

Case Report

Radio-diagnosis of Herlyn Werner Wunderlich Syndrome a rare case of urogenital abnormality

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Abstract

Herlyn-Werner-Wunderlich syndrome (HWWS) is a very rare urogenital abnormality, which is characterized by Mullerian duct anomaly with associated mesonephric duct anomaly. This syndrome is also known as OHVIRA (Obstructed hemivagina with Ipsilateral Renal Anomaly). The incidence of Mullerian Duct Anomaly is 2-3%, and incidence of OHVIRA is 0.16 to 10% of that. The three important components of Herlyn-Werner-Wunderlich (HWW) syndrome are didelphys uterus, obstructed hemivagina and renal agenesis on the same side. Typically presents with pelvic pain in young females after menarche. Presentation in the reproductive age group is unusual. The most common renal anomaly associated with this condition is renal agenesis. Other renal anomalies include renal dysplasia, duplication of kidneys and ureters, crossed fused ectopia and ectopic ureter. Ultrasound and Magnetic resonance imaging are considered as the vital modalities for detection. MRI is the gold standard modality for assessing the anatomical characteristics of the uterus, cervix, and vagina. Early diagnosis helps to prevent complications such as endometriosis, pyocolpos, adhesions, infertility. The unique feature of our case is a presentation in the reproductive age group. Only very few case reports of OHVIRA with a presentation in the reproductive age group are available in the literature. Whenever there is a renal anomaly or renal agenesis, screening of pelvic organs is important in a female child for early detection of Mullerian duct anomalies and prevention of further complications.

Key words

Herlyn-Werner-Wunderlich Syndrome, OHVIRA, Uterus Didelphys Hematometocolpus, Obstructed hemivagina, Renal agenesis, Mullerian duct anomaly.

Introduction

Herlyn-Werner-Wunderlich syndrome (HWW) is a very rare urogenital abnormality, characterized by Mullerian duct anomalies with associated mesonephric duct anomalies. This entity is also known as OHVIRA (obstructed hemivagina and ipsilateral renal anomaly). The incidence of Mullerian Duct Anomaly is 2-3%, and OHVIRA is 0.6 to 10% of that. Typically presents with pelvic pain in young females after menarche. Presentation in the reproductive age group is rare. The condition is most commonly diagnosed by imaging with ultrasound or computed tomography (CT) scan, although more recently magnetic resonance imaging (MRI) has emerged as the most sensitive diagnostic method. Treatment is carried out through excision of the vaginal septum, with good results; ultimately, around 80% of the patients are able to conceive. Therefore, it is important that physicians, who see patients with renal abnormalities, as well as those with endometriosis, maintain a high degree of suspicion for the condition, to guarantee a timely diagnosis and avoid complications from the syndrome.

Case report

A 26-year-old female P1L1A3 came to the hospital with severe pain during menstruation for past 3 months. The pain was relieved after menstruation. History of spontaneous abortion 3 months back, and after that, she developed severe pain during menstruation. No history of fever, nausea, vomiting, and diarrhea. She attained menarche at the age of 13, and then she had 3/30 regular cycles with normal menstrual flow accompanied by cyclical dysmenorrhoea. She was married for the past 4 years and had a history of three spontaneous abortions in the past. Third pregnancy she delivered the full-term baby by lower segment cesarean section one year back. Bowel and bladder habits were normal. No history of systemic hypertension, diabetes

mellitus, tuberculosis, bleeding disorders in the past. The general physical examination was normal and vitals were stable. On abdomen examination, there was tenderness in the pelvic region more on the left side. On per vaginal examination, fluctuant intra vaginal mass was noted. She was referred to the Department of Radio Diagnosis for pelvic imaging. Initially ultrasound examination was done and subsequently, Magnetic Resonance Imaging of pelvis was done. The study period was between 2017-2018 in the department of radiology and imaging sciences, Shri Sathya Sai Medical College and Research Institute. Oral information was given to the patient's attenders regarding the study.

