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Case Report

Herlyn-Werner-Wunderlich syndrome: Challenges in diagnosis and management

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Abstract

Herlyn-Werner-Wunderlich syndrome (HWWS), also known as OHVIRA syndrome (obstructed hemivagina and ipsilateral renal anomaly) is a complex congenital malformation characterized by a triad including uterine didelphys, hemivaginal obstruction, and ipsilateral renal agenesis. In this case report, we present a case of HWWS along with the challenges in diagnosis and multi-step treatment processes. A 25-year-old woman presented to Dr. Zainoel Abidin Hospital in Banda Aceh, Indonesia with a chief complaint of lower back pain for the past six months (two months after the marriage). The patient also complained of late menstruation, followed by thick yellow vaginal discharge resembling malodorous pus occurring after menstruation. Additionally, a history of fever and pain during intercourse was reported. Vaginal examination revealed purulent fluid emerging from a pinpoint hole on the right vaginal wall. Vaginal palpation revealed a two-branched uterus, along with a palpable cystic mass on the right vaginal wall. Ultrasound examination indicated the presence of the right and left hemi-uteri, measuring 4.7x1.35 cm and 5.7x1.26 cm in size, respectively with both ovaries appearing normal. Fluid accumulation was observed in the right hemivagina, while the left kidney exhibited normal features, and the right kidney showed signs of hypoplasia. The patient was diagnosed with uterus didelphys, fluid accumulation in the hemivagina, and right kidney hypoplasia. Magnetic resonance imaging (MRI) confirmed uterus didelphys and revealed narrowing of the right hemivagina, suggestive of HWWS. Hysteroscopy was performed to resect the vaginal septum with laparoscopic guidance, along with drainage of hematocolpos, pyocolpos and placement of an intracervical mold. Despite HWWs having conservative gradual management, it was opted to perform vaginal septum resection, hematocolpos and pyocolpos drainage and placement of an intracervical mould in this case, in order to relieve symptoms and restore the reproductive and sexual functions.

Keywords: HWWS, OHVIRA, uterus didelphys, obstructed hemivagina, renal agenesis

Introduction

*H*erlyn-Werner-Wunderlich syndrome (HWWS), also known as OHVIRA (obstructed hemivagina and ipsilateral renal anomaly) is a congenital disorder of Müllerian duct anomalies (MDA) [1-5]. The three characteristics of this syndrome include uterine didelphys (double uterus), hemivaginal obstruction, and ipsilateral kidney agenesis [6,7]. HWWs' etiology and pathogenesis are unknown [8-10]. The incidence of HWWS is 0.6–10% of all Müllerian abnormalities (23%), 0.1 to 3.8% in the female population; up until 2011, only about 200 cases of

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Received: June 1, 2023 - Accepted: August 23, 2023 - Published online: August 28, 2023

HWWS have been documented worldwide [3,11-15]. The first case of uterine didelphys, together with hemivaginal obstruction was reported in 1922 while the triad was first reported in 1971 by Herlyn and Werner and re-reported in 1976 by Wunderlich [4,16]. The pathogenesis of HWWS involves defects of lateral fusion and defects in the caudal portion of the Mullerian ducts at the 8th to 12th week of gestation, as well as abnormalities associated with failure of absorption of the septum by the 20th week of gestation [1,2,9,17,18]. Unilateral renal agenesis occurs when one or both ureteral cysts fail to form, and the metanephric blastema does not differentiate into nephrons [9].

HWWS is classified based on the presence of vaginal blockage, allowing gynecologists to apply this classification universally. HWWS can be classified as either Class 1 or Class 2, depending on the degree of hemivaginal obstruction. The clinical manifestations of these two classes' are significantly distinct from one another [9,13,15,19,20]. Class 1 is characterized by higher susceptibility to conditions such as hematometra, hematosalpinx, and hemoperitoneum [21]. Several months post-menarche, acute abdominal discomfort, fever, and vomiting are typical symptoms [13]. Endometriosis is a frequent problem that, if left untreated, can develop into secondary endometriosis, pelvic adhesions, pyosalpinx, or pyocolpos [15,21]. Class 2 is frequently accompanied by symptoms of bloody or vaginal discharge, and even the occurrence of genital system infections [13]. In the beginning, most individuals experience chronic discomfort, then followed by regular menstrual cycles with prolonged menstrual periods. In case report, we present a case of HWWS and outline the corresponding management processes.

