Signature: © Pol J Radiol, 2016; 81: 395-400
DOI: 10.12659/PJR.897228

Polish Journal of Radiology
www.PolRadiol.com
CASE REPORT

Received: 2015.12.23
Accepted: 2016.01.18
Published: 2016.08.24

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

The Herlyn-Werner-Wunderlich Syndrome – A Case Report with Radiological Review

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Summary

Background: HWW syndrome is a very rare congenital anomaly of urogenital tract involving Mullerian ducts and mesonephric ducts. It is characterised by a triad of symptoms - uterus didelphys, obstructed hemivagina and ipsilateral renal agenesis. It can be classified based on a completely or incompletely obstructed hemivagina. It presents soon after menarche or shows delayed presentation depending on the type. It can exhibit acute pelvic pain shortly after menarche and may show non-specific and variable symptoms with resultant delay in diagnosis. The most common presentation is pain and dysmenorrhea, and pain and abdominal mass in the lower abdomen secondary to haematocolpos and/or haematometra.

Case Report: Presentation of a clinical case of a 13-year-old patient with HWW syndrome presenting with regular menses, dysmenorrhea and painful lump in hypogastric region on the left side of midline. We described the role of imaging modalities in diagnosis of the Herlyn-Werner-Wunderlich syndrome with a review of literature. USG and MRI showed left renal agenesis with compensatory hypertrophy of the right kidney, uterus didelphys with haematometra and haematocervix in the left uterus with evidence of blood in a dilated retort-shaped left fallopian tube and a normal right uterus. The unique feature of our case is haematometra and haematocervix with cervical and vaginal atresia found on the left side (classification 1.2) with associated left renal agenesis.

Conclusions: HWW syndrome can present early or late, depending on the type. In patients with uterine and vaginal abnormalities, a work-up for associated renal anomalies should be performed. Early intervention is needed to reduce the risk of endometriosis and infertility.

MeSH Keywords: Didelphis • Hematometra • Mullerian Ducts

PDF file: http://www.polradiol.com/abstract/index/idArt/897228

Background

The Herlyn-Werner-Wunderlich syndrome is a rare, congenital disorder characterised by uterus didelphys, unilateral obstructed hemivagina and ipsilateral renal agenesis, all being secondary to mesonephric duct-induced Mullerian anomalies. It is also known as obstructed hemivagina and ipsilateral renal anomaly (OHVIRA). It is generally observed in postmenarche adolescents and young women with dysmenorrhea, irregular menses, abdominal pain and pelvic mass [1].

The diagnosis is often difficult due to the infrequency of the syndrome, and a high index of suspicion is required. Early detection is important as surgical resection of obstructing vaginal septum can provide pain relief and prevent further complications. Around 80% of patients are able to conceive. A high index of suspicion in patients with renal anomalies and endometriosis is needed to detect the Herlyn-Werner-Wunderlich syndrome for timely diagnosis to avoid complications from the syndrome. Delay in diagnosis increases the risk of complications such as endometriosis and infertility [2]. The unique feature of our case is haematometra and haematocervix with cervical and vaginal atresia found on the left side (classification 1.2) with associated left renal agenesis.

