Case Report

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"Antipodal asymmetry" – The undiagnosed twin in the opposite uteri: A case report of dicavitary twin pregnancy in uterine didelphys

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Abstract:

Müllerian duct anomalies (MDAs) are congenital defects arising from probable teratogenic assault at 6–22 weeks of gestation.Uterine didelphys arises from complete lack of fusion of Müllerian ducts, resulting in two entirely separate hemiuteri, cervices and vaginas.The incidence of MDA is <5% and the frequency of uterine didelphys is 1 in 1000–30,000 women and twin pregnancy in uterus didelphys is only 1 in a million. This is a case of a gravida 1 para 0, with uterine didelphys and unilateral renal agenesis diagnosed of single live intrauterine pregnancy in the left half of uterine didelphys who had a spontaneous passage of meaty material from the right hemiuterus which were histopathologically consistent with degenerating products of conception, hence confirming a dicavitary twin pregnancy. Management should be wholistic encompassing preconception, prenatal, intrapartum, and postpartum period as any complications may arise at any point.

Keywords:

Abortion, normal spontaneous delivery, twin pregnancy, uterus didelphys

Introduction

Uterine didelphys is a Class III Müllerian duct anomaly (MDA) arising from complete lack of fusion of Müllerian ducts, between 10th to 17th week of intrauterine development, resulting in two entirely separate, nearly fully developed and normal appearing size hemiuteri, cervices and vaginas.[1-4] The incidence of MDA is <5% and the frequency of uterine didelphys is 1 in 1000–30,000 women. The incidence of twin pregnancy in uterus didelphys pregnancy is 1 per 1 million.[4] Only 20 cases of dicavitary twin or triplet gestation have been described in literature.[5] Hence, there is limited literature on uterine didelphys available at the present time to determine reproductive and gestational outcomes.

This is a case report on a 31 year old, gravida 1 para 0, with uterine didelphys and unilateral renal agenesis, who was initially diagnosed to have twin pregnancy in each uterine cavity retrospectively after passage of products of conception from the right hemiuteri.

Objectives

General objective

The objective of the study was to present a case of a 31 year old, gravida 1 para 0, with uterine didelphys and unilateral renal agenesis, with dicavitary twin pregnancy.

Specific objectives

1. To discuss the abnormal development of uterine didelphys
2. To identify the sequelae and complications of MDA
3. To review the appropriate management for such cases.

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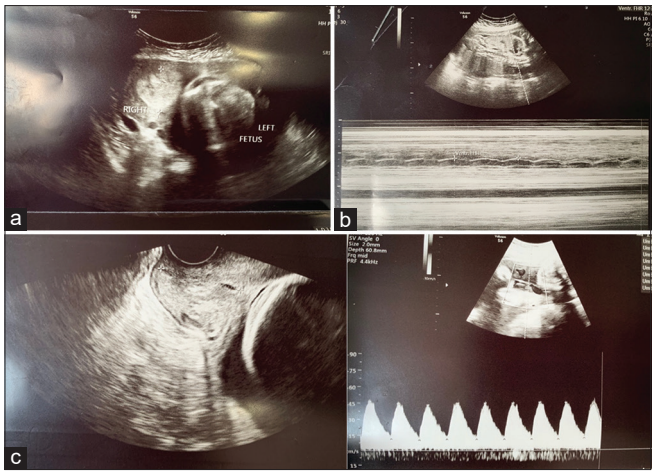
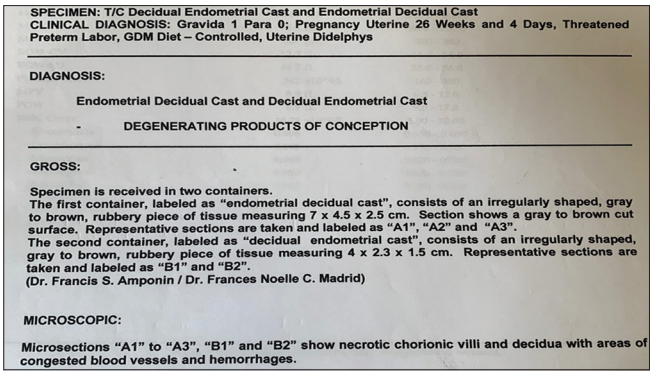


