

Herlyn Werner Wunderlich syndrome: a report of two cases*

BY CATHERINE MAE MUNOZ MORANTE, RN, MD AND ANNA BELEN I. ALENSUELA, MD, FPOGS, FPSREI

Department of Obstetrics and Gynecology, Jose R. Reyes Memorial Medical Center

ABSTRACT

The association of renal agenesis with ipsilateral blind hemivagina and uterus didelphys is reported as Herlyn-Werner-Wunderlich (HWW) syndrome. Presented herein are two cases of HWW syndrome, each with different set of clinical presentations but both with the same arranged diagnostic method and management executed. The first case, 15 year-old nulligravid, manifested severe dysmenorrhea since menarche and is worsening over the past months. On the other hand, the second case, 29 year-old Gravida 1 Para 0 (0010), exhibited cyclic hypogastric pain and gradually enlarging right pelvic mass. Both cases underwent computed tomography scan and ultrasound examination which revealed uterine didelphys, hemivagina obstruction and ipsilateral renal agenesis, yet each has different laterality of mullerian anomaly. Together were managed with full resection of the vaginal septum as well as drainage of the hematometrocolpos, which are, today, the main treatment for patients with HWW syndrome.

Keywords: Herlyn-Werner-Wunderlich syndrome, blind hemivagina, uterus didelphys, hematometrocolpos

INTRODUCTION

The Herlyn-Werner-Wunderlich (HWW) syndrome is a very rare congenital anomaly of the urogenital tract involving Mullerian ducts, and it is characterized by the triad of uterus didelphys, obstructed hemivagina and ipsilateral renal agenesis.⁴ This syndrome was first described in 1922 and was suspected in a young woman with regular menstruation, gradually increasing pelvic pain and a pelvic mass after menarche.¹ Reported incidence for this anomaly is 0.1-3.8% in the general population.² In the Philippines, there is no local incidence reported. However, the Pediatric Gynecology Unit of Philippine Children's Medical Center diagnosed 5 cases in its five years of existence. A similar case was encountered at St. Lukes Medical Center in 2011 and two cases in Negros Oriental Provincial Hospital, Dumaguete City reported for the past 20 years since 2012⁶. One documented case of HWW syndrome was engaged in Amang Rodriguez Memorial Medical Center in 2011.

The exact cause, pathogenesis, and embryologic origin of HWW syndrome are unclear and remain a subject of discussion. HWW syndrome is usually discovered at puberty with non-specific symptoms, like increasing cyclic pelvic pain and a palpable mass due to the associated hematocolpos or hematometra, which result from retained, longstanding menstrual flow in the obstructed vagina.⁴

CASE REPORTS

Case number 1

R.L., 15 year-old, nulligravid, who complained of severe dysmenorrhea, that occurred since the patient achieved menarche at 14 years of age; the patient also had irregular menstruation (4 menstrual cycles for 8 months), seven days duration consuming one pad per day. Six months prior to admission, there was a noted increase in the intensity of dysmenorrhea, hindering her daily activities which prompted her to consult a physician. Ultrasound of the lower abdomen and computed tomography scan of whole abdomen showed dual horn of the uterus with note of fluid accumulation in the cervical and vaginal region continuous with the left endometrial cavity, giving an impression of uterine didelphys with left hematocolpos. There appears to be two vaginas separated by a septum and there was hypodense soft tissue bulge at the left cervical and vaginal region possibly the left hemivagina was obstructed. Tubular septated structure at the left adnexa was noted and to consider left hydrosalpinx. There was no left kidney and the right kidney was enlarged reflective of compensatory hypertrophy right renal (Figure 1). She was advised to consult a gynecologist. Due to rarity of her case, patient was advised to seek a gynecology specialist in Manila for further evaluation and management.

Patient has no known co-morbidities and no history of surgical intervention. She has no history of sexual contact.