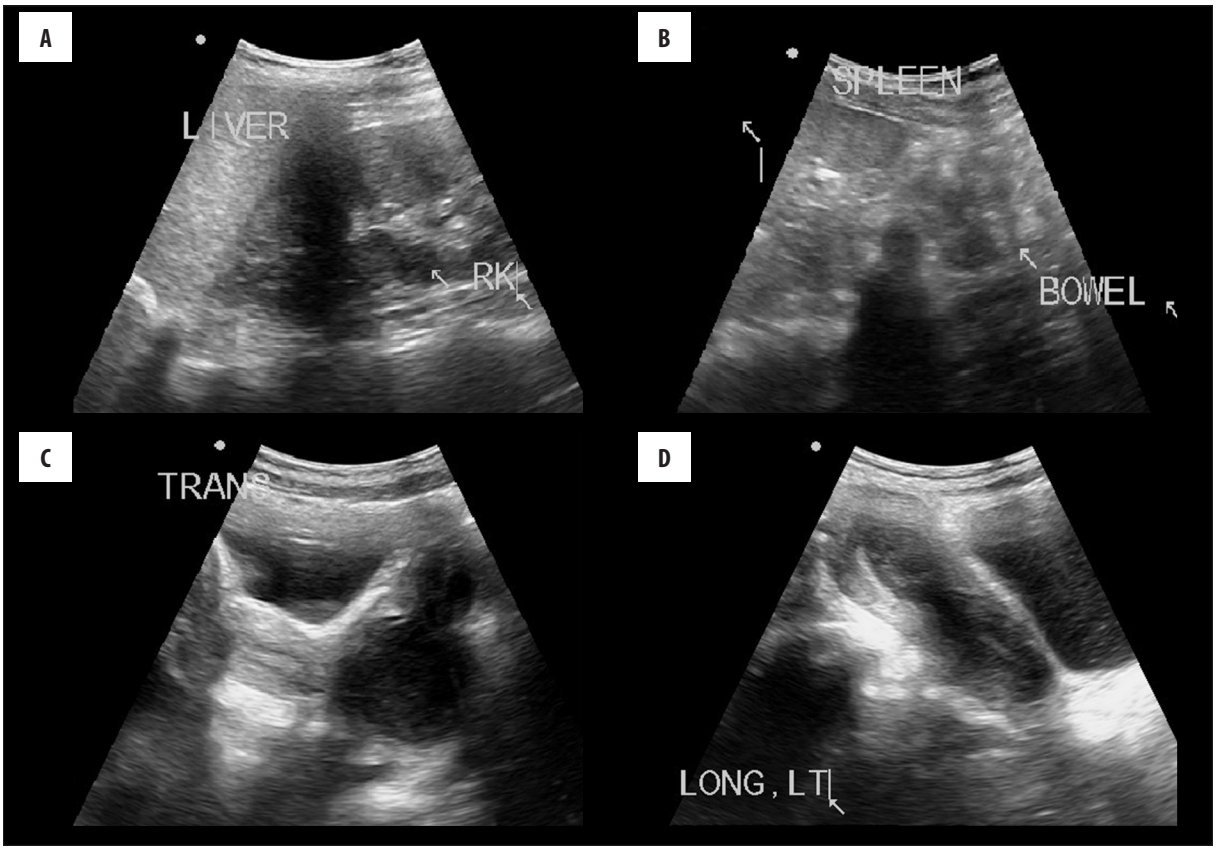

Figure 1. (USG of the abdomen and pelvis) – showing an absent left kidney, uterus didelphys, haematometra in the left uterine horn.

Case Report

A 13-year-old female patient presented with pain in the lower abdomen with lumpish feeling in the lower abdomen on the left side. She had menarche at 12 years of age and her menses were regular. There was no history of menorrhagia. She gave a history of dysmenorrhea and occasional vomiting. On examination, there was a tender lump in the hypogastric region on the left side of midline. PV examination was not done.

Vaginoscopy followed by hysteroscopy performed under general anaesthesia showed single vagina, cervix, uterus, and single ostium.

USG of the abdomen and pelvis revealed: absence of the left kidney in the left renal fossa which was occupied by bowel loops (Figure 1B) The right kidney showed mild compensatory hypertrophy and measured 11×5.6 cm (Figure 1A). Uterus didelphys was noted. The left uterine cavity and cervical canal showed a hypoechoic collection with multiple internal echoes suggestive of haematometra and haematotrachelos (Figure 1C, 1D). The right uterine horn and cervical canal appeared normal (Figure 1C). A well-defined elongated retort-shaped tubular anechoic cystic lesion measuring approx. 12.2×3 cm filled with multiple internal echoes was noted in the left adnexa. It was coursing superiorly over the uterine fundus and extending in the right adnexa – suggestive of left haematosalpinx. No obvious dilatation of the right fallopian tube was noted. Bilateral ovaries appeared normal.