Figure 1: Ultrasonographic results: (a) September 17, 2018: Single live intrauterine pregnancy compatible with 23 weeks and 6 days age of gestation by fetal biometry, fetus in cephalic presentation. Posterior Grade I high-lying placenta. Adequate amniotic fluid volume (SVP: 5.56 cm) and estimated fetal weight (679 ± 99 grams), appropriate for gestational age. Cervical length: Right = 2.42; Left = 3.72 cm. Endometrial thickness of right hemiuteri: 3.54 cm. (b) September 21, 2018: Single live intrauterine pregnancy compatible with 24 weeks and 4 days age of gestation by fetal biometry, fetus in cephalic presentation. Left posterolateral Grade II high lying placenta. Adequate amniotic fluid volume (SVP: 5.34 cm); estimated fetal weight (686 ± 100 g), appropriate for gestational age. Cervix (left hemi uterus): Normal, cervix (right hemi uterus): (1) Endocervical canal: 3.65 cm dilated, with heterogeneous echoes suggestive of blood/clots. (2) Internal os: 2 cm dilated. (c) October 2, 2018: Single live intrauterine pregnancy compatible with 24 weeks and 2 days age of gestation by fetal biometry, fetus in cephalic presentation. Posterior Grade I high-lying placenta. Adequate amniotic fluid volume (SVP: 3.80 cm), estimated fetal weight (725 g), is below the 10th percentile for age (Doppler studies of fetal umbilical artery: Decreased end-diastolic blood flow)

Case Report

This is a case of a 31 year old, gravida 1 para 0, with uterine didelphys and unilateral renal agenesis, who has been irregularly menstruating since menarche at 3–4 months' interval and was diagnosed to have single intrauterine pregnancy compatible with 4 weeks age of gestation in the left uterus on the 3rd month of missed period.

Pregnancy was unremarkable until at 24 weeks and 4 days of gestation, the patient consulted for scanty, vaginal bleeding associated with hypogastric pain and pelvic heaviness. Speculum and internal examination revealed minimal vaginal bleeding per os with soft and closed cervices. Biometry was done revealing a single live intrauterine pregnancy in the left hemiuterus, compatible with 23 weeks and 6 days age of gestation, cephalic, Grade I high-lying placenta, and adequate amniotic fluid volume, with appropriate fetal weight (679 ± 99 grams) for age. Right hemiuterus was noted to have thickened endometrium at 3.54 cm. Cervical length assessment revealed 2.42 cm right cervix and 3.72 cm T-shaped left cervix [Figure 1]. Urinalysis revealed urinary tract infection (UTI). The patient was admitted due to threatened preterm labor for tocolysis with calcium-channel blocker (CCB) (nifedipine) and



SPECIMEN: T/C Decidual Endometrial Cast and Endometrial Decidual Cast
CLINICAL DIAGNOSIS: Gravida 1 Para 0; Pregnancy Uterine 26 Weeks and 4 Days, Threatened Preterm Labor, GDM Diet – Controlled, Uterine Didelphys

DIAGNOSIS:

Endometrial Decidual Cast and Decidual Endometrial Cast

- DEGENERATING PRODUCTS OF CONCEPTION

GROSS:

Specimen is received in two containers.
The first container, labeled as "endometrial decidual cast", consists of an irregularly shaped, gray to brown, rubbery piece of tissue measuring 7 x 4.5 x 2.5 cm. Section shows a gray to brown cut surface. Representative sections are taken and labeled as "A1", "A2" and "A3".
The second container, labeled as "decidual endometrial cast", consists of an irregularly shaped, gray to brown, rubbery piece of tissue measuring 4 x 2.3 x 1.5 cm. Representative sections are taken and labeled as "B1" and "B2".
(Dr. Francis S. Amponin / Dr. Frances Noelle C. Madrid)

MICROSCOPIC:

Microsections "A1" to "A3", "B1" and "B2" show necrotic chorionic villi and decidua with areas of congested blood vessels and hemorrhages.

Figure 2: Histopathologic examination result of specimen labeled as decidual (Twin A)

for antibiotic therapy (cefuroxime) for UTI. On the 4th hospital day, there was a note of lesser vaginal bleeding and hypogastric and perineal pain. Repeat biometry with placental localization and cervical length assessment was done for re-evaluation revealing a blood/blood-clot-filled right hemiuterus with dilated right endocervical canal to 3.65 cm and internal os to 2 cms. The left cervix appears normal with cervical length at 3.09 cm, no funneling. The patient was referred to a perinatologist who included micronized progesterone 200 mg per vagina thrice daily (TID). She was then discharged improved.

