

รายงานผู้ป่วย

Case Report

รายงานผู้ป่วย : รกเกาะลึกและการรักษาด้วย Methotrexate  
Placenta Percreta and Methotrexate Treatment : A Case Report

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บทคัดย่อ

ภาวะรกเกาะลึกในการตั้งครรภ์ไตรมาสแรกเป็นภาวะที่พบน้อยแต่มีอันตรายต่อชีวิต โดยทั่วไปผู้ป่วยจะได้รับการรักษาด้วยการตัดมดลูก แต่มีการรักษาทางเลือกคือการให้ยา methotrexate ในกรณีที่ผู้ป่วยต้องการตั้งครรภ์ครั้งถัดไปและไม่มีภาวะตกเลือดที่เป็นอันตรายต่อชีวิต

รายงานผู้ป่วยนี้นำเสนอหญิงไทยอายุ 26 ปี ถูกวินิจฉัยว่าแท้ง ผลตรวจอัลตราซาวด์ทางช่องคลอดและคลื่นแม่เหล็กไฟฟ้ามีภาวะรกเกาะลึกทะลุกล้ามเนื้อมดลูก ได้รับการรักษาโดยให้ยา methotrexate ทุกสัปดาห์เป็นเวลา 3 สัปดาห์แทนการตัดมดลูก ผล  $\beta$ -hCG และอัลตราซาวด์ที่ 3 เดือนหลังการรักษาไม่พบรกในมดลูกซึ่งแสดงถึงความสำเร็จในการรักษาด้วย methotrexate

คำสำคัญ : ภาวะรกเกาะลึก, methotrexate, ประเทศไทย

ABSTRACT

Placenta percreta is a potential life-threatening condition. The detection of placenta percreta in the first trimester is rare. However, the physicians should have suspicion in case of incomplete abortion with predisposing factors, such as history of cesarean section. The conventional treatment of placenta percreta is hysterectomy. The conservative treatment, like methotrexate (MTX) remains alternative when patients have inactive bleeding and desire to preserve the fertility.

This case report examines a 26-year-old woman, at 12 weeks of gestation with a history of previous cesarean section, was referred for further management for incomplete abortion. The transvaginal ultrasonography (TVUS) and magnetic resonance imaging (MRI) confirmed the diagnosis of placenta percreta. MTX was administrated weekly for 3 weeks. The  $\beta$ -hCG gradually decreased to a normal level and ultimate resolution of placenta percreta from TVUS was observed at 3 months after treatment.

Keywords : Placenta percreta, methotrexate, Thailand

Introduction

Placenta percreta is the deepest penetrating subtype of placenta accreta, is characterized by absence of the decidua basalis and the chorionic villi pass through myometrium. Then, penetration of not only the serosa but

also neighboring organs such as urinary bladder and bowel. This condition could cause morbidity and mortality from severe massive bleeding, uterine rupture and infection<sup>(1)</sup>. Placenta percreta usually manifests with vaginal

bleeding during difficult placenta removal at delivery in the third trimester of pregnancy<sup>(2-3)</sup>. However, it may also complicate the first trimester pregnancy causing postabortal hemorrhage<sup>(4)</sup>. The diagnosis of placenta percreta in the first trimester is difficult. Retained placental could mimic unusual uterine mass, invasive mole and incomplete abortion<sup>(4-6)</sup>. If the physicians have not suspicion for this condition, the subsequent curette could cause catastrophic hemorrhage<sup>(3)</sup>. Furthermore, the treatment option of this condition is quite challenging. The definitive treatment for first-trimester postabortal placenta percreta consists of hysterectomy<sup>(3)</sup>. However, MTX effect resulting in placental necrosis and reducing placental vascularity, provided the justification for attempting one option of conservative treatment for patients with placenta percreta who desire to preserve fertility<sup>(7-11)</sup>. We report a case of a patient with 12-week incomplete abortion with two prior cesarean deliveries. The diagnosis of placenta percreta was confirmed by TVUS and MRI. And the patient was successful treated by MTX.

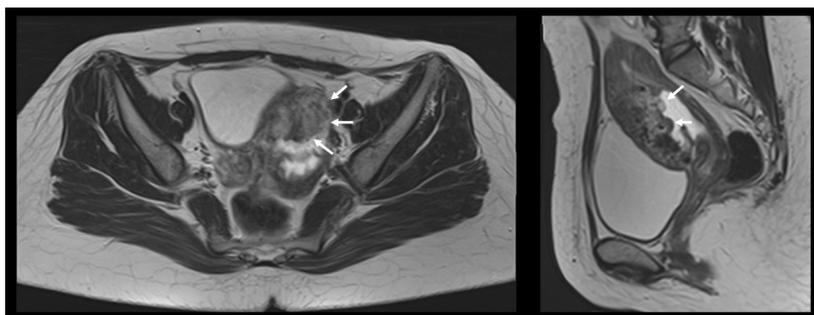
## Case

A Thai 26-year-old woman, at 12 weeks of gestation by last menstrual period with a history of 2 previously documented low transverse cesarean sections, was referred to our tertiary care hospital due to incomplete abortion. The patient had pelvic pain with persistent vaginal bleeding which soaked about three pads a day for ten days. She also had passage of tissue without the character of grape like cyst. The patient was hemodynamically stable. The pelvic examination revealed uterus corresponding to 12 weeks without tenderness

