

Repetitive hydatidiform mole in the cesarean scar: a case report and literature review

G.L. Liu^{1,2}, S.C. He², W.J. Shan², H.Y. Chen^{2,*}

¹ People's Hospital of Fu Yang, An Hui Province (P.R. China)

² The Third People's Hospital of Beng Bu, An Hui Province (P.R. China)

Summary

Objective: To report a case of Repetitive hydatidiform mole in the cesarean scar. **Case Report:** a 35-year-old woman presented to our hospital with irregular vaginal bleeding for more than one month. Transvaginal ultrasonography, serum hCG confirmed the cesarean scar pregnancy. The patient underwent a bilateral uterine artery embolization and a suction evacuation. The postoperative histologic examination of the tissue revealed a hydatidiform mole. Molar pregnancy in the cesarean scar is tough to differentiate from a normal cesarean scar pregnancy with serum hCG or sonogram. It was necessary to perform a histological examination of the post operative specimen for the cesarean scar pregnancy. **Conclusion:** A high index of suspicion is needed for early diagnosis and management of cesarean scar molar pregnancy. If we ignore it, it can be challenging to manage and can have potentially catastrophic consequences.

Key words: Repetitive hydatidiform mole; Cesarean scar pregnancy; Literature review; Case report.

Introduction

Cesarean scar pregnancy (CSP) is a rare type of ectopic pregnancy, with a frequency of 1 : 1800 to 1 : 2216 pregnancies, which may lead to uncontrollable hemorrhage [1]. Hydatidiform mole is a subtype of gestational trophoblastic diseases, with the incidence estimated at 1% [2]. Thus, molar CSP is exceedingly rare and may have a high risk of uncontrolled hemorrhage or uterine rupture. Patients with this condition often need blood transfusions, leading to hysterectomy. However, because of the extremely low incidence of molar CSP, the literature lacks information on the diagnosis and optimal management of cesarean scar molar pregnancy. Here, we report a case and review the literature on molar CSP, providing experience for further studies.

Case Report

The patient was 35 y.o. G4P1, LMP: December 15, 2018, admitted to the hospital with complaints of irregular vaginal bleeding for more than a month. The patient reported a history of having normal menstruations, with a 30 day interval and periods usually lasting 3 days. She denied any history of dysmenorrhea. Her pregnancy history included one full-term birth by cesarean section, two induced abortions. Vaginal bleeding occurred 48 days after her LNMP (last normal menstrual period) stopped. The patient did not pay attention to it and did not seek medical treatment. A urine HCG was positive 55 days after her LNMP. The patient was sent to another hospital for evaluation. A transvaginal ultrasound showed an anteverted uterus measuring $9.2 \times 8.3 \times 5.9$ cms, with a uniform muscular echo and an irregular echo of the uterine lining measuring

about $8.0 \times 6.0 \times 3.0$ cms, with multiple cystic echoes in the uterus, and no adnexal masses or abnormalities. Serum HCG level was 193079 IU/L was examined. No abnormalities were found in chest and abdominal radiographs as hydatidiform mole was considered. A large amount of hydatidiform molar tissue and 30 gms of blood clots were removed by ultrasound-guided uterine evacuation with no fetal tissue identified. Intraoperative bleeding was 20 mL. A postoperative ultrasound revealed a regular uterine lining with no retained tissue in the uterine cavity. Symptomatic treatment was given after the operation. The postoperative pathological report revealed a hydatidiform mole. The patient did not follow up regularly post operatively. The patient had irregular vaginal bleeding that occurred more than a month after the operation. The amount was similar to that of a normal menstruation, the color was bright red, and March 16, 2019 the patient was admitted to our hospital. An ultrasound revealed a normal sized uterus, left ovary measured 50×24 mms, with several anechoic areas seen measuring about 20×18 mms. The lower anterior wall of the uterus where the scar was located showed a mixed echoic pattern, resembling a honeycomb, measuring about 26×29 mm and which appeared to be slightly protruding outside the uterus. The myometrium display was not clear and increased color flow doppler was seen peripherally and internally. Physical examination revealed the previous lower transverse cesarean scar which was about 10 cm in length with no other obvious abnormalities observed in the rest of the physical examination. Gynecological exam revealed a normal female external genitalia, the vagina was regular with a moderate amount of brownish discharge that had no odor, the

