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Herlyn-Werner-Wunderlich syndrome and central placenta previa in a COVID-19 positive pregnant woman: a case report

Herlyn-Werner-Wunderlich syndrome and placenta previa

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Abstract

Background: The Herlyn–Werner–Wunderlich syndrome (HWWS) is an uncommon congenital anomaly, characterized by uterus didelphys, obstructed hemivagina, and ipsilateral renal agenesis. We report a unique case of association of HWWS and central placenta previa (CPP) in a COVID-19 positive pregnant woman.

Case presentation: A 39-year-old pregnant woman was admitted to our hospital for preterm labor risk at 32 gestational weeks. She referred a previous cesarean section (CS) and three miscarriages. Speculum examination allowed visualization of the left cervix, whereas the contralateral one was hidden under the obliterated vaginal septum. Ultrasound examination showed postero-lateral CPP, double uterus, and right renal agenesis. Subsequent Magnetic Resonance Imaging confirmed the condition of uterus didelphys and right renal agenesis, associated with CPP. The patient was treated with tocolytics and progesterone and was discharged in good physical conditions. At 35 gestational weeks, the patient became COVID-19 positive with few symptoms. Elective CS was performed at 36 gestational weeks, and she delivered a small-for-gestational-age newborn in good health conditions. The left womb was particularly bleeding on the lower uterine segment and ligation of the left uterine artery was necessary. The post-operative course was uneventful.

Conclusion: We describe a unique association of HWWS and CPP in a COVID-19 positive pregnant woman solved by means of elective CS and uterine artery ligation. Pregnancy in women with HWWS is possible, although obstetric complications may arise. When HWWS is associated with CPP, the risk of hemorrhage is the rule. A correct management determined positive both maternal and fetal outcomes.

Keywords: Herlyn-Werner-Wunderlich syndrome; Utero didelphys; Obstructed hemivagina; Renal agenesis; Case report

Introduction

The Herlyn–Werner–Wunderlich syndrome (HWWS) is a rare congenital malformation of the female urogenital tract, characterized by the triad: uterus didelphys, obstructed hemivagina, and ipsilateral renal agenesis [1, 2]. Since 2007 this syndrome was called with the acronym of OHVIRA syndrome (obstructed hemivagina, ipsilateral renal anomaly) [3]. It is caused by an abnormal development of the Müllerian and Wolffian ducts [4], and its estimated occurrence is very low [5]. It is usually misdiagnosed and mistreated owing to rare and variant clinical manifestations, understandably resulting in infertility and severe obstetric complications [6].

Central placenta previa (CPP) is defined as the condition where the placenta directly covers the cervix [7, 8]. It must be distinguished from low-lying placenta, where the placental edge is within 2 cm of the cervical os. Several risk factors have been identified, including previous cesarean sections (CS) [9]. Women with CPP have a higher risk of antepartum hemorrhage, CS, and occurrence of placenta accreta spectrum disorders. Diagnosis is performed with ultrasound examination (US) and should be confirmed ≥ 32 gestational weeks. For women with uncomplicated CPP, elective CS is recommended at 36+0 to 37+6 gestational weeks based on the presence of risk factors [7, 8].

In December 2019, a novel coronavirus spread in China. Responsible for the COVID-19 pandemic, it was identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Pregnant women who contract the infection have a greater risk than non-pregnant ones of developing severe general complications and being hospitalized in the intensive care unit (ICU). They are also more likely to develop pregnancy-specific complications, such as pre-eclampsia, premature rupture of membranes (PROM), preterm labor. Regarding neonatal outcomes, there was no evidence of teratogenicity of the virus when contracted in the embryonic period and no increase in the number of miscarriages was found. However, an association with intrauterine growth restriction (IUGR) and small-for-gestational-age (SGA) babies was found. The possibility of vertical transmission is not well understood, but seems to be possible [10–12], similarly to what happens with other viruses [13].

In this paper, we report a unique case of association of HWWS and CPP in a COVID-19 positive pregnant woman who delivered by elective preterm CS. Besides, literature review regarding HWWS and pregnancy outcome is carried out.