Case

A 25-year-old female patient was admitted to Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia, presenting with a chief complaint of lower back pain for the past six months (approximately two months following marriage). The patient denied experiencing vaginal bleeding but reported the presence of recurrent, thick, malodorous yellow vaginal discharge resembling pus occurring post-menstruation for the last two months. The patient also had a history of fever during the same period of time. The patient's menstrual cycle was regular, and the patient denied dysmenorrhea. The patient admitted pain during intercourse but denied postcoital bleeding. In a prior medical encounter, the patient had consulted a gynecologist due to a delayed menstrual cycle, leading to the diagnosis of uterus didelphys. Subsequently, the patient was referred to Dr. Zainoel Abidin Hospital.

The physical examination revealed a supine-state abdomen, palpable peristalsis, absence of palpable masses, absence of tenderness, and absence of undulation. The vagina and uterus were in a relaxed state. During pelvic examination, the cervix exhibited a smooth portio, a closed ostium uteri externum (OUE), negative fluxus, and negative fluoride test results. Additionally, the presence of purulent fluid coming out of a pinpoint hole on the right vaginal wall was observed. Vaginal toucher revealed a two-branched uterus, a palpable cystic mass on the right vaginal wall, an unenlarged cut, and a weak parametrium. No palpable masses were detected on either adnexa, and the Douglas cavity was not prominent. Based on the physical examination performed, it was still difficult to diagnose HWWS.

Follow-up examinations, including standard laboratory examinations, magnetic resonance imaging (MRI), transvaginal ultrasonography (USG), and anatomical pathology laboratory examinations were carried out. The results of laboratory investigations were within normal limits. Pelvic MRI of the axial, coronal, sagittal T1, T2, and T2 fat saturation slices without contrast exhibited duplication of the corpus uteri, cervix uteri, and vagina, suggesting uterus didelphys (**Figure 1**). There was also a narrowing of the right hemivagina accompanied by dilatation in the proximal segment (**Figure 1**). These MRI findings (uterus didelphys accompanied by a narrowing of the right hemivagina) were indicative of HWWS. A transvaginal ultrasound showed hemi uterus on the right and left side, visible hematocolpos, and visible shrinkage of the right kidney (**Figure 2**), confirming uterus didelphys and indicating right kidney atrophy.

Based on all the anamnesis, the patient's medical history, physical assessment, and supporting examinations, the patient was diagnosed with obstructed hemivagina dextra attributable to HWWS, accompanied by hematocolpos and pyocolpos. The patient then underwent a hysteroscopic-guided laparoscopy, which included excision of the vaginal septum,

drainage of the hematocolpos, and placement of an intracervical mould and catheter (**Figure 3**). The resected septum was subjected to histopathological examination, yielding findings correspondent with the characteristics of the vaginal septum. After the surgery, the patient received kaltrofen suppositories every eight hours, along with oral administration of clindamycin (300 mg every 12 hours) and cefixime (200 mg every 12 hours). The patient did not complain of post-operative pelvic or abdominal pain. After two days of observation, the gauze and catheter were removed (**Figure 4A**) and the patient was then discharged.

Ten days following the surgery, the cervical opening was still intact, with no ongoing bleeding observed (**Figure 4B**). The patient did not have any problems with urination or defecation, and no other complaints were reported.

