The important role of imaging in detecting Herlyn-Werner-Wunderlich syndrome

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Learning objectives

The aim of this paper is to describe radiologic findings in Herlyn-Werner-Wunderlich (HWW) syndrome.
Background

**Definition:** Herlyn-Werner-Wunderlich (HWW) syndrome, also known as obstructed hemivagina and ipsilateral renal anomaly (OHVIRA) is a rare form of uterovaginal duplication, with three characteristic anomalies namely, didelphys uterus, unilateral obstructed hemivagina and ipsilateral renal agenesis [1]. It was initially described in 1971 by Herlyn and Werner, then in 1976, Wunderlich described an association of right renal aplasia with a bicornuate uterus and simple vagina in the presence of an isolated hematocervix [2]. High index of suspicion of HWW syndrome is required in patients with Mullerian and mesonephric duct anomalies because delay in diagnosis may lead to complications like pelvic adhesions, endometriosis, pyocolpos, pyometra, and resulting in infertility [3-5]. If this syndrome is suspected, the diagnosis simply can be made by ultrasound and computed tomography and/or MRI of the abdomen and pelvis [6]. Resection of the vaginal septum is the treatment of choice for obstructive hemivagina [6-7].

**Epidemiology:** Müllerian duct anomalies have an incidence of 1-5% in the general population and 13-25% in women with recurrent pregnancy loss, with HWW syndrome constituting 0.16-10% of these anomalies [1]. Overall, the estimated occurrence of HWW syndrome is 0.1-3.8% [2].

**Pathogenesis:** HWW syndrome results from an embryologic aberration occurring during the 8th week of gestation that simultaneously involves the metanephric ducts as well as the Paramesonephric or Müllerian ducts. Failure of complete lateral fusion of the Paramesonephric ducts results in uterus didelphys and lack of development of the metanephric duct results in ipsilateral renal agenesis, but the exact cause are still unclear [1,8]. The probable causes are polygenic, multifactorial, teratogens or environmental [9]. Mehra et al. explained the embryonic origin of HWW syndrome as the following: embryonic arrest of the caudal portion of one of the Wolffian duct may result from an insult as early as 4th gestation week causes its maldevelopment, preventing the cross over and subsequent fusion of the Mullerian ducts. Paramesonephric duct on each side then develops fully with a separate well formed cervix and hemivagina, resulting in duplication of uteri (uterus didelphys). Complete nonunion between the paramesonephric ducts and the cranially migrating uterovaginal bulb results in a blind sac or vaginal atresia; while partial non fusion produces a remnant transverse vaginal septum which may be incomplete or complete with obstruction. Since the ureteric bud develops from the Wolffian duct and ultimately induces the metanephric blastema to form the kidney, absence of Wolffian duct leads to ipsilateral renal agenesis [1].
**Diagnosis and radiologic features:** The most frequently used system for classification of Mullerian duct anomalies (MDAs) was proposed by Buttram and Gibbons, which classifies them into six categories where HWW syndrome is a combination of Type III Mullerian anomaly (uterus didelphys) with mesonephric duct anomaly and vaginal septum [3,10]. But recent study conducted by Zhu et al. based on large population in China, managed to classify HWW syndrome patients into two new types [2].

**Classification 1, completely obstructed hemivagina**

Patients within this classification tend to have an earlier age of onset, with a short time from menarche to attack (hematocolpos, hematometra & hematosalpinx). This is the typical HWW syndrome presentation [11]. The presenting symptoms may include the acute onset of abdominal pain, fever, and vomiting. Also, patients may progress to secondary endometriosis, pelvic adhesion, pyosalpinx, and even pyocolpos faster if not treated in time [2]. This classification can be further divided into two types:

**Classification 1.1, with blind hemivagina:** the hemivagina is completely obstructed therefore the uterus behind the septum is completely isolated from the contralateral uterus. No communication is present between the duplicated uterus and vagina [2]. Abdominal USG may show absence of kidney with two structures in the pelvis demonstrating the shape, contour and echo pattern of a uterus. The endometrial cavity of one of the uterus may be distended with fluid contents and the vagina may not clearly appreciated in continuity with this structure (Fig. 2B). The other uterus may be of normal size and shape with the myometrium, endometrial cavity, cervix as well as vagina (Fig. 2A). Abdominal MRI may be performed for better characterization of pelvic anatomy. In sagittal MR images of the pelvis hematometrocolpos may be demonstrated indicating presence of vaginal septum. T2W coronal or sagittal MR images of pelvis may demonstrate the septum as a hypo intense band in the mid vagina (arrow) (Fig. 3) [1].
Fig. 1: with blind hemivagina


Fig. 2: Ultrasound of pelvis showing two uterine cavities in the pelvis. Right sided uterus with its cervix and vagina (white arrow in A) is normal in size, shape and echo texture with normal endometrial cavity. Left sided uterine cavity (yellow arrow in B) is grossly distended and filled with fluid containing fine internal echoes within.

