Pregnancy in Herlyn-Werner-Wunderlich syndrome: A case report and review of literature*

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ABSTRACT

Herlyn-Werner-Wunderlich Syndrome (HWWS) is a triad of uterus didelphys, unilateral obstructed hemivagina, and ipsilateral renal agenesis.

In the review of the locally published literature, there have been seven HWWS cases reported, none of whom were pregnant.

A 24-year-old was diagnosed with Herlyn-Werner-Wunderlich Syndrome during caesarean section of a term pregnancy, occupying the right hemiuterus with obstructed hemivagina. Ultrasound showed uterus didelphys with communicating endometrial cavities. MRI revealed uterus didelphys, two cervices and an obstructed right hemivagina. The patient refused excision of vaginal septum. Two years later, she delivered spontaneously to a live fetus, occupying the hemiuterus with the unobstructed hemivagina.

In pregnant women with HHWS, who did not undergo prior surgical intervention, the mode of delivery depends on the side of pregnancy. If it is located on the obstructed hemivagina, caesarean section is inevitable. If it is on the unobstructed side, there is hope for vaginal delivery.

Keywords: Mullerian duct anomaly, uterine didelphys, obstructed hemivagina, renal agenesis, Herlyn-Werner-Wunderlich Syndrome

INTRODUCTION

The association of uterus didelphys, obstructed hemivagina, and ipsilateral renal anomaly is well recognized. The triad has been described as Herlyn-Werner-Wunderlich Syndrome (HWWS).

It is difficult to estimate the exact incidence of obstructed Mullerian anomalies globally but is reported to be around 0.1 to 3.8 percent.[1] In our review of the locally published literature, seven cases were reported[2,3,4,5]. None of these cases described were pregnant (Table 1).

Treatment of HWWS involves excision of the obstructing lateral vaginal septum which should be undertaken if associated with obstruction, dyspareunia or infertility. Successful pregnancies after resection have been reported.[6]

This case report describes the course of two successive spontaneous term pregnancies involving the two horns of the didelphys even without the benefit of surgical excision of the vaginal septum.

CASE

T.A.M., a 24-year-old primigravid on her 40 weeks and one day AOG and not yet in labor, was admitted because of an ultrasound finding of oligohydramnios.

She had her menarche at the age of 14. Subsequent menses were regular, lasting for five days, using 3-4 pads per day, with mild dysmenorrhea on the first day of bleeding. Her first coitus was at the age of 17. She had eight years of primary infertility without consulting a physician.

Her prenatal check-up started on her seventh month of pregnancy, with unremarkable physical and laboratory findings, including an ultrasound determination. She was maintained on multivitamins and ferrous sulfate. At 40 weeks and one day AOG a non-stress test was done which was reactive, but biophysical profile showed oligohydramnios with an amniotic fluid index of 1.75 cm, and was thus subsequently admitted.

On admission she was conscious, coherent and not in any kind of cardio-respiratory distress. Vital signs were stable. She had pink palpebral conjunctivae and anicteric sclera. The abdomen was globular with a fundic height of 30 cm and fetal heart tone of 140 bpm, and no uterine contractions noted. Internal examination revealed a closed, long, uneffaced cervix without vaginal bleeding. Admitting diagnosis was G1P0, pregnancy uterine 40 1/7 weeks AOG, cephalic, not in labor; Oligohydramnios.