Ultrasound findings

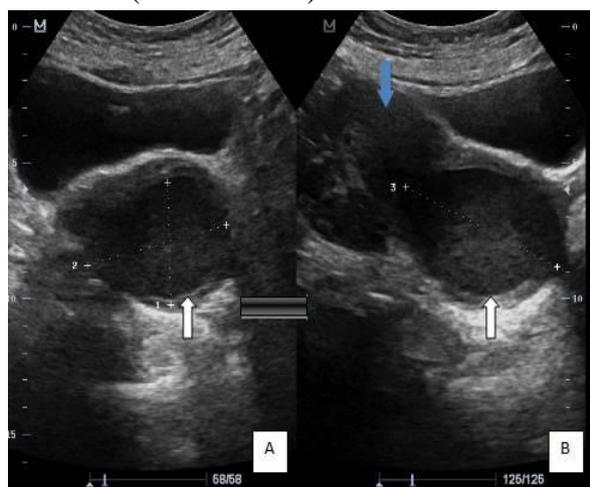
Two horns of the uterus with two endometrial cavities were identified separately. Hypo echoic fluid collection measuring 4.5x5.7x6.7cm with multiple moving internal echoes noted distending the endometrial cavity and cervix of the left horn of uterus (**Figure - 1A, 1B**). No evidence of abnormal vascularity (**Figure - 2**). The right horn of the uterus measures 9x3.5x4.5cm. The fundus, body, endometrial cavity, the cervix of the right horn was identified separately and appeared normal (**Figure - 3**). The right and the left adnexa appeared normal. Right ovary measures 3x2.2cm and left ovary measure 3.2x2.1cm. Ultrasound of the abdomen revealed the absence of the left kidney in the left renal fossa. Visualized other abdominal organs did not reveal any abnormal ability.

Magnetic resonance imaging of abdomen and pelvis

Two separate uterine cavities and cervixes are identified suggest that Uterine Didelphys (**Figure - 4**). Left uterine cavity, cervical canal, and proximal vagina are dilated and filled with fluid which was mildly hyperintense in T1WI, mixed-

signal intensity showing fluid-fluid level (hypointensity in the inferior half) in T 2WI, T2 STIR (**Figure - 5A, 5B**) the nd blooming noted in GRE sequence suggesting presence of blood products (**Figure - 7A, 7B, 7C, 7D**). Distension of the proximal the left vagina (**Figure - 6**) is due to the obstruction caused by the vaginal septum distally. Right horn of the uterus appears normal. Bilateral ovaries (**Figure - 8**) and adnexal region appeared normal. MRI of the abdomen revealed the absence of a left kidney (**Figure - 9**).

Figure - 1A and 1B: 26-year-old female, with Herlyn Werner Wunderlich syndrome. Transabdominal transverse section of uterus (Mind ray curvilinear probe 5MHz) demonstrating the right (blue arrow) and the left horn (white arrows) of uterus. Cystic dilatation of endometrial cavity with low level internal echoes is seen in the left horn of uterus (white arrows).



Diagnosis

Uterine didelphids with hematometrocolpos in left horn of uterus due to obstructed hemivagina left side with left (ipsilateral) renal agenesis-features suggestive of Herlyn Werner Wunderlich syndrome.

Treatment

Surgical left side vaginal septum resection, drainage of hematometrocolpos and vaginal repair has been done. The patient underwent the procedure very well.

Figure - 2: 26-year-old female with Herlyn Werner Wunderlich syndrome, Transabdominal transverse section of uterus (Mind ray curvilinear probe 5MHz) shows cystic dilatation of endometrial cavity (measuring 4.5x5.7x6.7cm) with low level internal echoes in the left horn of uterus. Colour Doppler image shows absence of vascularity.

