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CASE REPORT

Failed conservative management of cervical pregnancy despite falling beta-HCG

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CASE HISTORY

A 40-year-old gravida 2, para 1 Bangladeshi woman was referred to our clinic at 8 weeks' gestation for management after an ultrasound for early pregnancy bleeding revealed a cervical ectopic pregnancy. Her five-year-old daughter had been delivered by lower uterine segment Caesarean section for unknown complications in labour. Examination in the clinic revealed an enlarged boggy mass at the anterior cervix, and an irregular, enlarged uterus 12 weeks' gestation in size. The beta-human chorionic gonadotrophin (HCG) was 62,126 mIU/mL. The ultrasound performed by a specialist obstetrics and gynaecological ultrasonologist, had revealed a gestational sac of 2.4 cm in diameter with fetal cardiac activity evident. The fetal crown rump length was 19 mm. These findings were confirmed on repeat ultrasound at our hospital.

As bleeding was not severe, and another child was desired in the future, the patient was offered conservative treatment. Two stat doses of 50 mg IM methotrexate were given 24 hours apart. The possibility of local injection of methotrexate was considered, but rejected on the grounds that the risk of inducing severe bleeding would be too great. It was felt that feticide could be achieved with systemic chemotherapy alone. Indeed, a follow-up ultrasound scan one week after initial presentation revealed that although the pregnancy had not changed in size, fetal cardiac activity was no longer visible. beta-HCG was followed up, and declined rapidly with systemic methotrexate treatment (see graph in Figure 1). Management was on an outpatient basis, and per vaginam bleeding, although intermittent, was light.

Despite falling beta-HCG, an ultrasound performed four weeks after treatment revealed an enlarged gestational sac of 4 cm diameter, with a 6 cm diameter area of increased vascularity. Two days later, one month following initial treatment, the patient called from home to report heavier vaginal blood loss and moderate lower abdominal pain, and was advised to come in to hospital. On arrival, 750 mL of vaginal bleeding was observed, and ongoing bleeding was heavy. Examination was not possible due to discomfort, and the patient was consented for an examination under anaesthetic, with the understanding that a hysterectomy might be necessary to arrest bleeding. Blood was cross-matched, and a haemoglobin prior to theatre was 11.7 g/dL.

On examination under anaesthetic, an 8 weeks' gestation size uterus with bulky cervix and open os was found. A suction curette followed by sharp curettage of the ectopic sac was performed, and a size 20 French prostatic catheter filled with with 75 mL of water into the balloon was inserted to apply tamponade to the oozing area. Bleeding was controlled, and the patient returned to the ward.

Five hours later, the patient experienced further heavy vaginal bleeding around the balloon catheter. On examination the patient had cool peripheries, her blood pressure was 75/40 mmHg, and pulse rate 90/min. Her haemoglobin was 6.3 g/dL. A blood transfusion was commenced. Returning to theatre, a midline laparotomy revealed a fibroid uterus with a cervical ectopic adherent to the bladder. The decision was made to proceed with hysterectomy, as uterine artery embolisation was not available overnight. Pathology showed mild chronic endometritis in the cervical ectopic, which had ruptured into the endocervical canal. There were some scattered degenerate chorionic villi. The patient recovered uneventfully and, apart from grief over lost fertility, had no long-term ill effects.

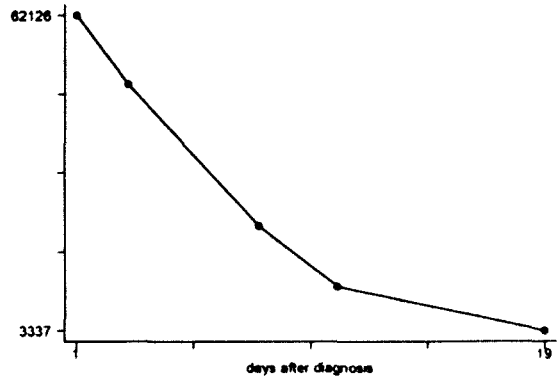

Figure 1 Maternal serum beta-HCG levels (mIV/mL) following diagnosis of cervical pregnancy and methotrexate therapy

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DISCUSSION

Cervical pregnancies are rare, accounting for < 1%[1] of all ectopics. Their incidence has been reported at one per 8628 deliveries.[2] Risk factors include anatomical anomalies, myomas, synechiae (as in Asherman's syndrome), and surgical interventions damaging the endocervical mucosa.[3] It has been postulated that previous Cesarean section, particularly if performed at or near the end of the first stage of labour, may predispose to cervical pregnancy if the scar is in the distal lower uterine segment or upper cervix.[2] Our patient had a past history of a Cesarean section in labour.

