ORIGINAL RESEARCH PAPER

Radio-Diagnosis

KEY WORDS: Herlyn–Werner–Wunderlich syndrome, ipsilateral renal agenesis, didelphic uterus, obstructed hemivagina, haematometrocolpos.

DIVERSITIES IN HERLYN-WERNER-WUNDERLICH SYNDROME: A CASE SERIES

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ABSTRACT

Herlyn–Werner–Wunderlich syndrome (HWWS) or Obstructed hemivagina, ipsilateral renal agenesis (OHVIRA) syndrome is a rare complex congenital developmental anomaly of the genitourinary tract characterized by a triad of didelphic uterus, obstructed hemivagina, and ipsilateral renal agenesis.A delay in diagnosis is often seen due to non-specific clinical features and inadequate evaluation.Ultrasound and Magnetic Resonance Imaging are helpful in confirming the diagnosis. In this article, we report case series of Herlyn–Werner–Wunderlich syndrome with extreme clinical symptoms at presentation with imaging showing features of OHVIRA with different uterine morphologies and few of them showing complications including pelvic inflammatory disease.The standard management of these patients is excision of vaginal septum and drainage of haematometrocolpos. Complications if any, have to be managed accordingly.

BACKGROUND

Herlyn–Werner–Wunderlich syndrome (HWWS) or Obstructed hemivagina, ipsilateral renal agenesis (OHVIRA) syndrome is a rare complex congenital developmental anomaly of the genitourinary tract characterized by a triad of didelphic uterus, obstructed hemivagina, and ipsilateral renal agenesis.[1] It was first reported in 1922.[2] The current overall incidence of Mullerian duct anomalies(including both major and minor anomalies) ranges from 7-10%, while excluding minor ones the incidence is 2-3 % and the incidence of obstructed müllerian agenesis is 0.1–3.8% in the general population which may be underreported due to the associated diagnostic dilemma.[1] The aetiology of the syndrome is unknown. However, it is thought to be multifactorial and is associated with Mullerian ducts fusion anomalies in utero.

Different variants of OHVIRA have been recognized with different uterine morphologies and varying vaginal obstruction(partial or complete).

Here, we present three cases of Herlyn–Werner–Wunderlich syndrome (HWWS) with varied clinical presentations, different uterine morphologies, few of them showing complications and management is also discussed in brief.

Case Description

Case 1

A18-year-old girl presented with cyclical abdominal pain and dysmenorrhea for 3 months. Her menstrual cycles were regular. On examination, the general condition was fair, BMI was 21.5, and secondary sexual characters were developed as per the age. Baseline laboratory analysis and hormonal profile were normal.

Imaging Findings:

USG Abdomen and Pelvis:

- separate uterine cavities with two separate cervices - **S/o uterine didelphys.**
- Well defined thick walled fluid collection with internal echoes posterior to urinary bladder(UB).(Figure 1)
- Non-visualization of left kidney in left renal fossa or pelvis with compensatory hypertrophy of right kidney.

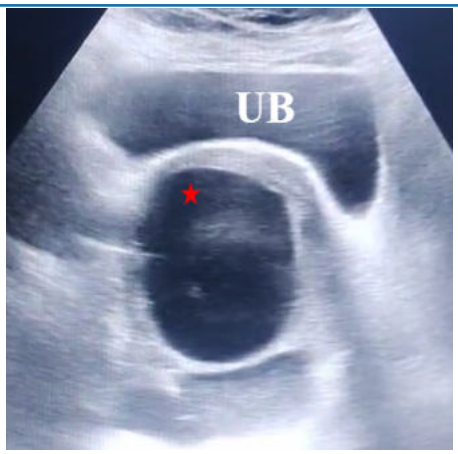


Figure 1. Axial transabdominal USG image(a) showing a well defined thick walled fluid collection with internal echoes(red asterisk) posterior to urinary bladder(UB).

