Cesarean Scar Pregnancy: Know what you are doing

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C-section rate within 22 developed countries between 1997 and 2008

Slide Courtesy of Prof. Stanojevic

Cesarean Rates (per 1,000 births), Industrialized Countries 1990-2004

Morbidly adherent placentae
1994-2002: 1 in 2000-2500

Cesarean scar pregnancy
2010: 1 in 2000-2500

Source: OECD Health Data 2006
Background

• The increasing incidence of cesarean scar pregnancy (CSP) is directly related to the increase in the rate of cesarean deliveries.
• I base this talk upon some of our previous work on the subject

Objectives

• 1. Teach practicing clinicians to Diagnose a cesarean scar pregnancy (CSP), using diagnostic criteria and RELIABLY differentiate it from an intrauterine and a cervical pregnancy.
• 2. Realize that there is a common histologic basis of CSP and morbidly adherent placenta (MAP) such as accreta, increta and percreta, and that CSP is its main precursor.
• 3. Construct an evidence based counseling and management plan taking into consideration patients’ obstetrical goals.

Outline

1. What is a cesarean scar pregnancy
   Incidence
   1. Diagnosis
   2. Natural history if left untreated
   3. Treatment
      1. Choices in the literature
      2. Management complications
      3. Best treatment: Is there any single one?
   4. Conclusions
1. What is a cesarean scar pregnancy (CSP)

**Synonyms in the literature:** Scar pregnancy, Cesarean section scar ectopic, Section scar ectopic

**The general knowledge in the community**

- CSP is an iatrogenic entity
- A blastocyst implants in a microscopic or macroscopic tract **on the uterine scar of in the “niche”** left by the incision, in the anterior uterine wall
- The mechanism is similar to implantations after uterine surgery (myomectomy, curettage, endometrial ablation, manual removal of placenta etc)
What is a cesarean section scar/niche and how does it look?
On US, most of the time it appears like this:

Watch!!! It has a width following the incision line!!
Asses size in the transverse plane

Remember: since the incision on the uterus is transverse, therefore the "niche" is larger in the transverse direction than it appears on a sagittal US image!
2. Pathogenesis

Sequence of events after fertilization
The **Extravillous Trophoblasts** appear, differentiate and start invading the decidua

- Normal implantation involves invasion of the uterine wall by two subgroups of **extravillous trophoblast**:
  - the **interstitial trophoblast** invades through the endometrium and the superficial one-third of the myometrium.
  - the **endovascular trophoblast** invades and remodels the maternal spiral arterioles *.

* Tantibrojn et al, Placenta 2008; 29:639

In early pregnancy, trophoblast cells invade the the uterus, where they transform spiral arteries to ensure the enhanced delivery of blood to the developing fetus at a low pressure

In a normal pregnancy there is a mechanism that stops the trophoblastic invasion: The **Fibrinoid Layers** between the decidua and the myometrium
By far, the biggest insult on the uterus is a cesarean section resulting in not only scaring but also leaves a dehiscence (“niche”) at the incision area.

- Propose that the extent of uterine wall "invasion" by placental villi (and resulting accreta vs. increta and percreta) may be dependent on the depth of the scar.

And that "placenta increta and percreta are not due to a further invasion of extravillous trophoblast in the uterine wall, rather they likely arise secondary to dehiscence of a scar, leading to the presence of chorionic villi deep within the uterine wall, and thus give extravillous trophoblast greater access to the deep myometrium."
Deficient lower segment Cesarean section scars: prevalence and risk factors.

D. Orellana, D. Johnson, C. M. Smith, and S. Gonzalez

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**Conclusion**

Deficient uterine scars are a frequent finding in women with a Hx of Pr C/S.

The risk of scar deficiency is increased in women with a retroflexed uterus and in those who have undergone multiple C/Ss.

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**Other theories of pathogenesis of CSP:**

- IVF centers use artificially "denuding" small area of the cavity to cause "inflammatory response" to increase implantation***
  
  

- The "exposed cellular matrix " attracting the trophoblast**
  
  Kaiman HJ et al, Placenta 1990; 11:349-367

- The theory of "low oxygen tension" in the scar that facilitates oocyte implantation*
  
  *Glenbacev et al Regulation of human placental development by oxygen tension. SCIENCE 1997; 277

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**Theories of the pathogenesis.**

Uterine interventions lead to the thinning or missing Nitabuch fibrinoid layer. The placenta will attach itself deeply into the uterine wall.