cervix was closed and without lesions or discharge or contact bleeding. The uterus was in an anterior position, consistent with 6-8 week size non-tender. There were no palpable adnexal masses or tenderness. Preliminary diagnoses were: 1. Hydatidiform mole implanted at cesarean scar, 2. Cesarean pregnancy. Serum HCG obtained at admission was 19600 IU/L. No obvious abnormalities were found in the patient's routine blood chemistries, normal coagulation function tests and immunological studies. A chest radiograph and other relevant examinations were also normal or negative. After admission, the patient experienced vaginal bleeding which was described as "period-like" flow. After symptomatic treatment, the patient improved. The patient was 35 years old, wished to preserve her was counseled that her risks with curettage could be more significant, such as experiencing uterine rupture, with possible life threatening massive bleeding and/ or hysterectomy therefore a uterine artery embolization was recommended. The patient consented and he next day a bilateral uterine artery drug infusion with an embolization was performed, Intra-operative infusion of 80 mg of methotrexate was administered and symptomatic treatment was given after the operation. On March 22, 2019, her serum HCG level was 9396 IU/L. An ultrasound-guided dilation and curettage was performed with about 20 gms of hydatidiform molar tissue and old blood clots evacuated. Post operatively, there was active bleeding from the uterine cavity, which failed initial medical treatment and subsequently responded to a uterine balloon compression device to stop the bleeding. Postoperative pathology revealed: uterine placental villi with mild hyperplasia of trophoblastic cells. A repeat serum HCG on March 26th was 3272 IU/L and her physical examination at this time revealed a normal uterine size and contour, with the internal model line in the middle, uniform echo at the base, hypoechoic at the anterior wall of the lower segment of the uterus, measuring about 13×11 mms. Receiving a second dose of MTX chemotherapy, the patient was discharged from hospital. Serum HCG levels were followed and were: 1598-850-828-608-367-286-200 IU/L. Mifepristone tablets were also given during this period. No obvious abnormalities were found in liver, kidney functions, ultrasound or chest radiographs.

Discussion

According to the study, the incidence of hydatidiform mole varies significantly from region to region, with a higher incidence noted in Asia, The incidence rates in Taiwan are 1 : 125, Japan 2 : 1000, Europe 1 : 1000, and the United States 1 : 1500 [3]. China has a large population base. Although its incidence rate is low, its overall incidence rate is not low, especially in the underdeveloped areas of China, which are restricted by medical conditions and have a high misdiagnosis rate. With the reform and opening up of China and the change of fertility concept, China has become the country with the highest cesarean section rate in the world in the past few decades. In recent years

China put forward the two-child policy, which led to many women with previous uterine scars to get pregnant again, making the incidence of scar pregnancy in China increases year by year. The incidence of hydatidiform mole at scar site of cesarean section is rare, and there is no clear diagnosis and treatment standard so far, but it can lead to serious consequences, such as uncontrollable life threatening hemorrhage, uterine rupture, hysterectomy, etc. of which our Chinese colleagues in Obstetrics and Gynecology should be aware of. Molar CSP, similar to that observed in our case, is exceedingly rare and may have a high risk of uncontrolled hemorrhage or uterine rupture. However, evidence on the optimal management of molar CSP is lacking, and currently available evidence is based on some case series or individual case reports. Only 4 cases were found in PubMed and to date, 3 of these cases were partial molar CSP and the other one remained unknown [4-7].

Wu *et al.* [4] reported the first molar CSP case in 2006. The patient was treated with dilation and suction curettage. However, the complex mass near the cesarean scar was not found in time, causing a repeat dilation and suction curettage.