Two days after discharge, the patient noticed brownish with watery pinkish vaginal discharge consuming three moderately soaked pads associated with intermittent crampy hypogastric pain of 8/10. No consult was done. Home medications continued. Three days after her discharge date, there was a note of continuous brownish vaginal discharge now with increased hypogastric pain intensity at 10/10, radiating to the lumbosacral area, occurring every 2–5 min. This prompted consult at our emergency department where internal examination revealed a 1 cm dilated right cervix with a closed left cervix. The patient was diagnosed with threatened preterm labor and was given terbutaline 250 mcg subcutaneously and betamethasone 12 mg TIM every 24 h for 2 doses for fetal lung maturity. She was subsequently admitted for tocolysis with a beta-agonist (Isoxsuprine drip: D5W 500cc + 10 ampules Isoxsuprine). Symptoms of bleeding and uterine contractions gradually resolved allowing transition to oral tocolytics. On the 5th hospital day, there was a note of recurrence of frequent moderate to strong uterine contractions occurring every 4–6 min, lasting for 40–60 s, associated with hypogastric pain at 10/10. The patient was placed on nothing per orem and Isoxsuprine drip was resumed which prompted no relief of symptoms. This was then followed by vaginal bleeding and passage of meaty material from the introitus. Internal examination was done revealing closed left cervix and 1 cm dilated right cervix. A meaty

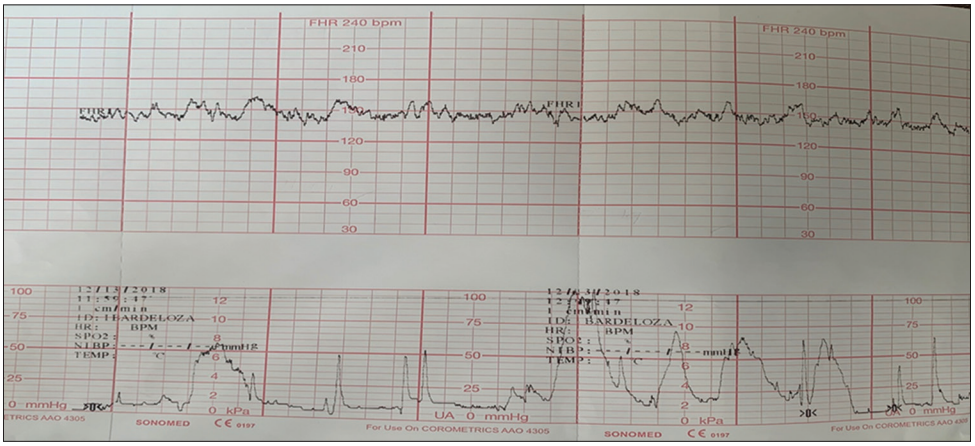


Figure 3: Baseline cardiotocography tracing during labor

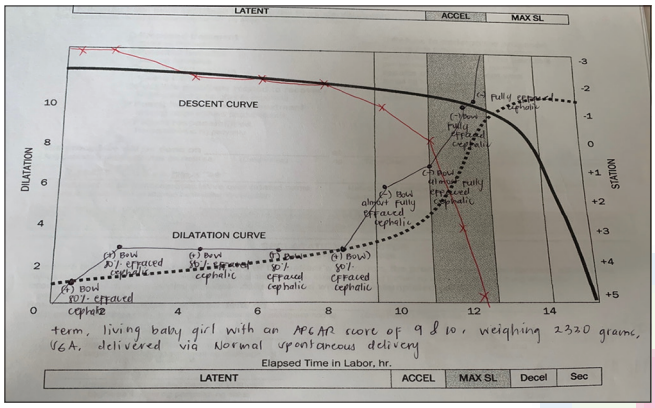
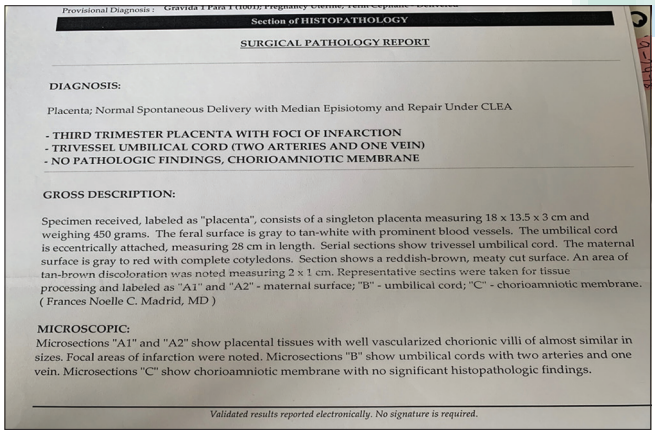


