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Case Report

Unusual clinical presentations, pathogenesis and radiological review of Herlin-Werner-Wunderlich syndrome: A case report and literature review ☆

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ABSTRACT

Herlyn-Werner-Wunderlich (HWW) syndrome is a rare anomaly of the female urogenital tract characterized by the combination of uterine didelphys, obstructed hemivagina, and ipsilateral renal anomalies. The exact incidence of the syndrome remains unknown, but it has been reported to be 1 per 2000 to 1 per 28,000 women. It is believed that the triad is a mesonephric duct-induced paramesonephric duct anomaly. In majority of the cases with complete hemivaginal obstruction, the pathology is diagnosed after menarche due to retained menstrual flow. While the common clinical presentations are dysmenorrhea, pelvic pain, intermenstrual bleeding, and pelvic mass, it can also manifest itself with unusual gastrointestinal and urinary tract symptoms. We present a case of HWW syndrome with gastrointestinal symptoms like worsening constipation and abdominal fullness.

The unusual clinical presentation of this syndrome makes diagnosis more challenging. To solve such medical puzzles and prevent complications, detailed history-taking and radiological guidance are critical.

Introduction

Herlyn-Werner-Wunderlich (HWW) syndrome, also known as Obstructed hemi vagina and ipsilateral renal anomalies (OHVIRA) is a rare congenital anomaly of the female urogenital tract which involves mesonephric and paramesonephric ducts [1]. Paramesonephric or Mullerian ducts as paired channels are present in both sexes during intrauterine life and regress in embryos with XY chromosomes under the influence of the Anti Mullerian Factor (AMF), produced by Sertoli cells [2]. Without AMF these ducts undergo 3 developmental phases; initiation, invagination, and elongation giving rise to fallopian tubes, uterus, and the upper part of the vaginal canal [2]. The mesonephric ducts better known as Wollfian ducts are located medially in relation to the Mullerian ducts

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and are derived from intermediate mesoderm. Wollfian ducts are present in both sexes initially and while they give rise to the epididymis, vas deference, and seminal vesicles in embryos with XY chromosomes, the ducts regress in embryos with XX chromosomes due to lack of testes-produced androgens [2,3]. Throughout several studies, it has been concluded that the Wollfian duct has significant role in the development of Mullerian duct [4]. Around 6-8 weeks postfertilization, it is the elongation phase of development in which Wollfian ducts act as physical guides for the Mullerian ducts to descend, fuse together, and reach the urogenital sinus [4]. In the absence or disruption of the Wollfian duct, the Mullerian duct shifts to the ipsilateral side and fails to fuse with the contralateral Mullerian duct. Furthermore, failure of the displaced Mullerian duct to connect with the urogenital sinus results in formation of a blind sac, an imperforated or obstructed hemivagina [5]. As a consequence, there are 2 hemiuteri, 2 endocervical canals and cervices, and blind ipsilateral hemivagina. As urinary and genital tracts have the same mesodermal origin, paramesonephric anomalies are highly likely to be associated with renal anomalies [6]. The most common renal anomaly present with uterine didelphys is ipsilateral renal agenesis followed by the multicystic, dysplastic kidney (MDK), a duplicated system of the contralateral kidney, and ectopic kidney [7]. Additionally, several studies concluded that hemivaginal obstruction and renal agenesis favor right side, however, this right-side predilection remains uncomprehended [8].

Case presentation

A 17-year-old, unmarried girl visited outpatient department of the French Medical Institute for Mothers and Children (FMIC) with primary complaints of worsening chronic constipation and abdominal fullness, for which she had visited many doctors and was treated with lactulose, omeprazole, suppositories, and enema, all resulted in short term relief of the symptoms. On further questioning the patient admitted episodic pelvic and rectal pain mostly during her menstrual cycles for which she was prescribed non-steroidal anti-inflammatory drugs (NSAID) with resultant improvement of the symptoms. She couldn't recall the exact period of her primary complaints but confirmed their presence for more than a couple of years. She did not have significant past medical or surgical history; her menarche occurred at age 14. She had irregular menstrual cycles during first year and normal cycles, occurring every 28-32 days and lasting for 5-6 days for the past 2 years. She admitted taking NSAID during her cycles, prescribed medications for constipation, and some herbal remedies. She refused a family history of congenital or gynecological disorders. She was not sexually active and did not report taking contraceptives and other hormonal pills.