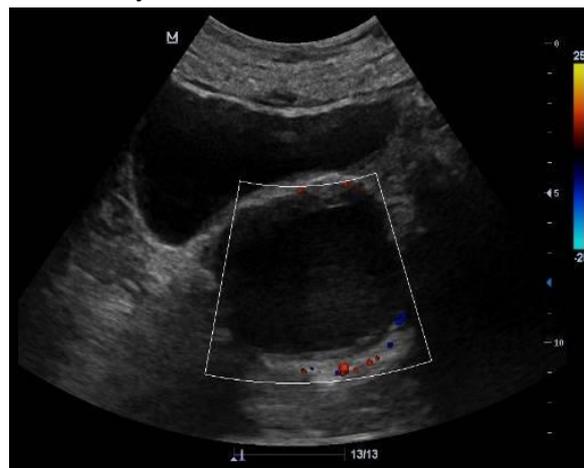


Figure - 3: 26-year-old female, with Herlyn Werner-Wunderlich Syndrome. Transabdominal longitudinal section of uterus (Mind ray curvilinear probe 5MHz) demonstrating the right horn of the uterus (blue arrow) and right ovary (white arrow). The right horn of uterus measures 9x3.5x4.5cm. The fundus, body, endometrial cavity, cervix was identified separately and appeared normal.

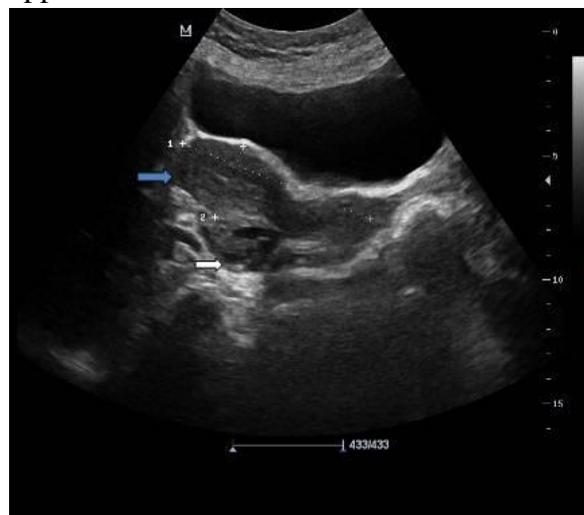


Figure - 4: 26-year-old female with Herlyn Werner-Wunderlich syndrome. Non-contrast coronal T2 weighted pelvic MRI (1.5 T, Philips TE: 80 TR:549) demonstrates two separate uterine cavities (right horn-blue arrow and the left horn-white arrow).



Figure - 5A and B: 26-year-old female, with Herlyn Werner Wunderlich syndrome. Non-contrast sagittal T2 weighted MRI of pelvis (1.5Tesla Philips TE: 80 TR: 462) demonstrates part of normal endometrial cavity and cervix, vagina on the right side (blue arrow), left sided endometrial cavity, cervical canal, proximal vagina is distended by the fluid collection (appears less hyperintense when compared with urine-white arrow).

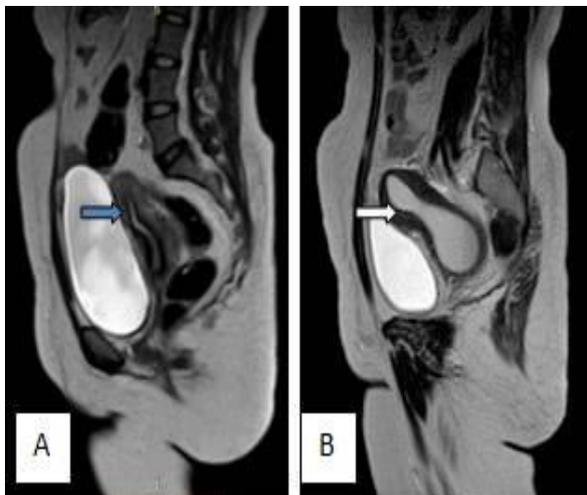


Figure - 6: 26-year-old female, with HWWS. Non-contrast coronal T2 Weighted MRI of pelvis (1.5 Tesla Philips TE: 80 TR: 549) demonstrates normal vagina on the right side. Isointense fluid collection is noted distending the proximal vagina on the left side (white arrow).

