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Cesarean scar gestational trophoblastic disease: two case reports

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Summary

Cesarean scar gestational trophoblastic disease (GTD) is very rare. With relaxation of China's fertility policy, the number of cases has increased. The authors admitted two patients with hydatidiform moles in 2005; ultrasound indicated a nidus located in a previous cesarean scar. Both patients underwent uterine artery embolization (UAE) followed by suction curettage or hysteroscopy and were subsequently diagnosed with cesarean scar gestational trophoblastic neoplasms, and chemotherapy was administered. The prognosis of both patients is good. The authors found that the trophoblastic cells on cesarean scar were more likely to cause myometrium infiltration and result in a high risk of bleeding. Ultrasound, UAE, and hysteroscopy play important roles in its diagnosis and treatment. When a cesarean scar gestational trophoblastic neoplasm is considered, chemotherapy should be promptly administered .

Key words: Cesarean section; Drug therapy; Gestational trophoblastic disease; Pregnancy; Neoplasms.

Introduction

Cesarean scar gestational trophoblastic disease (GTD) is GTD in a previous caesarean scar, which has the characteristics of both GTD and caesarean scar pregnancy (CSP). Although the morbidity of this disease was very low before, China has a high cesarean delivery rate (54% in 2011 [1]), and the Chinese government stopped its one-child policy in 2013. Consequently, the percentage of pregnant women with a history of cesarean section has increased dramatically with the demand for a second child, resulting in increasing rates of CSP and cesarean scar GTD. GTD on a cesarean scar is more difficult to diagnose and treat and further study of this disease is urgently needed.

Case Report

Case one

A 28-year-old female (gravida 4, para 1, cesarean delivery on 2014-05, last menstrual period (LMP) 2015-06-08) was diagnosed with miscarriage, due to irregular vaginal bleeding for seven days and menolipsis for 54 days. A suction curettage was performed in her local hospital. The present hospital's pathology consultation indicated decidua and a small amount of hydatidiform tissue and trophoblastic cells with moderate hyperplasia. The patient's serum human chorionic gonadotropin (hCG) level, which was 85,272 U/L before curettage, decreased and then increased, reaching a maximum level of 132,660 U/L on 2015-08-15. She suffered a large amount of vaginal bleeding on two occasions. According to B-ultrasound (BUS), there was an inhomogeneous echo pattern (6.0×3.4×5.1 cm) in the lower uterine cavity, thinning of a portion of the muscular layer of the anterior uterine isthmus (~0.14 cm), and strong blood flow in the muscular layer of the uterine isthmus. She was considered as an early-stage complete hyperplasia molar on cesarean scar. No abnormalities were found on chest X-ray or CT scan. Uterine artery embolization (UAE) was performed on 2015-08-19, and MTX 60 mg was injected into the uterine artery. Suction curettage under ultrasound guidance was performed 24 hours after UAE. Hemorrhage during operation was 400 ml. The postoperative pathology indicated a hydatidiform mole and trophoblastic cells with moderate hyperplasia. The patient once again suffered from a large amount of vaginal bleeding after the operation (which improved after conservative treatment), and her serum hCG level decreased unsatisfactorily after surgery. The patient was diagnosed with cesarean scar gestational trophoblastic neoplasm (GTN) (Stage I:4), according to the FIGO clinical staging system (2012). BUS prior to chemotherapy showed a honeycomb-like inhomogeneous echo pattern (5.1×3.9×3.4 cm) in the myometrium of the left wall of the isthmus (Figure 1). She received five courses of MTX chemotherapy since and two courses of consolidation chemotherapy.

Case two

A 29-year-old female (gravida 3, para 1, cesarean delivery in 2010, LMP 2015-01-22). She received suction curettage in her local hospital, due to menolipsis for more than two months, and BUS showed an inhomogeneous echo pattern in the uterine cavity. The postoperative pathology indicated a complete hydatidiform mole and trophoblastic cells with mild hyperplasia. Her serum hCG level was 114,725 U/L before curettage and decreased unsatisfactorily after surgery. She presented at the present hospital with persistent vaginal bleeding. BUS disclosed an inhomogeneous echo pattern (2.2×2.7×2.1 cm) above the uterine isthmus and in the muscular layer of the left lateral wall, the boundary of which relative to the myometrium was not clear, extending to the serosal layer and containing multiple dark fields, abundant blood flow was detected. Chest X-ray and CT scan findings were normal. UAE was performed on 25-04-07 and MTX 60 mg was injected into the uterine artery. Hysteroscopic surgery was performed together with laparoscopic examination, 24 hours after UAE. Shallow bluish- violet embossment was found on peritoneal reflection of the uterus and bladder by laparoscopy. Hysteroscopy

