CAESAREAN SCAR PREGNANCY – FULL CLINICAL GUIDELINE

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1. Introduction

Caesarean scar pregnancy is a rare type of ectopic pregnancy whereby implantation occurs at the myometrial defect of the previous Caesarean scar (uterine incision). These pregnancies may be ongoing potentially viable pregnancies or miscarriages within the scar. The prevalence of caesarean scar pregnancy is estimated to be approximately 1 in 2000 of all pregnancies and it constitutes 6.1% of all ectopic pregnancies diagnosed in women with one previous caesarean section. Since the first reported case in 1978, the frequency of caesarean scar pregnancies has been increasing, especially in the last few years. This may potentially be attributed to increasing awareness, better ultrasound diagnosis, rising caesarean section rates and possibly change in the uterine closure technique at Caesarean section. Caesarean scar pregnancy can cause severe maternal morbidity and even mortality.

2. Purpose & Scope

The purpose of this guideline policy is to provide the evidence-based guidance on diagnosis and management of caesarean scar ectopic pregnancy. The diagnosis and management of tubal and other non-tubal ectopic pregnancies and pregnancy of unknown location are discussed in another guideline titled “Diagnosis and Management of Ectopic Pregnancy and Pregnancy of Unknown Location - Full Clinical Guideline”.

3. Abbreviations

A&E	-	Accident & Emergency Department
AEPU	-	Association of Early Pregnancy Units
CSP	-	Caesarean Scar Pregnancy
HCG	-	Human Chorionic Gonadotrophin hormone
FBC	-	Full Blood Count
G & S	-	Group & Save
GS	-	Gestational Sac
IU/L	-	International Units per Litre
IV	-	Intravenous
LFT	-	Liver Function Tests
MRI	-	Magnetic Resonance Imaging
RCOG	-	Royal College of Obstetricians and Gynaecologists
TVS	-	Trans-Vaginal Scan
TAS	-	Trans-Abdominal Scan
US	-	Ultrasound

4. Definition and Risk factors

Caesarean scar Pregnancy (CSP)
CSP is a rare type of ectopic pregnancy in which the gestational sac is implanted in the scar caused by previous caesarean section. While two types of CSP – Type 1 or endogenic and Type 2 or exogenic- are described, management approach is the same. Type 1, or endogenic, CSP is where implantation occurs on the scar and the gestational sac grows towards the cervico-isthmic or uterine cavity with the potential to reach a viable gestational age but with the risk of massive bleeding from the implantation site. Type 2, or exogenic, CSP occurs when the gestational sac is deeply embedded in the scar and the surrounding myometrium and grows towards the bladder. In exogenic types, a layer of myometrium may be seen between the gestational sac and the bladder at an earlier stage; this becomes thin and eventually disappears, with bulging of the gestational sac through the gap as the pregnancy progresses, thus carrying a greater risk of earlier rupture. In two-thirds of cases the thickness of the scar may be less than 5 mm.

While most CSP occur after only one previous CS, there is no clear correlation between the risk of CSP and the number of previous Caesarean sections. Women who have an elective Caesarean section for breech presentation in a previous pregnancy appear to be at risk of future CSP and this may be related to the need for a higher uterine incision because of a poorly formed lower segment. It was estimated that 1 in 531 women with a cesarean scar would have a CSP.

5. Diagnosis

While most women present with slight vaginal bleeding and mild abdominal discomfort, some may present with acute pain and profuse vaginal bleeding. Incidental diagnosis is some times made in asymptomatic women on routine early pregnancy scanning or when attending Pregnancy Advisory TOP Services (see guideline). Haemodynamic instability and collapse in a suspected Caesarean scar pregnancy strongly indicates rupture with intra-abdominal bleeding. Given the potential for serious life-threatening complications, accurate and reliable diagnostic criteria are applied. A urine pregnancy test should be considered in any woman of reproductive age with unexplained abdominal pain – recommend catheterisation if necessary to obtain a urine sample. Full clinical assessment should be supplemented with transvaginal ultrasound scan and serum HCG to ascertain the location of pregnancy in women with a positive urine pregnancy test.

5.1 Imaging

Ultrasound is the primary diagnostic modality, using a transvaginal approach supplemented by transabdominal imaging if required. Key to the diagnosis of CSP are a high index of suspicion followed by an ultrasound assessment demonstrating characteristic features.