Figure 4: Labor progress form


Section of HISTOPATHOLOGY

SURGICAL PATHOLOGY REPORT

DIAGNOSIS:

Placenta; Normal Spontaneous Delivery with Median Episiotomy and Repair Under CLEA

- THIRD TRIMESTER PLACENTA WITH FOCI OF INFARCTION
- TRIVESSEL UMBILICAL CORD (TWO ARTERIES AND ONE VEIN)
- NO PATHOLOGIC FINDINGS, CHORIOAMNIOTIC MEMBRANE

GROSS DESCRIPTION:

Specimen received, labeled as "placenta", consists of a singleton placenta measuring 18 x 13.5 x 3 cm and weighing 450 grams. The feral surface is gray to tan-white with prominent blood vessels. The umbilical cord is eccentrically attached, measuring 28 cm in length. Serial sections show trivessel umbilical cord. The maternal surface is gray to red with complete cotyledons. Section shows a reddish-brown, meaty cut surface. An area of tan-brown discoloration was noted measuring 2 x 1 cm. Representative sectins were taken for tissue processing and labeled as "A1" and "A2" - maternal surface; "B" - umbilical cord; "C" - chorioamniotic membrane. (Frances Noelle C. Madrid, MD)

MICROSCOPIC:

Microsections "A1" and "A2" show placental tissues with well vascularized chorionic villi of almost similar in sizes. Focal areas of infarction were noted. Microsections "B" show umbilical cords with two arteries and one vein. Microsections "C" show chorioamniotic membrane with no significant histopathologic findings.

Validated results reported electronically. No signature is required.

Figure 5: Histopathologic examination result of specimen labeled as placenta (Twin B)

material, resembling decidual cast, passed out and was sent to laboratory for histopathologic examination. On the 6th hospital day, repeat sonographic studies revealed single live intrauterine pregnancy compatible with 24 weeks and 4 days age of gestation, left posterolateral grade II placenta, and adequate amniotic fluid volume with estimated fetal weight below the 10th percentile for age (725 g). Left cervix was noted to be long (3.37 cm) and closed, while the right cervix is 1.50 cm in length with a note of heterogeneous mixed echoes probably blood clots in the right hemiuterine endometrial cavity.

There was a gradual resolution of symptoms and the patient was shifted to oral tocolytic (nifedipine 30 gits Q8). On the 10th hospital day, histopathologic examination of "decidual cast" revealed necrotic chorionic villi and decidua with congested blood vessels and hemorrhages consistent with degenerating products of conception [Figure 2], hence a diagnosis of gravida 1 para 0 (0010), twin pregnancy, dichorionic diamniotic, pregnancy uterine 26 weeks and 5 days, complete abortion, and right hemiuterine pregnancy. The patient was subsequently discharged – improved on the 12th hospital day.

The rest of the pregnancy was delivered to term at 37 weeks by early ultrasound. Progress of labor was uneventful [Figures 3 and 4] until normal spontaneous delivery to a term living baby girl, with Apgar score of 9 and 10 and birth weight of 2330 g, appropriate for gestational age, on the 12th h of labor.

During the patient's stay at the postanesthesia unit, there was a note of moderate vaginal bleeding despite a well-contracted uterus. The patient was brought back to the operating room for genital tract inspection which revealed a 2.5 cm laceration at 9 o'clock of the left cervix, with a note of avulsed tissue. This is followed by removal of the avulsed tissue and repair of cervical laceration with vicryl 2-0 under subarachnoid block, which resulted to adequate hemostasis. The rest of the hospital stay was unremarkable and the patient was subsequently discharged on the 3rd hospital day. Delivered Placenta was sent to laboratory for examination revealing a third trimester placenta with foci of infarction [Figure 5].

Case Discussion

We present a case of a 31 year old, gravida 1 para 0, with

uterine didelphys and unilateral renal agenesis who was diagnosed to have single live intrauterine pregnancy in the left half of uterine didelphys. She was recurrently admitted due to preterm labor until with spontaneous of degenerating products of conception from the right half of uterine didelphys, hence confirming a dicavitary twin pregnancy – one delivered to term and the other probably was aborted in the past but was missed until with development of symptoms.