The advent of ultrasound and accurate serum tests for beta-HCG have dramatically improved our ability to diagnose cervical pregnancy at an early stage. A recent review of 117 cases revealed an increase in correct diagnosis of cervical pregnancy from 35 % in the years 1978–1982 to 87.5% in 1991–1994.[2] Early diagnosis allows conservative treatment to be initiated, avoiding the need for a hysterectomy, and enabling the retention of fertility. Options for conservative surgical treatment include dilatation and suction curettage accompanied by one of a variety of methods for achieving haemostasis (Foley catheter tamponade, angiographic uterine artery embolisation, Shirodkar cervical cerclage, intracervical injection of vasoconstrictive agents such as prostaglandins, or transvaginal ligation of cervical branches of the uterine arteries). Medical treatment options include local or systemic administration of chemotherapy, most commonly methotrexate, alone or in combination with some method of feticide (eg potassium chloride injection). There is no consensus on the best treatment regimen, largely due to the rarity of the condition.

The most popular type of conservative treatment in first trimester cervical pregnancy at present is methotrexate, either systemic, local or a combination.[4] Dosage regimens differ between different centres. A recent retrospective study of 62 cases[4] evaluated the effectiveness of methotrexate therapy for the treatment of cervical pregnancy. It was found that 34% of women overall required a concomitant procedure, and 9% subsequently required a hysterectomy. However, division of the pregnancies into viable and non-viable groups (based on presence of detectable fetal cardiac activity) showed that the higher risk viable cervical pregnancies had a 43% chance of requiring a further procedure. The largest case series to date, by Ushakov and colleagues[2] showed that viable cervical pregnancies are actually the majority (61.5%) of cervical pregnancies. Thus, the largest group of cervical pregnancies have the smallest chance of successful conservative treatment. Poor prognostic factors for successful treatment with methotrexate, based on a statistical analysis of 48 cases[5] include: (i) beta-HCG > 10,000 mIU/mL; (ii) gestation > 9 weeks'; (iii) detectable fetal cardiac activity; and (iv) crown rump length > 10 mm. Our patient had all of the above poor prognostic factors apart from advanced gestation.

In cases of high-risk viable cervical pregnancies, various adjustments to conservative treatment regimems have been suggested. These include: the use of local and systemic methotrexate together,[3,6] although with the caution that local injection into the gestational sac can induce heavy bleeding requiring surgery;[7] more potent chemotherapy such as etoposide, actinomycin D, or a combination with methotrexate;[3] and prophylactic embolisation.[6] Higher doses of methotrexate appear to be no more effective than lower dose regimens,[5] although a recent case was reported of the successful use of high dose IV methotrexate (300 mg total).[8] Concomitant feticide with systemic methotrexate significantly increases the chances of successful conservative resolution of the pregnancy.[5] In our case beta-HCG rapidly fell following feticide by systemic methotrexate, but the outcome was still hysterectomy.

There is no reliable method of predicting treatment failure. Even with falling beta-HCG levels, patients may experience severe haemorrhage necessitating surgical intervention, as our case demonstrates. In one reported case,[9] hysterectomy was necessary to control bleeding after four months of conservative treatment, despite undetectable levels of serum beta- HCG for four weeks. Trophoblastic invasion of blood vessels was still evident on pathology.

Our case demonstrates two points. First, that optimism with regards to conservative treatment for cervical pregnancy must remain cautious, particularly if the pregnancy is viable, and patients must be aware that their chances of requiring a second modality of treatment approach 50 %. Second, that following maternal serum levels of beta-HCG gives no guide as to risk of subsequent haemorrhage. Other methods for following up treatment success, such as serial measurements of gestational sac size, confirmation of fetal demise, and peritrophoblastic colour Doppler flow analysis may need to be employed.

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