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The application of contrast-enhanced ultrasound in the diagnosis of cesarean scar pregnancies

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Summary

Purpose: The aim of this study was to evaluate whether contrast-enhanced ultrasound (CEUS) could be used as a method for diagnosing cesarean scar pregnancy (CSP). *Materials and Methods:* This retrospective study reviewed medical records, CEUS results, and clinical outcomes of 30 women with CSP, admitted to the Hospital of Obstetrics and Gynecology. The women initially underwent transvaginal ultrasound followed by CEUS, using a contrast agent. The CSP lesions were classified into three types: first-trimester gestation sac type, first-trimester mass type, and second-trimester gestation sac type. *Results:* CEUS showed hyper-enhancement and rapid accumulation of contrast agents in the CSP lesions in the first two types and in the affected muscular layer in the third type, where the placenta accreta was confirmed histopathologically. *Conclusion:* CEUS can indirectly identify the intrusion of the lesion implanting into the muscular layer and give more diagnostic information before specific treatment for CSP.

Key words: Cesarean scar pregnancy; Transvaginal ultrasound; Contrast-enhanced ultrasound; Contrast agents; Cesarean delivery.

Introduction

Cesarean scar pregnancy (CSP) refers to embryo implantation in the cesarean scar. It is a rare type of ectopic pregnancy. The etiology of this condition is not clear. In recent years, the incidence of CSP has increased owing to increased cesarean delivery rate. Ultrasonography is the accepted first-line diagnostic tool for CSP. Contrast-enhanced ultrasound (CEUS) relies on the acoustic detection of gas-filled encapsulated microbubble contrast agents to provide high-spatial resolution imaging of microvascular perfusion [1]. The microbubble agents have a rheological profile similar to that of erythrocytes and show a high acoustic signal [2]. Embryo implantation is associated with vascular invasion. CEUS provides a sensitive method to assess vascular perfusion of the uterus during embryo implantation in macaques [3]. If CSP is not diagnosed and treated early, it may cause uterine rupture and then uncontrolled hemorrhage [4].

The aim of the present study was to detect microvascular perfusion of CSP, quantify pregnancy-associated increased blood flow and perfusion differences in the different regions of the uterus, and to evaluate whether CEUS could be used as a method for diagnosing CSP.

Materials and Methods

A study was conducted in 30 consecutive women with CSP who underwent transvaginal ultrasound followed by CEUS at the Hospital of Obstetrics and Gynecology, between September 2013 and December 2015. The patients were aged 21–39 years, with a median age of 32 years. Previous two cesarean sections were reported in nine (30%) of the 30 women. Their gravidity ranged from two to six. Informed consent was obtained from all patients before performing the CEUS and all patients consented to participate in the study. The study was approved by the Ethics Committee of Tianjin Central Hospital of Obstetrics and Gynecology (approval no. 2015KY001).

Ultrasonography was performed using an ultrasound system with a transvaginal probe (5–9 MHz). The examinations were performed by three sonographers who had more than five years' experience in using ultrasonography to perform gynecologic and obstetric examinations. Time-intensity curve was used to quantify microvascular perfusion.

The contrast agent used was a second-generation acoustic contrast agent. For each patient, a dose of 2.4 ml was injected as a quick bolus into the cubital vein. Echogenicity and contrast enhancement patterns were recorded. The entire CEUS process took more than three minutes, and parts of the video (lasting for three minutes) were stored in a hard drive.

Statistical analyses were performed with SPSS 19.0 software package. Tests of normality were used to evaluate data. Data were expressed as mean ± standard deviation. The differences between two groups were evaluated using paired *t*-test. A p value < 0.05 was considered statistically significant.

