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Evaluating ultrasonographic findings and pregnancy outcomes in cesarean scar pregnancy with the new Delphi Consensus Criteria: a retrospective three-years analysis

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Abstract

Objective: We reevaluated Cesarean scar pregnancies (CSP) diagnosed according to the modified Delphi method. Our aim was to discuss our ultrasonography (US) and Doppler US findings and treatment experiences.

Methods: Ultrasound images of pregnant women diagnosed with CSP were retrospectively reanalyzed using the modified Delphi method. Doppler US images were graded according to vascularity density. The treatment process, medical/ surgical applications, serum βhCG levels and hemogram results of the pregnant diagnosed with CSP were analyzed from the hospital data system.

Results: Ten cases were classified as Type1 CSP (35.7%), 12 cases as Type2 CSP (42.8%) and 6 cases as Type 3 CSP (21.4%). Residual myometrial thickness (RMT) was between 1.6-4.2 mm in Type 1 CSP cases and 1.0-2.7 mm in Type 2 CSP cases. In Type 3 CSP cases, the gestational sac (GS) was protruding from the serosa and RMT could not be measured. Adjacent myometrial thickness size was measured between 6.1-12.6 mm in all CSP cases. In Doppler images, it was observed that the vascularity around the GS was variable in Type 1 and Type 2 CSP cases. All Type 3 CSP cases had severe vascularity around the GS. Severe Doppler vascularity seen in Type 3 CSP cases wasn't observed in any Type1 CSP case.

Conclusion: The Modified Delphi methodology is one that facilitates the diagnosis of CSP. The severity of vascularity on Doppler US images may be useful in typing CSP and early diagnosis.

Keywords: Cesarean section, ectopic pregnancy, hysterectomy, methotrexate, scar, ultrasonography

Introduction

Due to the increase in cesarean (CS) birth rates in the last two decades, the possibility of complications after CS has also increased. While bleeding can be seen in the early postpartum period; conditions such as infertility, rupture, ectopic pregnancy, and placenta accreta spectrum (PAS) may occur in the late period.[1] Cesarean scar pregnancy (CSP) is one of the rare complications.[2] If the gestational sac (GS) is located at the CS niche and scar localization at the level of the lower uterine segment, if the myometrium is very thin or not visible between the GS and the bladder, and if there is intense decidual blood flow in this region on color Doppler examination, then the diagnosis of cesarean scar pregnancy (CSP) is made. At the same time, it is observed that the uterine cavity and endocervical canal are also empty.

Although Jurkovic D et al., stated that CSP was seen at a rate of 1/1800 to 1/2500 of all CS pregnancies in the early 2000s [3], it was reported that the frequency of CSP increased to 1/500 in the next decade.[4] In hemodynamically stable patients, treatment options include medical or surgical termination or continuation of the pregnancy. Observation, systemic or local chemotherapy, uterine artery embolization, dilatation and curettage, local excision and hysterectomy such as various CSP treatment options have been described in the literature, and different combinations have been tried.[5] However, considering the reported high morbidity rate, the most common clinical

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practice is the termination of pregnancy.[6]

In our study, we reevaluated retrospectively CSPs diagnosed between January 2019 and April 2022 according to the modified Delphi method.[7] We aimed to discuss the classification of our cases according to the Modified Delphi method, our new grading of Doppler US findings and our treatment experiences in the light of the literature.

Methods

A retrospective study was performed on pregnant women diagnosed with CSP at the radiology clinic of our hospital from January 2019 to April 2022, who met the evaluation criteria as presented in Table 1. Ethical approval, dated 16 June 2022 and numbered 477, was obtained from the ethics committee of our hospital. Since it was a retrospective study, an informed consent form was not obtained.