Case presentation

We describe a 39-year-old pregnant woman, admitted to our hospital for preterm labor risk at 32 gestational weeks. She referred a previous CS at term and three miscarriages. Non-Invasive Prenatal Testing (NIPT) revealed no alterations of 13, 18 and 21 chromosomes. Toxoplasmosis, Other agents, Rubella, Cytomegalovirus, and Herpes simplex (TORCH) screening was negative. Speculum examination allowed visualization of the left cervix, whereas the contralateral one was hidden under the obliterated vaginal septum. US showed posterolateral CPP (covering the left uterine cervix), double uterus and, in addition, right renal agenesis. Subsequent Magnetic Resonance Imaging (MRI) at 32 weeks + 2 days confirmed the condition of uterus didelphys and right renal agenesis, associated with CPP. Instead of the classic HWWS triad where the uteri are separated, in our case the uterine cavities were in communication, as an iatrogenic consequence of previous CS (Figure 1). The patient was treated with tocolytics and progesterone and was discharged 4 days later in good physical conditions. At 35 gestational weeks, despite a double Pfizer vaccination done two months earlier, the patient became COVID-19 positive with few symptoms. CS was performed at 36 gestational weeks. A Pfannenstiel transverse suprapubic incision was performed. After opening the cavity, a double uterus was visualized (Figure 2). A scar affecting both uteri and an abnormal vascularization were observed. We incised the left gravid

uterus transversally, and carefully a cephalic extraction was performed. A female SGA baby was extracted in good health conditions (birth weight = 2100 grams; Apgar score = 8/9). The left womb was particularly bleeding on the lower uterine segment and ligation of the left uterine artery was necessary. The post-operative course was uneventful for both mother and newborn. The timeline of the salient events is illustrated in Figure 3.

Discussion

Uterus didelphys and obstructed hemivagina association was reported for the first time in 1922 [14] and it became more popular in 1970s following the descriptions by Herlyn and Werner, and Wunderlich [1, 2]. However, there are still few relevant studies published on HWWS [15] and its estimated occurrence ranges between 0.1% and 3.8% [5].

The exact etiology and pathogenesis are still debated. The most accepted theory refers to an abnormal development of the para-mesonephric and mesonephric ducts [4]. The mesonephric ducts are precursors of kidneys and ureters and induce a correct Müllerian ducts fusion. Therefore, when a Wolffian duct is absent, the ipsilateral Müllerian duct is driven laterally to the urogenital sinus determining a blind sac, which corresponds to the obstructed hemivagina. The other Müllerian duct gives origin to the contralateral vagina [16]. The distal portion of the vagina originating from the urogenital sinus is not involved and develops normally [17]. On the side where the mesonephric duct is absent, the lateralized Müllerian duct cannot fuse with the contralateral one during the 8th week of embryogenesis, resulting in uterus didelphys [18].

Diagnosis usually comes after menarche, with a clinical presentation of dysmenorrhea, cyclic pelvic pain, and a pelvic mass due to the associated hematocolpos or hematometra, that results from retained menstrual materials in the obstructed hemivagina and can be complicated with an ascending infection; sometimes pyocolpos may arise and lead to mucopurulent vaginal discharge after accidental fissuring of the occluded hemivagina [19].

Early diagnosis is imperative to prevent long-term complications, such as infertility, endometriosis, pelvic adhesions, and obstetrical issue [20]. The initial imaging procedure is carried out by US [21]. MRI is considered the gold standard, having an accuracy of almost 100%, offering soft tissue details, being able to perform multiplanar image acquisitions, and differentiating among various classes (didelphys/bicornuate/septate uterus) [22]. Alternatively, Computed Tomography (CT) scan may be performed when pregnancy is excluded. Laparoscopy should be performed in absence of pregnancy only when the diagnosis by imaging is not clear or MRI is not available [23]. A differential diagnosis regards other pelvic disorders, such as endometriosis, pelvic inflammatory disease, complicated ovarian cyst, and tubo-ovarian abscess [23].

Vaginal septotomy is considered the treatment of choice for obstructed hemivagina, traditionally performed using scissors and scalpel [24]. Hysteroscopy, in addition to being an important tool in many other conditions [25–28], may be used for the resection as a minimally invasive, short, and safe alternative to the conventional method [29–31]. However, pregnancy is possible even without any treatment [32].