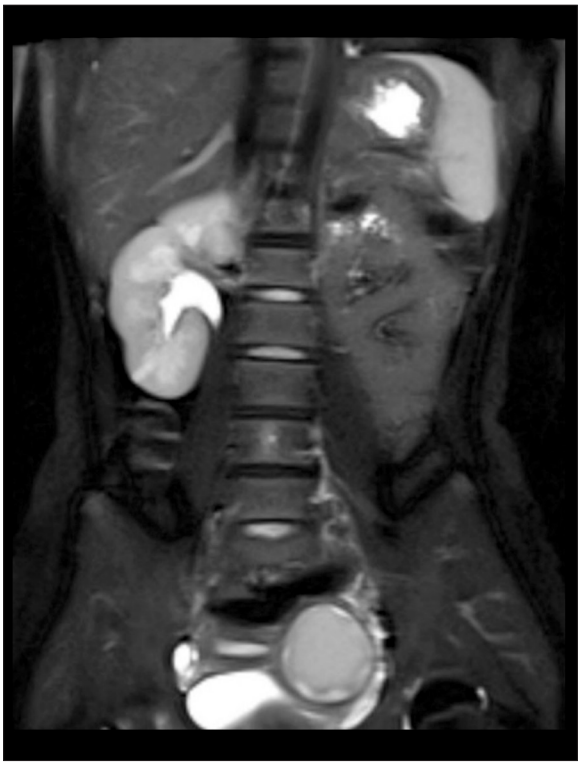

Figure 2. (Coronal STIR abdomen and pelvis) – showing absent left kidney with mild compensatory hypertrophy of the right kidney.

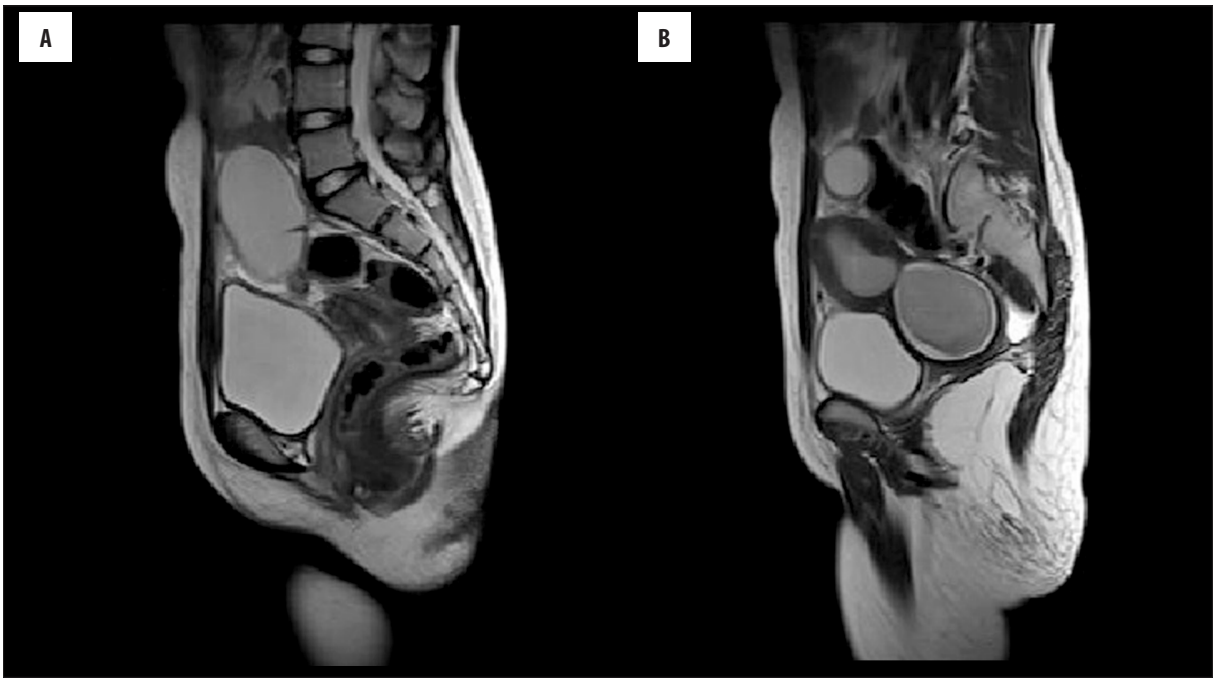

Figure 3. (Sagittal T2WI pelvis) – showing normal right uterine horn, haematometra and haematocervix in the left uterine horn and haematosalpinx overlying the urinary bladder dome.