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3. Incidence

C/S Scar Pregnancies

- True incidence is not known
- ~1 in 2000-2500 cesarean deliveries
- Rate increasing due to rising C/S rates
- 52% of CSP had only one prior C/S
- The more previous C/S, the more CSP, the more placenta previa and accreta

Wu S et al., Am J Obstet Gynecol 2005;192:1454-61
Miller DA et al., Am J Obstet gynecol 1997; 177:210
The inevitable consequences

Morbidly adherent placentae ("accreta") and CSP rates parallel the increasing CD rates

4. How do we make the diagnosis and which are the differential diagnoses?
The sonographic diagnosis is made by TVS.

As per some reviews the Dx by TVUS:
sensitivity 84.6%

This depends on the expertize
In our patients, the diagnosis was made in all cases.

Should you order MRI to diagnose or to confirm a sono diagnosis of a CSP?

Possible, but definitely not necessary!!

Sono criteria of CSP:
1. No fetal parts in the uterine cavity or cervix.
2. Thin myometrial layer between the bladder and gestational sac.
3. Triangular shaped gestational sac.
4. Gestational sac close to the bladder and anterior uterine wall.
5. Rarely: A-V malformation at the site of a CS

The differential diagnosis

1. **Cervical Pregnancy** – however – remember: Cx pregnancy is EXTREMELY rare & occur in intact uteri

2. **IUP in the process of abortion** – however – they very rarely have a beating heart!

Therefore:

If the chorionic sac is low, close to the cervix and the patient had a previous cesarean delivery: **IT IS A CSP!!!!**

Easy sonographic differential diagnosis between intrauterine pregnancy and cesarean delivery scar pregnancy in the early first trimester

On a panoramic, longitudinal, sagittal scan determine the location of the gestational sac by dividing the uterus in half by an imaginary line

- Sensitivity = 93.0%
- Specificity = 98.9%
- PPV = 96.4%
- NPV = 97.9%

If the gestational sac is above it: it is mostly a normal implantation

If the gestational sac is below it: suspect a CSP or a cervical pregnancy. Counsel accordingly

*Am J Obstet Gynecol February 2016*
EARLY sonographic appearance:
Placenta .... "on the scar" ...

EARLY sonographic appearance:
Placenta ..... "in the niche".

**Warning:**

At times (mostly after 7 weeks) the location of the sac may be misleading.

Rely on the patient’s Hx, location of the placenta and its vascular supply!!
In an anteverted uterus 7w2d

Color Doppler of the vessels at the scar implantation site

The sac may “move up”, but the placenta with its vessels stays at the implantation site

In a retroverted uterus 9w2d

Pregnancy growing fully into uterine cavity. Placenta with vessels stays anchored within the niche

9 weeks

The placenta remains anchored in the niche and determines its adherence
5. What is the natural history of CSP?

First question:
Are scar pregnancy and morbidly adherent placenta the same disease?

If they are the same disease they have to share the same histology.

2 Pathologists independently examined the microscopic images.

They could not identified which were CSP and which were MAP by histology.
• **Conclusions:**
  • This study supports our hypothesis, that **Cesarean Scar Pregnancy and Early Placenta Accreta** are one and the same histopathologic entity and are an early manifestation of the morbidly adherent placenta.

5. **What is the natural history of CSP?**

The second question is if scar pregnancy is precursor of morbidly adherent placenta?

**Our Hypothesis:** In the 1st trimester CSP is the clinical expression of placenta accreta and percreta.
The objective.

• The goal was to provide evidence that, based upon their natural history, cesarean scar pregnancies (CSP) are a precursor of morbidly adherent placentas (MAP).

Two examples of ten cases

CASE # 1

Giuseppe Cali MD
Timor-Tritsch, Montenegro, Cali et al UOG 2014.
Results

• Nine out of 10 patients diagnosed with 1st ∆ CSP delivered preterm or near term viable offspring
• One patient had a fetal loss and hysterectomy at 20 weeks
• Nine patients had cesarean deliveries and hysterectomies & 7 had significant bleeding
• All 10 patients had placenta percreta

Conclusion

• The cases in this series validate the hypothesis that CSP is a precursor of MAP, both sharing the same histopathology.

• Our findings provide evidence that can be used to counsel patients with CSP, to enable them to make an informed choice between 1st ∆ TOP and continuation of the pregnancy, with its risk of premature delivery and loss of uterus and fertility.
It is clear that there is no uniform and agreed upon definition of the type and depth of implantation placental and its correlation to outcome

Importance of measuring bladder-to-sac distance

- The literature is not only confusing as to the sac location, but…..
- Rarely is there information about bladder-to-sac distance or overlying myometrial thickness
- Furthermore, usually there is no distinction between “gestational sac” and “placenta”
- Lastly, there is rarely any mention about location of placental vascularization

To correctly measure the sac-to-bladder distance, we need a precise definition of implantation, since it may determine outcome

Sporadically, but increasingly, the literature makes a distinction between implantation “on the scar tissue” and “in the niche (dehiscence)”
No consensus (yet) on the scac location

- Comstock: “Low lying: versus—surrounded by myometrium”
- Twickler: < 1mm predicted MAP
- Naji: away from scar, close to scar, crossing the scar, inside the scar (CSP)
- Rac: smallest anterior myometrial thickness on 1st sonography significantly improved detection of morbidly adherent placenta.