Ultrasound ***diagnostic criteria*** for diagnosing CSP are:

Essential criteria

- Empty Uterine cavity
- Empty cervical canal
- Gestational sac or solid mass of trophoblast located anteriorly at the level of the internal os embedded at the site of the previous lower uterine segment caesarean section scar

Additional criteria

- A triangular/ round or oval-shaped gestational sac that fills the niche of the scar
- A thin or absent myometrial layer between the gestational sac and the bladder
- Discontinuity in the anterior wall of the uterus adjacent to the gestational sac
- Yolk sac, embryo and cardiac activity may or may not be present
- Evidence of prominent trophoblastic/placental circulation on colour flow Doppler examination
- Negative 'sliding organs' sign (see below)

The diagnostic criteria have not been subject to validation and are derived from descriptive case series, so to minimise the risk of false-positive diagnosis, it is recommended that all non-emergency cases of suspected scar pregnancy are referred to an experienced clinician to confirm the diagnosis. The clinicians, who can be contacted for a second scan in making a definitive diagnosis, are the Gynaecology consultant and/or Radiology consultants

The differential diagnoses are inevitable or impending miscarriage with gestational sac lying in the cervical canal and cervical ectopic pregnancy. In impending miscarriage, the gestational sac is often irregular and located within the uterine cavity and with absent or minimal Doppler signal. Gentle pressure with the transvaginal probe at the level of the internal os may slide the gestational sac against the endocervical canal – demonstrating 'sliding sign'. The sliding sign is absent in CSP. A cervical pregnancy is diagnosed when there is a barrel shaped cervix, gestational sac present in the cervical canal with ballooning of the cervix, gestational sac seen often below the level of the internal os, absence of sliding sign and prominent Doppler signals around the gestational sac.

Ultrasound (TVS +/- TAS) alone is often adequate in making a definitive diagnosis of CSP and a management plan can be adopted based on the ultrasound diagnosis. However, if the diagnosis is equivocal in cases of uncertain ultrasound features (as in women with large uterine fibroids or at a later stage of gestation), ***MRI*** can be requested as a second line investigation. The Radiology consultants can be contacted to request MRI. The long-term effect in children when they are exposed to Magnetic field in early pregnancy remain unknown (although safety has been proven with plain MRI not with Gadolinium contrast MRI) and this should be discussed with the patients before requesting the MRI.*

5.2 HCG

A serum HCG level is useful as a baseline prior to monitoring for treatment response, but it does not have a role in the diagnosis of caesarean scar pregnancy.

6. <u>Management of CSP</u>

A woman with a suspected CSP should be urgently reviewed directly by a senior gynaecologist. Women diagnosed with CSP should be counselled that such pregnancies can be associated with severe maternal morbidity (intra-abdominal rupture, severe vaginal bleeding, need for hysterectomy) and mortality. All women with suspected CSP should have a baseline FBC, group and save and baseline HCG levels done.

In principle, CSP should be treated as soon as possible after confirming the diagnosis, with the aim of removing/ resolving the gestational sac and the CSP mass to retain future fertility. While more than 30 CSP treatment regimens have been published, most recommendations are based on case series rather than randomized controlled trials. It is important to inform women that all treatment options carry a risk of haemorrhage and subsequent hysterectomy. Treatment should be individualised based on pre-treatment evaluation and after discussing with the consultants experienced in treating

CSP. Conservative approach has no or a limited role. Medical and surgical interventions with or without additional haemostatic measures should be considered in women with first trimester caesarean scar pregnancy.

Table 1: Management options for Caesarean scar pregnancy (CSP)

Expectant management	Limited or no role. Very rarely used in selected cases
Medical management	Systemic methotrexate
Local injection and Embolisation	Local injection of methotrexate with sac aspiration
	Local injection of other embryocides
	Uterine artery chemoembolisation
Surgical management	Dilatation and surgical evacuation under ultrasound guidance
	Hysteroscopic resection
	Laparoscopic excision and resuturing
	Combined laparoscopic and hysteroscopic procedure
	Hysterectomy
Combined or sequential management	Uterine artery embolisation followed by surgical evacuation or surgical resection in 24-48 hours
	Methotrexate injection followed by surgical evacuation or surgical resection after an interval

While there are various options available as tabulated above, there is insufficient evidence to recommend any one specific intervention over another for caesarean scar pregnancy. ***The current literature supports a surgical rather than medical approach as the most effective option.***

