



Case Report

Successful treatment of placenta accreta spectrum disorder using management strategy of serial uterine artery embolization combined with standard weekly and a 8-day methotrexate/folinic acid regimens at 7 weeks of gestation

Min-Min Chou^{*}, Jia-Chun Yuan, Yaw-An Lu, Sheng-Wei Chuang

Center for High Risk Pregnancy and Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, China Medical University Hospital, Taichung 40447, Taiwan

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ABSTRACT

Objective: We describe our experience with serial uterine artery embolization (UAE) combined with standard weekly methotrexate and a eight-day methotrexate/folinic acid (MTX/FA) treatment regimen in the management of placenta accreta spectrum (PAS) disorder at 7 weeks of gestation.**Case report:** A 38-year-old woman, gravida 2 para 0, with a history of myomectomy, was referred for ultrasound (US) evaluation due to suspected cervico-isthmic pregnancy. Transvaginal US image showed a viable embryo with a disproportionately bigger placenta encircling the fetus and completely covering the internal os of the cervix at 7 weeks of gestation. Color Doppler imaging revealed diffuse intraplacental and periplacental vascularity. Patient chose to terminate the pregnancy but attempted to preserve the uterus for future fertility following counseling. Serial UAE procedures were performed using Gelfoam and metallic microcoils. Two courses of a standard weekly MTX and a eight-day MTX/FA treatment regimen were administered to accelerate placental regression. The beta-hCG gradually decreased to a normal level, and an ultimate resolution of the PAS disorder was observed at 110 days after treatment.**Conclusion:** Early diagnosis of the PAS disorder could result in better obstetric outcome through earlier intervention using serial UAE combined with standard weekly and a eight day MTX/FA regimen in the first trimester of pregnancy.© 2020 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Placenta accreta spectrum (PAS) disorder encompasses a spectrum of disorders characterized by various degrees of placental invasion through the myometrium and uterine serosa. Early diagnosis of PAS disorder is crucial, because it may provide the option of a high chance of preservation of the uterus and future fertility in carefully-selected cases through earlier intervention in centers with a high level of management expertise in this challenging condition [1]. There are limited data regarding conservative treatment of PAS disorder in the first trimester in order to preserve uterine fertility [1–3]. We describe herein our experience of

employing serial uterine artery embolization (UAE) combined with standard weekly methotrexate and a eight-day methotrexate/folinic acid (MTX/FA) treatment regimen in the management of PAS disorder at 7 weeks of gestation.

Case report

A 38-year-old woman, gravida 2 para 0, with a previous history of myomectomy for multiple uterine fibroids (intramural 11 cm, 9 cm in the lower segment and intramural 5 cm, respectively) and uterine curettage, was referred for further evaluation due to suspected cervico-isthmic pregnancy with persistent vaginal spotting. Gray scale transvaginal ultrasound evaluation at 7 weeks of gestation revealed an intrauterine viable embryo with a crown-rump length of 1.02 cm. The placenta was disproportionately bigger in light of the gestational age, encircling the fetus and completely covering the internal os of the cervix. Many irregularly-shaped lacunae were observed (Fig. 1a). Color Doppler imaging (Voluson E10, GE Healthcare, United States) revealed an extensive

^{*} Corresponding author. Center for High Risk Pregnancy and Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, China Medical University Hospital, 2 Yude Road, Taichung 40447, Taiwan. Fax: +886 4 22086970.

E-mail addresses: mmchou1109@gmail.com, d95224@mail.cmuh.org.tw (M.-M. Chou).

turbulent blood flow perfusing throughout the whole surrounding uteroplacental tissues. Pulsed Doppler interrogation of the intra-parenchymal echolucent spaces and supplying high-pressure myometrial vasculature yielded a pulsatile venous flow within the lacunar spaces, and low resistance (resistance index = 0.34) arterial blood flow, respectively (Fig. 1b). Owing to a high risk of severe morbidity in this severe case, patient chose to terminate the pregnancy but attempted to preserve the uterus for future fertility following counseling. A UAE procedure was performed using Gel-foam and metallic microcoils. MTX (95 mg (50 mg/m²), 80 mg (1 mg/kg)) was administered weekly for 2 consecutive weeks as an adjuvant therapy because it was well-tolerated and preferred by the patient to promote involution and shedding of the morbidly adherent placenta. Furthermore, we administered MTX in a standard eight-day treatment regimen consisting of four administrations of MTX given at 1 mg/kg I.M. ("intramuscular injection"), on days 1, 3, 5, and 7 plus folinic acid 15 mg PO after each MTX dose on days 2, 4, 6, and 8 to accelerate placental regression because of persistent and extensive uteroplacental flow on color Doppler US and slightly slow regression of beta-hCG level. Multiple hypoechoic areas of abnormally invasive placenta-related enhanced

myometrial vascularity were noted at 21 days after treatment (Fig. 1c, d). Therefore, a second UAE was performed due to revascularization after the 1st UAE. Markedly decreased myometrial vascularity was noted at 90 days after treatment (Fig. 1e). The beta-hCG gradually decreased to a normal level (Fig. 2), and a normal uterus with an ultimate resolution of the invasive placenta was noted at 110 days after treatment (Fig. 1f). Mild and self-limiting elevations of serum alanine aminotransferase levels (52–79 IU/L) was noted during MTX treatment period. The patient had an uneventful recovery.