On physical examination, patient was conscious, coherent, not in cardiorespiratory distress, ambulatory. Vital signs were stable. The abdomen was flat, soft, no

*Second Place, 2015 Philippine Obstetrical and Gynecological Society (POGS) Midyear Residents' Interesting Case Paper Contest, April 17, 2015, Lounge, Subic Bay Exhibition & Convention Center

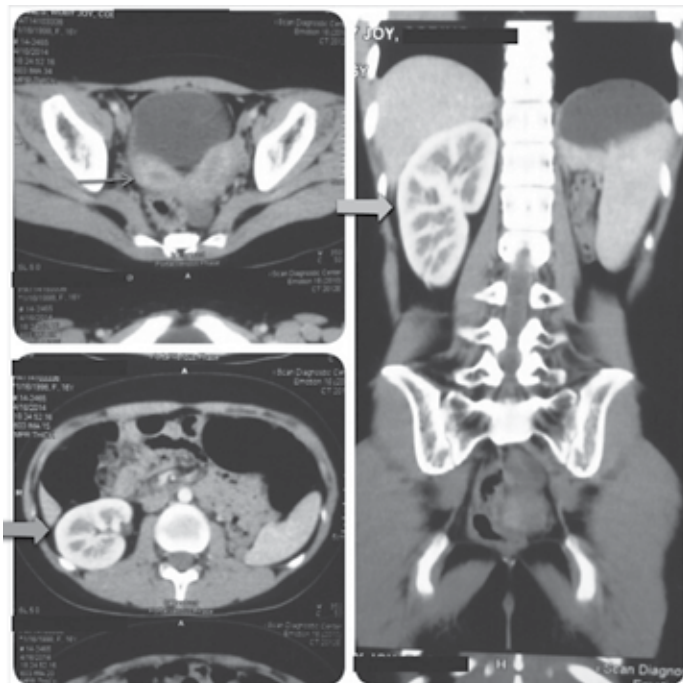


Figure 1. Case no.1. Computed tomography scan of whole abdomen. Non-visualized left renal with compensatory hypertrophy right renal (thick arrow), uterine didelphys (thin arrow) with apparently two vaginas

abdominal tenderness or mass palpated. On speculum examination, one cervix was visible which was pink, smooth, without erosions. On Internal Examination, cervix was firm, short and closed. Uterus was unenlarged and no adnexal mass or tenderness noted. A Nodular mass, solid, nontender at the left side of cervix was noted on rectovaginal examination.

Transvaginal ultrasound showed two uterine bodies, reflective of uterine didelphys, with respective cervix on each. The right uterus was with thin endometrium while the left uterus was with endometrial thickness of 0.9 cm and contains structures of mixed echoes suggestive of blood (Figure 2). The right ovary was normal while the left ovary, within were multiple follicles of varied sizes interspersed within the stroma with a centrally located cystic structures suggestive of multicystic ovary with endometriotic focus. And medial to the left ovary was the hematosalpinx. Double vagina was noted with dilated left vaginal canal fluid filled, to consider hematocolpos.

The initial assessment was Nulligravid, Herlyn Werner Wunderlich syndrome, Uterine didelphys, Double vagina with possible left longitudinal vaginal septum non-communicating, Left hematocolpos and left hematosalpinx, left renal agenesis.

She was advised excision of longitudinal vaginal septum and was done on the second day of her menstruation.

Intraoperatively, an obstructed hemivagina was identified with a longitudinal vaginal septum. An excised

