

Ectopic pregnancies in Caesarean section scars: the 8 year experience of one medical centre

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BACKGROUND: Our aim was to supplement the mostly individual case reports on the rarely occurring and life-threatening condition of ectopic pregnancy developing in a Caesarean section scar. **METHODS AND RESULTS:** Eight of all the patients treated in our department between 1995 and 2002 had been diagnosed for ectopic pregnancy that developed in a Caesarean section scar. They comprised this case series group. Four of them underwent methotrexate treatment; one had expectant management, one transcervical aspiration of the gestational sac and two by open surgery. All the non-surgically treated women had an uneventful outcome. One underwent a term Caesarean hysterectomy and the other first trimester hysterotomy and excision of the pregnancy located in the scarred uterus. Analysis of all these women's obstetric history revealed that five of them (63%) had been previously operated because of breech presentation, one had a cervical pregnancy and one had placenta previa. Four of them (50%) had multiple (≥ 2) Caesarean sections. **CONCLUSIONS:** The women at risk for pregnancy in a Caesarean section scar appear to be those with a history of placental pathology, ectopic pregnancy, multiple Caesarean sections and Caesarean breech delivery. Heightened awareness of this possibility and early diagnosis by means of transvaginal sonography can improve outcome and minimize the need for emergency extended surgery.

Key words: case series/methotrexate/pregnancy in scar/transvaginal sonography

Introduction

Implantation of a pregnancy within a Caesarean fibrous tissue scar is considered to be the rarest form of ectopic pregnancy and a life-threatening condition (Fylstra *et al.*, 2002). This is because of the very high risk for uterine rupture and all the maternal complications related to it (Herman *et al.*, 1995; Fylstra, 2002; Jurkovic *et al.*, 2003). Of the many theories for explaining its occurrence, the most reasonable one seems to be that the blastocyst enters into the myometrium through a microscopic dehiscence tract. This may be created throughout a trauma of a previous Caesarean section, any other uterine surgery (Cheng *et al.*, 2003), or even following manual removal of the placenta (Fylstra, 2002). Another mechanism for intramural implantation is IVF and embryo transfer, even in the absence of any previous uterine surgery (Hamilton *et al.*, 1992).

The true incidence of pregnancy in scar has not been determined because so few cases have been reported in the literature: there are only 18 published cases in the English medical literature between 1978 and 2001 (Fylstra, 2002). Between 2002 and mid-2003, however, 25 additional cases were reported (Fylstra *et al.*, 2002; Ghezzi *et al.*, 2002;

Haimov-Kochman *et al.*, 2002; Lam and Lo, 2002; Hartung and Meckies, 2003; Jurkovic *et al.*, 2003; Salomon *et al.*, 2003), 18 of which took place in a single centre (Jurkovic *et al.*, 2003). This may reflect both the increasing number of Caesarean sections being performed and the more widespread use of the transvaginal scan that allows earlier detection of such pregnancies (Jurkovic *et al.*, 2003). Notwithstanding this recent trend, current knowledge continues to be based mainly upon individual case reports.

We present our medical centre's experience of eight ectopic pregnancies implanted in Caesarean scars.

Materials and methods

Subjects

The medical records and sonographic pictures of all pregnant women with an ectopic pregnancy in a Caesarean section scar that had been diagnosed in our department during the years 1995–2002 were collected and reviewed. There were eight women who had been diagnosed with this condition and they comprise the study cohort (Table I). Case 1 has been previously reported (Herman *et al.*, 1995). Cases 1–7 were detected during routine sonographic evaluations that were carried out by experienced sonographers (R.M. and A.H.). Case 8

(Table I) had been elsewhere incorrectly diagnosed as a threatened abortion and was followed conservatively until 8 weeks of gestation.

The clinical data and findings of all eight women with pregnancy in a Caesarean section scar are presented in Table I. The mean maternal age was 35 years (range 28–43) and their gravidity ranged from 3 to 8. The mean menstrual age at diagnosis was 7 weeks gestation (range 6–9). Seven of them had conceived spontaneously and one by IVF–ICSI.