Table I. Evaluation criteria in the diagnosis of CSP

Inclusion criteria	Exclusion criteria
- Empty monitoring of the uterine cavity - GS presence filling the caesarean section niche - Empty monitoring of the endocervical canal - Presence of embedded GS on the incision scar - Presence of vascularity around the sac in Doppler US - Monitoring of the thin myometrial layer between the GS and the bladder or inability to select the myometrium at the incision site	- GS displacing towards the cervix in US images (a positive "sliding sac sign") - Absence of Doppler US images - Treating the patient diagnosed with CSP outside of our hospital - If available images are insufficient for classification

US images of pregnant women diagnosed with CSP in the radiology clinic of our hospital were retrospectively reanalyzed according to the modified Delphi method. All ultrasonographic examinations and retrospective image analyzes were performed by a single radiologist (ST) with eighteen years of experience in obstetric and gynecological US and Doppler US using a 7.0 Mhz transvaginal probe on an Aplio 500 US device (Canon Medical Systems Corporation, Tokyo, Japan). According to the modified Delphi method published in 2022, sagittal US images and sagittal US video images, in which the uterine cavity that can be seen from the fundus to the external os were evaluated. In CSP, the position of the GS relative to the uterine cavity line (i.e., the imaginary line between the endometrium and myometrium on the anterior wall) and the serosal line (i.e., the imaginary line at the outer border of the myometrium) was examined. Accordingly, if a large part of the GS crossed the uterine cavity line and grew into the cavity, it was classified as Type 1 CSP (Fig.1). Was called Type 2 CSP (Fig.2), if the largest part of the GS was embedded in the myometrium, did not cross the uterine cavity line into the cavity, and did not extend outward from the serosal contour. If the GS was seen to protrude outward from the serosal contour, it was called Type 3 CSP (Fig.3). In Type 3 CSP cases, only the presence of the protrusion was evaluated, since the size of the protrusion may vary according to the gestational week, it was not included in the evaluation. In the midline of the GS, the thinnest myometrial thickness between the sac and the serosal surface of the uterus was taken as the "residual myometrial thickness" (RMT) measure in the sagittal plane where the uterus is best seen. If the GS was located asymmetrically at the incision site, the RMT measurement was taken from the thinnest point between the serosal surface of the uterus and the GS in the image in which the GS was best evaluated. In the image where RMT was measured, the adjacent myometrial thickness (AMT) was measured from the thickest part of the myometrium adjacent to the CSP.[7] High resolution Doppler images, made using advanced dynamic flow technique (ADF) were reevaluated. Intensities of decidual and myometrial blood supply around the GS of all cases were examined. According to the blood supply around the CSP; It was grouped as "+++" if intense peripheral blood circulation was observed (Fig. 4), "++" if peripheral but not severe blood supply was observed (Fig. 5), and "+" if there was mild vascularity that did not show complete circular blood supply (Fig. 1). Since the relationship between CSP and uterine arteries could not be determined in every archived case, it was not evaluated.

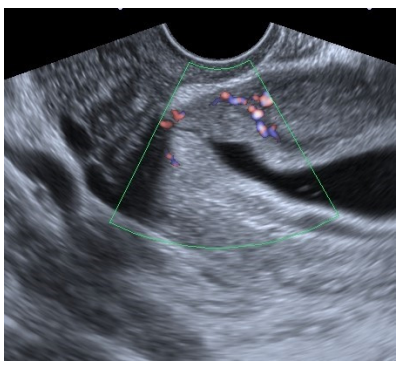
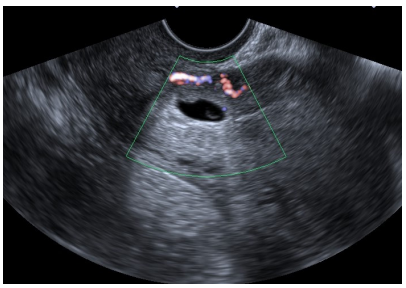


Fig. 1 Type 1 CSP; Most of the gestational sac extends into the uterine cavity (white arrow). Mild blood circulation pattern that was not completely circular around the CSP was evaluated as "+" color Doppler blood supply

Fig. 2 Type 2 CSP; Most of the gestational sac is embedded in the myometrium, the contour of the sac does not protrude from the serosal line

Fig. 3 Type 3 CSP; The gestational sac is observed to be protruding prominently from the serosal line

Fig. 4 "+++" Color Doppler blood supply; intense peripheral blood



circulation pattern is observed around the CSP

Fig. 5 "++" Color Doppler blood supply; peripheral but not severe blood supply pattern is observed around the CSP

Patients diagnosed with CSP had a history of at least one CS delivery. It was also investigated whether there was abortion, myomectomy, or any intrauterine surgical manipulation in their anamnesis. The treatment process, medical/surgical applications, serum βhCG (beta human chorionic gonadotropin) levels, and hemogram results of the pregnant diagnosed with CSP were analyzed from the hospital data system.