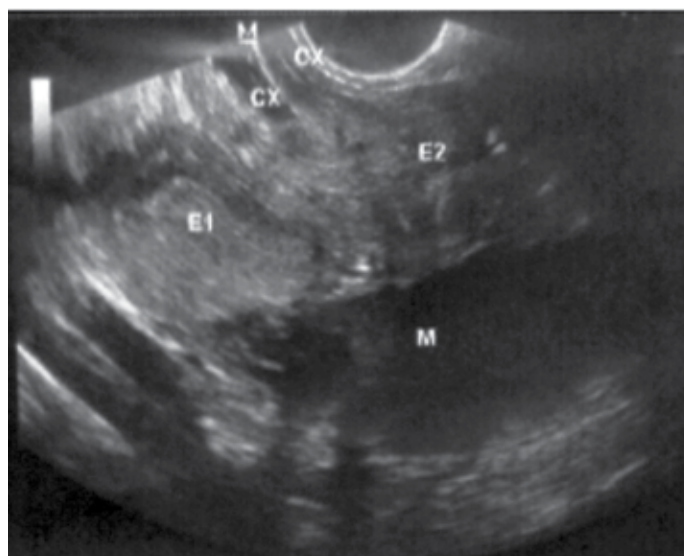


Figure 2. Case no.1. Transvaginal ultrasound. Uterine didelphys considered as described.

longitudinal vaginal septum measured 2 x 2 cm and was sent for histopathologic examination. Approximately 50ml of blood mixed with chocolate colored fluid was drained. Right and left cervixes were palpable.

Case number 2

K.B., 29 year-old, Gravida 1 Para 0 (0010) consulted at our institution with a chief complaint of severe hypogastric pain.

Patient had menarche at 15 years of age and had regular menstruation with four days duration consuming two pads per day, with no other signs and symptoms. Ten years prior to admission, when she was 19 years of age, she started experiencing cyclic hypogastric pain associated with gradually enlarging mass at right pelvic area. She self-medicated with mefenamic acid and noted temporary relief of pain. Seven years prior to admission, due to persistence of gradually enlarging pelvic mass, she consulted a gynecologist and was found to have a right ovarian new growth, probably endometrioma. She underwent Pelvic laparotomy and evacuation of hematometra. Final diagnosis was Pelvic endometriosis, hematometra. There was no further investigation done to determine the cause of the hematometra. Five years prior to admission, there was recurrence of the right pelvic mass accompanied by cyclic hypogastric pain. One month prior to admission, this time with a noted increase in the intensity of dysmenorrhea, associated with difficulty in urination and bowel movement. She consulted a gynecologist. Transabdominal and transvaginal ultrasound showed a thick walled cystic mass occupying the whole hypogastric area, etiology was unknown. The uterus was hard to delineate and the ovaries were normal. There was a tubular structure noted

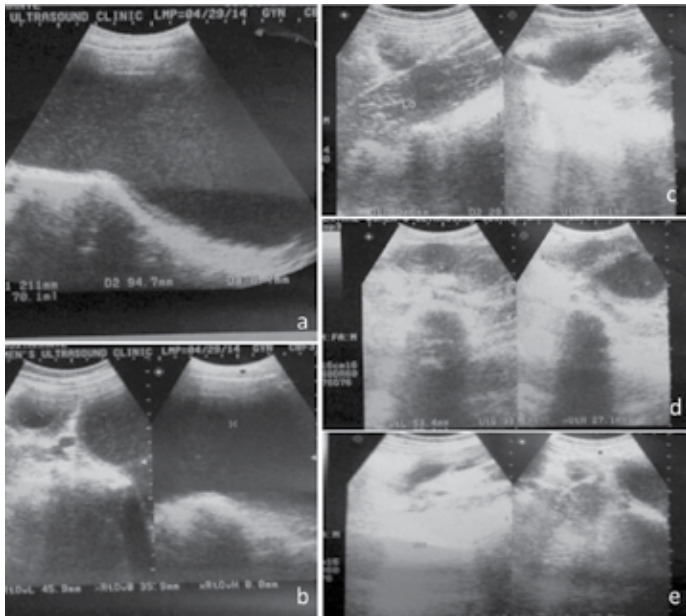


Figure 3. Case no. 2. Transabdominal and Transvaginal ultrasound prior to the operation. **A.** A thick walled cystic mass with low level echoes occupying the whole hypogastric area measuring 211 x 94.7 mm. **B,E.** Both ovaries are grossly normal. **C.** There is a tubular structure measuring 60.6 x 29.9 mm noted above the right ovary **C,D.** The Uterus is hard to delineate however on probe manipulation there is a thick walled cystic mass noted on the right iliac area measuring 51.1 x 36.9 x 35.0 mm and another homogenous mass noted on the left iliac area measuring 53.4 x 38.4 x 27.1 mm.