MRI Pelvis:

Uterine didelphys with left sided-hematocolpos and an obstructed left hemivagina(longitudinal obstructing septum).

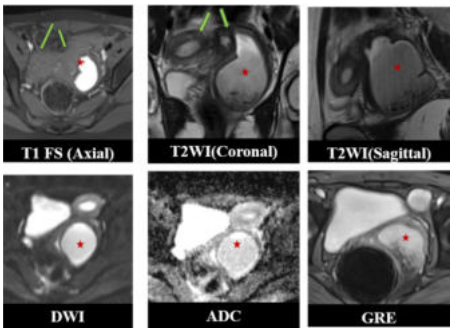


Figure. 2: MRI Findings: Uterine didelphys noted. (Green arrows).Longitudinal obstructing septum noted in left hemivagina with T1/T2 hyperintense collection(red asterisk) in left hemivagina, showing no diffusion restriction on DWI

and few blooming foci noted on gradient sequence. - S/o hematocolpos.

Final Diagnosis:
- **Ohvira** syndrome.

Uterine Morphology:
- ASRM Mullerian anomaly classification: **Uterine didelphys with obstructed left hemivagina.**
- ESHRE classification class **U3b C2 V2** (complete bicorporeal uterus, double"normal" cervix, longitudinal obstructing vaginal septum).

Management:
Examination under anaesthesia done.
Vaginoscopy done: Blind vagina on left side with hematocolpos.
Excision of vaginal septum with drainage of hematocolpos done.

Case 2
A 27-year-old nulligravid married woman presented with complaints of foul-smelling discharge per vagina for 1 year and fever since 3 days. She attained menarche at 14 years of age and continued with normal menstrual cycles. General and systemic examinations were unremarkable. Her secondary sexual characters were well developed. Baseline laboratory analysis and hormonal profile were normal.

Imaging Findings:
Usg Abdomen And Pelvis:
Uterine didelphys noted. Heterogeneous hypoechoic collection with coarse internal echoes in right cervical canal.

Bulky right ovary in right iliac fossa(RIF) forming an inflammatory mass with bowel loops adhered to the mass. Mesentery in RIF appears hyperechoic- Inflammed. Mild collection noted in RIF. Right renal agenesis with compensatory hypertrophy of left kidney.

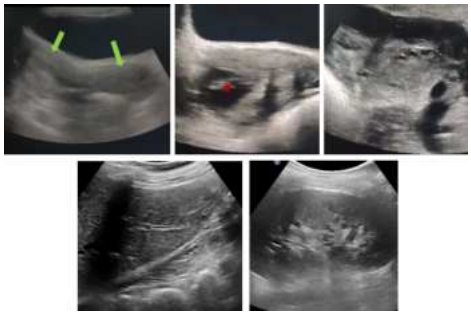
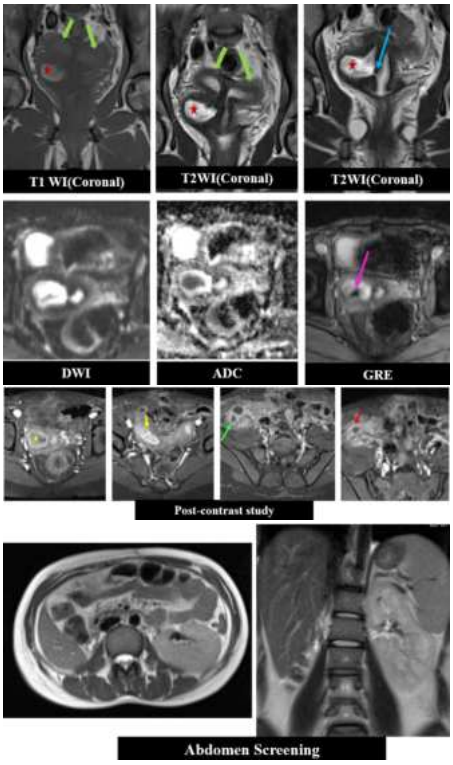


Figure 3. Transabdominal USG image showing bicorporeal uterus with two cervices with evidence of heterogeneous hypoechoic collection with coarse internal echoes in right cervical canal(Red asterisk).Fig. 5 shows bulky right ovary in RIF with surrounding hyperechoic mesentery and clumped up bowel loops adhered to the ovary.Fig. 6a and 6b shows right renal agenesis with compensatory hypertrophy of left kidney.

