Clinica Chimica Acta 486 (2018) 291–297

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/cca

Review

Application of ultrasonography in the diagnosis and treatment of cesarean scar pregnancy

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ARTICLE INFO

Keywords:
Ultrasonography
Cesarean scar pregnancy (CSP)
Doppler ultrasound
Contrast-enhanced ultrasound (CEUS)
Transvaginal ultrasound (TVS)

ABSTRACT

The morbidity of cesarean scar pregnancy (CSP) has shown an obvious ascending tendency with the increase of cesarean delivery in China and other countries. The timely diagnosis and treatment of CSP currently relies on medical imaging technology. In this article, we analyzed and compare the imaging methods in diagnosis of CSP. The imaging methods to diagnose CSP include traditional two-dimensional color/power Doppler ultrasound (2D-US), three-dimensional color/power Doppler ultrasound (3D-US), contrast-enhanced ultrasound (CEUS), and Magnetic Resonance Imaging (MRI). 2D-US provides important information including the location and size of gestational sac (GS), embryo with or without heart activity, and the relationship between the GS and scar. It can also divide CSP into different types, which are convenient for the choice of clinical treatment. CEUS can observe the perfusion of CSP in real-time, the arrival time of GS in CSP is earlier than that of the myometrium. It provides reliable evidence for diagnosis and evaluation of the treatment of CSP, which is helpful for making treatment plans and post-treatment follow-up. Combined use of ultrasound and CEUS could be a problem-solving method for CSP when conventional ultrasound is often inconclusive. Ultrasound has been accepted as the first-line imaging method and an important guiding method for CSP, supervising local methotrexate injection and curettage.

1. Introduction

Cesarean scar pregnancy (CSP) is a long-term complication associated with cesarean section. First reported by Larsen and Solomom [1], CSP is a rare form of ectopic pregnancy that the embryo is implanted at the site of scar caused by previous cesarean section. With the incomplete decidua reaction or lack of decidua, trophoblastic cells tend to invade into myometrium abnormally, which can lead to placenta accreta. During the pathogenesis of CSP, the embryo is implanted in the cesarean scar defect (CSD, niche) or in the site nearby, and the placental villus invade the scar gradually [2, 3]. Indeed, CSP and placenta accreta share some histological similarities, both characterized by abnormal placental growth into the myometrium. CSP can even lead to early placenta accreta in the first trimester [4, 5]. If not diagnosed and properly treated, continuing pregnancy with CSP may result severe outcomes such as uterine rupture [6, 7]. Blind curettage in patients with CSP can cause massive hemorrhage, which may lead to hysterectomy [8].

The incidence rate of CSP has been reported to range from one in 2500 to one in 1800 of pregnancies, and one in 531 of women having a history of cesarean section [8, 9]. Vaate et al. reviewed 21 literatures [10], and estimated that the prevalent rate of cesarean scar defect (CSD, niche) was from 24% to 74% by using transvaginal ultrasound (TVS). Moreover, using contrast-enhanced sonohysterography (SHG), the prevalence was found to vary between 56% and 84%. The World Health Organization (WHO) reported that the mean cesarean section rate of 9 countries in Asia was 27.3% in 2010, and it reached up to 46.2% in China [11]. By this consideration it is estimated that the incidence of uterus niche in China should be much higher than in other countries. In recent years, the morbidity of CSP has shown a clear trend of climbing with the increasing rate of cesarean delivery. The morbidity of CSP in China has significantly increased to one in 1221 pregnancies [12]. Thus, CSP is not a rare disease anymore, the morbidity has exceeded cervical pregnancy [1].

