

## Cesarean Scar Pregnancy: Some Management Options

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Cesarean scar pregnancy (CSP) is a rare form of an ectopic pregnancy wherein the trophoblast invades a defective and thinned out myometrium in a scar which is a remnant of a previous Cesarean section and with advancing penetration and implantation poses a grave risk to the patient. This is due to the massively increased vascularity associated with its growth in addition to the fact that the contractility of the lower segment being poor, once hemorrhage commences it is well nigh impossible to control it without some form of operative intervention. Other risk factors include trauma to the myometrium caused by dilatation and curettage, myomectomy or an adenomyosis excision, pelvic inflammatory disease, the use of assisted reproductive techniques

and prior placental pathology [1, 2] Delay in diagnosis and treatment could lead to complications like rupture, severe hemorrhage, hypovolemia and death. The incidence of CSP ranges from one in 1800 to one in 2216 pregnancies [2–4]. Regarding the number of previous Cesarean sections or the time interval between the occurrence of a CSP and the previous section, no definitive data are yet available. However, in one study 72% of patients of CSP had two or more Cesarean deliveries [3].

Like any other ectopic pregnancy, intervention is called upon soon after diagnosis which is usually made using ultrasound and/or magnetic resonance imaging. An ultrasound should show the sac in the region of the lower uterine segment with a thin layer of myometrium separating it from the bladder. Additionally, there should be a discontinuity in the anterior uterine wall which would indicate the defective area. Management options are plentiful, and consequently choosing the correct modality of

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treatment could be a dilemma. Since the patient is usually young an attempt is made to institute conservative management to try and preserve fertility. Early diagnosis could help in this endeavor. Differing management strategies range from conservative management using methotrexate (MTX) via different routes, endoscopic (laparoscopic and hysteroscopic) CSP excision, laparotomy to excise and repair the CSP site, hysterectomy if the deficit is too large, the use of uterine artery embolization (UAE) in combination treatment, intracervical injection of vasopressin prior to uterine evacuation of the CSP, etc. One study [5] compared the outcome in hemodynamically stable CSP cases who were randomized to two groups. One where UAE with systemic MTX (25 mg) was administered through the uterine arteries versus another where a direct injection of MTX (25 mg) into the gestational sac was done under ultrasound guidance. Serum beta ( $\beta$ ) human chorionic gonadotropin ( $\beta$ -hCG) levels were monitored on day four and seven as per the American Congress of Obstetricians and Gynecologists (ACOG) guidelines [6]. During follow-up, patients in both groups received systemic MTX injection(s) after day one. Patients were followed until serum  $\beta$ -hCG titers declined to less than 20 mIU/mL. Failure of conservative treatment led to surgery. The results were thus described in the article—“The two groups were similar in clinical characteristics, success rate (83.3 cf. 80.9%), time to normalization of serum  $\beta$ -hCG and percentage of patients receiving multiple doses of systemic MTX. However, within the failed cases, the percentages of patients with gestational sac  $>5$  cm (87.5%), or type II CSP (75.0%) was significantly higher than in the successful cases (13.5 and 18.9%, respectively;  $P < 0.001$ , both), without regard to treatment group. According to the logistic regression model, a gestational sac diameter  $>5$  cm or type II CSP was a independent risk factor for failed CSP management (gestational sac  $>5$  cm: OR 51.87, 95% CI 3.48–775.91,  $P < 0.01$ ; type II CSP: OR 15.54, 95% CI 1.25–193.36,  $P < 0.05$ ).” Both regimes were equally effective in the treatment of CSP patients. Either treatment was likely to fail for CSP patients with gestational sac  $>5$  cm or type II CSP. In a type II CSP, the progression is toward the bladder and the abdominal cavity, and thus it poses a greater threat than a type I CSP. Despite this study, conservative management in general is fraught with danger and the use of systemic MTX may not be as successful as in tubal ectopic pregnancies [7]. Sugawara et al. [8] reported three cases of CSP that were successfully managed by UAE and direct injection of MTX to the gestational mass and surrounding myometrium. In an extensive review of the literature [9] the authors conducted a Medline/Pubmed search of the English literature from January 1978 to January 2012 to study the efficacy of systemic MTX in CSP. In all 27 publications, 40 cases of CSP were

studied. The authors concluded that “administration of primary systemic MTX treatment was found to be ideal for a Cesarean scar ectopic pregnancy presenting before 8 weeks gestation, with a  $\beta$ -hCG concentration of  $\leq 12,000$  mIU/mL together with an absent embryonic cardiac activity (ECA) (OR 14.52, 95% CI 2.36–89.09).” The administration of systemic MTX seemed to be more efficacious when the  $\beta$ -hCG levels were less than 12,000 mIU/mL (OR 5.68, 95% confidence interval, CI 1.37–23.48) and absence of ECA (OR 4.80, 95% CI 1.14–20.08).