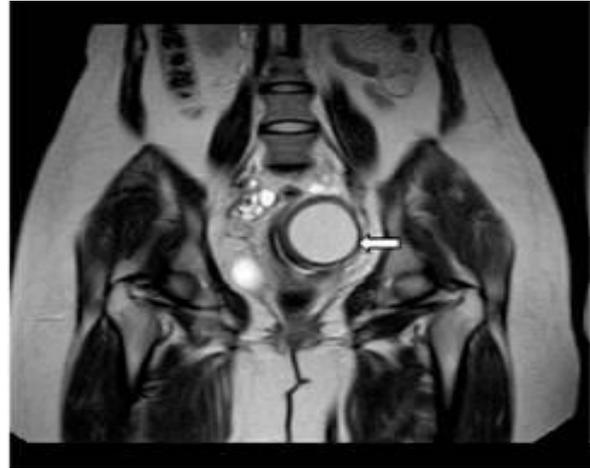


Figure - 7A, 7B, 7C, 7D: 26-year-old female, with HWWS. 7A (T1WI), B (T2WI), C (T2W STIR), D (GRE) non-contrast axial MR images (1.5Tesla Philips) are compared. Left uterine cavity, cervical canal and proximal vagina are dilated and filled with fluid which was mildly hyperintense in T1WI (blue arrow), mixed signal intensity showing fluid- fluid level (mild hypo intensity in the inferior half) in T2WI, T2 STIR (white arrows) and blooming in GRE sequence (Red arrow) - suggesting presence of blood products.

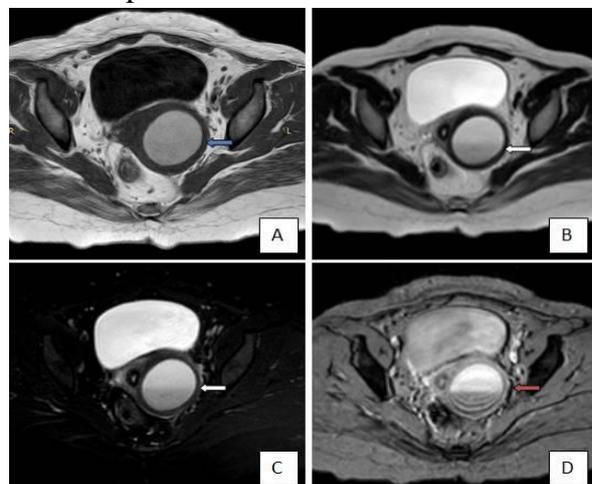


Figure – 8: 26-year-old female with Herlyn Werner Wunderlich syndrome. Non-contrast T2 Weighted coronal MR image of pelvis (1.5 Tesla Philips TE: 80 TR:549) demonstrates normally appearing right (blue arrow) and left (white arrow) ovaries.

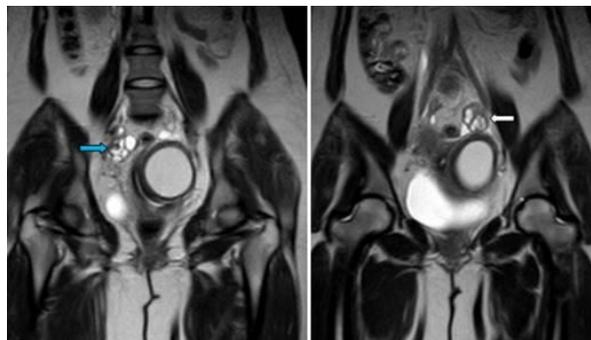
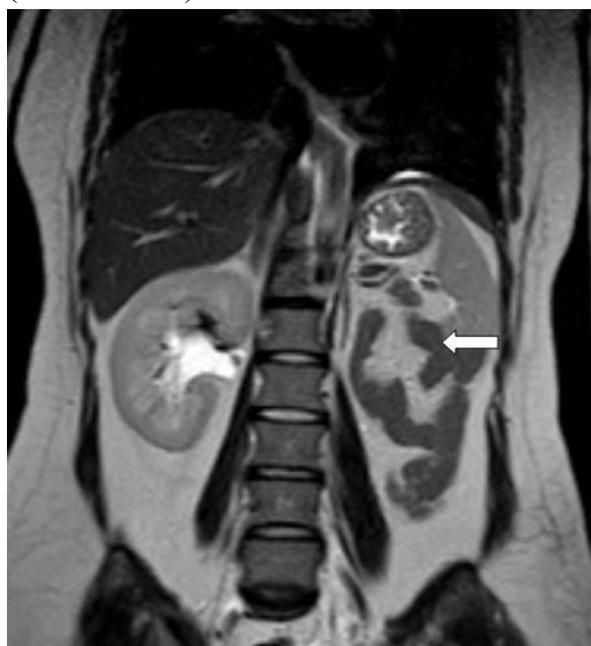