Discussion

Gray-scale US and color Doppler imaging are very useful tools for the evaluation of PAS disorders [4,5]. However, most cases of PAS were diagnosed in the second and third trimesters of pregnancy. The diagnosis and conservative management of PAS disorder in the first trimester is challenging because of the limited information in the literature. Recently, ultrasound features suggestive of PAS disorder, including a non-visible cesarean section scar, bladder wall interruption, thin retroplacental myometrium, presence of

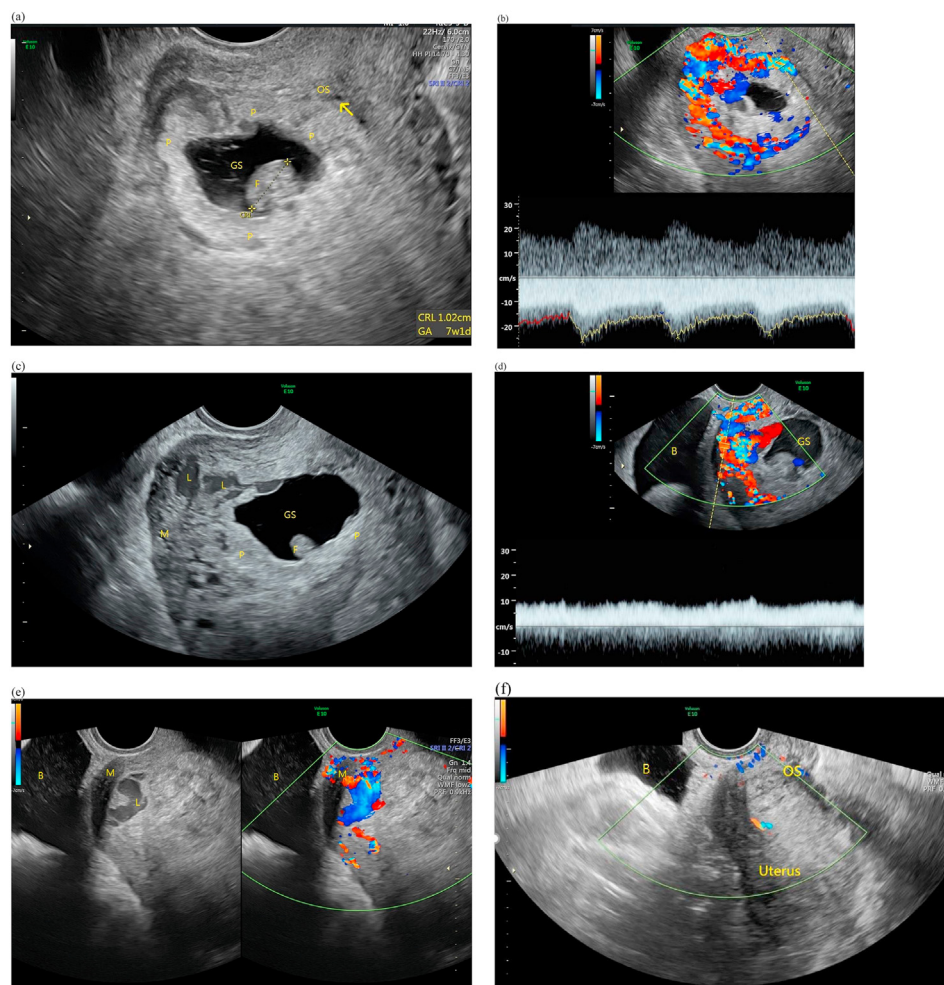


Fig. 1. (a). Transvaginal ultrasound image showing a viable embryo with a CRL of 1.02 cm, and a disproportionately bigger placenta with multiple hypoechoic areas encircling the fetus and completely covering the internal os of the cervix (arrow) at 7 + 1 weeks' gestation. (b) Transvaginal color Doppler image showing diffuse intraplacental and periplacental vascularity. (c) Gray scale ultrasound showing the presence of multiple irregular vascular spaces within the placental bed and myometrium at 21 days after treatment. (d) Color Doppler image showing areas of abnormally enhanced myometrial vascularity at 21 days after treatment. (e) Markedly decreased myometrial vascularity was noted at 90 days after treatment. (f) A normal uterus with ultimate resolution of the abnormal vascularity was noted at 110 days after treatment. B = bladder; CRL = crown-rump length; F = fetus; GS = gestational sac; L = Lacuna; OS = internal os of the cervix; P = placenta.