Treatments

Medical or surgical treatment options were evaluated according to the weeks of gestation, hemodynamic stability, and accompanying complications (such as the presence of subchorionic hemorrhage and rupture) of patients with CSP. All pregnant women who were diagnosed with CSP and had a fetal heartbeat (FHB) were informed about CSP and their treatment was planned by asking whether they wanted to continue the pregnancy. Emergency situations and what needs to be done were explained to the patients who wanted to continue their pregnancy. For those who want to terminate their pregnancy, medical treatment was performed with single[8,9]/ multidose[10] intramuscular methotrexate (MTX) (50 mg/m2) administration according to body surface area. As surgical treatment options, dilatation and curettage (D&C) or laparoscopic/open surgery and scar pregnancy excision and repair were performed under general anesthesia. If the pregnant woman didn't have severe active bleeding at the time of hospitalization and serum βhCG tends to decrease, serum βhCG follow-up and US control were performed. Intracavitary 16F Foley catheter (IFC) was inserted for twelve/twenty-four hours to provide hemostasis according to active bleeding status. If there was uterine rupture, ectopic pregnancy products on the scar were curetted and surgical repair was performed. After all the treatments, serum βhCG levels were measured until the level couldn't be detected, and bleeding and hemogram follow-ups were also performed periodically. US examination was repeated if clinically necessary.

Data analysis was done with the help of Turcosa (Turcosa Analytics Ltd Co, Turkey, www.turcosa.com.tr) statistic software. Descriptive statistics were presented as mean ± standard deviation for continuous-measure variables and as a number of cases and (%) for nominal variables.

Results

A total of 38 CSP cases were detected. A total of 28 cases meeting the evaluation criteria were included in the study. Ten CSP cases could not be evaluated because some images were not very optimal for typing due to the retrospective nature of the study and some patients were treated outside of our hospital. The average age of patients was 32.5±5. The num-

ber of pregnancies was between two and eight. The number of parities ranged from one to six. The gestational weeks at the time of diagnosis ranged from four to nine weeks. The total number of C/S of the patients ranged from one to six. None of the pregnant had an operation of myomectomy or infertility treatment other than CS. Also, none of the pregnant women had a history of ectopic pregnancy or IVF. Twelve pregnant had a previous abortion anamnesis and only three of them had D&C. 21 of 28 pregnant women applied with the complaint of vaginal bleeding, other CSP cases were detected in routine pregnancy examination. One case was diagnosed with uterine rupture and no embryo could be detected.

When the US images are examined; ten cases were classified as Type 1 CSP (35.7%), 12 cases as Type 2 CSP (42.8%), and six cases as Type 3 CSP (21.4%). A CSP case with menstrual cycle irregularity and diagnosed with rupture was evaluated as Type 3, the gestational week could not be determined because there was no US examination before the rupture.

In color Doppler images, it was observed that the vascularity around the GS was variable in Type 1 CSP and Type 2 CSP. Half of the Type 3 CSP cases had "++" and the other half had vascularity around the GS with a severity of "+++". In none of the Type 1 CSP cases, intense vascularity was observed as in the Type 3 CSP cases (Table 2).

Table 2. The classification of the cases according to the modified Delphi method is shown

