



Effectiveness, complications and reproductive outcome of selective chemoembolization with methotrexate followed by suction curettage for caesarean scar pregnancy - A prospective observational study



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ABSTRACT

Objective: Caesarean scar pregnancy (CSP) is a rare form of ectopic pregnancy implanted in a previous caesarean scar. Selective chemoembolization with methotrexate (SCEM) followed by suction curettage (SC) is one of the treatment options for CSP. The aim of the study was to assess the effectiveness, complications and reproductive outcome of SCEM followed by SC in the treatment of CSP.

Study design: All cases of CSP treated with SCEM followed by SC between 2015 and 2018 were prospectively followed-up to assess short and long-term outcome. All patients hospitalized with the suspicion of CSP during the study period were included in the study. Gelatine sponge was used as embolic material to avoid permanent damage of the uterus and minimise the possible impact on fertility. Haemoglobin (Hb) and beta human chorionic gonadotropin (β -hCG) levels, normalization of menstrual cycle, complications after the procedure and subsequent fertility were assessed.

Results: Twenty-two patients diagnosed with CSP underwent SCEM followed by SC. The procedure was effective in 20 cases (91%). In two cases additional SCEM was required before attempting SC due to persistent vascularity on ultrasound in one case and abnormal uterine bleeding in the second one. No complications were observed during the procedures, none of the patients required a hysterectomy. Follow-up ranged from 9 to 36 months. In short-term follow-up no significant complications occurred, only minor ailments such as uterine cramping and nausea were reported by 8 patients. In long-term follow-up 8 patients reported at least one complication, such as hypomenorrhea, amenorrhoea or were diagnosed with Asherman syndrome. Ten patients tried to conceive and 4 out of them achieved a pregnancy (all in less than 12 months) and delivered by caesarean sections between 35 and 39 weeks. One patient reported recurrent miscarriage.

Conclusion: SCEM followed by SC appears to be an effective treatment option for CSP. The method seems to be safe in short-term follow-up. However, complications were observed in long-term follow-up. Therefore, patients should be informed about the risk of complications interfering with future fertility, such as intrauterine adhesions and/or amenorrhea.

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Introduction

Caesarean scar pregnancy (CSP) is a rare form of ectopic pregnancy implanted in a previous caesarean scar. The prevalence has been estimated to range from 1/1000 to 1/2500 of all pregnancies with a history of previous caesarean section (CS) [1]. The number of CSP increases with the number of previous CS [2]. This condition may be associated with life-threatening

complications such as uterine rupture, placenta praevia or accreta and haemorrhage. Therefore, early diagnosis is crucial to decrease maternal morbidity and mortality. Ultrasonography has greatly improved the diagnosis of CSP. There is no universal treatment option for CSP and data about the complications of various management strategies are scarce [3]. In a recent systematic review the following therapeutic options were listed: expectant management, medical treatment by systemic and/or local methotrexate (MTX), uterine curettage, hysteroscopy, resection of CSP through a transvaginal approach, uterine artery embolization (UAE), laparoscopy, high-intensity focused ultrasound and combinations of these methods [4]. Although MTX is a preferred drug for CSP, side effects of the therapy and excessive bleeding after poor

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response to the treatment limit its application [5]. Even though dilatation and curettage (D&C) may be used to remove the CSP, it may be associated with excessive uncontrollable vaginal bleeding [6]. Performing suction curettage (SC) instead of D&C may decrease the risk of complications and therefore SC seems to be a safer method to remove debris from the uterine cavity. UAE is a widely used technique in both gynaecology and obstetrics. Selective uterine artery chemoembolization with intra-arterial methotrexate infusion (SCEM) followed by SC is one of the treatment options for CSP. In this study we investigated the effectiveness, complications and reproductive outcome of SCEM followed by SC in the treatment of CSP.

