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Termination of Twin Pregnancies with Hydatidiform Moles: a Case Series of Four Patients

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(Received 22 Apr 2014; accepted 11 Jun 2014)

Abstract

P A twin pregnancy with a complete hydatidiform mole with a coexistent foetus (CHMF) is a rare condition that typically results in poor pregnancy outcomes. For patients with refractory vaginal bleeding, termination of pregnancy is more appropriate. However, unified methods for termination remain to be explored. In the present study, we reviewed the termination measures in four cases of twin pregnancy with CHMF. Additional understanding of this condition will aid in the treatment of women with this condition and improve their pregnancy outcomes.

Keywords: Hydatidiform mole, Invasive mole, Pregnancy

Introduction

A twin pregnancy with a complete hydatidiform mole and a coexistent foetus (CHMF) is a rare, high-risk pregnancy with an incidence of 1/20,000-1/100,000 (1-3). With the increase in infertility and improvements in assisted reproductive techniques, the incidence of CHMF has increased. To date, there have been more than 200 cases of CHMF reported in the literature, suggesting that the incidence of hydatidiform mole with a coexisting foetus has increased because of the widespread use of ovulation-inducing medications and assisted reproductive techniques in recent years (4-6).

Treatment of CHMF remains a matter of controversy (7). Although the medical community has realised that pregnancies in CHMF patients can be continued if there are no foetal abnormalities or severe maternal complications, due to the deepened understanding of this condition and the increase in published reports concerning patients with surviving foetuses (8-10), the continuation is likely to lead to complications, such as refractory vaginal bleeding, hypertensive disorders in preg-

nancy, hyperthyroidism, premature rupture of membrane; when these complications occur or the patient presents with a noticeable increase in β -HCG or a suspected pulmonary metastasis, pregnancy termination is more appropriate (11, 12). Furthermore, CHMF patients have an incidence of persistent gestational trophoblastic tumours (PGTTs) as high as 55% (2, 13, 14), which is a sarcohyseric malignancy. For normal single pregnancies before 28 gestational weeks, termination methods primarily include induced abortion (vacuum aspiration), curettage, mifepristone in combination with misoprostol, amniotic cavity injection of ethacridine, induction of labor with water bag, and hysterotomy delivery (15, 16). However, not all of these frequently-used treatments are suitable for CHMF. Most CHMFs can only be diagnosed in the mid trimester of pregnancy. Although the pregnancy in CHMF patients without massive vaginal bleeding can be terminated using the abovementioned methods, emergent pregnancy termination methods are necessary for those complicated by massive vaginal bleeding. Howev-

er, termination with mifepristone + misoprostol, amniotic cavity injection of ethacridine and induction of labor with water bag all fail to realize a termination effect within a short period; induced abortion and curettage are not suitable for pregnancies with a long gestation duration; amniotic cavity injection of ethacridine is difficult to perform for pregnancies before 16 gestational weeks due to a small amniotic fluid volume; induction of labor with water bag may increase the risks of bleeding and infections for patients with vaginal bleeding; and hysterotomy delivery causes serious injury, which cannot be adopted unless necessary (17). To date, studies focusing on termination methods for CHMF are rare. Therefore, standard pregnancy termination procedures remain to be explored.

In this paper, we review the termination methods used for four patients with CHMF complicated by heavy bleeding. We analysed the similarities between these patients to provide references for the termination treatment of this disease.

Case report

From January 2012 to March 2013, four patients with CHMF received termination treatment at the Second Xiangya Hospital of Central South University, Changsha, China. Their clinical data before termination are summarized in Table 1.

This study was approved by the Ethics Committee of the Second Xiangya Hospital of Central South University. All patients signed an informed consent form.

The youngest of the 4 patients was 22 years old, and the oldest was 37 years old. The gestational ages ranged from 11+ to 24+ weeks. Of the patients, 3 had previously received human menopausal gonadotropin/human chorionic gonadotropin (hMG/hCG) after an in vitro fertilisation-embryo transfer to stimulate ovulation before pregnancy and 1 became pregnant by using Chinese medicine (including antler glue, dried human placenta, *ne-lumbo nucifera gaertn.*, *schisandra chineisis baill.*, and so on for the treatment of ovulation failure; 7 d/course) 10 years after getting married. All four patients had morning sickness early after their last

menstruation and presented to the hospital because of vaginal bleeding. Their β -HCG levels were 200,000 mIU/L or higher 6-8 weeks after the last menstruation. Their ultrasound acoustic images showed a live foetus generally consistent with its gestational age without structural abnormalities. All patients were hospitalised due to difficulties becoming pregnant, persistent vaginal bleeding, and a strong desire to take tocolytics. After hospitalisation, screening demonstrated a low risk for Down's syndrome, and ultrasound examinations identified no apparent foetal abnormalities in these patients. During the pregnancy, there were no signs of discomfort, such as headache, dizziness, cough, sputum, and haemoptysis. Of the four patients, two were mildly pale, and two had oedema (+). The gynaecological examinations showed dark red blood within the vagina in all of the patients. The patients experienced continued refractory vaginal bleeding accompanied by abdominal bloating during treatment. After informed of the risk of maternal complications if tocolysis continued, they made decision to commence pregnancy termination.