Michener [5] reported the second case in 2009, wherein the patient was treated with intra gestational sac methotrexate injection. The patient underwent emergency hysterectomy as intervention owing to the recurrence of vaginal bleeding after 10 months.

Ko *et al.* [6] reported the third case in 2012, wherein transvaginal ultrasonography findings led to the suspicion of molar pregnancy. Bilateral femoral arterial sheaths were inserted preoperatively, and ultrasound-guided suction evacuation was performed. Tissue was obtained, and histologic examination confirmed a partial hydatidiform mole. The patient has a good prognosis.

Chen Ling *et al.* [7] reported the four case in 2018. Transvaginal ultrasonography, serum hCG and pelvic MRI confirmed the cesarean scar pregnancy. The patient underwent bilateral uterine arterial embolization and suction evacuation. The postoperative histologic examination of the tissue revealed a partial hydatidiform mole. This case suggested us that it was necessary to perform a histological examination of postoperative specimen for cesarean scar pregnancy.

On the first visit to the patient, postoperative examination of the patient suggested that the diagnosis of hydatidiform fetal mass and hydatidiform mole was established. No residual pelvic ultrasound was found after postoperative examination, but the patient was lost to follow up after discharge, and blood HCG and ultrasound status were not regularly reviewed after surgery. Three possibilities should be considered at the second visit: Hydatidiform mole tissue residue, erosive hydatidiform mole, repetitive hydatidiform mole. When the patient was admitted for the first time, ultrasound showed that the pregnancy was in the uterine cavity, not in the scar site of the uterine incision, the second visit showed that the lesion was located in the scar

area of cesarean section in the lower segment of the anterior wall of uterus with abundant blood flow, although the disease was detected in hydatidiform mole tissue after the second clear operation, combined with its HCG 19000 IU/L, the decrease was obvious compared with the previous one. The two chest radiographs and pelvic ultrasound showed no metastatic lesions, and the first clear operation had clearly indicated no residual in the uterine cavity, so it was more likely to be diagnosed as repetitive hydatidiform mole.

Diagnostic criteria for CSP: (1) no evidence of uterine pregnancy (2) no evidence of cervical pregnancy (3) the growth of the pregnancy capsule is in the anterior wall of the lower uterine segment (4) there is a defect in the myometrium between the pregnancy sac and the bladder, if no obvious pregnancy sac is detected by ultrasound, it will appear as uneven isthmus Echo [8]. However, hydatidiform mole is a hyperplastic placental villous trophoblast cell after pregnancy, with interstitial edema, forming blisters of different sizes. The diagnostic rate of transvaginal ultrasonography for hydatidiform mole, invasive hydatidiform mole and choriocarcinoma was up to 90-95%, but the placental trophoblastic tumor lacked specific ultrasonographic manifestations. For hydatidiform mole, ultrasonic examination showed “snowflake” and “honeycomb” mixed echo. For erosive hydatidiform mole and choriocarcinoma, ultrasound examination showed rich blood supply, presenting “lake” and “dry branch” manifestations.

For invasive hydatidiform mole and gestational trophoblast tumor, the clinical diagnostic criteria mainly include: serum HCG is the most important diagnostic basis; Ultrasound examination is the most commonly used method to diagnose primary uterine lesions. The main manifestations of ultrasound are hyperechoic masses in the myometrium with clear boundary but no capsule. There is an echo uneven area or mass in the myometrium with unclear boundary and no capsule. It can also be manifested as diffusely increased echogenicity throughout the uterus, accompanied by irregular hypoechogenicity or non-echogenicity. Color doppler ultrasound mainly displays abundant blood flow signals and low resistance blood flow spectrum. In addition, there are other auxiliary diagnostic methods such as chest X-ray, CT and MRI, mainly for patients with metastatic lesions. MRI was performed to further evaluate the mass and blood flow near the cesarean scar. Yamada and Ohira reported a preoperative diagnosis of ectopic molar pregnancy. MRI revealed a right cornual mass with iso signal intensity on T1WI and high signal intensity on T2WI, and they detected hydropic villi that are small vesicles in the mass presenting low signal intensities on T1WI and high signal intensities on T2WI. In their opinion, ectopic molar pregnancy is characterized as molar tissue-like tiny cystic lesions, intratumoral hypervascularity, and dense enhancement on MRI. However, this was the only case reported wherein ectopic molar pregnancy was diagnosed before surgery using MRI, and further investigation using MRI in the preoperative diagnosis is needed