Cervical priming with intravaginal dinoprostone was started, followed by labor induction with oxytocin drip. After eight hours of regular uterine contractions, internal

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Table 1. Summary of Clinical Features of Herlyn-Werner-Wunderlich Syndrome in Local Literature

Author's Year	**Cruz Oblepias (2009)**	**Cruz Oblepias (2009)**	**Cruz Oblepias (2009)**	**Atencio (2009)**	**Dy-Fernandez, Tan (2010**	**Isidto, Tan (2012)**	**Isidto, Tan (2012)**	**Sucayan-Sta. Ana, Gorgonio (2014) *unpublished***
Age of Diagnosis	19	24	21	12	14	12	24	24
Symptoms	dysmenorrhea, foul-smelling discharge	right lower quadrant pain, foul-smelling discharge	foul-smelling discharge	dysmenorrhea	dysmenorrhea, constipation	right lower quadrant pain	dysmenorrhea, dyspareunia	none
Diagnostics								
Ultrasound	hematocolpos Hematometra, no right kidney	hematocolpos, right tubo-ovarian complex hematosalpinx vs pyosalpix, no right kidney	hematocolpos, Hematometra, no left kidney	uterine didelphys hematocolpos	hematometra, no right kidney	hematocolpos, Hematometra, no right kidney	hematocolpos, cystic mass left iliac area, uterus didelphys	uterine didelphys, no right kidney
MRI (CT Scan)	not done	not done	not done	(MRI) uterus didelphys, no right kidney	(MRI) uterus didelphys, right hematosalpinx, right renal agenesis	(CT Scan) Right lliac cystic mass no right kidney	not done	(MRI) uterine didelphys, 2 cervices, right blind hemivagina
IVP	no right kidney	not done	not done	not done		not done	no left kidney	not done
Laparoscopy ± Hysteroscopy or Vaginoscopy	laparoscopy	not done	not done	vaginoscopy	vaginoscopy hysteroscopy laparoscopy	not done	not done	not done
Laparotomy	not done	not done	not done	not done	not done	not done	not done	uterus didelphys, no endometriosis, no pelvic adhesions
Laterality of Vaginal Obstruction	right	right	left	not specified	right	right	left	right
Presence of Communication	uterine communication	vaginal communication	uterine communication	none	none	none	vagina communication	uterine communication
Treatment	excision of vaginal septum	excision of vaginal septum	excision of vaginal septum	excision of vaginal septum	marsupialization of blind hemivagina	marsupialization of blind hemivagina	excision of vaginal septum	none
Reproductive Outcome	lost to follow up	lost to follow up	not mentioned	not mentioned	not mentioned	not mentioned	not mentioned	G_1-Term, CS G_2-Term NSD

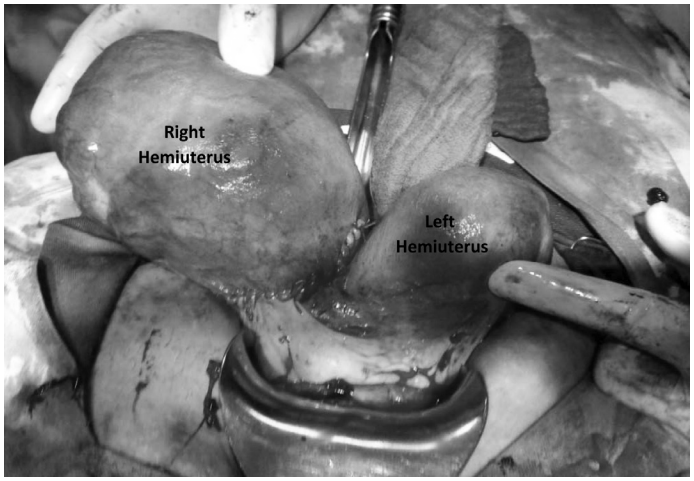

Figure 1. Anterior view of the didelphys uterus, with right gravid uterus showing repaired low segment transverse incision.