Figure - 9: 26-year-old female with Herlyn Werner Wunderlich syndrome. Non-contrast coronal T2 weighted MRI of abdomen (1.5Tesla Philips TE: 80 TR: 549) demonstrates the absence of left kidney (white arrows).



Summary of findings was as per **Table – 1**.

Discussion

The Herlyn-Werner-Wunderlich Syndrome was initially described by Herlyn and Werner in 1971. Herlyn-Werner Wunderlich syndrome (HWWS) is a very rare urogenital abnormality,

which is characterized by class III Mullerian duct anomaly with associated mesonephric duct anomalies [1]. The three important components of Herlyn-Werner-Wunderlich Syndrome are a didelphys uterus, obstructed hemi vagina and renal agenesis on the same side [1]. This syndrome is also known as OHVIRA (Obstructed hemivagina with Ipsilateral Renal Anomaly) [2]. The incidence of Mullerian Duct Anomaly is 2-3%, and OHVIRA is 0.16 to 10% of that [2]. In 1979 Buttram and Gibbons have formulated a classification for Mullerian duct anomalies [3]. The modified classification was given by the American Society for Reproductive Medicine. It is the most frequently used classification and uterine didelphys is classified under class III MDA [4].

Most common renal anomaly associated with this condition is the absence of ipsilateral kidney. The other renal anomalies which can be associated include renal dysplasia, duplication of kidneys and ureters, crossed fused ectopia, ectopic ureter, IVC duplication, ovarian malposition, intestinal malrotation, and high-riding aortic bifurcation [5, 6]. The right-sided renal anomaly is more common than the left side [7, 8].

Typically presents with pelvic pain in young females after menarche. Presentation in the reproductive age group is rare and only few case reports has been reported in the past. The lower urinary tract and internal genitalia are developed from two paired structures known as the Wolffian (Mesonephric) and Mullerian (paramesonephric) ducts. Uterine didelphys occurs due to abnormal embryological development during the 8th week of gestation [9]. The etiopathogenesis of Herlyn Werner Wunderlich syndrome is not yet known completely [10].

Robbins, et al. simplified the embryological process into 3 stages [10]:

1. Development of the ducts.
2. Fusion of the ducts.
3. Resorption of the septum.

Table - 1: Summary.

Modality	Findings
USG	Two horns of the uterus with two endometrial cavities were identified separately. Hypoechoic fluid collection measuring 4.5x5.7xx6.7cm with multiple moving internal echoes noted distending the endometrial cavity and cervix of the left horn of uterus.
MRI	Two separate uterine cavities, services are identified suggesting Uterine Didelphys. Left uterine cavity, cervical canal, and proximal vagina are dilated and filled with fluid which was mildly hyperintense in T1WI, mixed-signal intensity showing fluid-fluid level (mild hypointensity in the inferior half) in T2WI, T2 STIR and blooming in GRE sequence- suggesting the presence of blood products. Distension of the proximal left hemi vagina is due to the obstruction caused by the vaginal septum distally. Right horn of the uterus appears normal. Bilateral ovaries and adnexal region appeared normal. MRI of the abdomen revealed the absence of the left kidney.
Diagnosis	Uterine didelphys with hematometrocolpos in left horn of uterus obstructed hemivagina left side with left (ipsilateral) renal agenesis-features suggestive of herlyn Werner Wunderlich syndrome.