above the right ovary probably dilated tube, to consider right hydrosalpinx (Figure 3). Computed tomography scan of whole abdomen showed a large cystic mass in the abdominopelvic region which causing superior displacement of the uterus, to consider hematocolpos. The uterus appears to have two endometrial cavities suggestive of uterine didelphys. The adjacent ovaries were normal. The right fallopian tube was filled with fluid and dilated, suggestive of hydrosalpinx. The right kidney was not demonstrated while the left kidney was enlarged with mild left ureteropelvic ectasia (Figure 4). She was advised surgery but transferred to our service due to financial constraints.

Patient has no known co-morbidities. She was 20 year-old when she had her first sexual contact with only one sexual partner. She had her first pregnancy one year after but unfortunately, it was completely aborted. She denies use of contraceptive drugs.

On physical examination, she was conscious, coherent, not in cardiorespiratory distress, ambulatory, vital signs were stable. Abdomen was globally enlarged, soft with firm, movable, non-tender mass measures, from symphysis pubis to 1 cm above the umbilicus, 16 x 15 cm.

On examination of the genitalia, a soft bulging

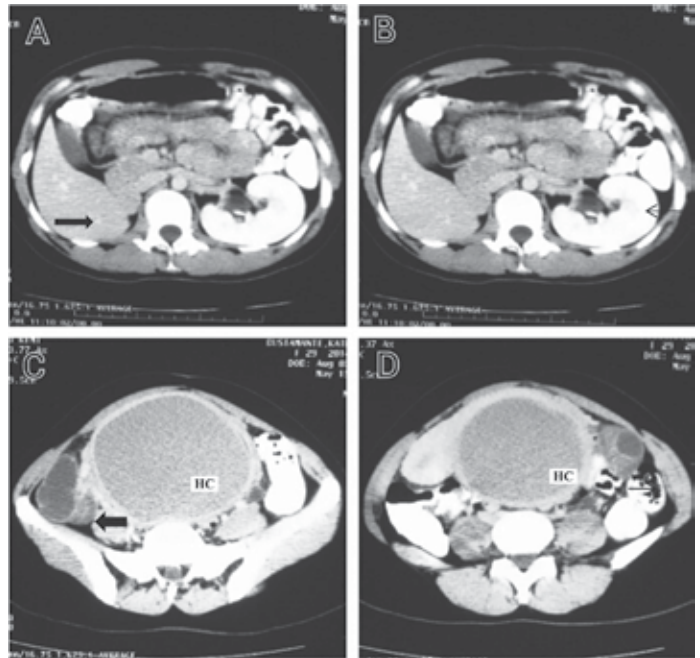


Figure 4. Case. No.2. Computed tomography scan of whole abdomen. **A,B.** Non-visualized right kidney (thick arrow) and mild left ureteropelvic ectasia (thin arrow). **C,D.** There is a large cystic mass in the abdominopelvic region measuring 19.7 x 11.7 x 9.7 cm which causing superior displacement of the uterus up to the level of L3 vertebral body. The uterus appears to have two endometrial cavity. To consider hematocolpos (HC), probable uterine didelphys, multiple ovarian cysts (thin arrow), maybe physiologic.

mass measuring 5x5 cm at right vaginal wall was noted obstructing the view of the cervix. The cervix was flushed to the vault pushed anterior and cephalad in the vaginal wall. There was a pelvoabdominal mass compatible with six months size, cystic, movable, non tender. Fullness of the cul de sac was noted on rectovaginal examination.

The initial assessment was Gravida 1 Para 0 (0010) Uterine didelphys, longitudinal vaginal septum non-communicating, hematocolpos, right hydrosalpinx, non visualized right kidney and mild left ureteropelvic ectasia, Herlyn Werner Wunderlich syndrome.

She was advised excision of longitudinal vaginal septum.