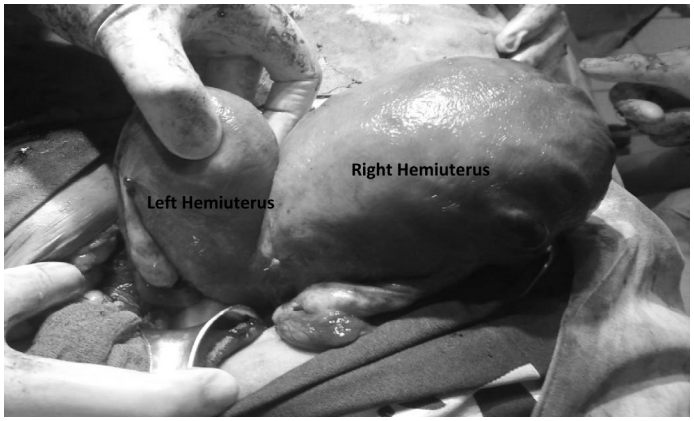

Figure 2. Posterior view of the didelphys uterus showing grossly normal bilateral adnexae

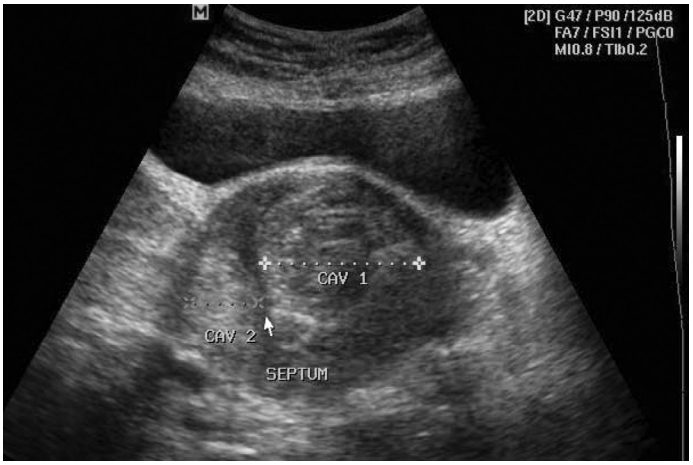

Figure 3. Transvaginal Ultrasound in transverse view showing the two hemiuteriwith a midline septum

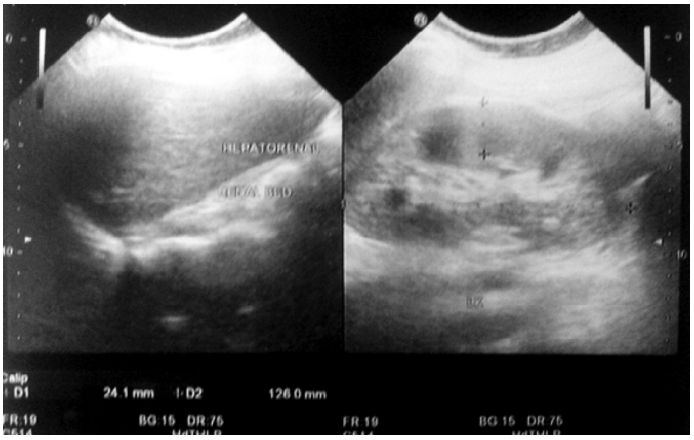

Figure 4. Tranabdominal Ultrasound showing the absence of the right kidney

examination showed no progress, with cervical dilatation admitting only a fingertip and beginning effacement. Induction of labor was temporarily discontinued and resumed the following day. After another eight hours of regular uterine contractions, internal examination revealed the cervix to be one cm dilated, 50% effaced, cephalic station -1 and with intact membrane. At that point she was then proposed for emergency caesarean section for oligohydramnios with failure of induction of labor.

She underwent a primary low segment transverse caesarean section under subarachnoid block. She delivered to a live term baby girl in cephalic presentation, with an Apgar Score of 8 and 9 and birth weight of 2,700 gm, birth length of 51 cm. It was at this point that she was found to have two uterine horns with a right gravid hemiuterus and a small left hemiuterus (Figure 1). Both fallopian tubes and ovaries were grossly normal (Figure 2).

On the third post-operative day, another pelvic examination was performed. On speculum examination, only one cervix was seen. What was previously noted as the right vaginal sidewall was likely a longitudinal vaginal septum separating the blind hemivagina from the unobstructed hemivagina. There was no distention of the lateral vaginal septum nor was a paravaginal mass noted.