Type	Diagnosis Week	Color Doppler blood flow	RMT	AMT	USG Finding (Diagnosis Time)	CS number	Arrival βhCG (U/L)	Hemoglobin	Treatment
1	6+4	+	2.7	6.4	FHB (+)	2	32547	12.8	CUGA
1	4	+	3.8	7.1	EMB (-)	1	2617	14	CUGA
1	6+5	+/++	3,4(2,2)	7.1	FHB(+)	3	5715	13.8	CUGA
1	5	++	3	10.1	EMB(-)	1	12070	13.1	S.ABORTUS
1	5+6	++	2.3	6.6	EMB(-)	3	7333	13.7	1 DOSE MTX+OP
1	5+2	+	4.2	7.9	EMB(-)	1			CUGA
1	6+3	++	2.6	7.1	EMB(-)	2	69037	13.2	CUGA
1	5+5	++/+++	3.5(2)	7.6	FHB(+)	1	24664	12.6	CUGA
1	4	+	2.6	6.1	EMB(-)	3	568	12.1	CUGA
1	4	++	1.6	7	EMB(-)	2	7789	13.3	CUGA
2	8	++	1.3	6.5	CHORIONIC BUMP, EMB(-)	3	21545	12.3	CUGA
2	5+3	+	1.1	6.1	4 GS, 1 FHB(-)	1	18251	13	OP
2	6+3	+++	1	8.4	CHORIONIC BUMP, EMB(-)	2	17511	12.7	5 DOSE MTX
2	9	++	1.3	6.7	EMB(-)	2	89762	11	CUGA
2	5+6	++	1	8.4	FHB(-)	2	8224	11	CUGA
2	6+3	+++	1.7	6.1	FHB(-)	2	20309	11.9	1 DOSE MTX+ CUGA + IFC
2	7+6	+	1.1	8.4	FHB(-)	2		11.9	CUGA
2	6+4	++	1.9	9	FHB(+)	3			HYSTERECTOMY, 36 WEEKS DELİVERY
2	8+6	++	1.7	7.7	FHB(+)	2	67119	14.1	CUGA
2	7+2	+++	2	9	FHB(+)	2	19480	10.4	CUGA +IFC
2	6+1	+	1.8	5.2	FHB(+) GS-CRL mismatch	2			S.ABORTUS
2	7+1	++	2.7	9	FHB(-)	2	31834	7.6	4 DOSE MTX
3	7+2	++	0	11	EMB(-)	6	18	13	S.ABORTUS
3	6	+++	0	12.6	FHB(-)	1	28715	12.6	CUGA
3	5+6	+++	0	11.4	FHB(-)	2	619	13.7	S.ABORTUS
3	4+6	++	0	8.3	EMB(-)	1	52	11.9	S.ABORTUS
3	9	+++	0	6.2	FHB(+)	3	36804	12.3	4DOSE MTX + CUGA
3	NOT KNOWN	++	0	9.7	RUPTURE	2	>10000	9.7	RUPTURE REPAIR

FHB: fetal heartbeat, EMB: embrio, GS: gestational sac, CRL: crown rump lenght, RMT: residual myometrial thickness, AMT: adjent myometrial thickness, MTX: methotrexate, CUGA: curettage under general anesthesia, IFC: intracavitary foley catheter, S.ABORTUS: Spontaneous abortus, OP: operation

RMT was between 1.6-4.2 mm in Type 1 CSP cases. In two patients who underwent control US both blood flow increased in Doppler US and RMT was thinned. RMT in Type 2 CSP cases was between 1.0-2.7 mm. In Type 3 CSP cases, the GS was protruding outward from the external serosa and RMT measurement could not be performed because the myometrial tissue was very thin. AMT size was measured between 6.1 and 12.6 mm in all CSP cases.

The classification of the cases according to the modified Delphi method and the treatment modalities are shown in Table 2.

Discussion

In our study, we reevaluated retrospectively CSPs according to the modified Delphi method. Our aim is to demonstrate the applicability of modified Delphi method to daily practice and to point out that Doppler US findings can also contribute to diagnosis and treatment planning. Ten cases were classified as Type 1 CSP (35.7%), 12 cases as Type 2 CSP (42.8%), and six cases as Type 3 CSP (21.4%).

Due to the increase in CS ratios in recent years, there has been an increase in the incidence of CSPs, which cause significant maternal morbidity and mortality.[11,12] Therefore, early and accurate diagnosis of CSPs is important. For this reason, various modalities have been proposed in recent years to diagnose CSP in the most accurate way.[7,13-15] Undiagnosed or misdiagnosed these cases may lead to PAS and as a result uncontrollable bleeding and hysterectomy.[2]