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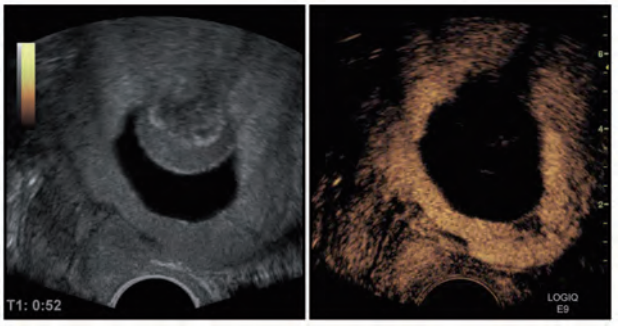

Figure 1. — CEUS images of the first-trimester gestation sac type imaging shows hyper-enhancement in the CSP lesions, as compared with the adjacent muscular layer.

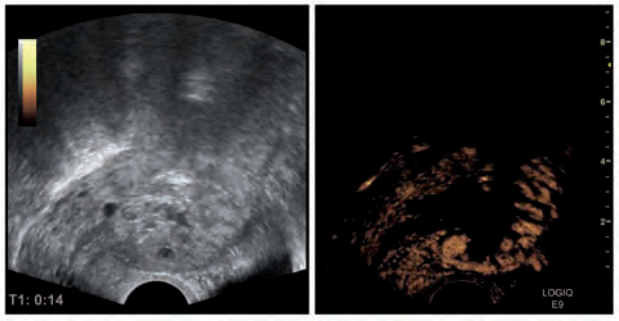

Figure 2. — CEUS images of the first-trimester mass type (case 2) imaging shows hyper-enhancement, heterogeneous enhancement in the lesions, and an obvious hyper-enhancement area in a part of the muscular layer. Placenta accreta was confirmed pathologically.

Results

CSP lesions can be classified into three types depending on CEUS findings: first-trimester gestation sac type (25 cases), first-trimester mass type (three cases), and second-trimester gestation sac type (two cases).

There were 25 cases of first-trimester gestation sac–type CSP. The median duration of gestation at diagnosis was 54.8 ± 10.8 (range 40–80) days. The average thickness of muscular layer in lesions was 2.34 ± 1.03 (range 1.0–5.5) mm. CEUS revealed hyper-enhancement and rapid accumulation patterns of contrast enhancement in the lesions, as compared with the adjacent muscular layer (Figure 1). The average contrast enhancement value was -42.30 ± 5.59 (range -53.31 to -31.86) dB in the lesions and -56.35 ± 5.36 (range, -67.20 to -48.00) dB in the adjacent muscular layer. The differences were statistically significant ($p < 0.05$). The boundary between the lesions and the adjacent muscular layer was distinct. Contrast enhancement was not found inside the gestation sac (including the fetus and umbilical cord). The contrast agents' duration was long in the lesions, as compared with the adjacent muscular layer. The contrast patterns in the lesions were fast accumulation and long duration of contrast agents. CEUS also showed homogeneous and heterogeneous enhancement of the lesions in 12 and 13 cases, respectively. Ultrasound-guided curettage was performed directly in 12 cases. Uterine artery embolization was performed followed by curettage in 13 other cases.

Three cases of CSP were identified as mass-type CSP. Conventional curettage was applied in two cases and medical abortion was performed in one case at local hospitals, resulting in severe hemorrhaging before their transfer to the present hospital. The clinical outcomes were the following: uterine artery embolizations were performed in cases 1 and 2, followed by curettage in case 1 and operation of local lesion resection in case 2. Local lesion resection was performed directly in case 3 according to patient requirements. CEUS showed hyper-enhancement, heterogeneous enhancement, and rapid accumulation patterns of contrast enhancement in the lesions in all three cases, as compared with the adjacent muscular layer. In case 2, CEUS showed one area with obvious hyper-enhancement in the muscular layer (Figure 2). Placenta accreta was confirmed pathologically in the resection specimen of case 2.

Second-trimester gestation sac–type CSP was identified in two cases. Both had delivered two babies by lower-segment cesarean section. Ultrasound revealed central type of placenta previa. A diagnosis of CSP was made in view of the history of cesarean section and they had induction of labor.