All those women had delivered by a Caesarean section for which the most frequent indication (5/8, 63%) was breech presentation. Previous >2 Caesarean sections were reported in 4/8 (50%) of the women. Two patients had associated complications, i.e. placenta previa (case 3) and cervical pregnancy (case 4). All eight parturient women fulfilled the criteria for sonographic diagnosis of pregnancy in scar: (i) an empty uterus; (ii) an empty cervical canal; (iii) on a sagittal view of the uterus a discontinuity in the anterior uterine wall when running through the amniotic sac is demonstrated (Vial *et al.*, 2000); (iv) the gestational sac is located in the anterior part of the isthmic portion of the uterus with a diminished myometrial layer between the bladder and the sac (Figure 1) (Godin *et al.*, 1997; Seow *et al.*, 2001; Fylstra, 2002). In addition, prominent peritrophoblastic flow has been demonstrated on Doppler flow sonography (Seow *et al.*, 2001), which was also found in our cases 2–7. β -hCG levels were determined using Micro particle Enzyme Immunoassay (MEIA) (Abbot AXSYM system; Abbot laboratories, USA). Pre-treatment maternal serum levels are presented in Table I.

Results

The clinical course of our eight patients represents a wide range of symptoms associated with this type of ectopic pregnancy. This is from a silent clinical picture in which the diagnosis was made coincidentally (cases 2–6), through slight vaginal bleeding with no other clinical complaints (cases 1 and 7), or profuse vaginal bleeding with abdominal discomfort (case 8) and finally missed abortion (cases 6 and 8). The image modality most frequently used was transvaginal sonography although transabdominal scan was added in two other cases. This combined modality helps to confirm the implantation site and reduces the risk of false diagnosis. The various treatment modalities which were applied and the outcome of all the eight pregnancies are summarized in Table I. Three cases were treated both by sonographically guided intra-amniotic injection of 25 mg methotrexate (MTX) and i.m. (systemic) administration of (50 mg/m²) on the basis of actual body weight (Stovall *et al.*, 1991; Stovall and Ling, 1993). Systemic MTX only was administered in case 7. This was because she was an obese woman who had a large fibroid uterus, which obscured the access for the intra-amniotic injection. For each case, where indicated, local MTX was injected only once. All procedures were conducted on an outpatient basis. The injection was performed transvaginally, under continuous ultrasound guidance and by using a 20-G needle. Neither antibiotic prophylaxis nor analgesia were administered. The gestational sac was targeted and the amniotic fluid was aspirated. This was immediately followed by the local MTX injected. Our adopted protocol for the systemic MTX administration and the patient monitoring was reported elsewhere (Stovall *et al.*, 1991; Stovall and Ling, 1993). Transcervical complete aspiration of the gestational sac under ultrasound guidance was performed without any complementary medical treatment in case 2,

although the exact aspiration of a very small gestational sac may also facilitate pregnancy absorption (Ravhon *et al.*, 1997; Jurkovic *et al.*, 2003). However, this unusual treatment approach should be addressed with great caution in the future. Since in case 6 the diagnosis was missed abortion, expectant management was chosen in this situation. Open surgery was needed only in two cases and both of them underwent an emergency laparotomy because of profuse haemorrhage. In one case (case 1) (Herman *et al.*, 1995), uterine rupture occurred at 35 weeks gestation. After delivery of a healthy infant, Caesarean hysterectomy was needed. In the second case (case 8; Figure 2), severe vaginal bleeding started during vacuum aspiration of an 8 weeks gestation missed abortion. Since in the specimens no products of conception were found, another ultrasound was conducted and only then was the correct diagnosis made (Figure 2b). Because of the combination of pregnancy in scar and heavy vaginal bleeding, emergency laparotomy (Figure 2C) and excision of the pregnancy located in the scar was carried out. Following surgery, portions of uterine wall consisting of endometrium and myometrium were retrieved. The final histology examination revealed clusters of trophoblast cells as well as scattered syncytiotrophoblast cells invading the myometrium. Decidual stromal changes were also noted and they were accompanied by foci of haemorrhage and disintegration of tissues (Figure 3). Immunostaining with β -hCG and desmin confirmed the presence of trophoblast cells within smooth muscle myometrial fibres.

Follow-up ranged between 4 and 16 weeks (with the exception of case 1). This was based on weekly serum β -hCG measurements. The women were tested for serum β -hCG levels within the community medical care system. In addition, sonographic examination was performed weekly in our outpatient clinic until pregnancy remnants could not be further detected. In all cases, following the original treatment, maternal recovery was complete and there was no need for additional interventions. No side-effects related to MTX treatment were recorded. The women who were planning future pregnancies were advised to have an early vaginal scan to confirm the intrauterine location of the new gestation. Two pregnant women (cases 4 and 6) have spontaneously conceived an *in utero* pregnancy. In one case (case 6), Caesarean section at term was performed because of fetal distress. No signs of previous pregnancy in scar were seen in the repeated operation. In the other case (case 4), the woman had two miscarriages following this event.