A 2D ultrasound was then requested. Transvaginal ultrasound report was as follows: The right hemiuterus measures 13.31 cm x 4.52 cm with dilated uterine cavity containing tissue debris of mixed echoes. Cervical canal is not prominent. The left hemiuterus measures 6.95 cm x 4.69 cm with cervical length of 3.63 cm. There is a midline echogenic tissue dividing the 2 horns of the uterus (Figure 3). A communication between the endometrium of the two horns of the uterus is noted at the lower portion of the didelphys.

The transabdominal ultrasound report was as follows: The separation of the two horns of the didelphys is visualized. On further evaluation of the retroperitoneum, right kidney is not visualized (Figure 4), while the left kidney is present, measuring 10.53 cm x 8.34 cm x 6.46 cm.

The patient was sent home on the sixth post-operative day. Prior to discharge, internal examination showed neither lateral vaginal wall distention nor vaginal mass. She was given home medications, advised to come

back for further work-up with plan of possible excision of the vaginal septum.

The patient was lost to follow-up until two years later when she sought consult at the Emergency Room for premature rupture of membranes of her second pregnancy at 35 weeks AOG. She claimed to have had regular prenatal check-up at the local health center with regular intake of multivitamins and ferrous sulfate.

Pertinent physical examination findings showed a globularly enlarged abdomen with a fundic height of 30 cm and FHT at 130 bpm. On speculum exam, clear watery discharge was noted in the vaginal vault, with a seemingly closed cervix. Internal examination revealed the cervix admitting the tip of finger, 50% effaced, cephalic, with watery vaginal discharge and no bleeding.

The admitting diagnosis was G2P1 (1001), pregnancy uterine 35 weeks age of gestation, cephalic, in beginning labor, premature rupture of membranes; previous low segment transverse cesarean section (right hemiuterus) for oligohydramnios and failed induction of labor; Uterine didelphys; Obstructed hemivagina with ipsilateral renal agenesis.

The plan was to deliver vaginally since this time the pregnancy was on the left hemiuterus with no previous uterine scar and unobstructed hemivagina. Induction of labor was started with oxytocin drip. After 16 hours of labor, she delivered spontaneously to a live, term baby girl in cephalic presentation, Apgar Score of 8 and 9; birth weight 2,700g; and birth length of 49 cm.

On follow up, Magnetic Resonance Imaging (MRI) was done. The sagittal section revealed uterine didelphys with two cervices. The right hemiuterus ended into a blind pouch,while the left hemiuterus showed no obstruction (Figure 5).

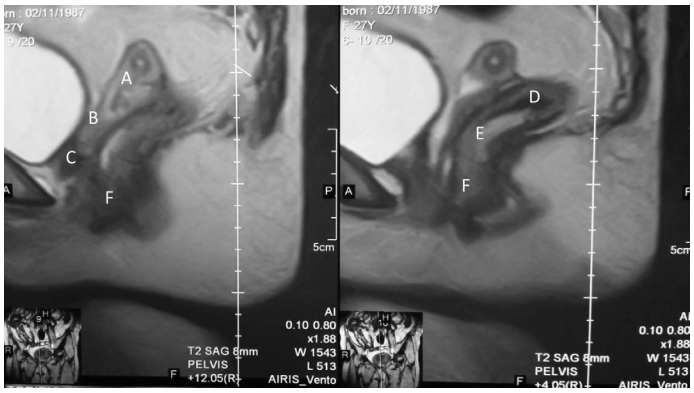

Figure 5. MRI Scan in Sagittal View (from right to left): Showing uterine didelphys. A – right hemiuterus; B – right cervix; C – blind pouch; D – left hemiuterus; E – left cervix; F – left vaginal canal

DISCUSSION

In 1979, Buttram and Gibbons proposed a classification system for Mullerian duct anomalies according to the type and degree of failure of normal development of the female genital tract. This was later modified by the American Society for Reproductive Medicine in 1988[6] (Table 2).[7] This case perfectly fits the Herlyn-Werner-Wunderlich Syndrome (Figure 6).