Kaelin AA et al.[15] divided CSPs into two groups according to their localization as “on the scar” and “in the niche”. They emphasized that the results of CSP located on the scar have better results than the CSPs located in the niche. They also emphasized that in the first trimester US examination, myometrial thickness less than 2 mm may cause severe placental adhesion. Timor-Tritsch’ et al.[16] In their article published in 2023, they investigated the effect of RMT on CSP results and divided them into two according to whether RMT was above or below 2 mm. They stated that the risk of preterm birth, hemorrhage, PAS and hysterectomy is high in CSP that starts below 2 mm. They emphasized that if the RMT is over 2 mm or the best is over 4 mm, less hemorrhage, near-term delivery or less severe PAS may occur. RMT was too low to be measured in Type 3 CSPs in our cases. In the control USs performed during the bleeding follow-ups in two patients with Type 1 CSP, both decreased RMT and increased blood flow were observed (shown in Table 2). In our case of Type 2 CSP, which resulted in hysterectomy, the RMT was 1.9 mm, bladder involvement was observed during the operation, which is consistent with the literature. However, more case studies are needed to evaluate the relationship between the thickness of the RMT and placental adhesion.

Timor-Tritsch IE et al.[14] in their article describing the diagnosis and pathogenesis of CSP, stated that the fifth and seventh gestational weeks are very critical weeks for the diagnosis of CSP. They also emphasized that many CSP cases were misdiagnosed as a miscarriage threat, missed abortion or normal pregnancy during this period. In the article published by Jordans IPM et al.[7], they stated that the diagnosis of CSP could best be made between the sixth and seventh weeks of pregnancy, but the diagnosis, evaluation and reporting of CSP can be made with the modified Delphi method until the 12th week. In our cases, the diagnosis weeks were between the 4th and the 9th gestational weeks, except for the pregnant woman who presented with uterine rupture, and most of them were between the 5th and 7th gestational weeks. Four CSP cases were diagnosed at 4 weeks of age, and six CSP cases were diagnosed at 5 weeks of age. The location of the sac, other US findings and Doppler images had supported CSP pregnancy. Our CSP diagnosis weeks were earlier compared to the modified Delphi method. In previous studies, it was stated that ADF showed higher resolution in obstetrics and general radiology compared to conventional Doppler US in color Doppler examinations performed using the ADF technique.[17-19] We think that the diagnosis of CSP can be made in the early weeks, as the vascularity around the GS can be clearly evaluated even in the fourth week of gestation in high-resolution Doppler images obtained with the ADF technique. Since 21 of 28 cases presented with vaginal bleeding, early US examination was performed and there was no delay in the diagnosis of CSP. Kuleva M et al.[20] as emphasized by, performing routine ultrasonographical examination of the lower uterine segment at the early gestational week and including it in the reporting is extremely important for the early diagnosis of CSP. It is very important to distinguish between cervical pregnancy and sliding pregnancy in the lower uterine segment from CSP.

The review published by Timor-Tritsch et al.[21] emphasized that FHB should be checked first in pregnancies diagnosed with CSP, and that if there is no FHB, it should be followed up with US follow-ups and until βhCG drops to zero. If there is a FHB and the continuation of pregnancy is desired, the myometrial thickness above the GS should be measured and it should be che-

cked whether the GS is on the scar or in a niche. It has been emphasized that the risk of PAS and CS hysterectomy is high if the myometrial thickness is less than 5 mm and the GS is in the niche. It has been emphasized that the risk of PAS and CS hysterectomy is less if the GS is on the scar or myometrial thickness is greater than 5 mm.