[9]. Therefore, for highly suspected scar pregnancy with abundant blood flow signals indicated by ultrasound, MRI examination is feasible to further clarify the diagnosis.

So far, more than 30 CSP treatments have been published, but the best method of CSP is still in dispute. The treatment of CSP patients is mainly based on the size of gestational sac, the presence or absence of fetal heart, blood hCG level, and the need for future fertility and experience to develop individualized treatment plans. CSP treatment including systemic or local injection MTX treatment, uterine artery embolization (uterine artery embolization, UAE), cervical dilation and curettage, transvaginal, hysteroscopy, laparoscopic or open lesion resection and hysterectomy. Many studies have shown that MTX intrathecal injection, cervical dilation and uterine clearance are not recommended as the first-line methods of CSP treatment, which have a high incidence of complications and a high rate of hysterectomy [10-11].

High risk factors for hydatidiform pregnancy: blood HCG was more than 100000 IU/L. The uterus was significantly larger than the corresponding gestational age with ovarian lutein cysts that were larger than 6cm in diameter. With the implementation of the “two-child” policy in China, the number of older women with repeat pregnancies increased significantly in a short period of time. Therefore, it is necessary to understand the relationship between gestational age and the potential risk of hydatidiform mole and the malignant change of hydatidiform mole. A British study shows that increasing maternal age will lead to increased incidence of hydatidiform mole [12]. According to the data analysis of Peking Union Medical College Hospital, the malignant transformation rate of patients over 35 years old increased obviously. Studies have found that half of patients aged 40-49 years with hydatidiform mole developed gestational trophoblastic neoplasia (GTN) after treatment with clear uterus, and 60% of patients aged 50 years and above developed GTN after treatment with clear uterus, indicating that patients aged 40 years and above had a high probability of developing GTN, and often needed other adjuvant therapy [13]. For this patient, blood HCG was more than 100,000 IU/L. She was 35 years old and did not pay attention to these two factors during her first visit, which led to her not receiving further treatment, therefore, in the process of the second visit to the doctor, MTX drug infusion was carried out along with UAE to necrotize the villus tissue and reduce blood flow, making it safe in the process of uterine evacuation with curettage thereby reducing blood loss. But despite this, uncontrolled bleeding still occurred during the ultrasound guided curettage and uterine balloon compression was performed for 48 hours postoperatively. After the operation, MTX and mifepristone tablets were continued, and the decrease in the levels of blood HCG were satisfactory. This suggests that we in the process of treatment of patients with high risk factors that are diagnosed with hydatidiform mole, we should pay special attention to and, recommend further chemotherapy drugs, along with

removal of the specimen and scar pregnancy perform routine pathologic examination in order to diagnose hydatidiform mole pregnancy and thereby avoid delays in treatment time. In our case, we did not directly perform uterine evacuation surgery, but we carried out MTX pretreatment before the decision of uterine evacuation, and did administer MTX chemotherapy in the pregnancy sac. The procedure was performed under ultrasound guidance to reduce the risk of uterine perforation. Other modalities to reduce the risk of bleeding, such as bimanual compression, oxytocin infusion, and uterine artery embolization, also can be considered. On the other hand, local methotrexate injection, if used in a patient with cesarean scar molar pregnancy is undesirable and potentially can be dangerous [5].