HWWS represents a failure of both lateral fusion of the Mullerian ducts and their vertical fusion with the urogenital sinus that eventually forms the distal vagina.[6] In HWWS, there is a complete failure of fusion of both Mullerian ducts at the cranial portion giving rise to uterine didelphys. Incomplete resorption of the septum at the caudal portion of the urogenital sinus resultsin an obstructed hemivagina. Since the urinary and genital systems both originate from the same fold of mesoderm arising from the dorsal body wall, both depend on normal development of the mesonephric system. Therefore, abnormal differentiation of the mesonephric (Wolfian) and paramesonephric (Mullerian) ducts may also be associated with anomalies of the renal organs, of which renal agenesis is the most common associated anomaly.[8]

The diagnosis of this syndrome is usually delayed. After menarche, patients have regular menstrual flow

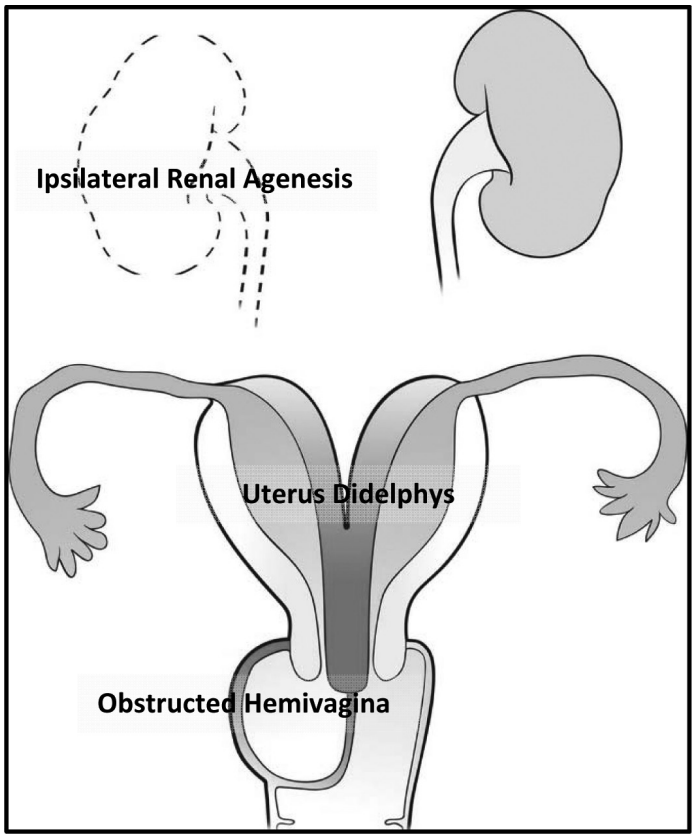

Figure 6. Diagram of Herlyn-Werner-Wunderlich Syndrome taken from *www.jhrsonline.org*

Table 2. Classification of Mullerian duct anomalies according to the American Society for Reproductive Medicine

Class I	*uterine hypoplasia or agenesis*
Class II	*unicornuate uterus:* A banana - shaped uterus with a single fallopian tube. A rudimentary horn (communicating or non-communicating) may be present
Class III	*uterus didelphys:* Two complete uteruses, each with its own cervix. A sagittal vaginal septum is seen in the majority of cases
Class IV	*bicornuate uterus:* Two uterine cavities with one cervix. MRI shows widely separated uterine horns with an intercornual distance of >4 cm and concavity of the fundal contour or an external fundal cleft of >1 cm in depth.
Class V	*septate uterus:* A fibrous septum is seen that appear hypointense on T2W images. While the muscular septum appears intermediate in intensity. MRI criteria includes a convex or flat external fundal contour or external fundal cleft of <1 cm in depth.
Class VI	*arcuate uterus:* it is a normal variant and is characterized by an external convex contour of the fundus with fundal endometrial indentation.
Class VII	*diethylbestrol-induced:* exposure to this synthetic estrogen antenatally can result in a T-shaped, hypoplastic and constricted uterus.

