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Caesarean Scar Pregnancy Managed Noninvasively with Systemic Methotrexate

Abstract
A woman with eight weeks amenorrhea and bleeding per vaginum was diagnosed with caesarean scar pregnancy. Since her S. HCG level was less than 10,000 miu/ml, she was taken up for systemic multiple dose methotrexate regimens. The patient was administered 4 doses of methotrexate on alternate days. S.HCG level declined gradually and at 21 days her S.HCG level was zero. The grave emergency thus was managed very simply on an outpatient basis.

Keywords: Caesarean scar pregnancy; Serum human chorionic gonadotrophin; Methotrexate

Introduction
A higher rate of caesarean section in the past few decades has led to an increase in the incidence of caesarean scar pregnancy. It is a serious emergency and presents often with one or more near fatal bouts of uterine hemorrhage. Caesarean scar pregnancy is a rare type of ectopic pregnancy where the embryo implants in the myometrium of lower segment at the site of previous caesarean section scar. The possible mechanism of this condition is the penetration of the blastocyst through a micro tubular tract between the caesarean scar and endometrial canal and thereby implantation into the myometrium. The clinicians are still not aware of the presentation and frequently misdiagnose it as a case of incomplete abortion. In one report as the dilator was put for an attempt to suction and evacuation, patient bled profusely and went into shock and developed obstetric collapse [1].

Case Description
A 30 year woman with 8 weeks pregnancy presented with bleeding per vaginum for 1 day. On ultrasonography, no gestation sac was seen in the uterine cavity. However a hypoechoic area 17x15 mm, the gestation sac, was visible in the anterior part of isthmus of uterus at the site of previous caesarean section scar (Figure 1).

A fetal node could be visualized in the sac and on doppler study blood flow was visible around the gestation sac (Figure 2 & 3).

Serum HCG assay was done and found to be 5623.0 miu/ml. A prior history of caesarean section and the ultrasonic pictures helped us to make a diagnosis of Caesarean scar pregnancy. Jurcovic’s criteria for diagnosis of caesarean scar pregnancy on ultrasound, as stated below were considered and fulfilled in this case:

i. An empty uterine cavity with a clearly demonstrable endometrial.
ii. The gestational sac visualized as a "double ring" sign in the anterior part of isthmus of uterus.
iii. Presence of gestational sac embedded and surrounded by myometrium.
iv. Thin or absent myometrium between gestational sac and the bladder.
v. Peritrophoblastic flow around the gestation sac [2].

As the S.HCG was value below 10,000miu/ml; conservative treatment with intramuscular methotrexate in multiple dose regimens was begun. Four injections of methotrexate were given on days 1,3,5,7 in a dose of 1mg/kg body weight. Leucovorin rescue 0.1 mg/kg body weight was given on alternate days. On day 3, S.HCG had declined to 4718.8miu/ml, and on day 8 it was 2419.2 miu/ml. Serum HCG decreased to 405.64miu/ml on day 21.
14 and became 0 on day 21. The gradual decline and then the complete absence of S.HCG implied a complete resolution of the scar pregnancy (Table 1).

**Table 1:** S.HCG measurement and values.

<table>
<thead>
<tr>
<th>Day of S.HCG Measurement</th>
<th>S.HCG Value in mi.u./ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>5623.0 mi.u./ml</td>
</tr>
<tr>
<td>Day 3</td>
<td>4718.8 mi.u./ml</td>
</tr>
<tr>
<td>Day 8</td>
<td>2419.2 mi.u./ml</td>
</tr>
<tr>
<td>Day 14</td>
<td>405.1 mi.u./ml</td>
</tr>
<tr>
<td>Day 21</td>
<td>0.0 mi.u./ml</td>
</tr>
</tbody>
</table>

**Discussion**

Caesarean scar pregnancy is being reported more frequently and if not treated aggressively and quickly, may lead to excessive uterine hemorrhage; with resulting maternal morbidity and mortality.

Various methods being used to treat this condition include:

a. Scar Resection - Laparoscopic or Open resection.

b. Hysteroscopic resection of the pregnancy sac after vasopressin injection.

c. Hysterectomy, if patient is hemorrhaging profusely.

d. Methotrexate intramniotic injection in the scar pregnancy sac.

e. Systemic Methotrexate therapy.

f. Surgical uterine artery ligation.

g. Uterine artery embolisation [3-5].

A simple algorithm has been given for management of caesarean scar pregnancy based upon the S.HCG level and the hemodynamic status of the patient [1] (Chart 1).

In our hospital we had 3 cases of caesarean scar pregnancy in 8 years. One patient had severe hemorrhage and went into hypovolemic shock when evacuation was tried, because of a wrong diagnosis of incomplete abortion. She was resuscitated and treated with systemic methotrexate therapy. In this patient the initial S.HCG level was below 10,000 miu/ml and the scar pregnancy completely resolved with methotrexate. The second patient had S.HCG level more than 10,000 miu/ml. Systemic methotrexate was again tried as first line therapy, but as she kept hemorrhaging, she was finally managed with laparotomy and scar resection [1].

Methotrexate competitively binds to the enzyme dihydrofolate and prevents conversion of dihydrofolate to tetrahydrofolate, thereby inhibiting synthesis of deoxy ribonucleic acid. MXT hence inhibits cell proliferation in the actively dividing cells of trophoblast and also causes cytolysis of the earlier formed cells.

In a recent study methotrexate instilled into the gestation sac in caesarean scar pregnancy was compared with systemic MXT therapy. They found that the mean time for gonadotrophin normalization, uterine mass disappearance was less with local intragestational MXT instillation. They also opined that the dose of MXT instilled in gestation sac was much less as compared to that given in systemic therapy. However, the cure rate was 100%, and similar in both intragestational and systemic MXT therapy [6]. In one case report, local intramniotic MXT was combined with uterine artery embolisation to control the hemorrhage [7]. It is time now that with plenty of case studies and case reports regarding caesarean scar pregnancy available in literature, standard guidelines and protocols should be formulated to bring uniformity in management of this serious condition.

**Conclusion**

Systemic Methotrexate therapy is a simple, safe and inexpensive technique for treatment of caesarean scar pregnancy in women who are haemodynamically stable and have S.HCG levels less than 10,000 miu/ml.
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Chart 1: Chart showing algorithm for management of caesarean scar pregnancy.

Haemodynamically stable

- Do Serum HCG
  - S. HCG less than 10,000 I.U./ml
    - Conservative therapy
    - Systemic alternate day Methotrexate
  - S. HCG more than 10,000 I.U./ml
    - Surgical treatment
    - Intraamniotic Methotrexate under ultrasound guidance

Haemodynamically unstable

- Surgical treatment
  - Combined intraamniotic and Systemic Methotrexate

- Resuscitate
  - Blood transfusion
  - Antifibrinolytic agent (Tranexamic acid)
  - Dopamine & Mephenine

References