Fig. 3: T2W Coronal, Sagittal MR images of pelvis demonstrating the septum as a hypo intense band in the mid vagina (arrow) causing obstruction and hematometrocolpos.


Classification 1.2, cervicovaginal atresia without communicating uteri: the hemivagina is completely obstructed; the cervix behind the septum is maldeveloped or atresic, and menses from the uterus behind the septum cannot outflow through the atresic cervix (Fig.4)[2].
Fig. 4: cervicovaginal atresia without communicating uteri


Classification 2, incompletely obstructed hemivagina

These patients have a later age of onset. The attack often comes years after menarche and usually mild. Purulent or bloody vaginal discharge can be the chief complaints. Patients often have ascending genital tract infection. Complications often develop gradually [2]. This classification also has two sub types:

Classification 2.1, partial reabsorption of the vaginal septum: a small communication exists between the two vaginas, which make the vaginal cavity behind the septum incompletely obstructed. The uterus behind the septum though, is completely isolated from the contralateral uterus. The menses can outflow through the small communication, but the drainage is impeded (Fig.5) [2].

Fig. 5: partial reabsorption of the vaginal septum


Classification 2.2, with communicating uteri: hemivagina is completely obstructed, and a small communication exists between the duplicated cervices. Menses from the uterus behind the septum can outflow through the communication to the offside contralateral cervix. However because the communication is small, the drainage is still impeded (Fig.6)[2].
**Fig. 6:** with communicating uteri


**Fig. 7:** Classification of HWW syndrome

Images for this section:

Fig. 1: with blind hemivagina

**Fig. 2:** Ultrasound of pelvis showing two uterine cavities in the pelvis. Right sided uterus with its cervix and vagina (white arrow in A) is normal in size, shape and echo texture with normal endometrial cavity. Left sided uterine cavity (yellow arrow in B) is grossly distended and filled with fluid containing fine internal echoes within.


![Ultrasound images of pelvis showing two uterine cavities](image)

**Fig. 3:** T2W Coronal, Sagittal MR images of pelvis demonstrating the septum as a hypo intense band in the mid vagina (arrow) causing obstruction and hematometrocolpos.

**Fig. 4:** cervicovaginal atresia without communicating uteri


**Fig. 5:** partial reabsorption of the vaginal septum

**Fig. 6:** with communicating uteri


**Fig. 7:** Classification of HWW syndrome
Findings and procedure details

Three patients were identified with HWW syndrome during period of observation from July until December 2016. The clinical data of these patients was collected from both medical records and history taking. Radiological features on abdominal CT, Ultrasonography, and MRI were demonstrated with simple description. Abdominal US examination was performed with curve probe type. Abdominal CT was performed on a 128 slice CT scanner. Abdominal MRI examination was performed on a 1.5 Tesla MRI scanner. Images acquisition done on multiple planes with T1-weighted (TR 631 ms; TE 9 ms) and T2-weighted Turbo Spin Echo (TR 5330 ms; TE 87 ms) sequences; fat-suppressed T2-weighted TSE images (TR 5838 ms; TE 87 ms). Informed consent was obtained from either the parents or the patient herself.

Patient 1

A 16-years-old female presented with severe right lower abdominal pain accompanied with high fever. There was also history of intermittent abdomino-pelvic pain since one year prior to admission which worsened a month before. Gynecologic history revealed menarche at 13 years of age followed by irregular menses and dysmenorrhea. Any recent abdominal trauma, nausea, vomiting, diarrhea was denied.