MRI Pelvis with Screening Abdomen(Figure 5):
- Uterus didelphys with communicating two hemiuteri.
- Peripherally enhancing T1/T2 hyperintense collection within right cervical canal- **S/o hemato-pyometra.**
- Features
- Right renal agenesis with compensatory hypertrophy of left kidney.

Figure 5: Uterine didelphys noted(green arrows). Right vaginal atresia with T1/T2 hyperintense collection in right cervical canal(Red asterisk) showing Diffusion restriction noted on DWI and few blooming foci on GRE(pink arrow).Communication between two hemiuteri.(Blue arrow). On post-contrast study, the collection shows peripheral enhancement(Yellow asterisk). Marked hyperenhancement of endometrium of right horn(yellow arrow)noted. - S/o endometritis. Mildly dilated right fallopian tube with wall thickening and enhancement(red arrow). – S/o salpingitis. Bulky and edematous right ovary with few peripherally enhancing fluid collections(green arrow) consistent with oophoritis and intra-ovarian abscesses.Inflammatory mass formation noted in RIF with bowel loops adhered to the mass.Abdomen screening shows right renal agenesis with compensatory hypertrophy of left kidney.



Final Diagnosis:
OHVIRA syndrome with features of pelvic inflammatory disease(PID)(Right Hemato-pyometra, endometritis, salpingitis,oophoritis with tubo-ovarian inflammatory mass formation)

Uterine Morphology:
- ASRM Mullerian anomaly classification: **Uterine didelphys with communicating hemiuteri and right vaginal atresia.**

Management:
The patient underwent exploratory laparotomy.
Uterine didelphys and right hemato-pyometra noted.
Intraoperatively, features of pelvic inflammatory disease noted in the form of right thickened fallopian tube forming a tubo-ovarian mass adhered to bowel loops.
Few endometriotic cysts noted and excision done.
Right uterine horn excision and right salpingo-oophorectomy done.

Case 3
A 14-year-old girl presented with continuous lower abdominal pain,difficulty in passing urine and acute urinary retention since 2 days.History of catheterization for the same present 2 days back.She attained menarche at the age of 13 years and complained of severe dysmenorrhea from the outset.

Imaging Findings:
USG Abdomen and Pelvis:
Septate uterus noted.

Heterogeneous hypoechoic collection with coarse internal echoes noted below cervical canal on right side.

Right renal agenesis with compensatory hypertrophy of left kidney.

MRI Pelvis:
Complete septate uterus with right sided-hematocolpos and an obstructed left hemivagina(longitudinal obstructing septum).

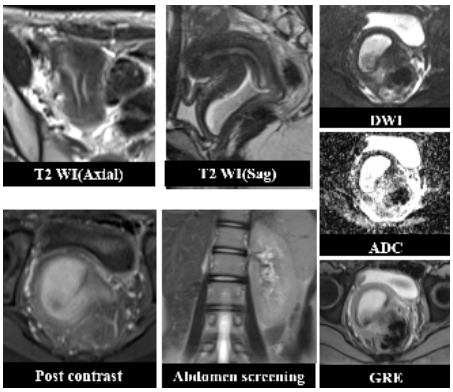


Fig.9: Complete septate uterus noted(green arrows).T2 hyperintense collection noted in right hemivagina(Red asterisk) with longitudinal obstructing septum noted.No diffusion restriction noted on DWI.Few blooming foci noted on GRE.No postcontrast enhancement noted.On Abdomen screening, Right renal agenesis with compensatory hypertrophy of left kidney noted.