CSP has no distinctive clinical symptom, and often shows some similarity to ectopic pregnancy and/or spontaneous abortion. Most patients visit the hospital with complaint of vaginal bleeding, sometimes with abdominal pain. Clinical diagnosis relies on a history of cesarean section, a baseline serum human chorionic gonadotropin (HCG) concentration, and medical imaging technology. The choice of therapeutic

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https://doi.org/10.1016/j.cca.2018.08.012
Received 4 July 2018; Received in revised form 9 August 2018; Accepted 10 August 2018
Available online 11 August 2018
0009-8981/

methods is often based on imaging classification, risk of hemorrhage, and reproductive needs by the patient. A timely, accurate and detailed imaging is important to provide guidance for an effective treatment to reduce patients' suffering and avoid severe complications. CSPs with typical images, such as outwards growing gestational sac (GS) located inside the niche, are relatively easy to diagnose. However, not all CSP fulfill the diagnostic code [13, 14], and many cases have no clinical symptom in early stage. Thus, the diagnosis of CSP needs to be further refined considering the fast development in the application of imaging technology.

Currently, the main imaging methods to diagnose CSP include traditional two-dimensional color/power Doppler ultrasound (2D-US), three-dimensional color/power Doppler ultrasound (3D-US), contrast-enhanced ultrasound (CEUS), and Magnetic Resonance Imaging (MRI). MRI offers potential advantages in the evaluation of CSP, including a higher soft tissue contrast and better spatial resolution, multi-plane imaging, better resolution of the pelvic anatomy, and the ability to assess the possibility of myometrial invasion as well as bladder involvement [15, 16]. Contrast-enhanced MRI provides detailed features of GS and tissue nearby, and a clearer demonstration of placental invasion [17]. Furthermore, CSP may lead to early placenta accreta, which is better detected by MRI [18]. However, MRI could not identify the embryo with or without heart activity [15]. Disadvantages such as the high cost, time consuming, and complicated operation make MRI less frequently used in clinical practice. Ultrasound has been accepted as the first-line imaging method for CSP. In this review, we analyzed the use of ultrasound in diagnosis, evaluation of treatment and follow-up of CSP.

2. Two-dimensional color/power Doppler ultrasound (2D-US)

Ultrasound has advantages of being simple, safe, noninvasive, lower expense, radiationless, and real-time. It is considered to be the preferred diagnostic method for CSP. The current sonographic criteria of diagnosis for CSP are following: 1) An empty uterine cavity and cervical canal; 2) GS or placenta embedding in the cesarean section scar; 3) In early stage gestations (≤ 8 weeks), a triangular GS fills the niche of the scar; in the gestations > 8 weeks, the GS shape may be round or oval; 4) A thin (1–3 mm) or absent myometrium between the GS and bladder; 5) Cervical canal is closed; 6) Presence of embryo and/or yolk sac with or without heart activity in the GS; 7) A high velocity and low impedance blood flow surrounding the GS and the scar detected by color Doppler ultrasound [5, 19]. The sensitivity of ultrasound for detecting CSP has been reported to be 84.6% [8].

During the transvaginal ultrasound (TVS), the probe is close to the cervix, avoiding the interference of intestinal gas, and clearly presenting the location of the GS, without the need of filling the bladder. It can provide information on the size and shape of GS, myometrium thickness around the scar as well as the embryo, and demonstrate the yolk sac and heart beat in the GS (Fig. 1). On the other side, transabdominal ultrasound (TAS) needs a proper filling of the bladder, but it sometimes clearly shows the relationship between GS and bladder. Color and power Doppler ultrasound can evaluate the blood flow of the mass, and reveal abundant low impedance flow signals (Fig. 2) [8, 20]. Pulse Doppler has been reported to have practical significance by its capability to measure the velocity of blood flow in CSP masses, when setting 39 cm/s as the threshold value for undergoing uterine artery embolization (UAE) [21]. There seems to be a consensus that combined use of TVS and TAS is of great significance for diagnosis, treatment options and prognostic evaluation for CSP [3, 19, 20].