Materials and methods

This is a prospective observational study of patients referred to the 3rd Chair and Department of Gynaecology of the Medical University of Lublin, Poland between 2015 and 2018, with the suspicion of CSP. On admission patients' demographic and clinical data such as age, number of previous pregnancies, gestational age, number of previous C-sections were collected and laboratory tests were performed to assess haemoglobin (Hb) and beta human chorionic gonadotropin (β -hCG) levels. The diagnosis was confirmed by two independent sonographers by transvaginal ultrasound examination using the following ultrasonographic criteria for CSP: empty uterine cavity, empty cervical canal, location of the gestational sac in the anterior part of the isthmic portion of the uterus, circular blood flow around the gestational sac [7]. After being informed about the possible risks and complications all patients signed an informed consent for both SCEM and SC. SCEM was performed in the Department of Interventional Radiology and Neuroradiology. Twenty five mg of MTX was infused bilaterally into the uterine arteries for a total of 50 mg. Finally both uterine arteries were embolized with gelatine sponge particles to avoid permanent damage of the uterus. Twenty four hours after SCEM the absence of vascularity of CSP was confirmed on ultrasound and SC was performed (Fig. 1). In case of a visible vascular pattern SCEM was repeated. Both SCEM and SC were performed during the hospital stay. After performing these procedures all patients were monitored in the hospital for at least 24 h. During short-term follow-up, which was performed immediately after the procedure and 30 days after, complications of the management, normalization of menstrual cycle, β -hCG level, Hb level were assessed. Then the patients were regularly contacted, in 3 months intervals, to assess long-term outcome. In long-term follow-up, the desire for subsequent pregnancy, pregnancy outcome, need for additional medical interventions, pain and other ailments were assessed. The study was approved by a local Research Ethics Committee. This study was prepared and performed according to the STROBE Statement Checklist for observational studies. The study protocol was approved by a local Bioethics Committee (KE-0354/6/2010).

Written informed consent to participate in the study was obtained from all patients.

Results

During the study period 22 patients were admitted to the Department between 6 and 10 weeks of gestation with the suspicion of CSP. All patients were of Caucasian racial origin. All patients were hemodynamically stable and were scheduled for combined treatment of SCEM followed by SC. SCEM with SC was performed in 22 patients and in 20 patients the procedure was successful. One patient required additional SCEM due to abnormal bleeding and another one due to rich vascularization of CSP. After repeated SCEM patients were scheduled for SC, which were uncomplicated. Pain after the procedure was mild and did not require treatment beyond standard over-the-counter medications. None of the patients required a hysterectomy. The follow-up ranged from 9 to 36 months. In short-term follow-up no significant complications occurred, 8 patients reported minor ailments: 6 uterine cramping and 2 nausea. Median of the regression time of β -hCG level was 30 days (range 7 to 90 days). Four patients were lost to long-term follow-up. In the remaining 18 patients 10 women normal menses occurred 1 month after the intervention. Two patients had regular menses 3 months after but the duration of bleeding was shorter. In one case normalization of menstrual cycle occurred 6 months after and in the other one after a year. Four women experienced menstrual cycle disturbances: 2 suffered from amenorrhea and two reported hypomenorrhea. Hb level was within normal values in all patients before the procedure. After SCEM followed by SC only in 1 case iron supplementation was necessary. In two patients Asherman syndrome was diagnosed after 9 months. In these two cases we performed hysteroscopies, during which intrauterine adhesions were confirmed and removed. Four women complained of severe pain in the CS scar, one of them had a caesarean scar defect and required surgical correction. In total, 8 out of 18 patients reported at least one complication. Ten out of 18 patients expressed the desire for subsequent pregnancy. Five patients conceived within a year after the procedure. Two pregnancies ended in CS at 35 and 38 weeks. These pregnancies were complicated by placenta praevia in one case and by cervical insufficiency in the second one. Two others were scheduled for elective CS at 39 weeks with no complications. The fifth patient had five early miscarriages. Five patients did not achieve a pregnancy.

Comment

The main finding of the study is that SCEM with SC is an effective treatment for CSP: most of the patients with CSP were successfully treated (91%), only two required additional SCEM. However, a significant number of complications was observed in

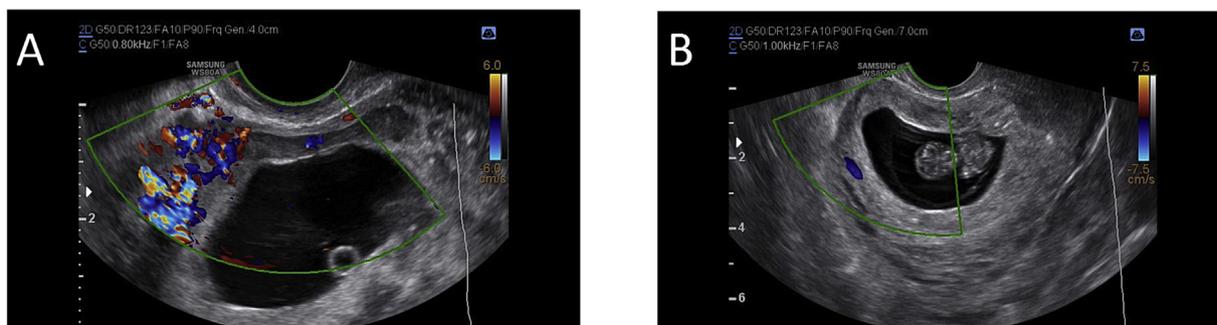


Fig. 1. Vascularization of caesarean scar pregnancy before (A) and after (B) selective chemoembolization with methotrexate.

long-term follow-up. Finally, some of these complications may have a negative impact on fertility.