The female and the male genitalia cannot be differentiated till 6 weeks of embryogenesis. Müllerian inhibiting factor production occurs after 6 weeks and its production is associated with the presence of the Y chromosome. As the Mullerian inhibitory factor is absent in female fetus, there occurs development of paramesonephric ducts on the lateral aspect of each mesonephric ducts on both sides. Any defective embryogenesis at this period can lead to the aplastic or hypoplastic uterus. Uterovaginal primordium is formed in the midline by the crossover and the fusion bilateral paramesonephric ducts. This leads to the development of the uterus, cervix, and the proximal two-thirds of the vagina. Mesonephric duct regression takes place simultaneously. Any maldevelopment in this process leads to the formation of didelphys uterus and bicornuate uterus. The resorption of uterovaginal septum occurs after the 9th week of embryogenesis. Any defect in the embryogenesis at this period leads to the septate an arcuate uterus. The process of resorption can occur in both caudal and cranial directions [11, 12]. The distal portion of the vagina is formed from the urogenital sinus. In case of HWWS, as there is the absence of Wolffian duct, the Mullerian duct on the same side gets displaced on the lateral aspect and fails

to fuse with the Mullerian duct of the contralateral side. This process leads to didelphys uterus [2, 9]. Partial or complete longitudinal or transverse vaginal septum is commonly associated with uterine didelphys in the Herlyn-Werner-Wunderlich syndrome. [9]. A longitudinal vaginal septum develops during embryogenesis when there is an incomplete fusion of the lower parts of the two Mullerian ducts. A transverse septum forms during embryogenesis when the Mullerian ducts do not fuse with the urogenital sinus. The vaginal septum causes obstruction in the ipsilateral horn which leads to retrograde menstruation causing haematometrocolpos. When it is left untreated, this can lead to complications such as endometriosis and pelvic inflammatory disease [6, 9] Lan Zhu et al. conducted a study and reviewed the characteristics and clinical features of HWWS. A new classification has been formulated based on the obstruction caused by the vaginal septum [13]. The obstruction can be complete or incomplete. The clinical symptoms vary depending on the type of obstruction [13]. In case of complete obstruction, the presentation of symptoms is at the earlier age, soon after menarche. In case of incomplete hemi vaginal obstruction, there is small communication between two vaginas or between the duplicated

services. As incomplete obstruction allows drainage of menstrual flow to some extent, the condition may take years to present after the onset of menarche [13]. This leads to delay in diagnosis of this condition. Another cause of delayed diagnosis would be the prescription of oral contraceptive pills which eliminates and suppresses the menstruation [6]. Early diagnosis helps to prevent complications such as endometriosis, pyocolpos, pyometra, adhesions, infertility and pelvic inflammatory disease [2]. Ultrasound and Magnetic resonance imaging are considered as the vital modalities for detection. MRI is the gold standard modality for assessing the anatomical characteristics of the uterus, cervix, and vagina. It also helps in assessing the type of vaginal obstruction, the characteristics of the obstructed contents in the uterus and other complications such as endometriosis [6].

Treatment

Laparoscopic or surgical vaginal septal resection is the treatment of choice. Laparoscopy is a diagnostic and therapeutic modality. The advantages include therapeutic drainage of hematomata or hematocolpos, vaginal septectomy, and marsupialization [14, 15].

Treatment of choice for HWWS is laparoscopic vaginal septum resection.

Prognosis

Successful pregnancy is achieved in 87% of patients and 23% have the risk of miscarriages [6]. Most of the patients need cesarean section [6]. Some of the rare complications that have been described on the side of obstruction include adenocarcinoma of the cervix and clear cell carcinoma of the vagina [6].

Conclusion

The three important components of Herlyn-Werner-Wunderlich syndrome are didelphys uterus, obstructed hemi vagina and renal agenesis on the same side. Everyone should be aware of this rare condition, as early detection can prevent further complications such as endometriosis,

infertility, pyocolpos. The presentation can be typical as well as atypical. The obstruction of hemi vagina can be complete or incomplete. Whenever there is a renal anomaly or renal agenesis, screening of pelvic organs is important in a female child for early detection of Mullerian duct anomalies and vice versa. MRI is the gold standard modality for assessing the anatomical characteristics of the uterus, cervix, and vagina. It also helps in assessing the type of vaginal obstruction, the characteristics of the obstructed contents in the uterus and other complications such as endometriosis. The unique feature of our case is presented is in the reproductive age group and after the delivery of a full-term normal fetus by cesarean section.

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