Among the patients, one (case 1) with a gestational age of 13+ weeks directly received emergency clamping and uterine evacuation. However, her β -HCG did not return to normal at 70+ days after three uterine evacuations. In case a PGT was present, the patient was subjected to five courses of chemotherapy with 5-fluorouracil (26-27 mg/kg·d) combined with kengshengmycin (KSM; 6-7 μ g/kg·d). Each course lasted 8 d, and the interval between courses was 21 d. Three courses were administered for consolidation. Another patient with a gestational age of 13+ weeks was strongly suspected to have an invasive hydatidiform mole because of an abnormal increase in β -HCG. She underwent three uterine evacuations after the first course of chemotherapy with 5-FU+KSM (six courses in total, including three consolidation courses). Two cases had a mid-gestational foetus of 20+ to 24+ weeks. For them, the clamping technique would not work because the cervical opening was not large enough, and a caesarean section abortion was not suitable because this procedure would have caused trauma to

the pregnant mother. Considering that the hydatidiform mole was the likely cause of the refractory vaginal bleeding, we followed the protocol for the treatment of hydatidiform moles and evacuated the uterus using a large pipette; the procedure was performed in an operating room that was prepared for transfusion and equipped for surgery. After most of the molar tissues were evacuated and the bleeding was significantly decreased, oxytocin was administered to promote uterine contractions and dilatation of the cervical opening. While waiting for the cervix to dilate, we clamped the foetal body using tissue forceps laid firmly against the cervix. This treatment not only promoted cervical dilation but also strengthened the uterine contractions. The clamping technique was performed until the cervical opening was approximately the size of the foetal biparietal diameter. During this process, there was not much blood loss, and the clamping procedure proceeded well in all three patients. The foetuses and placental tissues were all successfully clamped within 3-6 hours after the molar evacuation. Post-operative pathological examinations suggested pregnancy with a complete hydatidiform mole in all four patients. The karyotypes of the foetal heart blood and hydatidiform mole were normal in three patients, while the remaining patient (case 3) refused to undergo the chromosome examination. The results are summarized in Table 2.

After labour induction, the β -HCG levels in the 4 patients decreased to normal at approximately 3-17 weeks, and their menstruation recovered at approximately 4-24 weeks. All patients were followed up for one year and the examinations included β -HCG determination, chest X-rays, hyperthyroidism test, ultrasound examination and gynaecological tests. The treatment outcomes are summarized in Table 2.

Discussion

We reviewed the treatment of four cases of CHMF and explored the termination methods utilised. Determining whether a pregnancy with CHMF should be terminated is difficult (7). If the patient is in a

stable condition, the ultrasound examination suggests a live foetus, the karyotype is normal, and the patient is in agreement, the pregnancy should continue with close observation (3). However, CHMF is subject to a high-risk pregnancy, which can lead to complications, such as refractory vaginal bleeding, hypertensive disorders in pregnancy, hyperthyroidism and premature rupture of membrane and has a high possibility of developing into PGTT (2, 13, 14). Therefore, pregnancy termination is the safest choice for the patients with serious clinical complications, such as severe vaginal bleeding or preeclampsia, or for those with increased levels of β -HCG or suspected pulmonary metastasis (18, 19). In this study, the four patients described had similar clinical manifestations, such as having early postmenopausal vaginal bleeding, having difficulty becoming pregnant, undergoing ovulation-inducing drug treatment before pregnancy, having high expectations for the foetus, and having a strong desire to maintain the pregnancy; however, considering long-lasting and refractory vaginal bleeding accompanied by abdominal boating and the consideration of the risk of developing obstetrical complications, all patients agreed to discontinue the tocolytic treatment and proceed with emergency pregnancy termination. However, not all of frequently-used termination methods for normal single pregnancies are suitable for CHMF (17). According to literature (12), for early CHMF pregnancies, the direct clamping technique and evacuation are the most commonly used methods; for mid-gestational pregnancies with a relatively large foetus and little vaginal bleeding, routine induced labour can be performed, i.e., the cervical opening is dilated under the action of labour drugs until the foetus can be delivered through the vagina; and for mid-gestational pregnancies with emergency bleeding, caesarean section may be preferred over artificial rupture of the foetal membrane, oxytocin infusion-induced labour, or rivanol amniotic cavity injection-induced labour to avoid implantation into the peritoneal cavity and life-threatening haemorrhaging caused by the molar tissues being squeezed into the peritoneal cavity through the oviducts during uterine contractions.