Fetal survival has been reported [32], although obstetric complications may include recurrent miscarriage, preterm delivery, IUGR, PROM, abnormal fetal presentation, and post-partum hemorrhage [33]. Unlike other Müllerian duct anomalies that cause cervical incompetence [34, 35], uterus didelphys is not usually associated with this condition, so cerclage is not routinely used. Of note, most of the pregnancies (64%) occur in the uterus contralateral to the obstructed hemivagina, as observed in our patient [36]. Moreover, the present case involves the left part of the body, while usually the right side is affected [19]. However, there are still few reports on the association between HWWS and near term/term pregnancies. Our imaging procedures also showed the

presence of CPP, covering the left uterine cervix (Figure 1), a condition potentially associated with antepartum and post-partum hemorrhage, either intracesarean or postcesarean hysterectomy, in addition to perinatal mortality [37]. In accordance with the obstetric complications mentioned above, our patient referred three miscarriages and was admitted for preterm labor risk. However, none of the other obstetric conditions occurred and the woman had only a few symptoms caused by SARS-CoV-2 infection. These findings were inconsistent with the previous literature, according to which COVID-19 in pregnant women is associated with a low rate of maternal mortality, but great rates of complications and admission to ICU [10, 38].

A planned near term/term CS is recommended when obstetrical course is uneventful [7, 8]. Uterine artery ligation is considered an important procedure contemplated in obstetric guidelines to stop bleeding and allow uterus preservation [39].

The woman delivered an SGA newborn in good health conditions. However, a large multinational cohort study [11] showed that COVID-19 in pregnant patients is associated with a high rate of perinatal death and low birthweight was one of the main determinants of adverse perinatal outcomes. In this regard, early diagnostic tests could be useful for these high-risk patients to diagnose the most frequent pregnancy-related complications (such as IUGR), give an opportunity for early prevention, and improve maternal and fetal outcomes. Even though some authors demonstrated a relatively easy and feasible detection of some microRNAs in maternal peripheral blood for early diagnosis of IUGR, costs of these tests should be reduced in order to increase cohorts and have stronger evidence. Therefore, further studies are needed to identify other markers [40, 41].

Conclusion

We report a unique association of HWWS and CPP in a COVID-19 positive pregnant woman solved by means of elective CS. The study confirms that pregnancy in women with HWWS is possible, although obstetric complications may include recurrent miscarriage, preterm labor risk, and IUGR. When HWWS is associated with CPP, the risk of hemorrhage is the rule. Preservation of left uterus was allowed after ipsilateral uterine artery ligation. A correct management in the absence of guidelines may be complex and a close follow-up in such patients should prevent both maternal and fetal complications.

Compliance with Ethical Standards

Authors contribution: V.L., G.G.I.: Writing – original draft. M.G., D.I., S.G.C.: Writing – review & editing. M.P.: Conceptualization and supervision.

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Figure legend

Figure 1. MRI at 32 gestational weeks with HWWS and CPP.