According to our 2016 study of 17 CSP cases who continued their pregnancy:

- 6 patients with CSP implanted “on the scar” had a substantial better outcome (1 hysterectomy for accreta), compared to 11 patients with CSP implanted “in the niche” (all had hysterectomy for percreta)
- Myometrial thickness below 2mm in the 1st trimester US was associated with Morbidly Adherent Placenta at delivery.

6. Treatment of CSP
1. First trimester treatment choices, if continuing the pregnancy is NOT an option

The major treatment modalities

- Surgical requiring general anesthesia
  - Major: laparotomy
  - Minor: Laparoscopy, Hysteroscopy; D&C
- Minimally invasive: Local injection (MTX/KCl)
- Systemic
  - Major: UAE
  - Minor: IM Methotrexate (single/multiple)
- Different combinations of the above
  - Simultaneously
  - Sequentially
Primary treatment in 751 cases

1. Hysteroscopic excision
2. Hysteroscopy by TAS guidance
3. Hysteroscopy & Mifepristone
4. Laparotomy & excision
5. Laparotomy with elective TAH
6. Laparotomy & systemic MTX
7. Laparotomy & hysteroscopy
8. TAS guided local MTX injection
9. TAS guided local KCl injection
10. TAS guided local & systemic MTX
11. TVS guided local MTX injection
12. TVS guided local KCl injection
13. TVS guided local & systemic MTX
14. Local injection of Vasopressin
15. UA embolization alone

After 2012 an additional 5-6 treatments were published

- Hysteroscopic excision
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- Local injection of Vasopressin
- UA embolization alone

16. UA embolization & systemic MTX
17. UA embolization & local MTX
18. D&C alone
19. D&C & systemic MTX
20. D&C & Shirodkar cervical suture
21. Laparoscopic excision
22. Laparoscopy & hysteroscopy
23. Laparoscopy & systemic MTX
24. MTX systemic alone
25. MTX systemic & hysteroscopy
26. Expectant management
27. Trichostatin
28. Transrectal US guided aspiration
29. Hysteroscopy & Vasopressin
30. Hysterotomy by vaginal approach
31. Combination of ≥3 Rx. Modalities

After 2012 an additional 5-6 treatments were published.

Are there guidelines??

- It is obvious that none of the countries, USA included, have a set of guidelines at hand when a patient with an early placenta accreta or a cesarean scar pregnancy presents.

2. Treatment complications

Before treating: know the complications!
Complication rate in the 751 cases
Overall: 331 (44.1%)

Most and least complications by mode of treatment

<table>
<thead>
<tr>
<th>Most frequently used single &amp; combination Rx</th>
<th># of cases</th>
<th># of complications</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX Alone</td>
<td>87</td>
<td>54</td>
<td>62.1</td>
</tr>
<tr>
<td>D&amp;C Alone</td>
<td>305</td>
<td>189</td>
<td>61.9</td>
</tr>
<tr>
<td>UA embolization</td>
<td>64</td>
<td>30</td>
<td>46.9</td>
</tr>
<tr>
<td>Hysteroscopy</td>
<td>119</td>
<td>22</td>
<td>18.4</td>
</tr>
<tr>
<td>Local injection of MTX/KCl (TAS or TVS guidance)</td>
<td>81</td>
<td>8</td>
<td>9.6</td>
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</tbody>
</table>

Some of the treatments of CSP
Totally dismissed the minimally invasive treatments

Systemic MTX alone
- As a single agent treatment had a 64.6% complication rate.
- Its slow action may take days
- Questionable ability to stop the heart Often require additional treatment.

Sequential, multidose systemic MTX
- Be aware of its side effects.
- Even such treatment fails at times
- However MTX can be used as an adjuvant therapy with other treatments

Transabdominal or transvaginal US guided local, intra-gestational sac injection of MTX/ KCl
About 100 cases in the literature with about an 9.6% (0-15%) complications

Michaels et al JUM 2015; Timor-Tritsch et al 2015; Zosmer et al UOG 2015
Operative hysteroscopy alone or in combination

About 119 cases reviewed in the literature with the second lowest (about 18%) complication rate (mostly bleeding).

Suction aspiration and/or SHARP D&C alone or in combined with inflation of Foley balloon

3D US display of rich vascular supply surrounding the choriocarcinoma of a scar pregnancy

This explains the possible bleeding complication of a D&C when the scar pregnancy is subjected to curettage.

