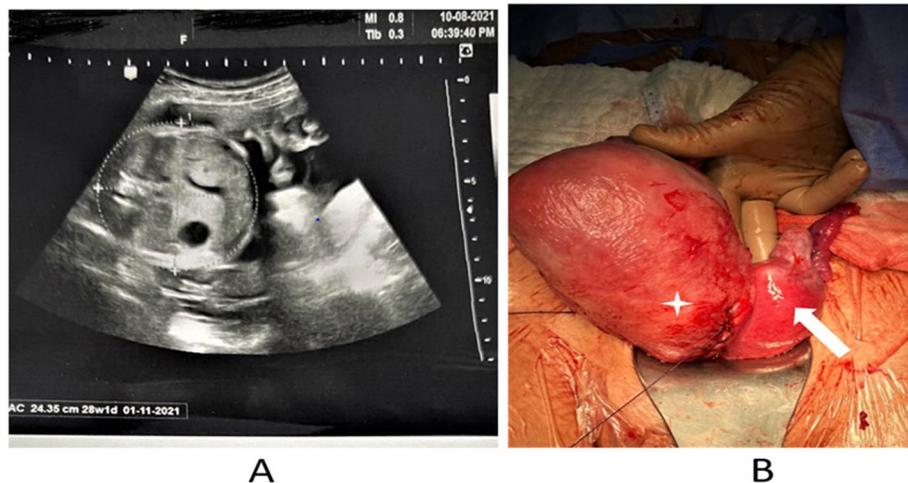


Fig. 5 The 2nd pregnancy at 2021 showed **A** ultrasound during pregnancy and **B** right hemi-uterus lower segment CS after suturing (star) and left hemi-uterus with tube and ovary (arrow)

anomalies and simultaneously assess for associated urinary tract anomalies. It is rarely necessary to perform surgery to diagnose a uterine anomaly [1]. Laparoscopy remains the gold standard for the diagnosis of female genital tract abnormalities but is only used when MRI is unavailable or fails to establish a diagnosis [26].

Mullerian abnormality does not necessitate surgical correction if the patient is asymptomatic and not obstructed. The aim of early diagnosis in relation to normal menarche and treatment is normal menstrual flow, sexual function, relief of pain, and decrease risk of endometriosis, with preservation of reproductive potential [1, 23]. Our patient received early management of obstructive didelphys anomaly with relieved of pain and successful two conceive pregnancies in the surgically treated right obstructed hemi-uterus with healthy two boys, without any maternal or fetal complications. A study by Wang et al. reported 52.9% ipsilateral pregnancies after vaginal septum excision [27]. In HWWS, successful pregnancy outcomes ranged from 57 to 68%, but abortion rates ranged from 30 to 33%, with a 3.6% perinatal mortality rate, 21–29% pre-term labor, and a higher prevalence of fetal malpresentation [3, 28, 29]. Prior to surgical therapy for blocked hemi-vagina, 54% (15/28) of women with HWWS conceived and delivered their first babies at term [30].

Conclusions

To avoid difficulties and protect future fertility, it is critical to have a quick and precise diagnosis of female reproductive tract illnesses, such as HWW syndrome. Early detection of this very uncommon illness would allow for prompt and effective surgical treatment.

Abbreviations

ASRM: American Society for Reproductive Medicine; CT: Computed tomography; ESHRE: European Society of Human Reproduction and Embryology; MDA: Mullerian Duct Anomalies; HWW: Herlyn-Werner-Wunderlich; MRI: Magnetic resonance imaging; MRKH: Mayer-Rokitansky-Kuster-Hausen Syndrome; OHVIRA: Obstructed Hemi-vagina and Ipsilateral Renal Anomaly; US: Ultrasonography.

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Authors' contributions

EA.A: responsible for doing surgery to patient and follow-up of the case and wrote the manuscript; LIS: responsible for follow-up and deliveries of the patient and shared in writing the manuscript; WOB, MAE, and FSA: responsible for the collection of the examination and investigation of the patient and shared in writing methodology and investigations of the patient. The authors have read and approved the final manuscript.

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Availability of data and materials

The authors are in the best disposition to provide all the documentation that is requested in case it is required by the editorial committee. All the original data and sources will always be available to anyone who wants to consult them.

Declarations

Ethics approval and consent to participate

The authors declare that ethical approval was obtained from the Ethical Committee of King Abdelaziz University Hospital, Jeddah, Saudi Arabia. The authors declare that they have the autograph consent of the patient to receive these interventions.

Consent for publication

The authors agree that this article is published and distributed on the platforms of this journal. The authors declare that they have the autograph consent of the patient for the publication of the information generated from here.

Competing interests

The authors declare that they have no competing interests.

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