from the unobstructed vagina, which eludes suspicion. After some time, however, there is retention of menstrual blood in the obstructed hemivagina leading to progressive and recurrent pelvic painandto the development of hematometra and/or hematocolpos. Other long-term complications include endometriosis and adhesions from retrograde menstruation.[6]

The women reported in the locally published literature presented with all or a combination of symptoms of progressive dysmenorrhea, pelvic pain, foul-smelling discharge, vaginal mass, constipation,or dyspareunia. Three patients presented with hematocolpos, one with hematometra, and three with hematometrocolpos.[2,3,4,5] None of these signs and symptoms were present in this patient.

Mullerian anomalies may also be discovered only during evaluation for infertility problems, and reports of successful pregnancies have been reported only after resection of the obstructing vaginal septum. Pregnancy is usually associated with obstetrical complications such as recurrent pregnancy loss, preterm labor, abnormal fetal presentation and prematurity due to uterine anomalies. Although it took her eight years to get pregnant, none of the other complications were present in this patient.

Due to the absence of any of these classic symptoms, the anomalies in this patient escaped clinical recognition Even without the benefit of surgical excision of the lateral vaginal septum, there was spontaneous conception. If it were not for the caesarean section, the syndrome would have remained undetected.

In the majority of pregnancies in women with HWWS, implantation occurs at the uterine cavity of the unobstructed hemivagina, as in this patient's second pregnancy. Peculiarly, her first pregnancy was on the same side as the obstructed hemivagina. Fertilization may have occurred through either of these two mechanisms: First, a communication between the two hemivaginas or two hemiuteri may exist, as has been reported in a few cases in the literature.[2,3] The sperms could have travelled from one hemivagina to the other or from one hemiuterus to the other. Second, there may have been transperitoneal transmigration of sperm, such that sperms deposited in the left hemivagina exited from the ipsilateral fallopian tube and fertilized an ovum that implanted in the right uterine cavity.

The interconnection between the two hemiuteri as seen in the ultrasound of this patient has given this patient countless benefits. It has allowed the lateral flow of menstrual debris, preventing the retention and pooling of blood on the obstructed side and saved her from potential hematometrocolpos, pain, vaginal mass, as well as from other complications arising from retrograde menstruation. A slightly similar case reported by Johnston-MacAnanny et al. was that of a 19-year-old patient on whom a communication between the two uterine horns was identified on 3D sonography, had no evidence of pelvic or vaginal mass on bimanual examination. She only presented with symptoms of constant thick brown vaginal discharge.[9]

Interconnection between the two sides, however, is not full-proof guarantee of absence of symptoms. Two patients in the local literature were reported to have had uterine communication,[4] and two others had vaginal communication[2,4], all of whom were symptomatic.

This patient's first pregnancy was on the obstructed side. Ordinarily, lochial debris and blood is expected to gravitate at the obstructed hemivagina producing distention of the vaginal wall. Pelvic examination on this patient on her third post-operative day, however, did not

reveal any bulging, distention, or mass at the lateral vaginal septum. The interconnection between the two hemiuteri has allowed the lateral flow of the lochial debris from the postpartum hemiuterus to the other, producing partial spontaneous decompression of the affected hemiuterus and hemivagina.

In the diagnosis of Mullerian anomalies, a high index of suspicion based on clinical presentation with the aid of imaging modalities is the key. In the local studies, several diagnostic modalities were used, namely—ultrasound, MRI, intravenous pyelography, vaginoscopy, laparoscopy, and hysteroscopy.