MDAs arise from the probable teratogenic assault at 6–22 weeks' age of gestation. This may include abnormalities in elongation, fusion, canalization, or septal resorption.[1,4] Uterine didelphys (Class III MDA) arises from a complete lack of fusion of Müllerian ducts, between 10th and 17th week of intrauterine development, resulting in two entirely separate, nearly fully developed hemiuteri, cervices and vaginas.[2-4] The incidence of Müllerian duct anomaly is 0.5%–-5% in the general population and the frequency of uterine didelphys is 1 in 1000–30,000 women.[5] Women with uterus didelphys have an 80% chance of becoming pregnant, with a greater risk of complications,[7] but the incidence of dicavitary twin pregnancy in a didelphic uterus, which is usually biovular, is 1 per 1 million.[6]

Most women with didelphys uterus are asymptomatic and are diagnosed late until menarche or coitarche when dysmenorrhea, dyspareunia, and/or infertility are noted,[1] usually through sonographic studies. Our patient has been asymptomatic until menarche when she noted irregular menstruation at 3–4 months' interval associated with severe dysmenorrhea at a pain scale of 10/10. She consulted a private gynecologist where laboratory and imaging tests were done revealing uterine didelphys and unilateral renal agenesis. She was offered correction of the anomaly but refused. There is a high association between uterine anomalies and maternal congenital renal abnormalities due to close association of Müllerian and Wolffian duct development. The mesonephric ducts serve as the origin of kidneys and inductor of elements for adequate Müllerian duct fusion. Therefore, a developmental anomaly of the caudal portion of one of the mesonephric ducts may be the cause of unilateral renal agenesis. The Müllerian duct ipsilateral to renal agenesis site is displaced laterally; hence, fusion with the contralateral duct is impaired resulting in didelphic uterus.[7] Women with absent or ectopic kidneys should be evaluated for uterine malformation and vice versa.[4]

MDA are associated with poorer pregnancy outcomes such as increased incidence of spontaneous abortion (30%–38%), premature rupture of membranes (53%), premature labor (95%), malpresentation (43%), and fetal mortality.[1,6] These complications may be secondary to premature transition from myometrial tranquility to preparation of labor phase. One of the numerous factors that may contribute to this transition is the uterine stretch, which may be secondary to the more limited capacity of a nonfused hemiuterus for fetal growth. Uterine stretch increases expression of connexin-43, oxytocin receptors, and other agonists for smooth muscle contraction.[2]

Our patient presented with recurrent admissions due to preterm labor starting at 24 weeks of gestation. Several drugs and interventions have been used in prevention of preterm labor, but none has proven completely effective in controlling preterm labor. Studies have shown that they do not markedly prolong gestation but may delay progress of labor up to 48 h for the completion of steroid therapy for fetal lung maturation. CCB (nifedipine) reduces the entry of calcium ions, ultimately reducing myometrial activity and contractions. CCB is a safer and more effective tocolytic agent than beta-agonist. Administration of CCB in our patient reduced the frequency but did not totally resolve uterine contraction hence addition of micronized progesterone 200 mg TID per vagina. Different clinical trials revealed that micronized progesterone significantly prolonged pregnancy and decreased the number of preterm births.[9,10] The only medicinal therapy currently recommended for prevention of preterm birth is prophylactic micronized progesterone (P4) therapy via vaginal suppository from 24th to 34th week of gestation. The exact mechanism for the role of P4 in the prevention of preterm birth is still unknown but may involve replenishment of functional progestin deficiency or nonprogestin mechanisms such as acting as a precursor for fetal adrenal gland cortisol production, hence limiting inflammatory activities[10] that may lead to premature transition to Phase II of parturition. With combined CCB and P4, hypogastric pain and vaginal bleeding resolved; hence, the patient was subsequently discharged.

Vaginal bleeding and 10/10 hypogastric pain radiating to the lumbosacral area recurred hence readmission for tocolysis and betamethasone therapy for fetal lung maturation. Terbutaline[11] was given which temporarily relieved hypogastric pain. This is then shifted to Isoxsuprine drip. Both are beta-agonists hence act by decreasing intracellular calcium ions available for binding with myometrial contractile proteins. Symptoms of bleeding and uterine contractions gradually resolved allowing transition to oral tocolytics until recurrence of bleeding on the 5th hospital day followed by passage of a meaty material resembling a decidual cast, which may be formed as endometrial response to hormones of pregnancy.[2] This resulted in the gradual resolution of uterine contraction and hypogastric pain.