MRI of the abdomen and pelvis revealed: absence of the left kidney in the left renal fossa, along its course of ascent and in ectopic location – suggestive of agenesis. The right kidney showed mild compensatory hypertrophy (Figure 2). Two pear-shaped structures were noted in the pelvis – suggestive of uterus didelphys. Two cervixes were noted. The right uterus was of normal in size and was anteverted. No collection was noted in the right uterine cavity. The right cervix appeared normal (Figure 3A). The left uterus was enlarged due to fluid collection in the uterine cavity and cervical canal measuring 8.7 (L) ×4.3 (AP) ×4.1 (T) cm causing stretching of the myometrium. Fluid collection appeared hyperintense on T1WI, T1 FAT SAT; it showed intermediate signal intensity on T2WI suggestive of blood – suggestive of haematometra and haematotrachelos (Figure 4A, 4C, 4D, 5). The lower end of fluid collection in the cervix showed inferior convexity – suggestive of obstruction at the level of the cervix or proximal hemivagina on the left side (Figure 3B). A large retort-shaped tubular lesion, approximately 12.2×3 cm in size, was noted in the left adnexa arising from the left uterus extending superior to and draping over the uterus and urinary bladder dome – suggestive of a dilated fallopian tube. It appeared hyperintense on T1WI, T1 FAT SAT with intermediate signal intensity on T2WI – suggestive of haematosalpinx (Figure 4B, 4D, 5). The right fallopian tube was not dilated and hence not seen. Bilateral ovaries appeared normal.

A diagnosis of uterus didelphys with left haematometra, hameatotrachelos and haematosalpinx with left renal agenesis – suggestive of the Herlyn-Werner-Wunderlich syndrome (classification 1.2) was made. Obstruction was at the level of the cervix or proximal hemi-vagina. Transabdominal resection of the left uterine horn with ipsilateral cervix was performed.

Discussion

The Herlyn-Werner syndrome (renal agenesis with ipsilateral blind hemivagina) was initially described by Herlyn and Werner in 1971. Wunderlich in 1976 described association of right renal agenesis with a bicornuate uterus and simple vagina in the presence of an isolated haematocervix [3].

Mullerian duct abnormalities cover a wide range of developmental anomalies, resulting from non-development, defective fusion or defects in regression of the septum during foetal development. It is classified as type III Mullerian duct anomaly (MDA) associated by mesonephric duct anomaly. It accounts for approximately 5% of MDAs [4,5].

The estimated overall prevalence of MDA is 2–3% of women. Uterus didelphys constitutes 11% of MDAs. Hypoplasia or agenesis of the uterus and proximal vagina constitute 5–10% of MDAs. Associated renal anomalies are present in approximately 43% [5,6].

About 75% of patients with didelphys uterus have a partial or complete vaginal septum which is commonly longitudinal in the Herlyn-Werner-Wunderlich syndrome, which reflects a disorder of lateral fusion between the inferior portions of two Mullerian ducts [7]. Studies of uterine organogenesis have implicated the Hox and Wnt genes as regulators of uterine morphology. However, specific gene mutations have not been identified as associated with most MDAs [2].

Mesonephric (Wolffian) and para-mesonephric (Mullerian) ducts are two paired urogenital structures from which internal genital organs and lower urinary tract are derived. The exact etiopathogenesis of HWW syndrome is still not known. Wolffian ducts play an important role in the