Ultrasound is a non-invasive, readily available tool. Due to its low cost, ultrasonography is the easiest and preferred investigation tool. It offers helpful information of both internal and external uterine contour while at the same time allowing the evaluation of the kidneys.[6] In the local report, most of the cases were diagnosed by ultrasound examination.

MRI is the ideal imaging modality for documenting uterine anomalies. Due to its multiplanar and tissue characterization capabilities, it correctly differentiates the type of Mullerian anomaly in 96% of cases. Distance from the perineum to the obstructed vagina can be easily calculated as when necessary. It also assists in the evaluation of the urinary tract, which may show developmental abnormalities in 30% of women with Mullerian anomalies.[4]

Hysteroscopy and laparoscopy can be employed to help with the diagnosis as well as potential treatments. In the report of Dy-Fernandez and Tan (2010), laparoscopy was used to diagnose uterus didelphys while hysteroscopy was used to visualize two cervices and to resect the vaginal septum.[3] Though diagnostic laparoscopy is more expensive and invasive, it may aid in ruling out other gynecologic pathology and in treating endometriosis and adhesions.[1]

The management is straightforward—relief of symptoms and preservation of future reproductive capabilities by excision of the obstructing vaginal septum.[4] Resection, however, is undertaken only if associated with obstruction, dyspareunia or infertility. Unless indicated, hemihysterectomy with or without salpingo-oophorectomy is avoided to provide the best chances for future reproductive plans.[6] In the review of the local literature, excision was done to relieve the patients of their symptoms.[2,3,4,5]

In Müllerian malformations reproductive challenges are typically attributed to pregnancy maintenance rather than conception. Uterine didelphys has a relatively good prognosis for achieving pregnancy. Candiani reported that out of 36 cases with HWWS, pregnancy rate is 80% and live birth rate is 77%.[10]

The importance of early recognition of Mullerian anomaliesin pregnancy is vital, not only because of the challenge of carrying the pregnancy to term, but also to appropriately plan the mode of delivery. This patient's first pregnancy was on the right horn with obstructed hemivagina, and ended up in caesarean section. If the anomaly was detected and corrected prior to her first pregnancy, caesarean section would have been avoided. Since the anomaly was not yet recognized, had she progressed to full dilatation, the fetus would have been trapped. Left undetected, it would have caused rupture of the hemivagina or hemiuterus.

For her second pregnancy, with HWWS already diagnosed, the impression was that the fetus was occupying the unobstructed left horn of the didelphys since on speculum examination amniotic fluid was noted coming out from the left cervix of hemiuterus. She was allowed to deliver vaginally since the left horn with unobstructed hemivagina had no uterine scar.

Based on this case report, a flow chart for the management of pregnant patient with HWWS is proposed. (Figure 7)

1. In a symptomatic patient who has undergone resection of vaginal septum and got pregnant, spontaneously delivery is possible.
2. In an asymptomatic patient who has not undergone resection of the vaginal septum, the mode of delivery will depend on the side where of the pregnancy:
   a. If pregnancy is on the same side as the obstructed hemivagina, a caesarean section is indicated.
   b. If the pregnancy is on the same side as the unobstructed hemivagina, trial vaginal delivery may be done.

This patient is not open to surgical excision of the obstructing vaginal septum. Her indifferent attitude towards further management may be attributed to the fact that she has no fertility problems, had no pregnancy complications, and she remains completely asymptomatic. But one important take-home advice to the patient was to have prenatal consult as soon as she gets pregnant again.

SUMMARY

A review of locally published literature highlights the uniqueness of this case. A flow chart was proposed for the management of a pregnant patient with HWWS.

Lucky for this patient, despite the potential hazards, all it takes is a minute communication between both sides not just for sperms to gain access to an ovum on the other side, but more importantly for her to be spared from gruelling symptoms and long-term complications.