Ultimately, CSP has to be differentiated from intrauterine pregnancy (IUP), Naboth cyst, unavoidable abortion, and other forms of ectopic pregnancy such as cervical pregnancy, and uterine isthmus pregnancy [20]. CSP is difficult to be distinguished from IUP, unavoidable abortion, and uterine isthmus pregnancy, when the majority of the GS was in the cavity above the cesarean section scar, and only a small part of the GS insets into the niche [22]. Blind curettage with a false diagnosis may result in massive hemorrhage. Moreover, residual villous tissue by improper curettage continues to grow and infiltrate the myometrium, which forms mass-based CSP. This kind of CSP is often shown as a heterogeneous mass composed of different components in the anterior wall of the lower uterine segment [23]. CSP is also difficult to be differentiated from hysteromyoma/adenomyoma in the isthmus of the anterior uterine wall, endometriosis in the cesarean section scar, and trophoblastic tumor with the use of conventional ultrasound [24].

In order to improve the accuracy of diagnosis, and to reduce the incidence of severe consequences, ongoing study effort for better diagnosis of CSP has never stopped. Timor et al. retrospectively analyzed 242 images with CSP, and suggested an easy method in differentiating an intrauterine pregnancy (IUP) from a CSP between 5 and 10 gestational weeks [22]. In their study, a straight longitudinal line was drawn from the external OS of the cervix to the uterine fundus, and the center of that line was defined as the midpoint of the uterus. They concluded that most CSPs were located proximally to the midpoint of the uterus, whereas most normal IUPs were located distally from the midpoint of the uterus. Using the location of the center of GS as a marker of CSP yielded sensitivity of 93% and specificity of 98.9%. While it is realtively easy to estimate the location of the GS, simply measuring the distance of gestational sac to the midline of the uterus. However, it might lead to misdiagnosis of some IUPs as CSPs, especially in later gestational weeks. Meanwhile, it remains to be a challenge to distinguish CSP from cervical pregnancy in some cases. Using merely the location of the GS to diagnose CSP may not deliver satisfactory results.

3. Three-dimensional color/power Doppler ultrasound (3D-US)

Three-dimensional ultrasound is able to display transverse, sagittal and coronal plan simultaneously, and to show the position of CSP with steric image. It remedies the defect of traditional two-dimensional ultrasound that is limited in displaying coronal plan (Fig. 3). The geometric shape of GS at the cesarean scar and the relationship of GS with the cesarean scar could be demonstrated visually by the three-dimensional ultrasound [25]. Furthermore, application of three-dimensional ultrasound affords a better visualization of thin anterior myometrium and the bladder-uterus interface, which significantly improves the detection of early placenta accreta [5]. Three-dimensional color/power Doppler ultrasound could further reveal the blood flow, enhance our ability to identify subtle details and ascertain the diagnosis [26, 27]. Hence, three-dimensional color/power Doppler ultrasound is considered to be a useful supplement to two-dimensional ultrasound.

4. Contrast-enhanced ultrasound (CEUS)

CEUS is widely used in clinical practice, which utilizes microbubble contrast agent to be bolus injected through elbow veins to visualize blood flow and microcirculation perfusion in organs, with obvious advantages in blood flow imaging [28, 29]. Compared with Enhanced Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), CEUS has remarkable advantages including: 1) Unparalleled time resolution. CEUS can trace the contrast agent in real time; 2) Split screen mode. CEUS provides an opportunity to display gray-scale ultrasound image and enhancement image simultaneously, with gray-scale image being a locating guide; 3) Safety of the contrast agents. The microbubble contrast agent is metabolized by pulmonary circulation, with no nephrotoxicity and no need of hypersensitive test; 4) Low cost makes it easier to be accepted by patients [30].

Even though there were only several literatures reported application of CEUS in CSP management, CEUS appears to be a suitable tool for this line of usage. Xiong et al. compared conventional ultrasound and CEUS in suspected CSP women with GS located at the lower section of the uterus. Of the 92 cases-studies, 52 cases were CSPs, and 40 cases were IUPs [31]. The sensitivity, specificity, positive predictive value,