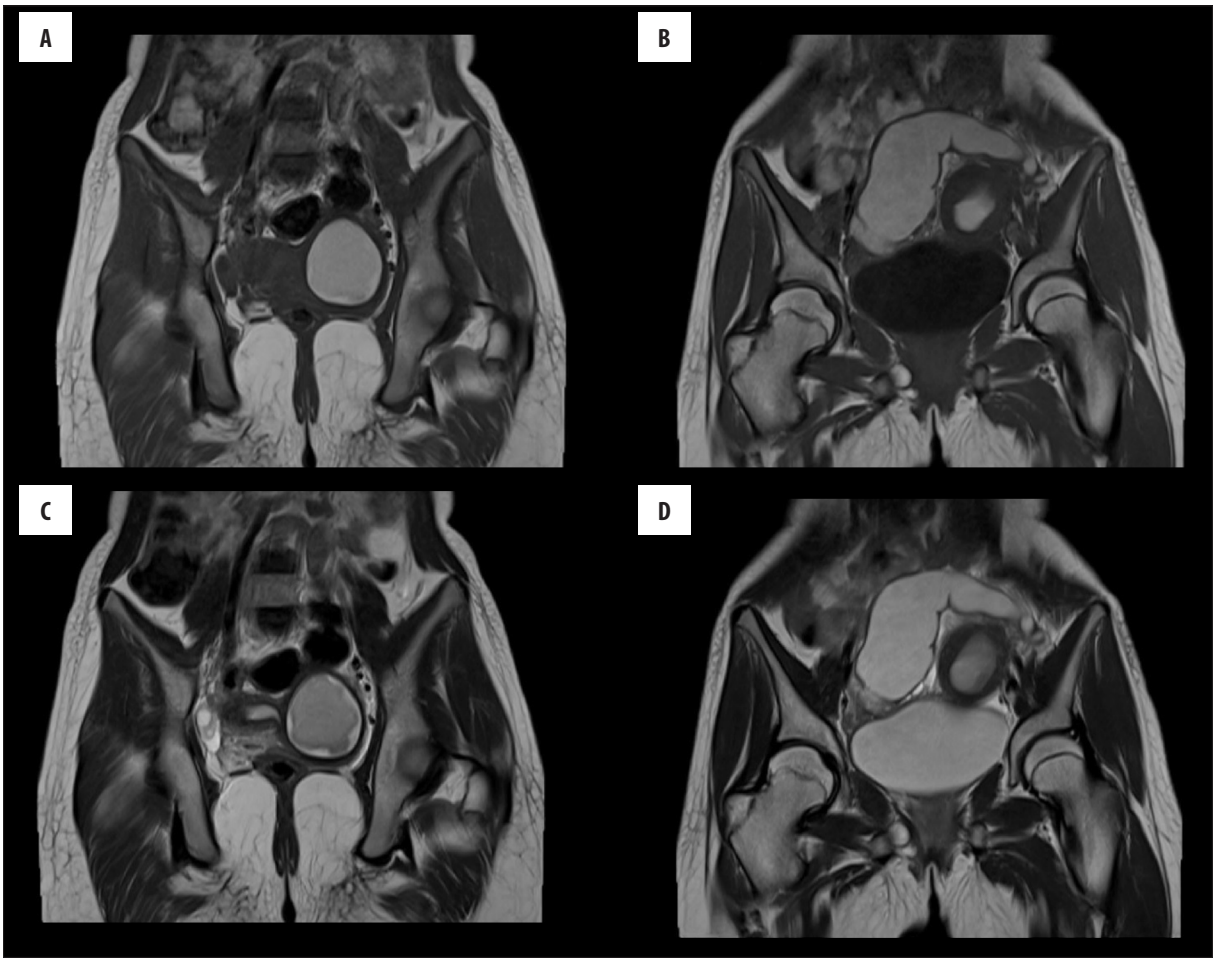

Figure 4. (T1WI and T2WI coronal pelvis) – showing uterus didelphys, haematometra in the left uterine horn, left haematosalpinx. (**A, B**) T1W-coronal; (**C, D**) T2W-coronal.

development of internal genital organs and give rise to kidneys [8]. They are inductor elements for adequate fusion of the Mullerian ducts. If one of the Wolffian ducts is absent, the ipsilateral kidney and ureter will fail to fuse in the midline. This process can be complete or incomplete. Uterus didelphys is formed if failure of fusion is complete. The Mullerian duct on the side lacking the Wolffian duct displaces itself laterally and cannot come into direct contact with the urogenital sinus in the centre with the resultant formation of a blind sac, imperforate or obstructed vagina. The distal third of vagina developing from the urogenital sinus is not affected. A didelphic uterus results due to embryologic arrest during the 8th week of gestation. This ultimately affects the Mullerian and metanephric duct [9].