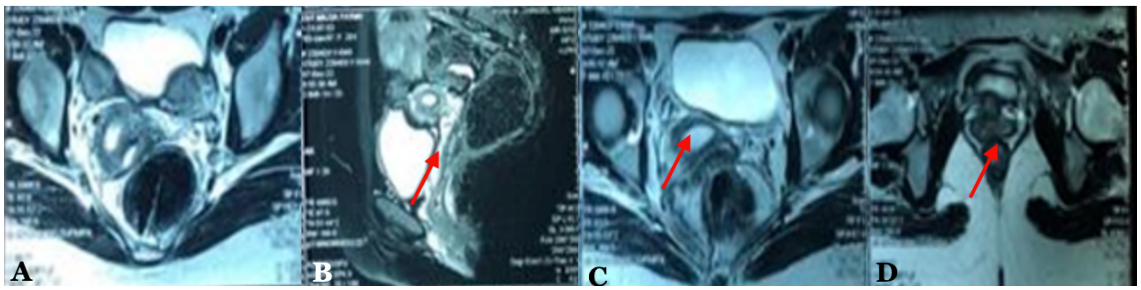

Figure 1. Magnetic resonance imaging (MRI) examination indicates (A) duplication of the uterus, cervix, and vagina; (B-C) obstructed right hemi-vagina with cystic mass (hematocolpos) appearance in the proximal segment (red arrows); and (D) hematocolpos and pyocolpos (red arrow).

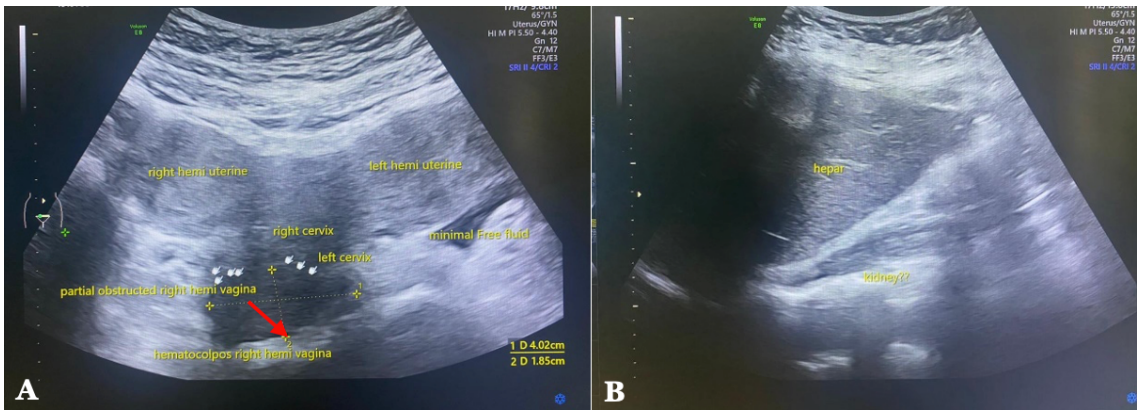

Figure 2. Ultrasonography examination shows (A) the right and left hemi-uterus, right and left cervix, hematocolpos (red arrow) on the right hemi-vagina and (B) right kidney atrophy.