In conclusion, as China's one child policy changes significantly and we see older pregnant women the incidence of scar pregnancy will increase significantly. Physicians may encounter more cases of cesarean scar molar pregnancy, which is a more difficult diagnosis to deal with. We need high vigilance in establishing the diagnosis and we need to establish a cesarean section scar hydatidiform mole pregnancy diagnosis standard so we can avoid delay in management. Time is of essence to minimize the potential complications associated with cesarean scar molar pregnancy.

Ethics Approval and Consent to Participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the Third People's Hospital of Beng Bu.

Acknowledgments

I would like to express my gratitude to all those who helped me during the writing of this manuscript.

Conflict of Interest

The authors declare no conflict of interest.

Submitted: July 21, 2019

Accepted: March 19, 2020

Published: August 15, 2020

References

- [1] Litwicka K., Greco E.: "Caesarean scar pregnancy: a review of management options". *Curr Opin Obstet Gynecol*, 2013, 25, 456–61.
- [2] Niemann I., Vejerslev L.O., Froding L., Blaakær J., Maroun L.L., Hansen E.S. *et al.*: "Gestational trophoblastic diseases - clinical guidelines for diagnosis, treatment, follow-up, and counselling". *Dan Med J*, 2015, 62, 5082.
- [3] Marki C., Jerbi E., Hsayaoui N., Zouari F., Brahim E.B., Oueslati H.: "Molar tubal ectopic pregnancy: report of two cases". *J OBSTET GYNAECOL res*, 2015, 6, 985-988.
- [4] Wu C.F., Hsu C.Y., Chen C.P.: "Ectopic molar pregnancy in a cesarean scar". *Taiwan J Obstet Gynecol*, 2006, 45, 343–5.
- [5] Michener C., Dickinson J.E.: "Caesarean scar ectopic pregnancy: a single centre case series". *Aust N Z J Obstet Gynaecol*, 2009, 49, 451–5.
- [6] Ko J.K., Wan H.L., Ngu S.F., Cheung V.Y.T., Ng E. H. Y.: "Caesarean scar molar pregnancy". *Obstet Gynecol*, 2012, 119, 449–51.
- [7] Chen L., Zhao J.T., Qi X.R.: "Partial molar pregnancy in the cesarean scar A case report and literature review". *Medicine*, 2018, 97, 26-27.
- [8] Wang Y.L., Su T.H., Chen H.S.: "Operative laparoscopy for unruptured ectopic pregnancy in cesarean scar". *BJOG*, 2006, 9, 1035-1038.
- [9] Yamada Y., Ohira S.: "Ectopic molar pregnancy: Diagnostic efficacy of magnetic resonance imaging and review of the literature". *Case Rep Obstet Gynecol*, 2016, 6, 761-62.
- [10] Kanat-Pektas M., Bodur S., Dundar O., Bakir V.L.: "Systematic review: What Is the best first -line approach for cesarean section ectopic pregnancy?" *Taiwan J Obstet Gynecol*, 2016, 2, 263-269.
- [11] Petersen K.B., Hoffmann E., Larsen C.R., Nielsen H.S.: "Caesarean scar pregnancy: a systematic review of treatment studies". *Fertil Steril*, 2016, 4, 958-967.
- [12] Savage P., Williams J., Wong S.L., Short D., Casalboni S., Catalano k., *et al.*: "The demographics of molar pregnancies in England Wales from 2000 to 2009". *Reprod Med*, 2010, 78, 341-345.
- [13] Elias K.M., Shon I.M., Bernstein M., Goldstein D.P., Berkowitz R.S.: "Complete hydatidiform mole in women age 40 to 49 years". *J Reprod Med*, 2012, 56, 254-258.

Corresponding Author:

HONGYING CHEN, M.D.

The Third People's Hospital of Beng Bu

No.38 Sheng li zhong lu Yuhui District Beng Bu,

Anhui Province (P.R. China)

e-mail: lg119881027@126.com