Lan Zhu et al. reviewed characteristics of all HWWS patients at Peking union medical college hospital (PUMCH) and suggested a new classification for the syndrome based on the presence of a completely and incompletely obstructed vaginal septum [3]. The new classification allows for earlier diagnosis and treatment. The syndrome is classified by complete or incomplete obstruction of the vagina as classification 1 (completely obstructed hemivagina) and classification 2 (incompletely obstructed hemivagina). The clinical findings in these two types are distinctly different (Figure 6, Table 1).

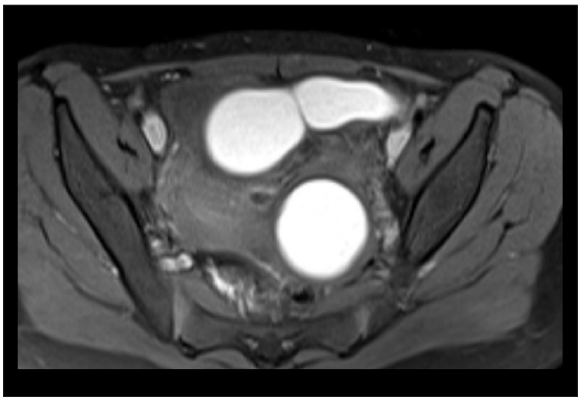

Figure 5. (Axial T1FS pelvis [T1 FATSAT]) – showing left haematosalpinx overlying the urinary bladder dome, uterus didelphys, haematometra and haematocervix in the left uterine horn, normal right uterine horn.

Incomplete hemivaginal obstruction, normal menstruation from the non-obstructed side, and rare occurrence of the syndrome result in a delay in diagnosis. Patients presenting with cyclical dysmenorrhea are often prescribed oral contraceptive pills and NSAIDs which suppresses or eliminates menses with a further delay in diagnosis of the condition [2].