Discussion

Although a recent report was published by Jurkovic *et al.* (2003) describing the outcome of 18 cases of pregnancies implanted in scarred uterus, we believe that additional case series are needed for further elucidate this issue. Vial *et al.* (2000) proposed that there were two different types of such ectopic pregnancies, both of which were encountered among our patients. The first is due to the implantation of the gestational sac on the scar with progression towards either the cervico-isthmic space or towards the uterine cavity. Such a

Table 1. Characteristics of the eight patients with pregnancy located in a uterine scar^a

Case no.	Maternal age (years)	Gravidity and parity	Obstetric history	Presenting symptoms	Gestational age (by LMP) at diagnosis	Fetal heart beat	Pre-treatment hCG levels (IU/l)	Imaging modality	Management of the pregnancy in the scar	Length of follow-up pregnancy	Maternal outcome	General remarks and pregnancy following this event
1	28	G ₃ P ₁	● 1 early abortion	Vaginal bleeding	7 weeks	+	N/K	Transvaginal sonography	Conservative follow-up until 35 weeks of gestation	Throughout pregnancy	Emergency Caesarean hysterectomy (healthy infant)	-
2	38	G ₄ P ₂	● C/S: breech at term, puerperal fever ● C/S at term: CPD	-	6 weeks	-	N/K	Transvaginal sonography	Transcervical aspirational of gestational sac under ultrasound guidance	4 weeks	Uneventful	-
3	32	G ₅ P ₂	● C/S at term: CPD ● C/S at term: breech	-	8 weeks	+	16 620	Transvaginal sonography	Intra-amniotic MTX injection and systemic treatment under ultrasound guidance	4 weeks	Uneventful	-
4	36	G ₈ P ₃	● C/S at 34 weeks: placenta previa ● 1 early abortion ● C/S (+T incision) at 37 weeks: transverse lie	-	6 weeks	+	7700	Transvaginal sonography	Intra-amniotic MTX injection and systemic treatment under ultrasound guidance	16 weeks	Uneventful	2 spontaneous pregnancies, both miscarried at 17 weeks gestation
5	35	G ₄ P ₁	● C/S at term ● Cervical pregnancy: MTX treatment ● C/S at 36 weeks: breech ● 2 early abortions ● 1 early spontaneous abortion	-	6 weeks	-	12 000	Transabdominal and transvaginal sonography	Intra-amniotic iMTX injection and systemic treatment under ultrasound guidance	12 weeks	Uneventful	-
6	31	G ₅ P ₂	● C/S at term: breech ● 1: early spontaneous abortion ● 2 term vaginal deliveries	-	6 weeks	-	N/K	Transvaginal sonography	Expectant management of a missed abortion	8 weeks	Uneventful	C/S at term because of fetal distress. No other complications

Table 1 Continued

Case no.	Maternal age (years)	Gravity and parity	Obstetric history	Presenting symptoms	Gestational age (by LMP) at diagnosis	Fetal heart beat	Pre-treatment hCG levels (IU/l)	Imaging modality	Management of the pregnancy in scar	Length of follow-up	Maternal outcome	General remarks and pregnancy following this event
7	43	G ₃ P ₂	● 1 term vaginal delivery	Vaginal bleeding	7 weeks	-	1400	Transabdominal and transvaginal sonography	Systemic MTX treatment	10 weeks	Uneventful	Large fibroid uterus
8	37	G ₅ P ₂	● C/S term breech ● C/S at term: fetal distress ● C/S at term: oligohydramnios	Vaginal bleeding	8 weeks	-	N/K	Transvaginal sonography	Laparotomy and excision of a missed abortion	3 weeks	No post-operative complications	Septated uterus

^aAll operations were performed in the lower uterine segment. C/S = Caesarean section; CPD = cephalo-pelvic disproportion; MTX = methotrexate; LMP = last menstrual period; G = gravida; P = para; N/K = not known.



