CASE REPORT

Cervical pregnancy with massive bleeding after treatment with methotrexate

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Professor Theera Tongsong,
ttongson@mail.med.cmu.ac.th**SUMMARY**

This report describes a catastrophic bleeding following methotrexate treatment of cervical pregnancy and dramatic response to Bakri surgical obstetric silicone (SOS) balloon tamponade in controlling massive bleeding. A 42-year-old woman was diagnosed for cervical pregnancy with a viable fetus at 12 weeks by transvaginal ultrasound. Conservative treatment with intrafetal potassium chloride injection and systemic methotrexate were instituted. On the sixth day of therapy, catastrophic bleeding lead to hypovolemic shock. After resuscitation and blood transfusion, we attempt to control the bleeding with evacuation and curettage but was unsuccessful. Bakri SOS balloon tamponade was applied with immediate and effective response. Nevertheless, total abdominal hysterectomy was performed. In conclusion, conservative treatment of cervical pregnancy with systemic methotrexate could be catastrophic in some patients. Control of active bleeding with Bakri SOS balloon tamponade may possibly be helpful in case of uncontrolled bleeding in selected cases.

BACKGROUND

Cervical pregnancy is a rare type of ectopic pregnancy, but potentially life-threatening. It is defined as an implantation of a fertilised ovum in the cervical canal, occurring between 1 in 1000 and 1 in 95 000 pregnancies, accounting for less than 1% of all ectopic pregnancies.^{1 2} Traditionally cervical pregnancy has been managed surgically, typically by total abdominal hysterectomy, owing to higher risk of massive bleeding. Nevertheless, with the advent of transvaginal ultrasound and the rapid sensitive assay of serum β human chorionic gonadotropin (β hCG) in the past two decades, most ectopic pregnancies, including cervical pregnancies, have often been diagnosed in earlier gestation. Consequently, management of cervical pregnancy with radical modalities has shifted to more conservative approaches.³⁻⁹ Most reports have demonstrated high efficacy and safety of conservative treatment of cervical pregnancy either by medical treatment with methotrexate administration, uterine artery embolisation, or hysteroscopic resection or dilatation and curettage with Foley's balloon tamponade. None in such reports found serious complications with conservative management, though failure might be seen in few cases. The objectives of this report were to describe catastrophic bleeding secondary to methotrexate treatment of cervical pregnancy and to illustrate the dramatic response to Bakri surgical obstetric silicone (SOS) balloon

tamponade in controlling massive bleeding from cervical pregnancy, rarely described elsewhere.

CASE PRESENTATION

A 42-year-old woman, G2 P0010, first presented for antenatal care at 12 weeks of gestation. She was healthy and asymptomatic at first visit without history of in vitro fertilisation treatment and with no vaginal bleeding. Her first pregnancy ended with spontaneous abortion at 9 weeks of gestation, without any interventions. On physical examination, the patient was healthy with stable vital signs. Pelvic examination revealed enlarged barrel-shaped cervix, 1 cm dilation, minimal effacement and no sign of vaginal or cervical bleeding. Transabdominal ultrasonography was performed for nuchal translucency, using 3.5 MHz transducer (Voluson E8; GE Medical Systems, Zipf, Austria). An ultrasound examination revealed a gestational sac with fetal cardiac activity situated 1 cm above the external os. A cervical ectopic pregnancy was diagnosed and was confirmed by transvaginal ultrasound (5 MHz transducer) based on the findings of an empty uterus, an enlarged barrel-shaped cervix which was larger than the uterine corpus. The gestational sac was located below the level of the uterine arteries, absence of the sliding sign (the gestational sac did not slide against the endocervical canal when pressure from the transducer was applied to the cervix) and high vascularisation around the gestational sac on colour flow mapping (figure 1 and video 1). The fetus had cardiac activity with crown-rump length of 5.5 cm. The placenta was localised in the markedly enlarged cervical canal. The uterine corpus and fundus were

Figure 1 Transvaginal colour Doppler ultrasound, sagittal scan of the uterus, showing conceptive product occupies the whole cervix; note: vascularisation of the placental site and empty uterine corpus.

