Sequential methotrexate treatment with and estrogen and progestin in a retained adhesive placenta

T. Mizuno¹, H. Takagi², K. Matsunami², A. Imai²

¹Department of Obstetrics and Gynecology, Gifu University School of Medicine, Yanagido, Gifu ²Department of Obstetrics and Gynecology, Matsunami general Hospital, Kasamatsu, Gifu (Japan)

Summary

Background: Hysterectomy is the definite and recommended treatment of a retained adhesive placenta. Case: A 33-year-old woman at 38 weeks plus one day of gestation had a cesarean delivery due to previous history of myomectomy. On ultrasound placental retention was noted thus curettage was attempted two weeks postpartum but it induced moderate fresh bleeding. A contrast-enhanced computed tomography scan depicted the multiple vessels within the intrauterine mass and the absence of deep myometrial invasion. The patient received four doses of 50 mg of methotrexate intramuscularly every other day, alternating with four doses of 15 mg of folic acid. An attempt to evacuate the necrotic tissue along with withdrawal bleeding was successful after three courses of sequential conjugated estrogen (0.25 mg)-progestin (5 mg) therapy. Conclusion: The use of estrogen and progestogen together with methotrexate in combination may be simple and potentially effective for placenta accreta and placenta increta.

Key words: Placental adhesive disorders; Methotrexate; Placenta increta; Placenta accreta.

Introduction

The incidence of placental adhesive disorders has drastically increased in recent years, due to the increasing cesarean rates in most countries [1]. Though hysterectomy is the definite and recommended treatment, conservative management may be considered in patients desiring future pregnancy [2, 3]. We present a successful case of conservative treatment with methotrexate and estrogen-progestin.

Case Report

A 33-year-old woman, gravida 1, para 1, at 38 weeks and one day of pregnancy had a cesarean delivery because of previous history of myomectomy. On ultrasound a finding of placental retention was noted, thus curettage was attempted two weeks postpartum but moderate fresh bleeding was induced. She was referred to us for further management. On admission, since the uterus became firmly contracted and the patient was hemodynamically stable, she wanted to conserve her uterus. Magnetic resonance imaging showed a retained placental mass with rough borders. The mass, which measured 75 x 70 x 65 mm, was lodged on the posterior wall with minimum myometrial invasion (Figure 1a). Contrast-enhanced computed tomography depicted the multiple vessels within the intrauterine mass and the absence of deep myometrial invasion. Neither solid components nor calcifications could be identified (Figure 1b). Her human chorionic gonadotropin (HCG) level was 78.0 mIU/ml, and a general examination revealed no other abnormality. The patient received four doses of 50 mg of methotrexate intramusculary every other day, alternating with four doses of 15 mg of folic acid. She was carefully monitored for vaginal bleeding and sepsis. After four cycles (one cycle per 2 weeks), color Doppler ultrasound scan showed that the placenta had shrunk in size and decreased in its vascurality, indicative of necrotic tissue. Serum HCG became negative. An attempt to evacuate the necrotic tissue along with withdrawal bleeding was successful after three courses of sequential conjugated estrogen (0.25mg)-progestin (5 mg) therapy. Subsequent ultrasonographic examination documented an empty uterine cavity.

Discussion

Methotrexate affects placental tissue by decreasing vascularity leading to necrosis [1]. The sensitivity of chorionic tissue to methotrexate is well documented by its use in gestational trophoblastic neoplasia, abnormal pregnancy, and medical termination of pregnancy [1]. There are some reports of successful use of methotrexate in cases of placenta accreta or placenta increta [2, 3]. This report adds another and justifies its use in selected cases. The patient in this report received estrogen and progestin derivatives to effectively protect the endometrium, induce regular withdrawal bleeding and hasten expelling retained necrotic placenta. Combined sequential estrogen replacement regimens with progestin given very rarely fail to protect the endometrium, rather than surgical curretage [4]. The use of estrogen and progestogen and of methotrexate in combination may be simple and potentially effective for placenta accreta and placenta increta. Though experience in the management of placental adhesive disorders with this protocol is limited and should be strictly supervised, it should be taken into consideration if the patient desires future fertility.





Figure 1. — Retained adhesive placenta. a; sagittal T2-weighted MRI showing a placental mass embedded in the uterine posterior wall with minimum myometrial involvement (arrow), in accord with placenta accreta. b; horizontal contrast-enhanced CT showing the highlighted area of increased vascularity that does not cross the uterine wall (arrow).

References

- [1] Bretelle F., Courbière B., Mazouni C., Agostini A., Cravello L., Boubli L. et al.: "Management of placenta accreta: Morbidity and outcome". Eur. J. Obstet. Gynecol. Reprod. Biol., 2007, 133, 34.
- [2] Crespo R., Lapresta M., Madani B.: "Conservative treatment of placenta increta with methotrexate". *Int. J. Gynaecol. Obstet.*, 2005, 91, 162.
- [3] Mussalli G., Shah J., Berck D., Elimian A., Tejani N., Manning F.: "Placenta accreta and methotrexate therapy: Three case reports". *J. Perinatol.*, 2000, 20, 331.

[4] Burch D., Bieshuvel E., Smith S., Fox H.: "Can endometrial protection be inferred from the bleeding pattern on combined cyclic hormone replacement therapy". *Maturitas*, 2000, *34*, 155.

Address reprint requests to: A. IMAI, M.D. Institute of Endocrine-Related Cancer Matsunami General Hospital Kasamatsu, 501-6062 (Japan) e-mail: aimai@matsunami-hsp.or.jp