Figure 1. Ultrasound follow-up at 5, 6 and 7 weeks gestation. At 5 and 6 weeks gestation (A and B), a midline sagittal transvaginal image demonstrating a gestational sac implanted at the isthmic region between the cervix and the empty uterine cavity (small arrows), i.e. anatomical location of a previous Caesarean section scar (large arrow). At 7 weeks gestation (C), a midline longitudinal transabdominal scan demonstrating an empty uterine cavity. The tip of the sac is bulging towards the bladder (large arrow).

situation may progress to a viable birth, but with an increased risk of life-threatening massive bleeding from the site of implantation (Herman *et al.*, 1995). The second is a deep implantation into a post-Caesarean section defect with progression towards rupture and bleeding during the first trimester of pregnancy. Some authors (Ghezzi *et al.*, 2002) believe that the difference between those two types of pregnancy is of paramount importance. In the former, when there is a continuous connection to the cavum uteri, expectant management is justified since pregnancy may continue until a viable birth. In the latter, the risk of late first-trimester life-threatening bleeding is increased if immediate treatment is not undertaken.

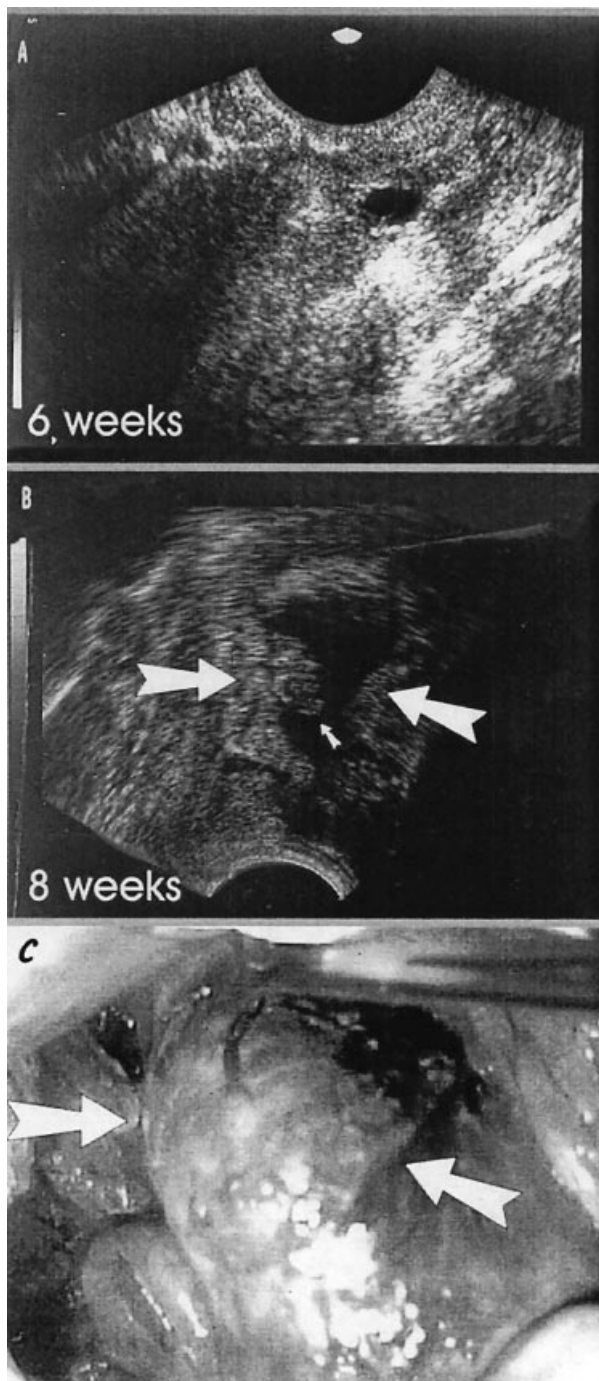


Figure 2. Ultrasound follow-up at 6 and 8 weeks gestation (case 8). At 6 weeks gestation (A), a midline sagittal transvaginal image demonstrating a gestational sac implanted in the isthmo-cervical region. At 8 weeks gestation (B), note the gestational sac located at the isthmic region between the uterus and the cervix (large arrows). The fetal pole is seen within the sac (small arrow). The same case at laparotomy (C). Note the bulging uterine isthmus (between the large arrows), just before the gestational sac has been excised.