On physical examination, the patient had palpable pelvic mass and mild suprapubic tenderness. Her development and secondary sex growth were normal otherwise, her hemodynamic was stable and there was no distress. Her vital signs were also within normal range and basic laboratory investigations did not find significant derangement. The patient was ordered an abdomen and pelvis ultrasound during which a distended cystic structure with low-level echoes was appreciated in the pelvis. The right kidney was not seen in the abdomen and pelvis. Subsequently, the possibility of HWW syndrome was raised. MRI confirmed duplication of uterus, cervix, and vagina. The right blind-ended hemivagina had a longitudinal septum resulting in ipsilateral hematometrocolpos, measuring 10 cm (SI) x 6.7 cm (AP) x 6.5 cm (TR) (Fig. 1), the right kidney was not seen in the abdomen and pelvis and the left kidney was compensatory enlarged (Fig. 2). There was no imaging evidence of endometriosis, hydro/pyosalpinx. The pathology was described to the patient and her family and surgical treatment was offered. The patient and her family did not consent to surgical intervention due to damage to the hymen tissue and subsequently, the contact was lost. After 4 months the patient again visited the gynecology department with a chief complaint of increased menstrual flow after the septectomy and evacuation were performed in one of the governmental hospitals.

Discussion

Mullerian duct developmental anomalies cover a wide range of pathologies that mostly involve uterus. These defects are mainly a result of deficient development (agenesis, rudimentary horn, unicornuate uterus), nonfusion (didelphys or bicornuate uterus), or failure of canalization (septate uterus) [9]. Didelphys uterus happens to be the least common Mullerian Duct Anomaly (MDA) [10]. It is classified under class III of MDA and accounts for 11 % of the MDA [11]. MDA is highly associated with different renal anomalies. A study titled "A Retrospective Analysis of Female Mullerian Duct Anomalies in Association with Congenital Renal Anomalies" recorded the renal status of 186 women with confirmed MDA of which congenial renal anomalies were present in 90 of them consisting 48.4 % of all the cases. The study also concluded that congenital renal anomalies in the form of unilateral kidney agenesis were mostly seen in women with duplex uterus and obstructed hemivagina [7]. HWW syndrome is a rare anomaly characterized by the triad of didelphys uterus, obstructed hemivagina, and ipsilateral renal anomalies. Although the true incidence of this syndrome is unknown, the incidence of uterine didelphys as part of this syndrome is estimated to be 1/2000-1/28000 [12].

The new classification of HWW syndrome by Zhu et al., (Table 1) is based on presence of complete or incomplete obstruction of hemivagina [13]. Multiple studies have also recommended the same classification pattern [14]. Additionally, the new classification of HWW syndrome assists in determining the clinical onset, presentation, and details of the pathology [13]. The onset of clinical manifestations is earlier and more severe in type I compared to type II [13]. A study conducted by Tong et al., concluded that age at onset of clinical symptoms significantly differs between those with complete obstruction vs those with incomplete obstruction (12.86 ± 1.84 vs 20.68 ± 7.43 years; $P < .05$). Dysmenorrhea, endometriosis, and acute pelvic inflammation are the most common gynecological concerns associated with HWW syndrome [8].