The use of a single balloon Foley catheter as adjuvant to local, intragestational injection of MTX
Our treatment approach for CSP in the last 3-4 years

- Place single balloon as single treatment OR
- Inject locally & place balloon

New treatment for CSP and Cervical pregnancy

New minimally invasive treatment – Placing a double cervical ripening balloon

Reasons for its use:
- To simplify treatment; Minimize patient discomfort
- Simultaneously
  • Stops heart
  • Prevents bleeding
- Adapt a catheter familiar to Obstetricians who use it in the labor room
- Use it for cervical pregnancies too

The use of a double, cervical ripening balloon catheter as a single, minimally invasive treatment of CSP and CxP

Obstetrics
A new minimally invasive treatment for cesarean scar pregnancy and cervical pregnancy

Timor-Tritsch & Monteagudo
Am J Obstet Gynecol March 2016

Timor-Tritsch et al AJOG 2016
The New York experience: 3 centers*

- 21 +5+1 CSPs and 3 CxPs 30 pts were treated.
- Catheter placement & balloon inflation tolerated well.
- Oral pain medication and antibiotics were given.
- Last 8 patients received paracervical block (1% Lidocaine).
- Balloons deflated, catheter removed 1-3 days.
- Minimal, "old", dark blood was seen after removal of the catheters from intra-cavitary accumulation of blood.
- In all cases almost total resolution of the hCG, the sac site & its vascularity was seen within 20 -60 days.
- In the last cases we used adjuvant systemic MTX.

* NYU/Bellevue Medical centers: 24 cases.
* Carnegie Imaging (Drs Rebarber and Monteagudo): 5 cases.
* Lenox Hill, MPH (Dr Bornstein): 1 case.

Suggested management of CSP:

- **FH +**: CSP
  - Available evidence based counseling
  - Patient requests TOP
  - Select most appropriate Rx, stop heart with no or least delay!
  - Monitor hCG weekly. Scan by gray scale & Doppler: Watch for possible EMV

- **FH -**: CSP
  - No FH
  - Recheck q3 days
  - Patient interested in continuing pregnancy
  - Determine if placenta/ gestational sac is on the scar or in the niche. MEASURE MYOMETRIAL THICKNESS
  - Monitor hCG weekly: Follow hCG until zero! Do last US exam

- **No FH after 3 scans or at 7 wks by reliable dating**: Stop heart with no or least delay!
- **≥ 5 mm**: Low risk for MAP (accreta, percreta) and cesarean hysterectomy
- **≤ 5 mm**: High risk for MAP (increta, percreta) and cesarean hysterectomy
Evidence based counseling

The choices are:

1. Continue the pregnancy risking 2nd and 3rd trimester complications, delivering a live neonate and possibly having hysterectomy for morbidly adherent placenta BASED UPON THE ARTICLES BELOW


2. Terminating the pregnancy and plan for another one. BASED UPON THE FOLLOWING ARTICLES


7. Summary and conclusions
Summary: diagnosis/management of CSP
1. Early Dx of CSP is difficult, but possible.
2. Best diagnostic tool for CSP and for MAP (its vascularity) is TA & TVUS with color Doppler
3. Implantation site ("on the scar or in the niche") may be important to select to continue or to terminate the pregnancy
4. CSP is a precursor of MAP
5. CSP can result in a live neonate with a high risk of MAP and of hysterectomy
6. All patients with a previous C/S should have a 5-7 week TVUS scan to rule in or out CSP.

7. MRI does NOT add to the diagnosis.
8. The earlier the diagnosis is established, and treatment is given the faster the resolution
9. Evidence based counseling crucial
10. Systemic MTX: good adjuvant to treatment
11. Placement of a single Foley balloon catheter is useful after local injection
12. Double cervical ripening balloon treatment is minimally invasive and deserves additional evaluation

Last Suggestion:
Early recognition of CSP starts with patient education.

At the time of discharging women from the hospital after a CD, she should be advised that in case of a future pregnancy, an early visit (1-2 weeks after a missed period) at the obstetrician for a TVS is of paramount importance.
Is there a “best treatment”? 
This is what I do: 
• Evidence based counseling!!! 
• If no heart beats: just watch (hCG, US) 
• Heart beats: Individualize treatment 
• If treat: do it promptly! Stop the heart beats! 
• If TV US guided TV local MTX sac injection selected use back-up Foley catheter 
• Lately: use Double Cervical Ripening Balloon (up to 8w) 
• F/U hCG and US until hCG "0" or sharply declining 
• If pregnancy is desired:> close US monitoring 
• Counsel for possible developing a MAP

Thank you for listening!