Intraoperatively, an obstructed hemivagina was identified with a longitudinal vaginal septum (Figure 5). An excised longitudinal vaginal septum measured 3 x 4 cm and was sent for histopathologic examination. Approximately 1500ml of chocolate colored fluid was drained (Figure 5). Right and left cervixes were palpable.

Post-operative period was uneventful. Patient followed-up ten days after the surgery with repeat transvaginal ultrasound showed Uterus didelphys, proliferative endometriums, normal ovaries, to consider right hydrosalpinx (Figure 6). On speculum examination, the right vaginal opening remained patent (Figure 7).

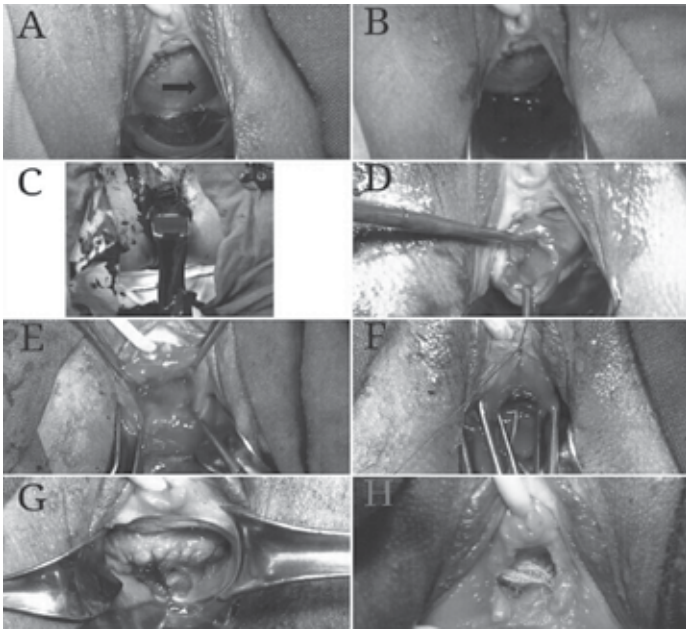


Figure 5. Case no. 2. **A.** An obstructed hemivagina with a longitudinal vaginal septum (black arrow). **B, D, E, F, G.** Longitudinal vaginal septectomy was performed measuring 3 x 4 cm and repair by continuous interlocking. **C.** Chocolate colored fluid was drained. **H.** Vaseline gauze was inserted to maintain patency of the right vaginal canal.

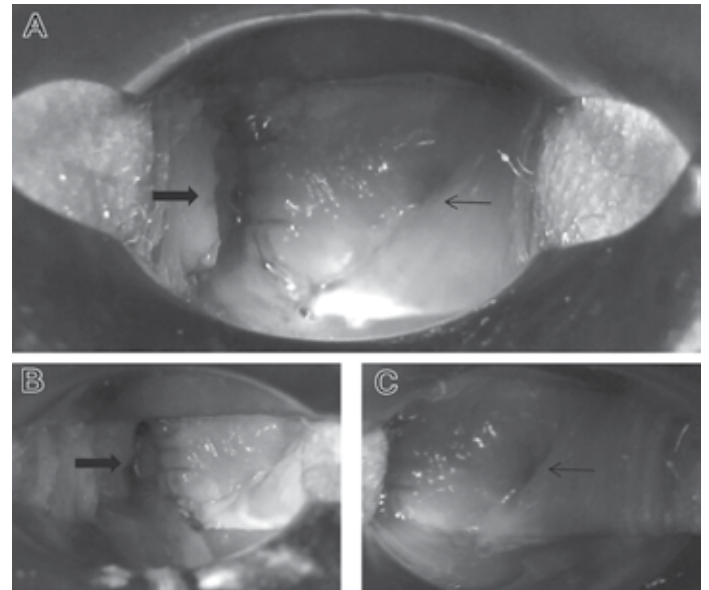


Figure 7. Case no.2. Ten days after the surgery. Right (thick arrow) and Left Vaginal opening (thin arrow).