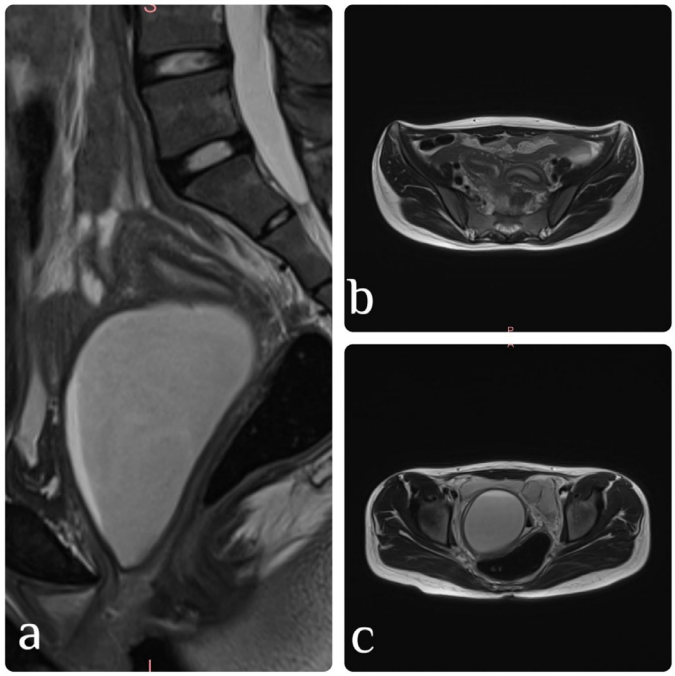


Fig. 1 – (A) Sagittal T2, demonstrating blind right hemivagina, containing bright fluid with fluid-fluid level. (B) axial T2 shows 2 separate uteri. (C) axial T2 demonstrates dilated hemivagina, abutting rectum.

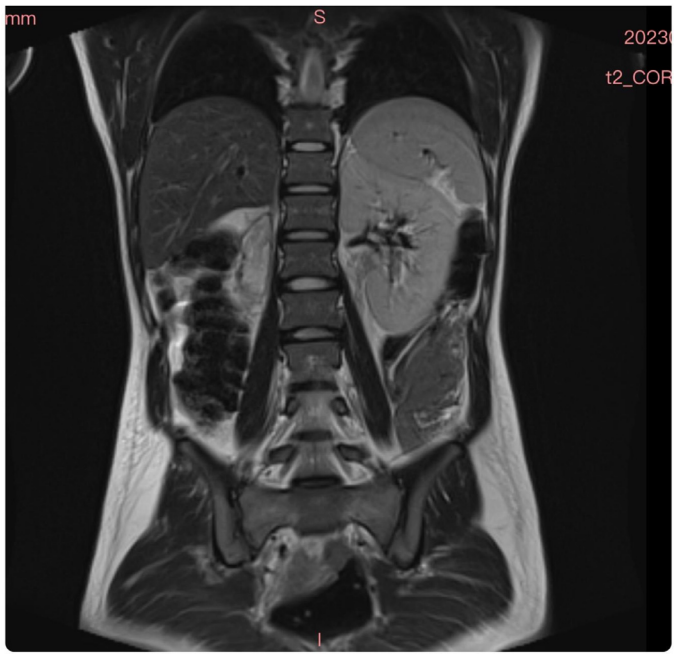
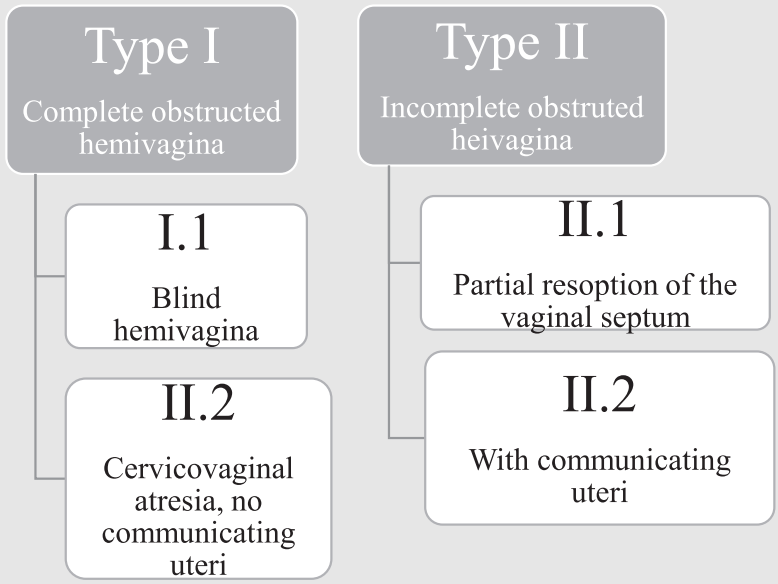


Fig. 2 – T2 Coronal shows absence of normal appearing right kidney and compensatory enlarged left kidney.