6.1 Surgical evacuation under ultrasound guidance

Dilatation of cervix and evacuation under ultrasound guidance is suitable for endogenic CSP with myometrial thickness of at least 2 mm thickness, symptomatic CSP and particularly with HCG levels of >5000 IU/L. ***Consider this method as the first-choice treatment option in all clinical circumstances once the diagnosis of CSP is confirmed***. It should be performed under ultrasound guidance to aid complete tissue removal and to do the procedure in a quick time. Various techniques to reduce the bleeding during and after the procedure have been reported. Cervical cerclage applied prior to surgical evacuation and tied after the procedure is an effective method of reducing bleeding following evacuation. Other haemostatic techniques include the use of intrauterine Foleys catheter insertion intra-/post-operatively and pre-operative UAE.

The suggested procedure steps based on our local experience are:

Pre-op (in GAU or Day case unit)

- Operator to do a scan (TVS and TAS) to reassess the CSP (if not done before) to ensure suitability for surgical evacuation
- Ensure 2 units of blood cross matched as there is a risk of severe bleeding intra-op and immediate post-op
- Consent - inform women risks of infection, bleeding, hysterectomy rarely though, need for follow up, recurrence of CSP in future pregnancy and need for blood transfusion. Inform women that a trans-rectal scan may be needed just in case if abdominal ultrasound is not giving a satisfactory image (in cases of very early CSP or woman's high BMI)

Intra-op (in theatre)

- Lithotomy position
- Cleaning and draping

- Do an ***abdominal ultrasound*** and obtain a sagittal view of uterus, cervix and CSP. Transrectal ultrasound could be used if CSP not clearly visualised on TAS.
- ***IV antibiotics*** and then oral antibiotics for 5 days
- 800 mcg ***misoprostol*** P/R in the theatre (to aid uterine contraction post-operatively) just before starting the procedure
- Consider applying ***cervical suture*** as high and safe as possible using Merseline tape, start anteriorly and end anteriorly, but do not tie at this stage
- Dilate the cervix to one level above the suction size that planning to use under US guidance.
- Ensure the suction machine is working well before inserting into the cervical canal, keeping the suction power to maximum
- Evacuate the decidua from the uterine cavity first under US guidance
- Then evacuate the sac and pregnancy tissue from CSP under US guidance
- Ergometrine 0.5 mg given IV straight after the procedure is complete.
- Finish the procedure as quickly as possible as blood loss will be maximal during the procedure
- Once CSP tissue evacuated, tie the Merseline tape anteriorly (if the cervical suture is applied).
- If cervical suture is applied as a haemostatic measure, plan for suture removal in 2-4 days time at GAU
- Discharge home the same day or next day if stable

Post-op (in GAU)

- Remove cervical suture (if applied) in 2-4 days, consider doing in the OP hysteroscopy procedure room with Entonox on standby
- Do HCG levels, senior clinical review, plan further follow up as appropriate (at least in 1 week)
- If remaining asymptomatic and HCG levels falling, scan in 7-10 days time post-op
- Follow up until pregnancy test is negative
- Consider methotrexate injection if, at any time, suspecting residual pregnancy tissue

6.2 Medical Management

Systemic methotrexate may be offered to suitable women with CSP (asymptomatic, very early pregnancy, no visible cardiac activity on scan and low HCG levels of <5000 IU/L, no evidence of intrauterine pregnancy). ***Consider this treatment option only if 'surgical evacuation under ultrasound guidance' is not suitable or appropriate.*** The methotrexate dose regimen and follow up for CSP is the same as that used for tubal ectopic pregnancies. It should never be given at the first visit, unless the diagnosis of ectopic pregnancy is absolutely clear and a viable intrauterine pregnancy has been excluded.

Discuss with the gynaecology consultant on call prior to administration of methotrexate

Prior to its administration, all women receiving methotrexate should have a baseline full blood count, and liver and renal function tests. Adequate counselling should be provided regarding the likelihood of prolonged follow up, repeated HCG tests, the need for additional treatment doses and the possibility of surgical intervention including hysterectomy.
If HCG levels are rising on serial measurement, one must positively exclude intrauterine pregnancy before starting methotrexate treatment.