DISCUSSION

Developmental anomalies of the müllerian duct system represent some of the most fascinating disorders that obstetricians and gynecologists encounter. The müllerian ducts are the primordial anlage of the female reproductive tract. When an interruption or dysregulation occurs in any of the dynamic processes of differentiation, migration, fusion, and canalization, a wide spectrum of müllerian duct anomalies can result. Didelphys uterus arises when midline fusion of the müllerian ducts is arrested, either completely or incompletely¹⁰. The incidence of uterus didelphys related to HWW syndrome is approximately 1 in 2,000 to 1 in 28,000 and it is accompanied by unilateral renal agenesis in 43 % of cases.⁴

The triad of uterus didelphys, blind hemivagina and ipsilateral renal agenesis results from a unilateral hypodevelopmental anomaly of the mesonephric and paramesonephric structures.⁷ In most cases, the etiologic factors are unknown, but may include an insult during the first trimester or polygenic/multifactorial inheritance.² Familial occurrences are reported, though definitive genetic associations have not been identified¹⁰.

In our patients who presented with multiple congenital anomalies, obstructed unilateral hemivagina with uterus didelphys associated with ipsilateral renal agenesis, these findings were compatible with Herlyn Werner Wunderlich Syndrome, a rare but well-established anomaly. There were no mentioned illnesses, medications taken aside from prenatal medications or any insult during the first trimester of the pregnancy of their mother.

Jiali Tong, et al, 2013, published a study of Clinical characteristics of 70 patients with Herlyn Werner

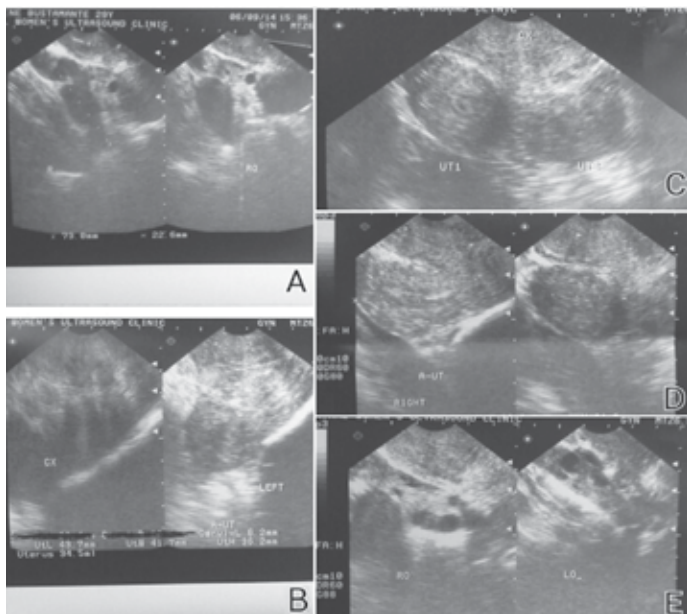


Figure 6. Case no. 2. Transvaginal ultrasound ten days after the surgery. **A.** Previously seen tubular structure with incomplete septations noted lateral to the right ovary measures 73.0 x 22.6 mm, to consider Right hydrosalpinx. **B.** There are two endocervical canals seen. Cul de sac unremarkable. **C.** Uterus Didelphys. Two normal sized anteverted uterus with homogenous pattern. **D.** Proliferative Endometrium, both endometrium are intact with isoechoic shadow. **E.** Both ovaries are grossly normal with small follicles.

Wunderlich Syndrome, to confirm different clinical presentations, among women with HWW syndrome by comparing the clinical characteristics and anatomic variations of patients. It was reported that there were significant differences between patients with complete obstruction and those with incomplete obstruction in terms of mean age at diagnosis (13.00 + 2.05 years vs 24.74 +7.73 years; $P < 0.05$) and mean age at onset of symptoms (12.86+1.84 years vs 20.68 +7.43 years; $P < 0.05$). Median time between menarche and symptom onset was 1 year. The primary gynecologic complaint is dysmenorrhea. Intermittent mucopurulent discharge (40%) and metromenorrhagia (25.7%) are also reported⁸.