Although gynecological symptoms are common in patients with HWW syndrome, many cases have been reported in which the pathology has manifested itself with gastrointestinal or urinary symptoms. The primary complaint in our case was chronic worsening constipation showing less relief with medical treatment. Because the patient was regularly taking NSAID while menstruating, she did not complain of dysmenorrhea. Similar to our case, a case of HWW syndrome is reported in a 13-year-old girl who primarily complained of rectal and perianal pain, abdominal fullness, and worsening constipation [11]. Another case of a 13-year-old girl with imperforated hymen resulting in hematometrocolpos is reported in which she had cyclic lower abdominal pain and constipation for which she was self-medicating with anti-helminthic

Table 1 – New classification of the HWW syndrome.



medications [15]. In another young female of the pediatric age group, the HWW syndrome was manifested with right lower abdominal pain and tenderness simulating acute appendicitis [16]. Furthermore, several other cases of HWW syndrome were reported in pediatric and early adolescent age group patients complaining of acute abdominal pain [17–19].

Patients with HWW syndrome have also been presented clinically with unusual urinary symptoms. Dogan et al., have reported HWW syndrome diagnosed in 2 girls at pubertal period who actually presented with cyclical abdominal pain and urinary incontinence. Both had hysteroscopic resection of the vaginal septum after which the urinary incontinence was also completely resolved [20]. Additionally, many cases of HWW syndrome have been reported in which patients were presented with urinary retention. "An Unusual Cause of Recurrent Urinary Retention in an Adolescent Female" is the title of a case report in which a 16-year-old female presented to the pediatric emergency ward with complaints of worsening dysuria, bladder fullness, and decreased urinary output for 4-5 hours. Her associated complaints were constipation, rectal pain, and feeling a lump in the rectum while she was straining to defecate. Subsequently, her bladder was catheterized and 800 mL of urine was drained. Later she underwent an ultrasound and MRI that confirmed HWW syndrome [21]. Similarly, urinary retention as a primary complaint was reported in a few other cases of HWW syndrome [22,23]. Urethrovaginal fistula is also reported to be present in some patients with HWW syndrome. "A Rare Case of Herlyn Werner Wunderlich Syndrome with Urethrovaginal Fistula" is the title of a case reported by Meher-un-Nisa et al., in which a 27-year-old lady presented with hematuria and urinary retention was diagnosed with HWW syndrome. The patient had only a single opening in the vulva through which urine and menstrual flow were drained [24].

In almost all of the cases of HWW syndrome with or without unusual clinical presentations, sonography helped raise suspicion of the pathology and MRI confirmed it. While ultrasound is of benefit because of its availability, affordability, and safety, MRI has proved to be superior. A study by Yavus et al., aimed to evaluate the merits of sonography and MRI for accurate diagnosis and management of patients with HWW syndrome concluded that sonography was able to reveal the diagnosis, however, MRI provided extra information in most of the cases [25]. Another study by Zhang et al. concluded that although sonography is the primary imaging modality for the evaluation of MDA, MRI provides optimal characterization of complex malformations due to its excellent tissue contrast and large field of view. The study also suggests that MRI can better identify the site of obstruction and provide reasonable preoperative guidance [26]. Moreover, MRI is able to demonstrate detailed information in regards to uterine morphology, fluid content nature, and character of the vaginal septum. It is also of importance in diagnosing complications of pathology like endometriosis, pelvic inflammation and adhesions. Lastly it can help surgeons in picking the most accurate treatment options to maintain patient's fertility [1].

In conclusion, although the HWW syndrome is a rare female urogenital abnormality, it is not rare for it to manifest itself with gastrointestinal and urinary tract symptoms such as acute abdominal pain mimicking appendicitis, constipation, abdominal fullness, rectal pain, urinary incontinence, urine retention, dysuria, and hematuria rather that gynecological symptoms. It is of great importance for pediatric and early adolescent age group practitioners to be familiar with the diverse clinical presentations of HWW syndrome. Furthermore, detailed clinical history should be obtained as patients might be prescribed medications to alleviate gynecological and other

symptoms. Imaging facilities, specifically MRI should be utilized for timely diagnosis, detection of associated findings, and tailored treatment options.

Patient consent

Dr Mursal Amini confirms that I have obtained written informed consent for publication from the patient and her legal representative.

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