Management of Cervical Pregnancy: Case Series and Literature Review

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ABSTRACT

Cervical pregnancy is a rare form of ectopic pregnancy and clinical diagnosis is a challenge to physicians. At present, there is no consensus for standard treatment, but medical treatment becomes the first line treatment. We have reported four cases of cervical pregnancy and reviewed literatures regarding the diagnosis and modalities of treatment for this condition.

Keywords: Cervical pregnancy; conservative treatment; methotrexate

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INTRUDUCTION

Cervical pregnancy is a rare form of ectopic pregnancy, of which the conception implants at endocervical canal. The incidence of cervical pregnancy is 1:1,000 to 95,000 pregnancies and it accounts for less than 1% of all ectopic pregnancies.1 Risk factors of cervical pregnancy were mentioned in many literatures2,3 such as previous uterine curettage, previous cesarean section, use of assisted reproductive technology, and presence of uterine fibroids. Cervical pregnancy can cause significant morbidity and mortality, because it is difficult to make diagnosis and to control serious complication, i.e. intractable hemorrhage. In the past, hysterectomy was the treatment of choice. Nowadays, cervical pregnancy can be diagnosed at an earlier gestational age, because of high resolution ultrasound and sensitive serum beta human chorionic gonadotropin (β-hCG) test. Consequently, conservative treatment with surgical and/or medical methods can be achieved without the need for hysterectomy and fertility can be preserved. Many treatment options such as methotrexate (MTX), cervical curettage, intra-cervical balloon tamponade, cervical cerclage, and uterine arteries embolization (UAE), have been introduced to treat cervical pregnancy.

We have reported four cases of cervical pregnancy being managed at the Faculty of Medicine Siriraj Hospital, a tertiary care referral hospital, between 2005 and 2015. We also reviewed literatures regarding the diagnosis and modalities of treatment for this condition.

CASE REPORT

Case 1
A 27-year-old primigravida had painless light vaginal bleeding for 2 weeks. Her gestational age (GA) was 8 weeks by last menstrual period (LMP). Her obstetric and gynecological histories
were unremarkable. Transvaginal ultrasonography revealed a gestational sac (GS) of 19.6 mm in mean sac diameter at cervical canal, containing an embryo of 5.4 mm in crown lump length (CRL). (Fig 1 and 2) Cardiac activity of the embryo was detectable. Initial serum $\beta$-hCG was 4,259 mIU/mL. The patient was hospitalized and treated with multidose intramuscular MTX (1 mg/kg) on days 1, 3, 5 and 7, and intramuscular leucovorin (0.1 mg/kg) on days 2, 4 and 6. Pelvic examination on day 8 after completion of treatment demonstrated bleeding necrotic tissue at the cervical os. The patient then underwent evacuation and curettage. Histopathology report of the curetting revealed products of conception. Serum $\beta$-hCG was monitored weekly and the level returned to 1.2 mIU/mL at week-4 after starting MTX. Subsequently, the patient had two successful term pregnancies.

Case 2
A 28-year-old, gravida 4 para 1, presented to our hospital for her first episode of painless light vaginal bleeding. Her LMP was 6 weeks ago. She had one term vaginal delivery, surgery for tubal pregnancy and uterine curettage for illegal abortion at 8-week gestation. Transvaginal ultrasonography revealed a GS at cervical canal, containing an embryo of 5.4 mm in CRL.

Transvaginal ultrasonography revealed a GS at cervical canal. There was an embryo of 7.7 mm in CRL and cardiac activity was detectable. Initial serum $\beta$-hCG was 55,799 mIU/mL. During hospitalization, she developed heavy vaginal bleeding. Pelvic examination showed profuse bleeding through an open cervical os. Her vital signs included blood pressure 80/50 mmHg and pulse rate 90/minute. Then she underwent emergency evacuation and curettage under intravenous anesthesia. Estimated blood loss during the operation was 250 mL. Her hematocrit immediately after the operation was 28% and she received one unit of packed red cell (PRC). Histopathology report of the curetting confirmed trophoblastic villi. Two weeks after the operation, she still had persistent light vaginal bleeding through one-cm dilated cervical os and had serum $\beta$-hCG of 493 mIU/mL. Transvaginal ultrasonography showed retained product of conceptus in the cervical canal. The patient was re-hospitalized and treated with multidose intramuscular MTX (1 mg/kg) and intramuscular leucovorin (0.1 mg/kg) using the same protocol as in Case 1. On the 5th and 9th day of treatment, the patient had profuse vaginal bleeding with hypovolemic shock. She had PRC transfusion. The bleeding spontaneously stopped without any intervention. Serum $\beta$-hCG was monitored weekly and the level returned to normal level at week-4 after starting MTX. Subsequently, the patient had one successful term pregnancy.