A 33-year-old woman with G5P2 was admitted at 18 weeks of gestation, complaining of vaginal spotting. CEUS revealed hyper-enhancement and rapid accumulation patterns of contrast enhancement in the lesions (in the placenta and one area of the muscular layer), as compared to the adjacent muscular layer. The maximum contrast enhancement value was -47.80 dB in the placenta, -45.31 dB in the affected muscular layer lesion, and -57.55 dB in the normal muscular layer (Figures 3 and 4).

Another 24-year-old woman with G3P2 was admitted at 23 weeks of gestation, complaining of vaginal spotting. The CEUS curve showed that the maximum contrast enhancement value was -44.69 dB in the placenta, -34.36 dB in the affected muscular layer lesion, and -62.37 in the normal muscular layer (Figures 5 and 6).

Uterine artery embolizations and cesarean section were performed in two cases. Placenta accreta was confirmed histopathologically. No contrast agent–related complications occurred. All patients recovered well after treatment.

Discussion

Ultrasound has been applied as the first-line diagnostic tool for CSP. The disadvantage of this ultrasound imaging modality is its limited sensitivity. Magnetic resonance im-

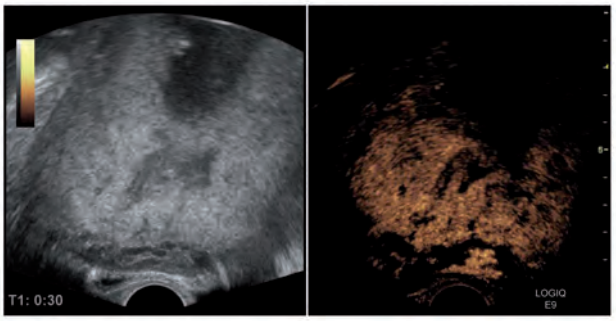

Figure 3. — CEUS images of CSP (18 weeks of gestation) imaging shows hyper-enhancement in the lesions (in the placenta and part of the muscular layer), as compared with the adjacent muscular layer. Placenta accreta was confirmed pathologically.

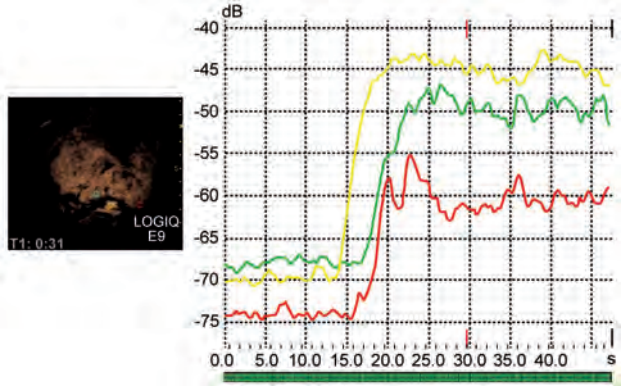

Figure 4. — Time-intensity curve of CSP (18 weeks of gestation). Yellow: affected muscular layer lesion (maximum intensity, -45.31 dB). Red: normal muscular layer (maximum intensity, -57.55 dB). Cyan: placenta (maximum intensity, -45.31 dB).

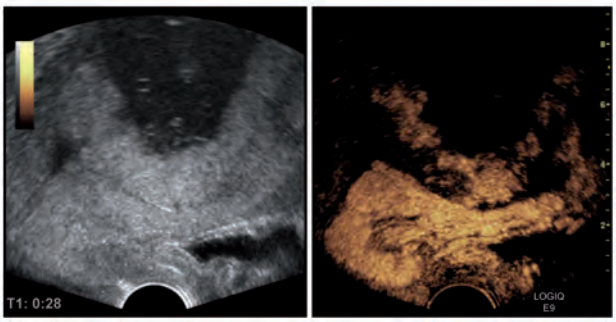

Figure 5. — CEUS images of CSP (23 weeks of gestation) Imaging shows hyper-enhancement in the affected muscular layer lesion. Placenta accreta was confirmed pathologically.