Contraindication to Methotrexate Treatment

- Any hepatic dysfunction, thrombocytopenia (i.e. platelets <150 x 10^9 /L), blood dyscrasia (WCC<3 x 10^9/L)
- Difficulty or unwillingness of patient for prolonged follow up (average follow up 35 days).
- Women on concurrent corticosteroids
- Sensitivity /allergy to methotrexate
- Renal impairment

Treatment Protocol

- Provide information leaflet about medical management of ectopic pregnancy
- Obtain written informed consent from patient

- Take blood for FBC, U&Es, LFTs, blood group
- Measure height and weight
- Prescribe methotrexate 50mg/m^2; send the prescription with height and weight documented to pharmacy to prepare the medication
- Check blood results, give methotrexate intramuscularly in buttock or lateral thigh
- Rest for up to one hour, check for any local reaction. If local reaction noted consider antihistamine or steroid cream (very rare).

Arrange **follow up** in GAU:

- Day 1: serum HCG and methotrexate
- Day 4: serum HCG
- Day 7: serum HCG, FBC, U&E, LFT. Second dose of methotrexate if HCG decreases <15% day 4-7. 15% medical treatment will require second dose

If HCG decreases >15%, repeat HCG weekly until less than 20IU/L.

Up to 75% women experience pain on days 3-7, due to tubal miscarriage/ placental separation. Side effects of the drug are minimal but may include nausea, vomiting and stomatitis. Patient advised to maintain ample fluid intake, avoid alcohol and folic acid-containing vitamins during treatment, avoid sexual intercourse (risk of rupture), and avoid exposure to sunlight.

Avoid pregnancy for 3 months following methotrexate because of a possible teratogenic effect. Patients may use reliable barrier method or hormonal contraception.

6.3 Local injection of Methotrexate

Gestational sac aspiration with the administration of methotrexate into the sac is the preferred approach for exogenic type of CSP with thin myometrial tissue between the gestational sac and bladder. This approach alone or combined with systemic administration of methotrexate appears to have a better success rate and requires fewer additional interventions. In this effective technique the gestational sac is aspirated and methotrexate injected into it under ultrasound guidance. While transabdominal and transvaginal injection approaches are both feasible, the transvaginal approach is recommended as it has the advantage of being anatomically closer to the target lesion and so helps to avoid visceral injury. The time required for complete resolution of the ectopic mass correlates with the initial sac size and HCG levels.

The dose of the methotrexate, pre-procedure evaluation, counseling and follow up are similar to that for systemic methotrexate injection.

7. Anti-D rhesus Prophylaxis

Offer anti-D prophylaxis at a dose of 250IU (50 microgram) as per national protocol to all RhD-negative women who have surgical removal of CSP, or where bleeding is repeated, heavy or associated with abdominal pain.

Do not use a Kleihauer test to quantify feto-maternal haemorrhage.

Do not offer anti-D rhesus prophylaxis to women who solely receive medical management for an ectopic pregnancy.

8. Support and Information Giving

Provide women with early pregnancy complications information and support in a sensitive manner, considering their individual circumstances and emotional response. Throughout a woman's care, give her and, with her agreement, her partner information in a variety of formats. This should include:

- When and how to seek help if existing symptoms worsen or new symptoms appear
- What to expect during the course of her care (including expectant management) such as the potential length of treatment and extent of pain and or bleeding, and possible side effects, as appropriate.
- Where to access support and counseling services, including leaflets, web addresses and helpline numbers.

Women should be advised, whenever possible, of the advantages and disadvantages associated with each approach used for the treatment of CSP, and should participate fully in the selection of the most appropriate treatment.

What is the risk of recurrence?

Most women have a normal pregnancy following a CSP. The risk of recurrence has been reported as 3.2–5.0% in women with one previous CSP treated by dilatation and curettage with or without uterine artery embolisation.

9. Monitoring Compliance and Effectiveness

As per agreed business unit audit forward programme

10. References

Green-top Guideline No. 21 (2016) - Diagnosis and Management of Ectopic Pregnancy. RCOG/AEPU Joint Guideline November 2016

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Petersen KB, Hoffmann E, Larsen CR, Nielsen HS (2016), Cesarean scar pregnancy: A systematic review of treatment studies. Fertility and Sterility 105: 958-967

Eastwood KA, Mohan AR. Imaging in pregnancy.
The Obstetrician and Gyanecologist 2019;21:255-62.

Burton Hospitals:

If a diagnosis of CSP is suspected, consider referral to Royal Derby Hospital (RDH), as appropriate. Consultant on call at Burton to liaise with Gynae consultant on call at RDH to discuss management and arrange the referral.

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