Sometimes after menarche, the retention of menstrual blood in the obstructed hemivagina leads to the formation of hematocolpos, which is clinically detected as a pelvic mass⁶ as in the second case presented.

In our patients, the first case with early onset and less severe symptoms, manifested only with severe dysmenorrhea that is present since menarche and is worsening over the past months in spite of no other associated symptoms. On the other hand, the second case, a 29 year-old Gravida 1 Para 0 (0010), with late onset of symptoms and was asymptomatic for four years, exhibited cyclic hypogastric pain and gradually enlarging right pelvic mass associated with difficulty in urination and bowel movement probably due to hematocolpos which gets worse with each menstrual period. Rarely, this may lead to intestinal obstruction or hydronephrosis by pressure on contiguous structures.

In the presence of a menstrual outflow obstruction, hematometra, hematosalpinx, and endometriosis were the main reasons for cyclic pelvic pain and metromenorrhagia⁸.

The potential acute complications of this syndrome include pyohematocolpos, pyosalpinx or pelvipерitonitis, while long-term complications are endometriosis, pelvic adhesions and increased risk of abortion or infertility.⁴ The fertility of women with HWW syndrome was good. Only 6 women were diagnosed with primary infertility postoperatively, indicating that there is no increased incidence of primary infertility among women with HWW syndrome. There were no pathologic pregnancies or pregnancy complications, so it could be considered that primary infertility among women with HWW syndrome may be caused by factors such as endometriosis and pelvic abscesses rather than by uterus didelphys⁸.

The diagnosis may be difficult due to the rarity of this syndrome and most of the time pelvic mass and dysmenorrhea are the only presenting sign and symptom of HWW syndrome patients in the clinical settings. The said manifestations are very general or are not pathognomonic to the said syndrome, which can be misdiagnosed with ovarian new growth. Henceforth, it cannot be omitted

that there is a chance that one might fall in the late diagnosis or even misdiagnosis of the disease like what happened in the second case presented in this report. Ergo, to avoid such shortcomings, imaging techniques are strongly suggested to be done. Likewise physical examination and high suspicion are indispensable. Diagnostic methods include hysterosalpingography, transvaginal ultrasound, computed tomography, magnetic resonance imaging, laparoscopy, and hysteroscopy. Hysteroscopy can detect intrauterine adhesions and communication between the duplicated endometrial cavities. Magnetic resonance imaging has 96–100% accuracy in classifying uterine anomalies while transvaginal ultrasound has 85–92%, and hysterosalpingography has 6–55%.⁹ Magnetic resonance imaging is the most effective method and helps to prevent unnecessary surgery. Because of the high cost, ultrasonography and computed tomography are commonly used.³ Embryologically the reproductive system develops in close relationship with the urinary system – paramesonephric and mesonephric ducts, respectively.⁷ Therefore, it is important to examine the urogenital system when genital anomaly is identified and vice versa.³

In order to avoid the associated morbidity of delayed management, surgical intervention should be considered as first line therapy.⁹ Full resection of the vaginal septum is the main treatment for patients with HWW syndrome⁸ and drainage of the hematometocolpos.⁴

Zurawin et al., 2004, reported that laparoscopy should now be considered the gold standard for the complete evaluation of congenital anomalies of the female reproductive tract. MRI picked up only 53% of the Mullerian anomalies that were found at the time of laparoscopy. Ultrasonography, CT scan, and MRI are the initial steps for its diagnosis; however, laparoscopy is a crucial tool for confirmation of the diagnosis.⁹

In our patients, together were managed with full resection of the vaginal septum as well as drainage of the hematometocolpos, repaired by continuous interlocking. Vaseline gauze was also inserted to maintain patency of the vaginal canal.