Case 3
A 36-year-old gravida 3 para 2 presented with moderate vaginal bleeding with pelvic pain. Her LMP was 8 weeks ago. She had prior two cesarean sections at full term pregnancies. Transvaginal ultrasonography showed GS at cervical canal. An embryo with a CRL of 20 mm and cardiac activity were identified. Initial serum $\beta$-hCG was 60,663 mIU/mL. She was hospitalized and treated with multidose intramuscular MTX (1 mg/kg) and intramuscular leucovorin (0.1 mg/kg) using the same protocol as in Case 1. On the 4th day of treatment, the physician and the patient discussed about the treatment options, and hysterectomy was performed.
Case 4

A 21-year-old primigravida was referred to our hospital due to suspicion of cervical pregnancy. Her gestational age was uncertain. She presented with painless light vaginal bleeding. Her gynecological history was unremarkable. Transvaginal ultrasonography showed a GS-liked structure of 3 cm at cervical canal. Fetal echo could not be identified. Neither intrauterine GS nor adnexal mass was demonstrated. Her initial serum $\beta$-hCG was 2,824 mIU/mL. She was hospitalized and treated with single-dose intramuscular MTX 50 mg/m$^2$. Magnetic resonance imaging (MRI) was performed at one week after treatment and the finding was compatible with cervical pregnancy. Serum $\beta$-hCG was monitored weekly and the serum $\beta$-hCG level returned to normal level at week-4.

DISCUSSION

Cervical pregnancy is a rare condition and clinical diagnosis is a challenge to physicians. The common presenting symptom is painless vaginal bleeding. Pelvic examination usually shows enlarged cervix with partially dilated external orifice and closed internal orifice, and almost normal uterine corpus. Ultrasonography is one of the diagnostic tools. The criteria for diagnosis consist of (i) GS or placental tissue visualized within the cervix, (ii) cardiac motion noted below the level of the internal os, (iii) no intrauterine pregnancy, (iv) hourglass uterine shape with ballooned cervical canal, (v) no movement of the sac with pressure from transvaginal probe (“sliding sign” that is typically seen with incomplete abortions), and (vi) closed internal os. All of our cases had classical symptom of vaginal bleeding and ultrasonogram met the criteria for diagnosis, except for the last case, which needed MRI to confirm the diagnosis of cervical pregnancy.

The etiology of cervical pregnancy is still inconclusive, but many literatures proposed various risk factors for this condition. In our patients, the potential risk factors included previous uterine curettage and cesarean section.

Up-to-date, there is no consensus for standard treatment. In the past, hysterectomy used to be the treatment of choice. Nowadays, medical treatment has become the first line treatment because of its simplicity, high success rate, and ability to preserve fertility. Surgical treatment is then preserved for the case with failure of medication or profuse hemorrhage. Systemic MTX, either single dose regimen (50 mg/m$^2$ intramuscularly) or multidose regimen (1 mg/kg of MTX intramuscularly for up to four doses with 0.1 mg/kg of leucovorin intramuscularly on alternating day) has demonstrated successful outcome in many reports. Nevertheless, there is no consensus about the MTX regimen for cervical pregnancy. At presence, treatment regimen varies on physician’s preference. Krik et al., reported that the success rate of systemic MTX treatment was 83%. Factors affecting the success rate were GA, level of serum $\beta$-hCG, and presence of embryonic heart activity. Failure from MTX was significantly associated with GA ≥9 weeks, serum $\beta$-hCG ≥10,000 mIU/ml, CRL >10 mm, and presence of embryonic cardiac activity. The overall success rate of primary MTX treatment for cervical pregnancy without and with embryonic cardiac activity were 90.0% and 40%, respectively.

Using combined treatment of systemic MTX and feticide method, for example intra-cardiac potassium chloride (KCl), or intra-amniotic MTX, can increase the success rate. Local intra-amniotic MTX alone or with intra-cardiac KCl in case of presence of embryonic cardiac activity has also been described. Never theless, intra-amniotic injection requires experienced physician. In the present report, three cases were initially treated with medical treatment using intramuscular MTX, but only one case had successful result, whereas the others needed subsequent surgical treatment, curettage or hysterectomy. Both of our failure cases had embryonic cardiac activity, and one case had high level of $\beta$-hCG. Thus combined treatment with feticide method may minimize the risk of MTX failure and avoid surgical intervention.

Our second case required curettage because of profuse vaginal bleeding, but the surgical management failed because serum $\beta$-hCG showed plateau level. The failure of curettage may be caused by the deep invasion of placenta into the endocervical tissue. Hence, serial serum $\beta$-hCG
Cervical pregnancy is uncommon and currently there is no standard treatment. Conservative treatment, with either medical or surgical method, has high success rate and can preserve fertility.

**CONCLUSION**

Cervical pregnancy is uncommon and currently there is no standard treatment. Conservative treatment, with either medical or surgical method, has high success rate and can preserve fertility. Combination with adjuvant procedure, especially the feticide method, will increase success rate in case of cervical pregnancy with embryonic cardiac activity.
Declaration of conflicting interests
The authors declare that they have no conflict of interest.

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