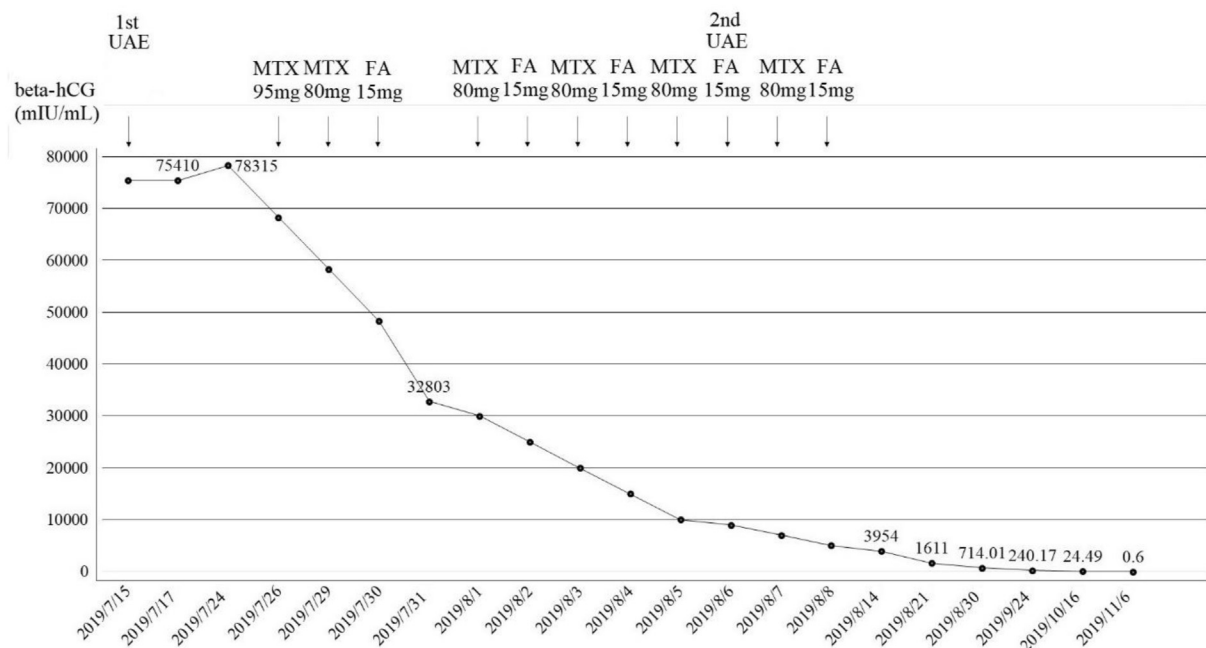


Fig. 2. Regression curve of beta-hCG against time with the various treatments including uterine artery embolization (UAE), weekly methotrexate (MTX) and an 8-day methotrexate/folinic acid regimen.

intraplacental lacunar spaces, presence of retroplacental arterial-trophoblastic blood flow, and irregular placental vascularization demonstrated by three-dimensional power Doppler have been reported [6,7].

Most reports in the literature suggest the operative strategy of a hysterectomy as the definitive treatment for first-trimester PAS disorder in severe cases with a high risk of maternal morbidity or mortality due to placental penetration of the maternal bladder or uterine parametria [1,6,8]. However, even though the diagnosis has been made in the first trimester, the surgical procedure might still be very bloody and problematic in some severe cases [9,10]. We also agree the view that either UAE or systemic MTX as a primary treatment in uncomplicated case of early PAS disorder should be avoided or used sparingly [8]. There is little prospective experience in the conservative treatment of PAS disorder using UAE alone in the first trimester [2,3,8]. Therefore such approach is still of an experimental and investigational nature. Our experience with conservative strategy of serial UAE in the treatment of PAS in the first trimester of pregnancy was published as a case report in 2006 [2]. Unfortunately, satisfactory vessel occlusion could not be achieved because of recurrent placental revascularization which likely reflects the known resistance of placental tissue to hypoxia [3,11,12]. The resistance of the placenta to hypoxia, the release of inflammatory cytokines and the expression of angiogenic growth factors may account for persistent enhancing placental tissue and vascularity on subsequent recanalization following UAE and hysterectomy was ultimately performed 2 weeks after the second UAE [2,13,14].

However, conservative treatment can be implemented in certain selected cases with strong desire for uterine preservation, and multiple adjuvant treatment modalities of UAE and/or systemic MTX, either alone or in combination, have been introduced to promote the passing or absorption of the morbidly adherent placenta under close monitoring [15]. After the uterine arteries and other supplying collateral blood vessels have been occluded by serial UAE, combined with the much higher efficacy of cytotoxic effect of aggressive MTX treatment regimen in early pregnancy,

invasive placental tissue does not survive prolonged period of uterine ischemia, and the high rate of trophoblasts turnover begin to undergo degenerative changes and are gradually killed and resolved. These results appeared to validate our findings that earlier intervention using serial UAE combined with standard weekly and a eight-day MTX/FA regimens is an alternative treatment in carefully-selected cases. However, the high rate of recurrence of PAS disorder in a subsequent pregnancy should be discussed with patient. Furthermore, intrauterine device placement to avoid uterine synechia and for contraception in the following 12 months due to potential uterine scarring damage caused by MTX and UAE. As this is the first report of its kind, however, the efficacy and safety of this management strategy need to be further examined.

Conflicts of interest statement

The authors declare no financial disclosures or conflicts of interest relevant to this manuscript.

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