The result of histopathologic examination of the "decidual cast" revealed necrotic chorionic villi and

decidua with areas of congested blood vessels and hemorrhages consisted of degenerating products of conception [Figure 2], hence a diagnosis of dicavitary twin pregnancy. Miscarriage in MDA is more likely to occur if the embryo implanted on the septum with disordered and decreased blood supply insufficient to support placentation and embryonal growth.[8]

Multifetal gestation may be a result of fertilization of two separate ova in a single ovulatory cycle, division of a single fertilized ovum, or less commonly, superfecundation and superfetation. Superfecundation is the fertilization of two separate ova in the same cycle from separate coitus and not necessarily by the same set of sperm. Considering the gap in gestational age of two separate hemiuterus (26 and 5 days versus an abortus), we may consider a probable case of superfetation versus a probable missed, undiagnosed abortion. Superfetation is a phenomenon yet to be proven since ovulation is suppressed due to upregulation of placental progesterone production, but cases were reported in the context of growth discordance.[13] This phenomenon was presumed in two cases, one of which is a case of twins from a pseudo-didelphic uterus. Mechanisms preventing superfetation include suppression of ovulation by hormonal influences of pregnancy, production of cervical mucus plug preventing sperm entry, occlusion of Fallopian tube by decidual reaction, and fusion of decidua capsularis and decidua parietalis obliterating possible implantation site for other embryo.[13] These inhibitory conditions may be superseded by the luteal out-of-phase phenomenon, an atypical increase in estrogen levels in the mid-luteal phase that may allow another ovulation between 1 and 3 weeks after ovulation, and the presence of dual endometrial cavities possibly receptive of another implantation. Only one reported that uterine didelphys superfetation was reported with a note of maturation discrepancy between two fetuses (23 vs. 28 weeks), which lead to intrauterine fetal death of the twin in the right horn and preterm delivery of the twin in the left horn.[14]

The undiagnosed twin of our case can also probably underwent missed abortion weeks prior to spontaneous expulsion at 26 weeks' age of gestation [Figure 2], while the other twin was delivered to term at 37 weeks [Figure 5], with 11 weeks' interval. Although there was a note of generalized hypogastric pain associated with uterine contractions, only one of the two cervices ultimately resulted in cervical dilatation. This may suggest that initiation of labor may be a localized rather than a systemic reaction. This suggestion is supported by the reports of deliveries of a dicavitary twins with wide-time interval of delivery from 3 h to 8 weeks between the delivery of twins.[4] Hence, salvaging twin pregnancies in an anomalous may be possible with modern medical therapies with early detection and diagnosis.

The rest of the pregnancy remained uneventful until vaginal delivery at 37 weeks. Uterus didelphys is not an indication for cesarean delivery unless with obstetric indications.[4]

Postpartum hemorrhage secondary to possible genital tract laceration was noted. Assessment revealed 2.5 cm laceration at 9 o'clock of the left cervix, with avulsed tissue, probably torn vaginal septum, which was subsequently excised and repaired via simple running suture with vicryl 2-0 for hemostasis. A complete or incomplete longitudinal vaginal septum may be present in uterine didelphys and may range from thin, easily displaced to thick, inelastic tissue which may cause dystocia.[4] The presence of vaginal septum may be a part of Herlyn–Werner–Wunderlich-Syndrome (HWWS), a rare congenital urogenital tract anomaly characterized by uterine didelphys, obstructed hemivagina, and ipsilateral renal agenesis. HWWS may be classified as to imperforate septum (Type I), perforate septum (Type II), and imperforate septum with cervical fistula (Type III). All the components of the triad of HWWS are all confirmed in our patient except presence of hemivagina, which may remain unrecognized clinically and radiographically, especially if no obstruction is present.[12] In our patient, no documentation of a longitudinal septum is available, but the presence of severe pelvic pressure before passing out meaty material, visualization and palpation of two cervices, and presence of avulsed tissue upon vaginal delivery, may support a Type II HHWS.

The rest of the postpartum period was unremarkable and the patient was eventually discharged-improved with a good baby outcome.

While available literature on uterine didelphys is currently quite limited to determine reproductive and gestational outcomes,[4] obstetricians should be more vigilant and give a wholistic care encompassing preconception, prenatal, intrapartum, and postpartum period as any complications may arise at any point.

Conclusion

Uterine didelphys is usually asymptomatic and may usually remain undiagnosed; hence, an accurate prevalence may be made if standardized diagnostic tests will be applied. Pregnancy is possible in an anomalous uterus, provided prompt detection and appropriate management be done. Vaginal delivery is considered the primary mode of delivery unless with obstetric indications. Wholistic care encompassing preconceptual to postpartum period should be given to women as any complications may arise at any point.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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