Final Diagnosis:
- **OHVIRA** syndrome.

Uterine Morphology:
- ASRM **class – Complete septate uterus with duplicate cervices and obstructed right hemivagina.**
- ESHRE class **U2b C2 V2** (complete septate uterus, duplicated cervices, longitudinal obstructing vaginal septum)

Management
Patient underwent exploratory laparotomy before MRI, being suspicious of having right adnexal mass- A bulge was seen on the right side of uterus extending till pouch of doughlas (Hematocolpos). Endometriotic spots noted on right ovary. No evidence of adhesions or pelvic inflammatory disease (PID).

Post surgery MRI done and diagnosed as OHVIRA. Patient underwent examination under anaesthesia and diagnostic hysteroscopy and vaginal septal excision done.

Summary
- Three patients had varied clinical presentations with pelvic pain being the most common presenting symptom.
- On imaging, obstructed hemivagina with ipsilateral renal agenesis is seen in all patients with different uterine morphologies and complications like pyometra and endometriosis.
- The standard management of these patients is excision of vaginal septum and drainage of haematometrocolpos. Complications if any, have to be managed accordingly.

DISCUSSION
Mullerian duct anomalies arise due to non-development, defective fusion or failure of resorption of the Mullerian ducts.[3] According to the classic theory of vaginal development, upper part of vagina develops from mullerian (paramesonephric) duct and the lower part from sinovaginal bulbs.Vaginal plate will be formed by the fusion of 2 sinovaginal bulbs which canalize later to form vaginal lumen. But this classic theory could not fully explain complex Müllerian malformations like OHVIRA and their association with renal anomalies.

Acien suggested that the uterus and cervix develop from fused paired paramesonephric ducts (2nd part) and diverging distal paramesonephric ducts (3rd part). In contrast, the vagina originates entirely from the mesonephric (Wolffian) ducts, though its lining includes Müllerian cells derived from the Müllerian tubercle. Thus, the paramesonephric ducts do not contribute to the formation of the vagina, but the Müllerian tubercle does, providing the cells that line it. Failure in proper positioning of paired paramesonephric ducts by mesonephric ducts results in fusion anomalies of uterus.

An early failure of development of metanephric diverticulum(around 5 weeks) from mesonephric duct leads to ureteric bud agenesis, which further leads to agenesis of ipsilateral ureter and kidney.

In OHVIRA syndrome,failure in development of distal hemivagina occurs due to arrest in development of ipsilateral mesonephric duct, hence resulting in obstructed hemivagina. The classic OHVIRA syndrome consists of uterus didelphys, unilateral vaginal obstruction, and ipsilateral renal agenesis, all components being secondary to mesonephric duct-induced müllerian anomalies.[4] Although the majority of the patients have uterus didelphys morphology, obstructed hemivagina may also be seen with other Mullerian duct anomalies such as a bicornuate and septate uterus.[5]

A delayed diagnosis can result in complications such as endometriosis, adhesions, infertility, and infections caused by prolonged cryptomenorrhea.

Treatment typically involves surgical excision of the vaginal septum to alleviate the obstruction, which not only relieves pain but also lowers the risk of pelvic endometriosis due to retrograde menstrual flow. After surgery, patients can usually have a normal sexual life, and most of them are able to conceive and carry a pregnancy to term.

CONCLUSIONS
- Early diagnosis of MDA is essential as it is associated with an increased risk of complications including endometriosis, pelvic inflammatory disease, infertility and abortions.
- MRI is the imaging investigation of choice for the diagnosis and detailed assessment of the type and complications of MDA.
- Diagnosis of OHVIRA syndrome requires a multimodal approach, which includes a detailed history, meticulous examination, and appropriate imaging studies.
- In conclusion, greater awareness of this rare entity and early diagnosis with timely intervention can prevent unnecessary surgeries and patients' future complications including infertility.

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