on palpation and blood clot per cervix os. TVUS demonstrated 4 cm ill-defined complex mass in the anterior site of fundus invading almost the complete thickness of myometrium and interface with urinary bladder (as figure 1), which was absence of vascular flow in the uterine wall. The magnetic resonance imaging (MRI) showed a bulked uterus containing abnormal mixed hypo-hypersignal intensity of T2W about 4.0x3.2x5.5 cm (WxAxL) along anterior aspect of uterus which involved myometrium without involving the serosa of urinary bladder (as figure 2). The findings were consistent with placenta percreta. The laboratory findings at admission were hemoglobin 12.3 g/dl,  $\beta$ -hCG 1,155 mIU/ml. In view of her desire for further childbearing and since there was no active bleeding, it was decided to conserve her uterus and to treat her medically. The patient was agreed to MTX course as adjunctive treatment to conservative management. She clearly understood about the toxicity and the uncertain efficacy of MTX treatment. The patient was administered MTX intramuscular in the doses of 1 mg/m<sup>2</sup> (1.5 mg) weekly as out-patient and was monitored with  $\beta$ -hCG, leukocyte counts and liver function. The placenta percreta was monitored by TVUS weekly and gradually decreased in size. Unfortunately, the patient was loss to follow-up after the third dosage of methotrexate. However, 3 months after the MTX treatment, the patient revisited as out-patient. TVUS showed that the retained placenta had totally resolved. The final  $\beta$ -hCG value was less than 5 mIU/ml.



**Figure 1.** Transvaginal ultrasonography. There was 4 cm ill-defined echogenic complex mass without vascular flow in the uterine wall of anterior part of fundal area (white arrow).



**Figure 2.** MRI. T2W imaging revealed bulked uterus containing abnormal mixed hypo-hypersignal intensity of T2W about 4.0x3.2x5.5 cm (WxAxL) along anterior aspect of uterus which involved myometrium without involving the serosa of urinary bladder (white arrow).

## Discussion

Placenta percreta is characterized by absence of the decidua basalis and the chorionic villi pass through myometrium. Then, penetration of not only the serosa but also neighboring organs such as urinary bladder and bowel. The reported incidence of placenta percreta is rare about 1 in 2400-7000 pregnancies<sup>(1)</sup>. The patient with placenta percreta usually manifests as the symptoms of uterine rupture, such as pelvic pain and shock<sup>(2)</sup>. In addition, the vaginal bleeding in third trimester or during delivery could be commonly seen<sup>(2)</sup>. This condition has been associated with placenta previa, previous uterine curettage, scarred uteri resulting from prior cesarean section, myomectomy, multiparity and elderly maternal age<sup>(3)</sup>. Most of cases are diagnosed by intraoperative finding

and histopathology, that mean the patient was performed unavoidable hysterectomy with the indication of postpartum bleeding<sup>(3)</sup>. Prenatal diagnosis is crucial to prevent the morbid postpartum hemorrhage. Meanwhile, some cases with placenta percreta in first trimester are missed and unfortunately diagnosed either during the abortive curettage or in the post abortive bleeding<sup>(4)</sup>. Relaying identifiable risk factors and finding to radiology is important to assist in further assessment. There are some features of placenta percreta from TVUS, including non visible cesarean section scar, non visible or thinning of the myometrium overlying placenta, presence of placental lacunae with turbulent flow, loss of retroplacental clear space, interruption of the interface

between the bladder and myometrium and presence of retro placental arterial trophoblastic blood<sup>(5)</sup>. MRI may be used when TVUS is not definitive or if the placenta located at posterior or fundal position. MRI protocol include a form of T2-weighted imaging. The finding of placenta percreta is uterine bulging, heterogenous placenta, thick T2 dark intraplacental bands and focal disruption of the myometrium<sup>(6)</sup>. In this case report, the patient was performed TVUS as first modality and was investigated by MRI to confirm the diagnosis and explore the extension of placental invasion.

The hysterectomy is definitive treatment for first trimester placenta percreta especially in case of uncontrolled hemorrhage. Even through the diagnosis has been made in the first trimester, the surgical procedure might be problematic in some severe cases<sup>(3)</sup>. Some patients desire to preserve their fertility and medical treatment with MTX is an alternative choice. The cytotoxic effect of MTX could induce placental necrosis and reduce the vascularity of placenta to expedite a rapid involution of placenta. In the literature review, there was ten cases which demonstrated the successful treatment of MTX, but all was placenta accreta in third trimester pregnancy with retained placenta following deliver<sup>y(7-11)</sup>. The MTX was administrated intramuscularly in the dose of 1 mg/m<sup>2</sup> weekly for 3-4 doses. None of the patients manifested drug toxicity.