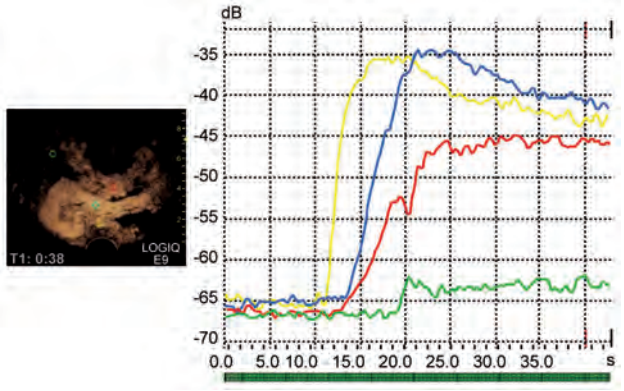

Figure 6. — Time-intensity curve of CSP (23 weeks of gestation) Yellow: affected outer muscular layer lesion (maximum intensity, -34.96 dB). Cyan: affected muscular layer (maximum intensity, -34.36d B). Red: placenta (maximum intensity, -44.69 dB). Green: normal muscular layer (maximum intensity, -62.37 dB).

aging has been previously used as an adjunct to ultrasonography [5]. The criteria for ultrasound have been described in the literature, such as an empty uterine cavity and cervical canal, development of a sac in the anterior part of the isthmic portion, and absence of healthy myometrium between the bladder wall and the gestational sac [6], but there has been no consensus. CEUS performed in this study was exploratory - to visualize differences in microvascular perfusion in the CSP and its adjacent structures. According to the findings of the present study, the CEUS features of CSP can be classified into three types. The first two types have common findings, such as hyper-enhancement and rapid accumulation patterns of contrast enhancement in the lesions, as compared with the adjacent muscular layer.

Based on the anatomical features, normal CEUS enhancement in a non-pregnant uterus is initially in the muscular layer, where the supplying artery is the arcuate artery, and then in the endometrium, where the supplying artery is the spiral artery. However, in this study, CEUS enhancement in a gravid uterus was initially in the endometrium (where decidual response occurs) and then in the muscular layer. This may be due to trophoblastic remodeling of the spiral artery in the process of the invasion of trophoblastic cells and blood flow accumulated in the placental intervillous space. Blood flow velocity was slow in the placental intervillous space, resulting in rapid accumulation of contrast agents in that area; thus, a villi tissue microvascular environment was formed.

Timor-Tritsch *et al.* [7, 8] reported that ten cases of CSP were identified early, in which the patients continued the pregnancy. All patients underwent hysterectomy at the time of cesarean delivery. Placenta percreta was the histopathological diagnosis in all ten cases. The cases in this series validated the hypothesis that CSP was a precursor of morbidly adherent placenta, both sharing the same histopathology. However, routine ultrasound has difficulty in diagnosing CSP with adherent placenta because of limited

sensitivity. In the present study, placenta accreta was confirmed histopathologically in case 2 in mass-type cases, and CEUS showed an obvious area of hyper-enhancement in an area of the muscular layer, which illustrated that the process of placenta accreta was associated with microvascular intrusion. CEUS can indirectly identify the intrusion of the lesion implantation into the muscular layer.

In the present study, two cases were identified as second-trimester gestation sac type. Both had early CSP. If placenta accreta occurred, a villi tissue microvascular environment was likely to form at first, leading to accumulation of contrast agents in the affected muscular layer. CEUS showed hyper-enhancement in the area. This could explain the occurrence of hyper-enhancement of the affected muscular layer in a second-trimester gestation sac–type CSP. As a result, CEUS is helpful in identifying whether placenta accreta has occurred. The present study also found that the hyper-enhancement with quantitative analysis was higher in the affected muscular layer than that in the placenta, which is worth considering.

Conclusion

The imaging features of CEUS may lead to a more accurate diagnosis before specific treatment of CSP.

Acknowledgement

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