Table 1: Clinical data before pregnancy termination

No	Age (yr)	G/P	Ovulation induction medication	Clinical symptoms	First vaginal bleeding time	β -HCG at first vaginal bleeding	Tocolysis	Time of vaginal bleeding (days)	Ultrasound findings
1	30	1/0	HMG/hCG	Vaginal bleeding, accompanied by abdominal bloating	8 w	1,069,300	Yes	10+	Dual live foetuses within the uterus, in accordance with the months of amenorrhea. A heterogeneous echo pattern of 3+ cm was detected within one of the foetal placental lower edges and the anterior uterine wall, which was increased to 10+ cm when examined for tocolysis; there were fine dark areas within it, which was alveolar without an apparent blood colour.
2	24	1/0	HMG/hCG	Vaginal bleeding, accompanied by abdominal bloating	9 w	1,425,000	Yes	10+	The intrauterine foetus stopped developing, and the placenta showed an alveolar echo.
3	37	2/0	Not pregnant for 10 years. Traditional Chinese medicine was administered orally	Vaginal bleeding, accompanied by abdominal bloating	10+ w	118,200	Yes	40+	Single intrauterine live foetus, approximately 10 weeks of gestation; the placenta showed an abnormal echo, suggesting close observation.
4	22	1/0	HMG/hCG	Vaginal bleeding, accompanied by abdominal bloating	11+ w	108,200	No	30+	Single intrauterine live foetus; the partial placenta was increased and accompanied by large amounts of vesicle-related fluid dark areas, suggesting follow-up.

Table 2: Clinical data at and after pregnancy termination

No.	Time of pregnancy termination	Methods for pregnancy termination	Karyotype of hydatidiform mole	Time of β -HCG (mIU/L) re-	Persistent trophoblastic disorders	Chemotherapy	Contents of follow-up	Time of menstruation recovery	Ultrasound examination after evacuation
1	13+ w	Direct evacuation for short period of amenorrhea	46,XY	115	Yes	5-FU+KSM	To test β -HCG once every week; chest film once every 3 weeks; hyperthyroidism test	182	Intrauterine high echo of 4*3*2 cm; evacuation was performed twice
2	13+ w	To remove most of the molar tissues by 5-FU+KSM and clamp the foetus after bleeding had decreased and the cervix had dilated under pro-cervical-opening-dilation medications	unknown	121	Yes	Yes	To test β -HCG once every week; chest film once every 3 weeks; hyperthyroidism test	191	Intrauterine heterogeneous high echo, with rich blood colour; continuous chemotherapy
3	20+ w	To remove most of the molar tissues and clamp the foetus after bleeding had decreased and the cervix had dilated under pro-cervical-opening-dilation	46, XX	28	No	No	To test β -HCG once every week; gynaecological test once every month	67	No abnormal acoustic image
4	24+ w	To remove most of the molar tissues and clamp the foetus after bleeding had decreased and the cervix had dilated under pro-cervical-opening-dilation medications	46, XX	35	No	No	To test β -HCG once every week; gynaecological test once every month	86	No abnormal acoustic image

However, because reports on termination of CHMF are rarely released, standard pregnancy termination procedures remain to be explored. In this study, of the two patients in early pregnancy (gestational age, 13+ weeks), one was subjected to direct emergency clamping and uterine evacuation, and the other underwent chemotherapy followed by uterine evacuation due to the high risk of an invasive hydatidiform mole. The two patients in mid-trimester pregnancy (gestational age, 20+-24+ weeks) both had the manifestations of massive haemorrhage and an insufficiently large cervical opening. Considering that vaginal bleeding may become aggravated or even become life-threatening during medical induction of labour and that direct caesarean section could cause serious psychic and physical traumas, we removed most molar tissues first during the massive haemorrhage and then administered cervical dilatation drugs until haemorrhaging noticeably decreased. By performing these procedures, we minimised the haemorrhaging that could occur while waiting for the cervix to dilate and reduced the risk for pulmonary embolism from the metastasis of trophoblastic cells into the uterine wall sinusoids under premature oxytocin use. Additionally, potential short- and long-term traumas due to caesarean section abortions were prevented. The successful treatment of the four patients in this study suggests that the method of pregnancy termination for a twin pregnancy with CHMF should be comprehensively determined according to the gestational age, blood loss, and cervical opening dilation. In addition, all patients reported in this study became pregnant with the aid of ovulation stimulants. Therefore, the association of CHMF with these drugs remains to be explored in the future.

Ethical considerations

This study was approved by Ethical Committee of Research in Chongqing Municipal Center for Disease Control and Prevention.

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission,

redundancy, etc) have been completely observed by the authors.

Acknowledgements

The authors declare no conflicts of interest.

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