In the literatures we found only 2 cases which is similar to ours. Chou et al<sup>(12)</sup>, reported 7 week of gestation with placenta accreta which was terminated the pregnancy by uterine arterial embolization (UAE) and subsequent systemic MTX treatment. The dosage of MTX was intravenous 50mg/m<sup>2</sup> weekly for 2 courses

and subsequent 1 mg/kg intramuscular every other day for 4 doses. Halal et al<sup>(13)</sup>, demonstrated 10 weeks of abortion with unsuccessful misoprostol termination. The patient was received the curettage and have post abortal hemorrhagic shock. After resuscitation, the patient was stable and was performed UAE and single dose of 80 mg/m<sup>2</sup> MTX intramuscularly. However, comparison with previous studies, neither of case report diagnosed after a first trimester that have treated by MTX alone. The information about the standardized protocol of dosing, frequency and route of administration is insufficient.

This case report demonstrates that hemorrhage could be avoided by avoiding attempt any curettage of placenta. This underscores the importance of radiographic diagnosis. In the view of the conservative treatment, we leave placenta percreta in situ with adjuvant treatment with MTX and waiting its resorption. Therefore, no expelled placenta for pathological assessment was identified.

As this is the first report of this approach, the efficacy and safety of this management strategy need to be further examined and the adjuvant MTX for placenta percreta treatment might be justified in selected cases.

## Conclusion

The diagnosis of placenta percreta in first trimester is crucial. Sonography is useful screening tool. In addition, MRI is worthwhile to confirm the diagnosis. Conservative treatment with MTX may be considered in patient desiring fertility and in whom bleeding could be controlled.

## Ethical approval

Ethical approval for this study was obtained from the Ethic Committee of Buriram Hospital (BR.0032.102.1/46).

## Consent

Written consent was obtained from the patient.

## Conflict of interest

The authors declare no conflict of interest.

## Reference

1. Breen JL, Neubecker R, Gregori CA, Franklin JE Jr. Placenta accreta, increta, and percreta. A survey of 40 cases. *Obstet Gynecol* 1977; 49(1):43-7.
2. Fox H. Placenta accreta, 1945-1969. *Obstet Gynecol Surv* 1972;27:475-90.
3. Wang YL, Weng SS, Huang WC. First-trimester abortion complicated with placenta accreta: A systematic review. *Taiwan J Obstet Gynecol* 2019;58(1):10-14. doi: 10.1016/j.tjog.2018.11.032.
4. Shah J, Matta E, Acosta F, Golardi N, Wallace-Huff C. Placenta Percreta in First Trimester after Multiple Rounds of Failed Medical Management for a Missed Abortion. *Case Rep Obstet Gynecol* 2017;2017:6070732. doi: 10.1155/2017/6070732.
5. D'Antonio F, Timor-Tritsch IE, Palacios-Jaraquemada J, Monteagudo A, Buca D, Forlani F, et al. First-trimester detection of abnormally invasive placenta in high-risk women: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2018;51(2):176-83. doi: 10.1002/uog.18840.
6. D'Antonio F, Iacovella C, Palacios-Jaraquemada J, Bruno CH, Manzoli L, Bhide A. Prenatal identification of invasive placentation using magnetic resonance imaging: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2014;44(1):8-16. doi: 10.1002/uog.13327.
7. Singh BY, Raghav V, Kapur A. Medical Management of Placenta Accreta with Methotrexate: Review of Two Cases. *J SAFOG* 2015;7:86-8.
8. Mussalli GM, Shah J, Berck DJ, Elimian A, Tejani N, Manning FA. Placenta accreta and methotrexate therapy: three case reports. *J Perinatol* 2000;20(5):331-4. doi: 10.1038/sj.jp.7200373.
9. Arulkumaran S, Ng CSA, Ingemarsson I, Ratnam SS. Medical treatment of placenta accreta with methotrexate. *Acta Obstet Gynecol Scand* 1986;65(3):285-6. doi: 10.3109/00016348609155187.
10. Heiskanen N, Kröger J, Kainulainen S, Heinonen S. Placenta percreta: methotrexate treatment and MRI findings. *Am J Perinatol* 2008;25(2):91-2. doi: 10.1055/s-2007-1004831.
11. Tong SY, Tay KH, Kwek YC. Conservative management of placenta accreta: review of three cases. *Singapore Med J* 2008; 49(6): e156-9.
12. Chou MM, Yuan JC, Lu YA, Chuang SW. 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. *Taiwan J Obstet Gynecol* 2020;59(6):952-55. doi: 10.1016/j.tjog.2020.09.027.

13. Halal HA, Shammary MA, Tawfeeq T, Mahmmod S, Jabari AA. Conservative management of abnormal placenta accrete complicating the first trimester abortion: A casereport and review of literature. Open J Clin Med Case Rep 2019;5:1-11.