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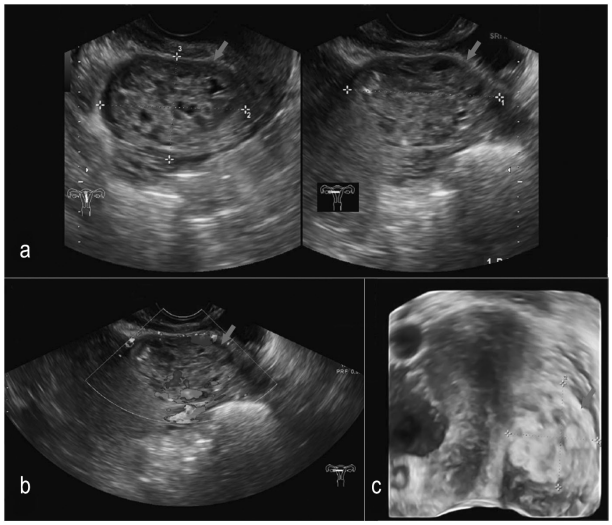

Figure 1. — BUS prior to chemotherapy in case one. **a)** A honeycomb-like inhomogeneous echo pattern (5.1×3.9×3.4 cm, red arrow) is detected in the myometrium of the left wall of the isthmus, extending to the serosal layer. **b)** Color Doppler ultrasound shows abundant blood flow inside the nidus (RI = 0.35). **c)** Three-dimensional ultrasound shows the nidus bulging outward.

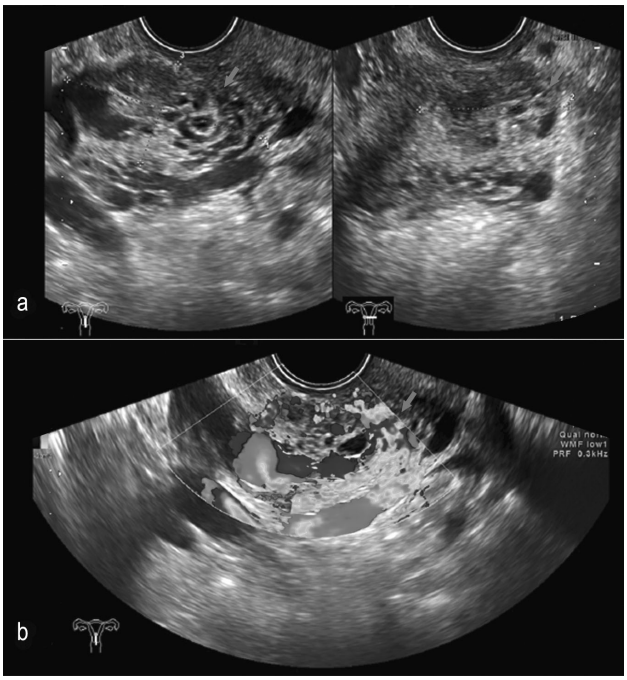

Figure 2. — BUS prior to chemotherapy in case two. **a)** An inhomogeneous echo pattern (4.7×3.4×2.5 cm, red arrow) is detected on the left anterior side of the uterine isthmus, bulging outward slightly, with multiple irregularly shaped dark fields inside. **b)** Color Doppler ultrasound shows abundant blood flow around and inside the nidus.

showed a 4×4×4 cm diverticulum on the left anterior wall of the lower uterine segment, bulging into the abdominal cavity, with little hydatidiform tissue, as well as a great amount of flocculent-appearing tissue and old blood clots. Some of the tissue adhered to the uterine wall, with unclear boundaries. The tissue in the diverticulum was removed, and hysteroscopy was performed again to verify no obvious residual material**.** The postoperative pathology indicated a hydatidiform mole and trophoblastic cells with moderate-to-severe hyperplasia. The patient was diagnosed with a postoperative residual hydatidiform mole at the site of the cesarean scar. However, the serum hCG level before surgery was 36,618 IU/ml and decreased postoperatively to approximately 10,000 IU/ml, after which it increased again. She was thus diagnosed with cesarean scar GTN (Stage I:3). BUS prior to chemotherapy showed an inhomogeneous echo pattern (4.7×3.4×2.5 cm) on the left anterior side of the uterine isthmus (Figure 2). She received three courses of MTX chemotherapy, which was switched to ACTD thermotherapy because of an unsatisfactory decrease in her serum hCG level. Her serum hCG level decreased to within the normal range after receiving two courses of ACTD chemotherapy, followed by two courses of consolidation chemotherapy.

This report was approved by Institutional Review Board, Women's Hospital, School of Medicine, Zhejiang University. Ethics board approval number is "20160014".