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Video 1 Transvaginal color Doppler ultrasound, sagittal scan of the uterus, shows conceptus occupies the whole cervix, Note: vascularization of the placental site and empty uterine corpus.

empty. The outline of uterine cavity and conceptive products were clearly delineated.

After proper counselling, the couples strongly requested for conservative management and the plan of management was outlined as follows. The patient was admitted to the hospital for inpatient management. Serum β -hCG was scheduled for follow-up as a standard protocol. Intrafetal potassium chloride (KCL) injection was administered under ultrasound guidance and the fetal activity disappeared immediately, followed by administration of systemic multidose regimen of methotrexate. She was haemodynamically stable, pain free, had no haemoperitoneum on ultrasound examination and had normal kidney and liver function. She received four doses of methotrexate (50 mg/m^2 of body surface area) given intramuscularly, alternating with four doses of oral folinic acid 5 mg daily.

Apart from mild nausea and gastritis, she tolerated the treatment well. Serum β -hCG levels slightly declined during the first, fourth and sixth day of treatment, $60\,826$, $53\,630$, and $47\,498 \text{ IU/L}$, respectively. On the sixth day of treatment, the patient had sudden massive bleeding per vagina leading to hypovolemic shock within a short time. Fluid replacement and blood transfusion was instituted and the patient was transferred to the operative room for surgical control of bleeding, soon after

Figure 3 Longitudinal section of the cervix depicts area of the placental site with adherens in the elongated cervix (12 cm in length).

resuscitation, to maintain haemodynamics. Under general anaesthesia, conceptive product was evacuated through cervical os followed by curettage to remove the remaining placental tissue. However, active bleeding still continued throughout the procedure and finally the vital signs became unstable again, despite blood transfusion. To control the active local bleeding, Bakri SOS balloon tamponade was applied, with inflation by normal saline (200 mL), at the implantation site in the cervix. The bleeding dramatically stopped. However, due to unstable vital signs and unsure of further bleeding after the balloon removal, decision to perform total abdominal hysterectomy was made. The balloon was removed after both of the uterine arteries were secured. No significant bleeding from the cervix was observed during hysterectomy. Overall estimated blood loss was approximately 5000 mL . Postoperatively, the patient suffered from acute tubular necrosis and disseminated intravascular coagulation, a consequence of the hypovolemic shock due to massive blood loss. However, the patient gradually improved to complete recovery without any serious sequelae and was discharged on the twelfth day after operation.

Pathological examination revealed markedly enlarged cervix containing cervical pregnancy with placenta increta along circumferential cervical canal with underlying typical cervical

Figure 2 Bivalved gross specimen showing conceptive product occupies the whole cervix; note: empty uterine corpus.

Figure 4 Microscopic findings of the cervix showing placental site with underlying connective tissue and glandular structures of the cervix.

tissue characterised by cervical connective tissue and mucin-secreting endocervical glands (figures 2–4). The cervical canal was stretched to 12 cm in length.

OUTCOME AND FOLLOW-UP

The patient was healthy without any serious sequelae on the follow-up visit at 6 weeks after operation.

DISCUSSION

Of note, the most common presenting symptom is vaginal bleeding, with previous curettage and caesarean delivery being the most common risk factors, which supports what has been reported previously in the literature.^{10–11} However, cervical pregnancy in the case presented here was asymptomatic at first visit and had no known risk factor, spontaneously occurring in the first pregnancy.

The diagnosis of cervical pregnancy in the case presented here was based on diagnostic criteria using transvaginal ultrasonography,⁵ including (1) empty uterine cavity above the internal os; (2) barrel-shaped cervix; (3) typical gestational sac was located below the level of the uterine arteries; (4) the absence of the 'sliding sign' (when pressure from the transducer is applied to the cervix, the gestational sac slides against the endocervical canal in case of imminent abortion but not in an implanted cervical pregnancy; and (5) the vascularisation around the gestation sac demonstrated by Doppler colour flow mapping.