At present there is no universal treatment or guidelines for CSP treatment. Timor-Tritsch et al. analyzed the different therapeutic approaches for CSP and found 31 primary treatment methods for the 751 reported CSP cases [2]. Recent literature data indicate that combination of various treatment options is more effective and safer for the patient than single method [4]. One of the frequently used treatment methods for CSP is UAE.

UAE has been a well-documented minimally invasive treatment method for different gynaecological pathologies, such as fibroids, postpartum haemorrhage and CSP. UAE was described as an effective method to block blood flow in the uterine arteries, which also decreases vascularization of CSP. Moreover the promotion of acute trophoblastic ischemic degeneration helps to avoid extensive bleeding in further procedures [8]. In general, in the treatment of CSP UAE was associated with a success rate of 93%, a risk of haemorrhage 5%, and a risk of hysterectomy 3% [9]. On the basis of our results and literature data the combination of SCEM with SC seems to be an effective uterine preservation method in the treatment of CSP and is associated with less blood loss in comparison to surgical management [10]. Some authors pointed out that scar tissue can be extremely fragile after UAE, especially after co-administration of MTX [11]. This is the reason why we decided to use SC instead of D&C to remove CSP tissues. Sarah Maheux-Lacroix et al. stressed that to achieve more successful outcomes, three factors should be highlighted: adequate MTX dosage, appropriate embolic material and complete embolization of target arteries [9].

The biggest concern associated with UAE in CSP treatment is its possible impact on future fertility. UAE may have a negative impact on various factors. It has been shown that UAE can lead to premature ovarian failure, hypomenorrhea and premature menopause [12]. Some studies reported a decrease in anti-Müllerian hormone (AMH), which is a marker for ovarian reserve was found after UAE in patients with symptomatic fibroids [13,14]. Moreover, a decrease in menstrual blood volume was observed in UAE patients. In contrast to fibroid treatment with UAE, where patients suffer from menorrhagia and the decrease in blood volume is considered a therapeutic success, in patients with CSP it might be recognized as a complication. In our study 4 out of 18 patients experienced hypomenorrhea or amenorrhea after SCEM with SC. Also Chen et al. reported a reduction in menstrual volume in half of the patients after UAE, which was considered to have a negative impact on the patients' quality of life [15]. Uterine or endometrial necrosis and intrauterine adhesions might be the cause of this condition.

In our study 2 cases of Asherman syndrome were diagnosed in the 22 CSP patients treated with SCEM with SC. The true prevalence of Asherman syndrome is unknown, but ranges from 2% to 48% after surgical evacuation of an early pregnancy loss [16]. While dilatation and curettage with a sharp curette is a known risk factor for Asherman syndrome, there are no reports of Asherman syndrome following suction curettage. We believe that in the cases that occurred in our study the chemoembolization could have contributed to the formation of intrauterine adhesions.

Despite the risk of the abovementioned complications, viable pregnancies after CSP treatment with UAE are possible. Yin et al. presented 13 cases of successful CSP treatment, in this group two patients were planning future pregnancy and conceived without any complications [17]. In the present study half of the patients achieved pregnancy. Similarly Krissi et al. reported a 50% successful pregnancy rate [18]. It has to be stressed that in all abovementioned studies absorbable embolic material was used instead of permanent particles to minimize the impact on fertility [18].

This study has some relevant limitations, which include relatively small number of the patients and different duration of follow-up. Further studies are required to assess the fertility after SCEM followed by SC.

The combination of SCEM with SC appears to be an effective treatment option. The method seems to be safe in short-term follow-up. However, complications were observed in long-term follow-up, including these interfering with future fertility. Patients should be informed about the possible risk of such complications. Future studies should focus on finding the optimal treatment protocol for CSP treatment in patients desiring subsequent pregnancies.

Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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Not applicable.

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