Discussion

In the two cases presented here, the authors detected cesarean scar GTD displaying some characteristics different from those of normal GTD. One of these was a high risk of bleeding. Both patients suffered multiple instances of massive hemorrhage or long periods of vaginal bleeding. Although UAE can control bleeding effectively, for some with refractory bleeding, there is no other choice but lesion resection or uterectomy. The persistent bleeding may be related to microvessel exposure or an arteriovenous fistula. In uterine cesarean scars, a diverticulum or microscopic dehiscence, together with poor vascularization often exists [2]. Thus, trophoblastic cells can infiltrate the myometrium more easily, leading to invasive moles or GTN morbidity. This is another characteristic of cesarean scar GTD. In the present authors' opinion, many of the hydatidiform moles seen on cesarean scars are actually invasive moles. This idea requires further study.

The diagnosis of cesarean scar GTD was based on imaging data, pathology, and variations in hCG serum levels. Transvaginal ultrasonography is a non-invasive and inexpensive medical imaging tool used for the diagnosis of cesarean scar GTD. Ultrasound is sensitive for the detection of GTD. "Snow-storm" appearance, "Swiss cheese" appearance or focal heterogeneous myometrial echogenic lesions containing fluid-filled cavities are characteristic appearances [3]. Fowler *et al.* reported that routine pre-evacuation ultrasound examination identifies 44-50% of hydatidiform moles [4, 5]. Transvaginal ultrasound is also highly accurate in detecting cesarean hysterotomy scars [6]. If the gestational sac is located within the anterior isthmic portion of the uterus (the location of the previous caesarean

scar) with prominent peritrophoblastic flow, and if the uterus and cervical canal are empty, CSP should be considered [7]. For patients with GTD, if an abnormal echo pattern is found in the anterior isthmic portion of the uterus, cesarean scar GTD should be considered. Other imaging modalities, such as chest X-ray, chest and abdomen CT scans, and brain MRI, are used to detect metastasis. Pelvic MRI is also useful for detecting myometrial invasion. The pathology of GTD shows abnormal proliferation of trophoblasts. Monitoring serum hCG levels is important for diagnosing cesarean scar GTN.

UAE is of significant value in treating certain hemorrhagic conditions in obstetrics and gynecology. For CSP, UAE followed by suction curettage appears to have more advantages and may be a preferred option [8]. Given that cesarean scar GTD also presents a high risk of severe, potentially life-threatening hemorrhage, UAE offers a powerful and minimally invasive non-surgical treatment used to control bleeding and preserve the uterus and future fertility of the patient. A high success rate and low complication rate have been shown with UAE. Pelvic pain and fever are the most commonly reported complications. Ischemia and necrosis of the ureter and bladder are rare. In the two cases presented here, the authors performed UAE before curettage or hysteroscopy, effectively reducing hemorrhage during surgery. Because the tissue of the cesarean scar hydatidiform mole was not easy to be cleaned up totally, the authors used MTX with UAE to damage trophoblastic cells in advance, and the side effects were minimal. The authors suggest that more frequent serum hCG monitoring after surgery could be adopted.

The differential diagnoses of cesarean scar GTN was mainly postoperative residual hydatidiform mole. Trophoblast cells on cesarean scars may infiltrate deeper than usual or hide within the diverticulum, making curettage more difficult, and because the risks of bleeding and perforation are high, surgeons tend to be more conservative than usual during operation, thus theoretically increasing the rate of hydatidiform mole residue. With the possibility of postoperative residual hydatidiform moles, we have the following choices: 1) Performing a second curettage: the uterine artery will reperfuse two to three weeks after embolization, and repeat UAE may be needed if a second curettage is considered; however, 100% removal of the uterine contents is not guaranteed. 2) Hysteroscopy: it has the advantage of visualization but still faces risks of bleeding and perforation. The rate of hydatidiform mole residue with hysteroscopy is smaller than that with curettage. If no obvious residual trophoblastic tissue is seen in the uterus by hysteroscopy, this supports a diagnosis of GTN. 3) Direct chemotherapy: short-term follow-up and serum hCG monitoring can be adopted if abnormal echo lesions in the uterus are small, the risk of repeat surgery is high, and there is no guarantee of removing the uterine contents completely. If variations in serum hCG levels correspond to a diagnosis of GTN (according to the FIGO guidelines), the authors suggest applying standardized chemotherapy. Especially for those patients with nidus in the myometrium under BUS or accepted hysteroscopy procedure before, the present authors are more inclined to administer chemotherapy promptly. In the present two cases, the effect of chemotherapy was deemed effective. During follow-up of the patients after chemotherapy, the nidus became gradually smaller and finally disappeared .

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