Physical examination by rectal toucher indicated uterus deviated to the right, also revealed palpable and tender pelvic mass, sized approximately 8 x 8 cm with limited mobility. Abdominal US was ordered and showed uterine cavities protruding to the right side and grossly distended, filled with fluid suggesting hematometra. Right kidney was absent (Fig.8). Infected ovarian cyst was suspected at first and abdominal CT was performed prior to surgery. Abdominal CT revealed uterus didelphys, right adnexal complex cyst, and left single kidney (Fig. 9-A-D). Exploratory laparotomy was done and omentum covered cystic mass, also enlarged uterus (suggesting uterus didelphys) were found (Fig.10). Then, right salpingo-oophorectomy, adhesiolysis, and omentectomy were carried out.
Fig. 8: Abdominal USG findings of a 16-years-old female presented with severe right lower abdominal pain and high fever, turned out to be HWW syndrome, revealed uterine cavities protruding to the right side and grossly distended, filled with fluid, suggesting hematometra. Right kidney was absent.

References: Department of Radiology, Dr. Soetomo General Hospital, Surabaya
Fig. 9: Abdominal CT images of a 16-years-old female presented with severe right lower abdominal pain and high fever, turned out to be HWW syndrome. A) Axial and C) coronal CT image showed uterus didelphys (yellow arrow). B) Axial CT image showed right adnexal complex cyst (red arrow) D) 3D reconstruction showed left single kidney.

References: Department of Radiology, Dr. Soetomo General Hospital, Surabaya

Fig. 10: Exploratory laparotomy of a 16-years-old female presented with severe right lower abdominal pain and high fever, turned out to be HWW syndrome, revealed omentum covered cystic mass (blue arrow), also enlarged uterus suggesting uterus didelphys (green arrow) were found. Left ovary seems normal (black arrow).

References: Department of Obstetrics and Gynecology, Dr. Soetomo General Hospital, Surabaya

Abdominal MRI performed afterwards revealed two separate uterine cavities and cervices suggestive of uterus didelphys with hematometrocolpos along right uterus cavity and cervical canal distension, also right kidney agenesis (Fig.11). Right hemivagina was dilated with blood products within, implicating the presence of an obstructing right vaginal septum with a small communication exists between the duplicated cervices.
Fig. 11: Post surgery abdominal MRI images of a 16-years-old female presented with severe right lower abdominal pain and high fever, turned out to be HWW syndrome. A) Coronal T2 MRI showed uterus didelphys (yellow arrow) and incomplete obstructed hemivagina, there was communicating outflow between left uterine to the contralateral (green arrow); B) red arrow showed right cervical canal distension; C) right sided hematometrocolpos was demonstrated, indicating the presence of vaginal septum which observed as hypointense band ± 4 mm in thickness at mid vagina (yellow arrow); D) Coronal T2 MRI image showed absent right kidney.

References: Department of Radiology, Dr. Soetomo General Hospital, Surabaya

The patient was diagnosed with HWW syndrome and since there was communication between the duplicated cervices it falls into classification 2.2 according to the new HWW syndrome classification. Transvaginal resection of the vaginal septum was done in order to drain the hematocolpos afterwards (Fig.12).
A 13-years-old female presented with left lower abdominal pain. Gynecologic history revealed menarche at 12 years of age also followed by irregular menses and dysmenorrheal after then. Palpable cystic mass, sized approximately 5 x 8 cm at suprapubic with limited mobility was detected on physical examination.

Abdominal US then performed and showed uterus enlargement with hematometra and hematocolpos also a second uterus-like mass (Fig.13). Abdominal MRI was performed for further evaluation and revealed uterus didelphys with left obstructive hemivagina (Fig.14A-C). The abdominal MRI also revealed agenesis of left kidney (Fig.14D). The findings were consistent with HWW syndrome (classification 1.1) and the patient also had transvaginal resection of the vaginal septum.
Fig. 13: Abdominal USG findings of a 13-years-old female presented with left lower abdominal pain, turned out to be HWW syndrome, showed uterus enlargement with fluid containing internal echoes suggesting hematometra (U) and hematocolpos (V) also a second uterus-like mass (red arrow).

References: Department of Radiology, Dr. Soetomo General Hospital, Surabaya
Fig. 14: Abdominal MRI images of a 13-years-old female presented with left lower abdominal pain, turned out to be HWW syndrome. A) Axial and C) Coronal T2 MRI image showed uterus didelphys (red arrow) with left obstructed hemivagina (orange star). B) Coronal T2 MRI image showed left obstructive hemivagina (orange star) indicating presence of vagina septum which observed as hypointense band, ± 2.7 mm in thickness (green head arrow), there is no communication between the duplication genital structure at any level C) Coronal T2 MRI image revealed left kidney agenesis.

References: Department of Radiology, Dr. Soetomo General Hospital, Surabaya

Patient 3

An 18-years-old female presented with lower abdominal and pelvic pain. Those complaints occurred since the patient experienced menarche at 12 years of age. There
was also a history of irregular menstruation and severe dysmenorrhea. Upon physical examination there were fluid collection in vagina and palpable mass as well.