Most cases of cervical pregnancy occur in women of reproductive life, many of whom desire to preserve fertility. In the past two decades with the advent of transvaginal sonography, which can facilitate an earlier diagnosis, conservative management is therefore more commonly practiced. A variety of approaches have been proposed,¹⁰ including dilation and evacuation combined with Foley balloon tamponade, methotrexate with/without KCL injection, uterine artery embolisation^{4–12} and ligation of cervical branches of uterine arteries. The most commonly reported medical treatments are methotrexate, either local injection (intra-amniotic or intrafetal)^{1–13–14} or systemic administration,^{2–3–7–9–15–17} commonly used in conjunction with fetal KCL injection.^{15–18} The outcomes of conservative management with methotrexate have been reported to be relatively safe and highly effective in more than 90% of cases earlier than 12 weeks of gestation,¹⁹ though the time to resolution varies largely.¹⁸ Furthermore, no evidence of adverse effects on subsequent pregnancies was shown.

Unlike reports between 1960 and 1980 in which most cases of cervical pregnancy underwent total abdominal hysterectomy,¹⁰ most recent studies have shown successful conservative treatment of cervical pregnancy without complications.^{1–2–5–9–11–13–14–20–22} In the past decade, failure cases of conservative treatment resulting catastrophic haemorrhage have been very rarely reported in literature. It is possible that the cases of failure and massive bleeding, leading to hysterectomy, might recently tend to be unreported or there is less opportunity to be published compared with those with successful treatment. Therefore, the number of fatal cases with conservative treatment may be underestimated and the effectiveness of medical treatment could be overestimated. Unlike several reports, our case signifies that cervical pregnancy could be catastrophic even in case of well-prepared, especially the cases with higher gestational age like our case. Medical treatment with methotrexate after fetal destruction with KCL is not always successful.

Owing to its large size, effectiveness in bleeding control was unlikely to be achieved with Foley catheter balloon fixation.²¹ We used Bakri SOS tamponade balloon for temporary bleeding control during total abdominal hysterectomy and such a

procedure yielded a high efficacy. The active and massive bleeding immediately stopped. To the best of our knowledge, this is the first report on controlling bleeding due to cervical pregnancy with Bakri SOS tamponade balloon. This experience suggests that Bakri SOS tamponade may be applied in conservative treatment as well, though we temporarily used it for preventing further blood loss during the switching of the procedure due to active bleeding with unstable vital signs in our case. Of note, we did not use an inflated Foley balloon catheter as a local tamponade in this case, as in previous reports, since it was expected to be too small to be effective in the markedly enlarged cervix.

While conservative management of cervical pregnancy in early gestation may be safe and effective, it seems to us that such a treatment at late first trimester or early second trimester, like our case, must be performed with extreme caution in well-prepared settings with available surgical team, anaesthetists and adequate blood components. It should be kept in mind that during the treatment of cervical pregnancy with methotrexate, catastrophic bleeding can unexpectedly occur, extreme cautions must be exercised, especially in the case of large gestational sac, like in our case. The acute massive bleeding without any warning signs in the case presented here was likely to be associated with some degree of partial separation of the placenta in response to methotrexate.

Insights gained from the case presented may be concluded as follows: (1) conservative treatment of cervical pregnancy with systemic methotrexate could be catastrophic and must be carried out with extreme precaution especially in case of higher gestational age. (2) Control of active bleeding with Bakri SOS balloon tamponade can be helpful and should be considered in case of uncontrolled bleeding especially from enlarged cervical canal, while fertility may possibly be preserved in some selected cases.

Learning points

- Ultrasound findings of cervical pregnancy in this case have been instructive, informative and inspire sonographers to alert on this problem.
- Catastrophic bleeding can suddenly occur during treatment with methotrexate.
- Bakri surgical obstetric silicone balloon tamponade can dramatically stop bleeding from large cervical pregnancy.

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Competing interests None.

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