In the review of Maheux-Lacroix S et al.[22] that included 63 studies in the literature, it was stated that surgical treatments (D&C, hysterotomy surgical resection, hysterectomy) had a higher success rate compared to medical treatment (intragestational or IM MTX). They stated that the success rates of combined treatments are high, but they also increase the cost of treatment and the possibility of side effects, so its superiority over monotherapy is uncertain. Cagli F et al.[23] In cases with CSP, they first aspirated the gestational sac and then administered 50 mg MTX locally. They emphasized that local MTX treatment guided by transvaginal US is an effective, safe and fertility-preserving treatment method for CSP. In our study, systemic MTX treatment was performed in 2 cases (7.14%) and surgical intervention was performed in 21(75%) cases. Three of those who underwent surgical intervention had previously received systemic MTX. Local MTX procedure was not applied to any case. The remaining five cases (17.9%) were resulted in spontaneous abortion without any medical (MTX) or surgical procedure, and βhCG values decreased. One of these cases was Type 1 CSP, one was Type 2 CSP, and interestingly, three of them were Type 3 CSP. This made us think that even in Type 3 CSPs with intense vascularity in color Doppler US, spontaneous abortion may result during hospital follow-up, if there is a gradual decrease in βhCG level and there is no sudden decrease in hemogram level that requires intervention. In our cases, the gestational weeks of Type 3 CSP with spontaneous abortion were 4+6, 5+6 and 7+2. Of these, cases with 4+6 and 7+2 weeks were anembryonic pregnancies; in the case with 5+6 embryos, there was no fetal heart activity. We think that due to non-viable pregnancies, the growth factors required for myometrial involvement were not sufficient, and spontaneous abortion could occur more easily even if "+++" Doppler intensity was present. The higher incidence of spontaneous abortion in Type 3 CSP cases, in which the probability of rupture is reported to be higher, suggests that this situation should also be taken into account in patient follow-up.

In a meta-analysis published by Calì G in 2018[24], it was stated that those with positive FHB CSP have a high risk of serious bleeding in the first trimester and clinical symptoms that require surgical/ medical intervention (bleeding, rupture). They stated that the majority of patients with CSP without a FHB had abortion without complications, and that the risk of uterine rupture and hysterectomy in the first trimester was negligible. In our study, FHB was positive in a total of eight CSPs. Of these, one case with Type 2 CSP was followed-up because she wanted to continue her pregnancy. Of the seven remaining CSPs with a heartbeat, CUGA alone was sufficient in five, while the remaining one aborted spontaneously, while the other received combined therapy. Since there was no previous US examination of the CSP Type 3 case presenting with rupture, information about presence of embryo and FHB could not be obtained. Various treatments were applied to CSPs without heartbeat or with anembriyonic pregnancy, depending on their clinical status, and no life-threatening complications were encountered. Due to the small number of our cases, CSP types, FHB and treatment methods couldn't be compared with each other. Because of this, studies with large case studies and meta-analyses are needed.

Pekar-Zlotin M et al.[25] conducted a retrospective cohort study of 36 women diagnosed with CSP and treated with combined local and systemic methotrexate (MTX), reevaluated according to the new Delphi consensus.[7 They found that βhCG levels and hospital stay were significantly lower in group A (i.e. Type 1 CSP) compared to the other two groups, whereas in group C (i.e. Type 3 CSP) the treatments were more complicated and longer lasting. They thought that it would contribute to patient follow-up and clinical practice according to the modified Delphi criteria.

The sample size in our study is relatively small (28 out of 38 cases were included in the study). Excluding 10 cases may reduce the reliability of the data collection process, in order to avoid any doubt in the classification, we did not include the cases that were in between, were difficult to evaluate, and whose interpretation might vary from operator to operator. In addition, our study only includes descriptive statistical information. A comparative statistical study could not be performed due to the decrease of cases when divided into groups. These are our limitations. However, we stated that in Type 3 CSP, spontaneous abortion occurs in half of the cases and that CSP diagnosis can be made earlier with Doppler USG findings. A larger number of cases study will shed light on these issues.

Various treatment options are available in CSP. Gestational age, decidual vascularity, hemodynamic stability, clinician experience, and equipment availability can guide the selection of the most appropriate modality for the patient. In addition, the patient's future pregnancy plans should be considered in treatment options, and mothers

with CSP who want to continue their pregnancy should be counseled in terms of bleeding, rupture and hysterectomy risk. In the presence of suspected CSP, it is important that the US is performed by an experienced doctor.

Conclusion

We think that the Modified Delphi Method will facilitate the diagnosis of CSP and the planning of appropriate treatment. In our cases, "+++" and "++" vascularity were observed in Doppler US in Type 3 CSPs, but spontaneous abortion rate was observed in 3 of 6 cases, which is one of the interesting results for us. Similarly, although the "+" vascularity was higher in Type 1 CSPs than in Type 2 and 3 CSPs, the rate of surgical intervention was higher. However, we think that it should be evaluated with more cases in order to determine the appropriate treatment protocols according to the types of CSP.

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