On abdominal US, uterus enlargement and fluid collection in vagina, consistent with hematometrocolpos were found. Uterus didelphys with obstructed hemivagina was suspected. Due to severe abdomino-pelvic pain, immediate incision was performed to drain hematometrocolpos before any further imaging. Abdominal MRI which was performed afterwards indicated uterus didelphys with two vaginas with vaginal septum ± 2.6 mm in thickness (Fig.15A-D). The presence of right kidney agenesis (Fig.15-E), made the patient diagnosed with HWW syndrome (classification 1.1).

![Abdominal MRI images of an 18-years-old female presented with lower abdominal and pelvic pain which turned out to be HWW syndrome. A-D) Axial and coronal T2 MRI image showed two separate uterine with two separate cervices (uterus didelphys) (right: yellow arrow, left :red arrow) with vaginal septum ± 2.6 mm in thickness; E) Coronal T2 MRI image revealed right kidney agenesis.](image)

**Fig. 15:** Abdominal MRI images of an 18-years-old female presented with lower abdominal and pelvic pain which turned out to be HWW syndrome. A-D) Axial and coronal T2 MRI image showed two separate uterine with two separate cervices (uterus didelphys) (right: yellow arrow, left :red arrow) with vaginal septum ± 2.6 mm in thickness; E) Coronal T2 MRI image revealed right kidney agenesis.

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The demographic, clinical characteristics and radiologic findings in all the 3 patients is summarized below (Fig.16 & Fig.17).
<table>
<thead>
<tr>
<th>Patients</th>
<th>Age (years)</th>
<th>Recent symptoms</th>
<th>Age at symptoms onset (years)</th>
<th>Age at menarche (years)</th>
<th>Physical examination findings</th>
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<tr>
<td>No. 1</td>
<td>16</td>
<td>severe right lower abdominal pain and high fever</td>
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<td>13</td>
<td>Uterus deviated to the right Palpable cystic and tender pelvic mass, size ≤ 8 x 8 cm with limited mobility</td>
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<td>Palpable cystic mass, size ≤ 5 x 8 cm, at suprapubic with limited mobility</td>
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<td>No. 3</td>
<td>18</td>
<td>lower abdominal and pelvic pain</td>
<td>18</td>
<td>12</td>
<td>Fluid collection in vagina and palpable mass</td>
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**Fig. 16:** Demographic and clinical characteristics of the 3 cases.

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<th>Patients</th>
<th>Abdominal USG</th>
<th>Modalities</th>
<th>Abdominal CT</th>
<th>Abdominal MRI</th>
<th>HWW syndrome classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 1</td>
<td>Uterine cavities protruding to the right side and grossly distended, filled with fluid containing within suggesting hematomata</td>
<td>Uterus didelphys</td>
<td>Right adnexal complex cyst</td>
<td>Uterus didelphys with hematometrolpos, along right uterus cavity and cervical canal distension</td>
<td>Classification 2.2</td>
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<tr>
<td></td>
<td>Absence of right kidney</td>
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<td>Left single kidney</td>
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<td>No. 2</td>
<td>Uterus enlargement with hematometra and hematocolpos</td>
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<td></td>
<td>Uterus didelphys with left obstructive hemivagina, non communicating</td>
<td>Classification 1.1</td>
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<td></td>
<td>Second uterus-like mass</td>
<td></td>
<td></td>
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<tr>
<td>No. 3</td>
<td>Uterus enlargement with fluid collection in vagina, assessed as hematometrolpos, suspected uterus didelphys with obstructed hemivagina</td>
<td>Not performed</td>
<td></td>
<td>Uterus didelphys with vaginal septum (MRI was performed after incision due to severe abdomino-pelvic pain)</td>
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Fig. 12: Transvaginal resection of the septum to drain hematocolpos

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Conclusion

Herlyn-Werner-Wunderlich syndrome is very rare and its non specific symptoms or findings upon physical examination may result in delay of diagnosis, though diagnosis simply can be made by imaging modalities. Early diagnosis and treatment will relieve acute symptoms also preserve fertility. Abdominal US is very useful in detecting mullerian duct anomaly, whereas abdominal MRI is the most accurate tools for diagnosis of HWW syndrome. A patient with single kidney without history of nephrectomy should raise suspicion of urogenital malformation, especially HWW Syndrome.
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References