SUMMARY

Clinicians must be aware and well-informed of this unusual obstructive malformation of the female genital tract, the Herlyn Werner Wunderlich syndrome, for a number of reasons: (a) to diagnose early and accurately, (b) to prevent complications, (c) to decrease morbidity and unnecessary surgical procedure, and (d) to preserve future fertility. Worthy to mention, its rarity and variable clinical features may contribute to a diagnostic delay for years after menarche. A high index of suspicion is required when

urogenital anomaly is identified and thus examination of the urogenital system is important to consider.

The exact cause, pathogenesis, and embryologic origin of HWW syndrome are unclear and remain a subject of discussion. The potential acute complications of this syndrome include pyohematocolpos, pyosalpinx or pelviperitonitis, while long-term complications are endometriosis, pelvic adhesions and increased risk of abortion or infertility. Nevertheless, in HWW patients with no other associated significant conditions, aside from the fact that their fertility is good, there are no pathologic pregnancies or pregnancy complications noted. Thus

it could be considered that primary infertility among women with HWW syndrome is caused by factors such as endometriosis and pelvic abscesses rather than by uterus didelphys.

Magnetic resonance imaging is the method of choice for diagnosing HWW. In the real setting however, because of its high cost, ultrasonography and computed tomography are commonly used. Moreover, laparoscopy is a crucial tool for confirmation of the diagnosis.

Full resection of the vaginal septum with drainage of the hematocolpos is the main treatment for patients with HWW syndrome.

REFERENCES

1. Ana Cristina Aveiro, Victor Miranda, António Jorge Cabral, et al. Herlyn–Werner–Wunderlich syndrome: a rare cause of pelvic pain in adolescent girls. *BMJ case report* 2011
2. IlkerInanArikan, MugeHarma, Mehmet Ibrahim Harma, et al. Herlyn–Werner–Wunderlich syndrome (uterus didelphys, blind hemivagina, and ipsilateral renal agenesis) - a case report. *J Turk Ger Gynecol Assoc.* 2010 Jun 1;11(2):107-9.
3. Jin-HwaJeong,MD, Youn-Jung Kim, MD, Chun – Ho Chang, MD, et al. A case Herlyn–Werner–Wunderlich syndrome with recurrent hemetopyometra. *Journal of Women’s Medicine* Vol.2.No.2 June 2009
4. Riccardo Del Vescovo, Sofia Battisti, Valerio Di Paola, et al. Herlyn–werner–wunderlich syndrome: MRI findings, radiological guide (two cases and literature review), and differential diagnosis.*BMC Medical Imaging* 9 March 2012, 12:4
5. DoronKabiri MD, YaaraArzy MD and Yael Hants MD. Herlyn–Werner–Wunderlich Syndrome: Uterus Didelphys and Obstructed Hemivagina with Unilateral Renal Agenesis. *IMAJ.* Vol 15. January 2013
6. Isidto Ma. Corazon A., MD and Nailani Z. Tan, MD, FPOGS. Herlyn–Werner–Wunderlich Syndrome: Report of Two Cases. *Philippine Journal of Obstetrics and Gynecology* Vol.36.No.3, July - September 2012
7. Cristina Vilhena, José L. Metello, Ester Casal, et al. Herlyn–Werner–Wunderlich syndrome: 3D ultrasonographic diagnosis in premenarche.*Middle East Fertility Society Journal.* 8 January 2014
8. Jiali Tong, Lan Zhu, Jinghe Lang. Clinical characteristics of 70 patients with Herlyn–Werner–Wundelich Syndrome. *International Journal of Gynecology and Obstetrics.* Volume 121, Issue 2, May 2013, Pages 173-175
9. Kamal M. Zahran., DaaEldeen M. Abd El Aal, Moustafa H.M. Othman, et al. Uterus didelphys with impeforatehemivagina and ipsilateral renal agenesis complicated by hematocolpos , hematometra and hematosalpinx.The challenge of intact hymen. *Middle East Fertility Society Journal.* Volume 16, Issue 4, December 2011, Pages 291-294
10. Lawrence S Amesse, MD, PhD, MMM, Teresa Pfaff-Amesse, MD. Mullerian Duct Anomalies. *Medscape;* Mar 5, 2012