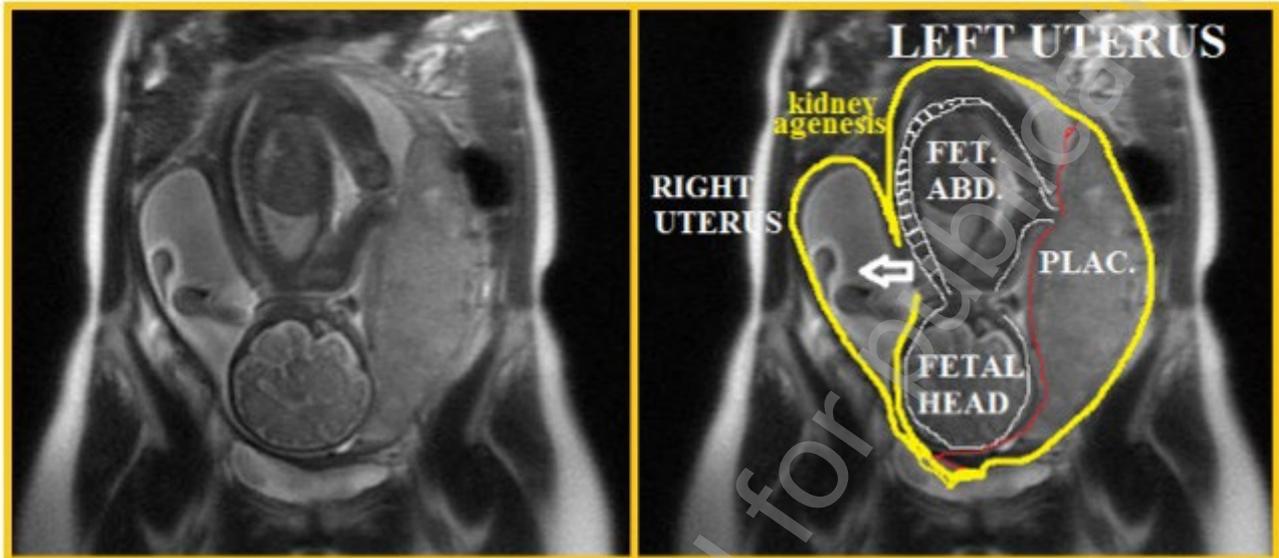


Figure 2. Exposition of both uterine cavities after fetal extraction.

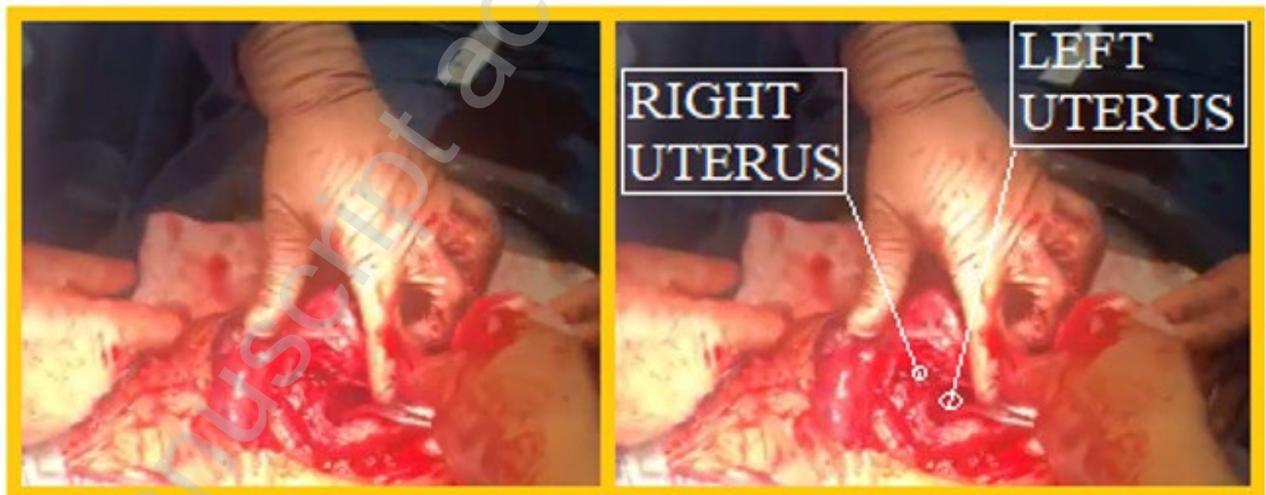
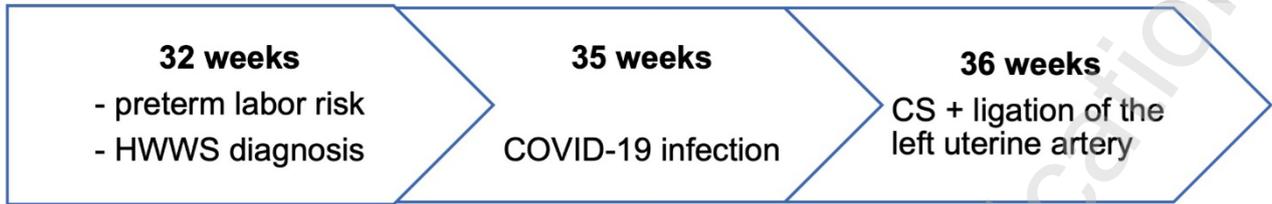


Figure 3. Timeline of the salient events.



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