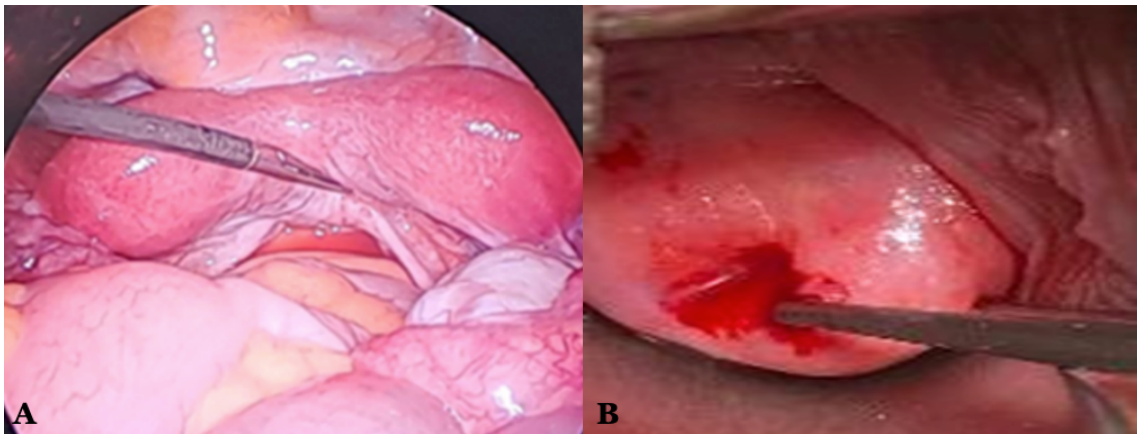

Figure 3. A laparoscopic view shows two hemi uteri, corresponding to uterine didelphys (A). Laparoscopy showing a seven cm-sized hole in the left uterus, the length of pin point from the right uterus was 2.5 cm and there was access to hole of the left cervix. (B). Inspeculo indicates vaginal septum.

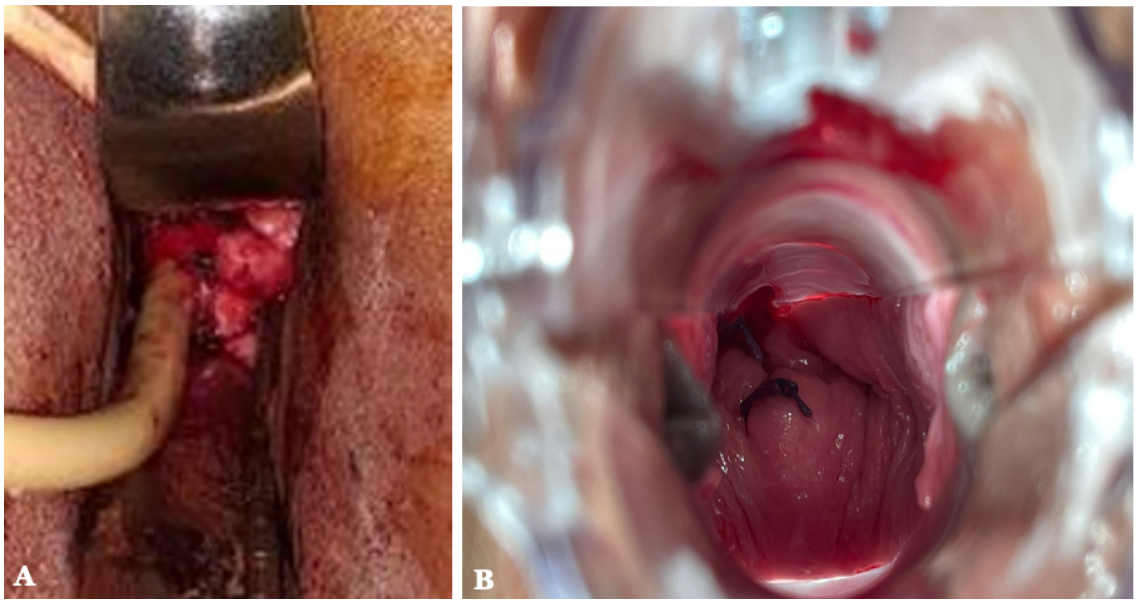

Figure 4. Vaginal conditions immediately following the surgical procedure (A) and at the ten-day post-operative mark (B). Persistence of an intact cervical opening observed during examination on the tenth post-operative day (B).

Discussion

HWWS or OHVIRA syndrome, is a rare congenital disorder, characterized by clinical manifestations including uterine didelphys, hemivaginal obstruction, and ipsilateral renal agenesis [1,2,9,22]. The incidence of uterine didelphys associated with HWWS is approximately 1 in every 2,000 to 1 in every 28,000 and is accompanied by unilateral renal agenesis in 43% of cases [23]. The incidence of unilateral renal agenesis is 1/1,100 and 25–50% of patients have genital abnormalities [1,5,24]. A partial or complete vaginal septum is found in 75% of patients with uterine didelphys [9,13].