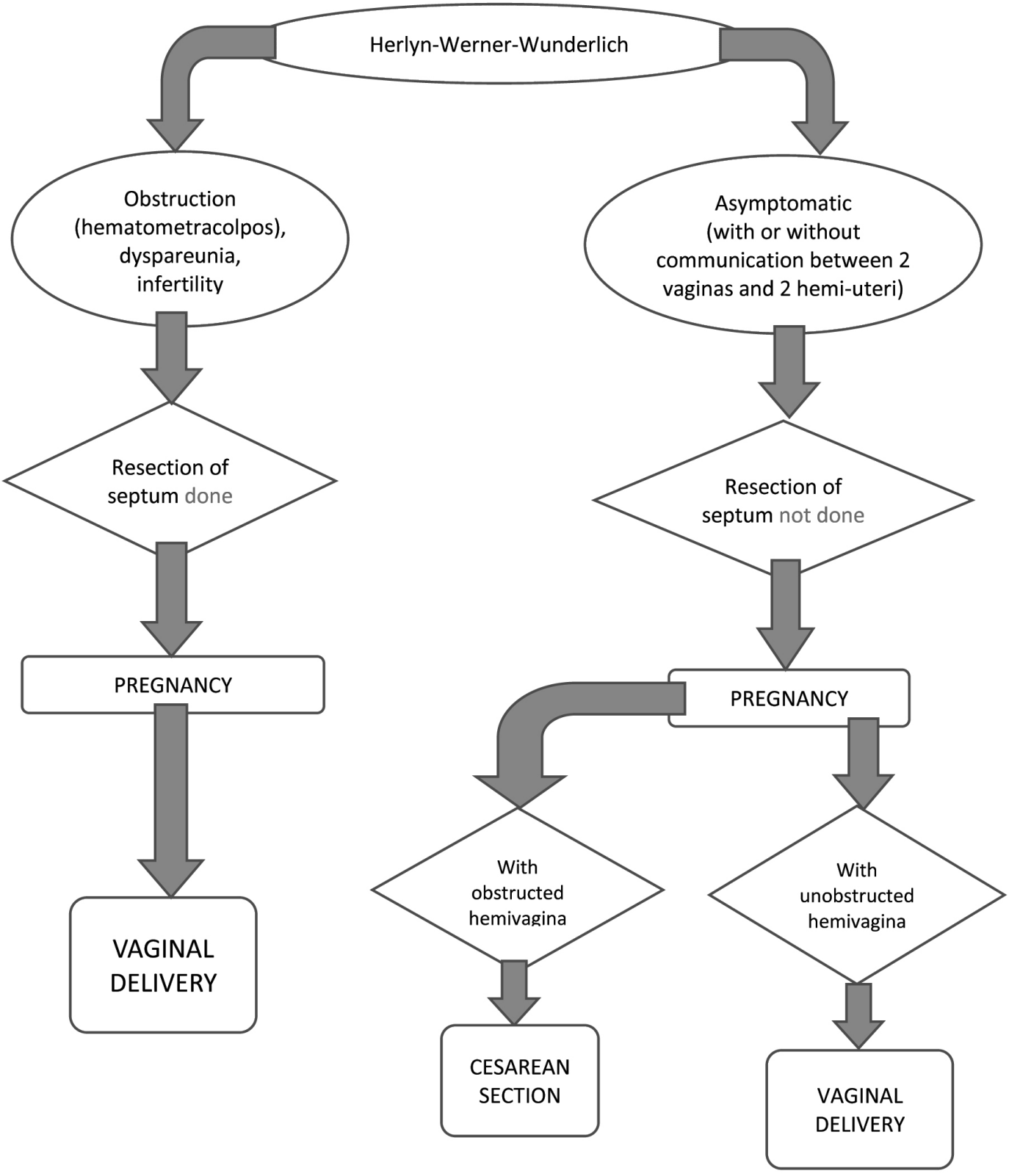

Figure 7. Proposed Flowchart in the management of patients with Herlyn-Werner-Wunderlich Syndorme

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