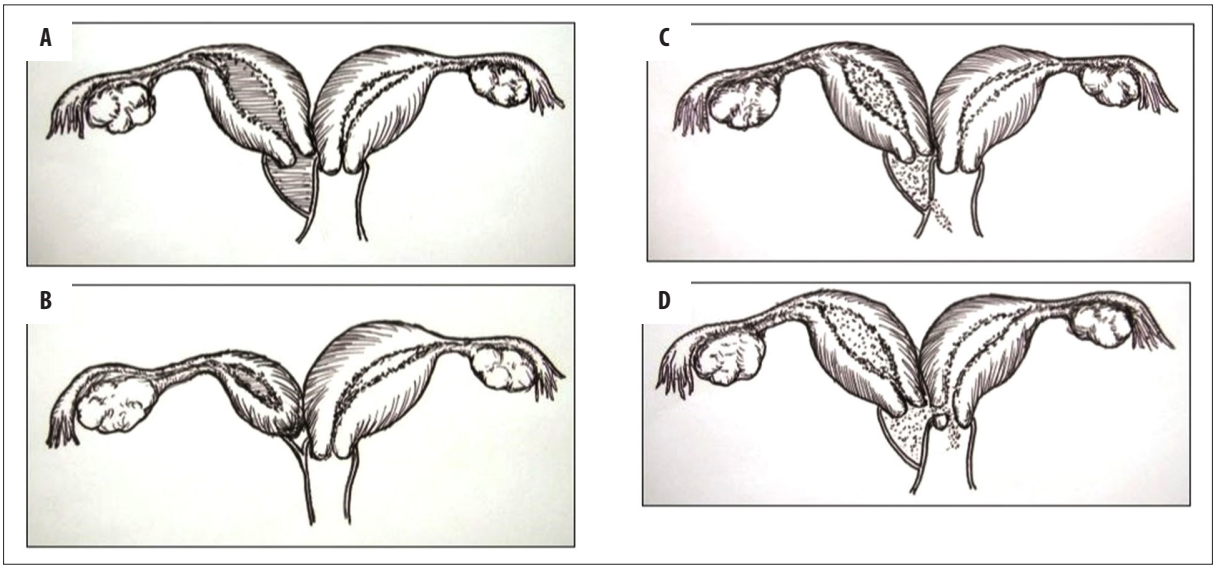

Figure 6. Classification 1 – Completely obstructed hemivagina. Classification 1.1 – with blind hemivagina (**A**). There is no communication between the duplicated uterus and vagina. Haematocolpos occurs a few months after menarche. Haemoperitoneum due to bleeding from the fallopian tube can be found at surgery [10]. If neglected, the condition can progress to secondary endometriosis, pelvic adhesions, pyosalpinx and pyocolpos [10,11]. Classification 1.2 – Cervicovaginal atresia without communicating uteri (**B**). Cervix behind the septum is atretic or maldeveloped. Menses from the uterus behind the septum cannot flow through atretic cervix. Hence, clinical features are similar to as in classification 1.1. Classification 2 – Incompletely obstructed hemivagina. Classification 2.1 – Partial reabsorption of the vaginal septum (**C**). A small communication exists between two vaginas with resultant incomplete obstruction. Patients have a late presentation. Classification 2.2, with communicating uteri (**D**). A small communication exists between two duplicated cervices with a completely obstructed hemivagina. Menses from the uterus behind the septum can flow through communication to the contralateral cervix. Drainage is often impeded due to small communication. Courtesy: *Zhu et al. New classification of Herlyn-Werner-Wunderlich syndrome. Chin Med J, 2015; 128: 222–25.*

Table 1. Showing clinical characteristics of a complete and incomplete type of HWWS.

Clinical characteristics	Classification 1 (Complete)	Classification 2 (Incomplete)
Age at symptom onset	Soon after menarche	Late presentation
Age at time of diagnosis	Soon after menarche	Late
Dysmenorrhea	Common	Less common
Irregular PV bleeding	Less common	More common
Intermittent mucopurulent discharge	Less common	More common
Abdominal pain, fever, vomiting	Common	Uncommon
Pelvic inflammatory disease	Uncommon	Common
Haematometra, haematosalpinx, haemoperitoneum	Common and early	Uncommon
Endometriosis	Common	Uncommon
Progression to secondary endometriosis, pelvic adhesions, pyosalpinx, pyocolpos	Quick and easy	Gradually

Other associated anomalies include renal dysplasia, duplication of the kidneys and ureters, ectopic ureter, high-riding aortic bifurcation, IVC duplication, intestinal malrotation and ovarian malposition [2]. Renal agenesis is ipsilateral to the dilated uterine cavity. The right side is affected twice more frequently than the left side [5,6].

Prognosis: Early detection and treatment result in good prognosis with preservation of fertility. As much as 80% patients with uterus didelphys conceive, with elevated rates of premature delivery (22%) and abortion (74%). Caesarean section is needed in over 80% of patients [2]. Rare complication of adenocarcinoma of the obstructed side of the uterine cervix and clear cell carcinoma of the obstructed portion of the vagina have been described [2].

Diagnosis

Ultrasonography and MRI are useful in its detection. Transvaginal sonography has an advantage of low cost, better imaging of the uterus and adnexa with no radiation exposure. MRI is considered as a gold standard for diagnosis and pre-operative planning of the Herlyn-Werner-Wunderlich syndrome. It evaluates uterine morphology, detects communication between vaginal and uterine lumen, characterises fluid contents, has the capability of multiplanar imaging but with no radiation, can detect associated renal agenesis and diagnose complications like endometriosis [2].

Treatment for patients with classification 1.2 is different from patients with other classifications. As cervical agenesis is difficult to correct surgically, laparoscopic or transabdominal resection of the affected ipsilateral uterus is suggested [3]. Resection of the vaginal septum is the treatment of choice for obstructed hemivagina with haematocolpos. Vaginal septotomy is usually done by hysteroscopic approach rather than laparoscopic technique [12].

Conclusions

HWW syndrome has variable onset of presentation. In patients with uterine and vaginal abnormalities, work up for associated renal anomalies should be performed. USG has advantage of low cost & real time imaging. MRI is considered gold standard for diagnosis. It evaluates uterine, cervical and vaginal morphology, detects level of obstruction, characterises fluid contents, has multiplanar imaging capability with no radiation hazard, can detect associated renal agenesis and can diagnose complications like endometriosis. It helps clinicians for planning, staging, assessing risk-benefit ratio of different treatment approaches. Early intervention is needed to reduce risk of endometriosis and infertility.

Conflict of interest

None.

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