Diagnosis HWWS is often challenging, as the disorder commonly manifests asymptomatically, or with predominantly non-specific symptoms [2,14]. The most common symptom is recurrent and progressive pelvic pain, and the severity of the symptoms is greatly influenced by the shape of the vaginal obstruction [11,15]. Pain usually occurs due to the presence of hematocolpos, hematometra, hematosalpinx, and or hemoperitoneum [13,14,18]. In addition, a mass in the pelvis may also be found with or without clinical symptoms. Other possible symptoms include endometriosis due to reflux of blood in the abdominal cavity and infertility. The patient in the present study complained of back pain which is assumingly associated with hematocolpos and pyocolpos. There was also a palpable cystic mass on the right side of her vaginal wall.

In terms of the diagnosis of HWWs, USG and MRI are useful imaging techniques [3,5,7,17,25]. Among these, MRI has been considered the best method for diagnosing HWWs and other congenital anomalies due to its capacity to produce superior anatomical images of the internal genital organs and its high sensitivity in detection of blood. The only time laparoscopy is utilized to diagnose anomalies of the female genital system is when an MRI is not available or does not reliably establish the diagnosis. Furthermore, the utilization of laparoscopy to facilitate interventions such as hematocolpos or hematometra drainage, vaginal septectomy, or marsupialization has made it as a gold standard diagnostic method [13].

In general, the exact cause and pathogenesis of HWWS is unknown, but experts suggest that this syndrome occurs due to disturbances in the formation and joining during the embryonic period [9]. Disruptions in developmental process of genital organs leads to various abnormalities in a woman's genital structure. Anomalies in these structures may arise from compromised canalization process, agenesis, and failures in the lateral and vertical fusion processes of the urogenital sinus and Müllerian duct [26]. The fusion process of the right and left Mullerian ducts is normally completed by 12 weeks of gestation, whereas the canalization process is completed at a gestational age approaching 20 weeks [26]. Failure of the vertical fusion process may

consequently impede the canalization process of the genital organs [26]. Furthermore, the absence or incorrect fusion of the two Müllerian ducts in the midline can result in the formation of two separate uteruses, cervix, and vagina [27,28].

To relieve symptoms and maintain fertility in patients with HWWs, surgery has been considered the most effective treatment. Resection of the obstructed vaginal septum is a key surgical procedure for patients with a blind hemivagina, partial reabsorption of the vaginal septum, and communicating uteri. Most patients recover completely after vaginal septal resection [3]. The best time to perform surgery on these patients, especially those with blind hemivagina, is during the menstrual phase due to the enlarged hematocolpos, which facilitates improved visualization and palpation. Laparoscopic evaluation, especially after the surgery, should be performed in patients with vaginal septal obstruction to avoid massive menstrual regurgitation, endometriosis, or pelvic adhesions, which cannot be detected by ultrasonography or MRI [29]. With early diagnosis, HWWs has a good prognosis, except for patients classified with of cervicovaginal atresia lacking communicating uteri. In complicated cases such as cervical atresia, consideration should be given to ipsilateral hysterectomy, as septal resection fails to alleviate symptoms of obstruction. This new classification of HWW syndrome can help provide early diagnosis and treatment to patients, thereby preventing potential development of secondary pelvic endometriosis and pelvic inflammation [13].

Conclusion

Late menstrual period, pelvic pain, and hematocolpos are among the symptoms of HWWS in our patient. We did transvaginal ultrasound and MRI to determine the congenital uterine abnormalities. Surgical intervention involving resection of the vaginal septum and establishment of vaginal drainage was conducted in this patient in order to relieve acute symptoms and to treat obstruction; therebefore possible endometriosis and infertility can be prevented.

Ethics approval

The patient provided written informed consent to be published as case report.

Competing interests

The authors declare that there is no conflict of interest.

Acknowledgments

We would like to express our gratitude to all participants elaborated in this study.

Funding

This study received no external funding.

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

How to cite

Roziana R, Nora H, Maharani CR, *et al.* Herlyn-Werner-Wunderlich syndrome: Challenges in diagnosis and management. Narra J 2023; 3 (2): e223 - http://doi.org/10.52225/narra.v3i2.223.

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