Operative interventions to treat CSP include dilatation and curettage, resection by laparotomy, laparoscopic excision, hysteroscopic resection, suction curettage and hysterectomy. At times unfortunately, one surgical procedure used primarily to evacuate a CSP may lead to a secondary major procedure (hysterectomy) being performed due to severe hemorrhage resulting as a consequence of the primary procedure. Dilatation and curettage can result in severe hemorrhage and perforation [10]. In a case reported by Koplay et al. [11], vacuum aspiration was used to evacuate a CSP which showed no evidence of a bulge at the previous Cesarean scar site when viewed by laparoscopy after incising the uterovesical peritoneum. The CSP was close to the endometrial cavity rather than the peritoneal cavity. Hence a Karman cannula number eight was used to evacuate the CSP without incident. However, this kind of management is open to questioning. One study compared the use of MTX alone versus a combined therapy of MTX and suction curettage [12]. The combined treatment acted in a shorter period of time, though both therapies could treat the majority of CSP cases successfully.

Hysteroscopic surgery too has been used in conjunction with UAE in the treatment of CSP. [13] Twenty-nine cases of CSP underwent UAE prior to hysteroscopy. CSP masses that progressed toward the uterine cavity were resected using a cutting wire loop electrode combined with curettage. Success rate and cure rate were 94% (31/33). While there was no uterine perforation, massive hemorrhage occurred in two cases and hysterectomy was performed. In one other study, [14] in a series of six cases, four were treated with primary removal of the CSP. In these cases, the median time for the return to  $<5$  mIU/mL  $\beta$ -hCG was 30 days. Two patients were treated with systemic MTX which failed. One of these was treated with hysteroscopic removal, the other with local treatment of MTX to the gestational sac. Management of CSP by a combination of operative laparoscopy and hysteroscopy has also been described [15]. In the two cases described by Colome et al. one underwent evacuation of the CSP by a combined laparoscopy hysteroscopy procedure. The other case involved an ultrasound guided injection of MTX into the gestational sac which failed. The CSP was evacuated using the combined laparoscopy and hysteroscopy procedure.

Intracervical injection of vasopressin has been described, in the evacuation of a CSP [16]. The bleeding is reduced following which an enhanced vision ensures easy operability.

Eleven patients of CSP were treated at a center between 1999 and 2004 [17], of these four underwent laparoscopic surgery, six underwent hysteroscopic treatment, and one was treated by a combination of laparoscopic and hysteroscopic surgical treatment. All uteri were successfully preserved. Laparoscopic surgery was successful in all 32 cases in another study [18]. In the same study of 39 cases treated by hysteroscopic surgery, two had to undergo abdominal hysterectomy due to the occurrence of severe hemorrhage.

High-frequency focused ultrasound (HIFU) was used in combination with dilatation and curettage in four cases of CSP at a center [19]. All four cases had elevated serum  $\beta$ -hCG and large lesions. In one case, laparotomy and repair was done due to a large defect though the  $\beta$ -hCG levels had returned to normal. HIFU was done under local anesthesia. The rationale of using HIFU was thus explained—“HIFU, by utilizing ultrasound energy to heat tissue at a focal point, is able to stop ECA and leads to a rapid reduction in serum  $\beta$ -hCG levels. Subsequent D&C under hysteroscopic guidance enables complete removal of products of conception following the HIFU procedure.” Exploratory laparotomy and hysterotomy for excision and repair of the mass can be a “rapid and safe option,” [20] one article argues. This argument is sustainable, and it may be the first definitive treatment initiated which may be life saving despite the lack of frills and sophistry associated with it.

Transvaginal hysterotomy along with MTX injection [21] during the operation was used as treatment for 12 cases of CSP. The authors felt that the safety and efficacy of this method needed further confirmation. With good reason in my opinion. Combination therapy in many permutations may be counterproductive and may result in several other procedures being performed to the detriment of the patient.

After going through the maze of options available to manage CSP it becomes a trifle confusing as to the use of the correct choice of treatment for each case. However, early diagnosis, the size and type of the CSP, the levels of serum  $\beta$ -hCG, the use of MTX, fertility preservation, etc., are variables which could influence the modality of treatment. In addition, there are always questions regarding future pregnancy, the occurrence of abnormal placentation and obstetric outcome. In the literature, almost “all of the women whose pregnancies were managed expectantly developed placenta accreta or increta, resulting in either a hysterotomy or hysterectomy with severe hemorrhage” [22]. Regarding future fertility potential one study [23] shows encouraging results for fertility (either

spontaneously or by IVF) and obstetric outcome after the treatment of CSP. However, the risk of recurrent CSP remains. In a ten year study, twenty-two cases of CSP were reviewed [24]. The conclusion was that there could be no consensus in the management of CSP.

One could envisage an increasing incidence of CSP being the trend in the future for obvious reasons. Therefore, as a preventive measure it would be prudent to monitor a primary labor well and perform a justified Cesarean section which would stand the scrutiny of any audit. A primary Cesarean scar invariably invites repeat scars and possibly more CSP. There should not be a desperation to conserve fertility at all costs to the detriment of the patient, and extirpative surgery may have to be resorted to as the first line of treatment. Any combination therapy should be performed after due process taking into consideration the circumstances of the patient. There can be no template as yet for the management of CSP.

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