In case 1 during first trimester of gestation after the diagnosis was made we decided to manage this pregnancy expectantly. This policy was adopted following discussion with the couple and reaching a mutual decision to avoid any intervention at that stage. It was judged that the sac, located in the isthmic region, would later coalesce with the uterine cavity and continue as a

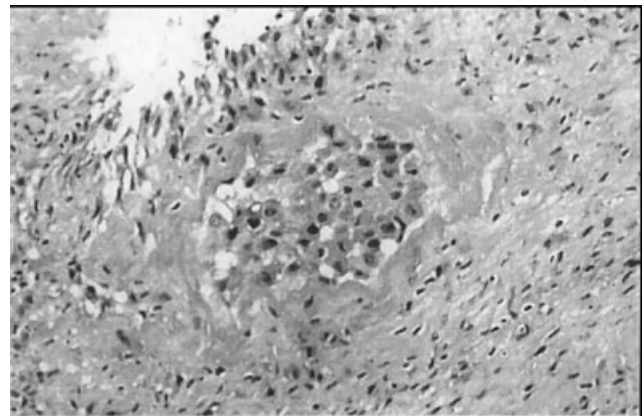


Figure 3. Photographs of sections through the myometrium showing a cluster of trophoblast cells present in-between smooth muscle bundles (case 8) (haematoxylin and eosin, $\times 200$).

normal pregnancy. Later on, the sac still remained outside the uterine cavity, but because of the increased risk of hysterectomy associated with termination at that stage, the expected management did not change (Herman *et al.*, 1995). We agree with Jurkovic *et al.* (2003) that in view of the lack of significant data, each woman should be given all the available information and the opportunity to decide on the management of her pregnancy. Nevertheless, based on our experience reported herein, we believe that the prognosis for an uneventful term pregnancy is still very poor and therefore our current policy is to recommend termination of such a pregnancy once the correct diagnosis is made.

We decided not to perform magnetic resonance imaging, and we agree that sonography combined with Doppler flow imaging is a very reliable tool for detecting these cases (Nawroth *et al.*, 2001; Jurkovic *et al.*, 2003). We now prefer to combine transvaginal scanning for obtaining fine details of the gestation and its relation to the scar with a meticulous abdominal scan with full bladder (Ravhon *et al.*, 1997). The latter provides a ‘panoramic view’ of the uterus and an accurate measurement of the distance between the gestational sac and the bladder. The importance of correct diagnosis is emphasized also in case 8, which originally was managed as an intrauterine non-viable pregnancy leading to massive bleeding and laparotomy.

Although no treatment policy should be based on anecdotal reports because of the infrequent occurrence of uterine scar gestation, much is to be learned from each report (Haimov-Kochman *et al.*, 2002; Jurkovic *et al.*, 2003).

Two principal management options may be considered, i.e. the medical or the surgical. The medical treatment mainly consists of MTX, administered either systemically (Ravhon *et al.*, 1997; Shufaro and Nadjari, 2001; Lam and Lo, 2002), locally (Lai *et al.*, 1995; Jurkovic *et al.*, 2003) or combined (Nawroth *et al.*, 2001). Theoretically, the combined approach might expose the patient to higher MTX dose and side-effects may result. However, this was not currently found. This is because such a pregnancy is surrounded by fibrous scar rather than by a normally vascularized myometrium. Therefore, systemic absorption of local MTX is minute. This also may

potentially limit the systemic absorption of the drug and delay complete resorption of the pregnancy (Ravhon *et al.*, 1997). Therefore, concomitant fine needle aspiration of the remaining fluid in the sac may be required (Ravhon *et al.*, 1997). Others have combined potassium chloride (KCl) injections directly into the fetal thorax, with MTX being injected into the sac and the surrounding myometrium (Godin *et al.*, 1997). Nevertheless, on rare occasions, rupture of the scar and heavy bleeding may occur following medical treatment (Lai *et al.*, 1995; Jurkovic *et al.*, 2003). This may occur even 15 days following MTX treatment (Lai *et al.*, 1995). Therefore, the medical approach may be combined with bilateral uterine artery embolization, thus minimizing such complications (Ghezzi *et al.*, 2002).

A number of reports support the surgical alternative, even in the presence of a non-bleeding patient (Rampen, 1997; Vial *et al.*, 2000; Seow *et al.*, 2001; Fylstra, 2002; Fylstra *et al.*, 2002). This includes elective laparotomy and excision of the gestational mass. These authors believe that even if recurrence is unlikely, the resection of the old scar with a new uterine closure can reduce the risk of recurrence. In addition, if no complication occurs, the follow-up period seems to be shorter compared with the medical treatment options.

A minimally invasive approach that has recently been described is endoscopic surgery (Lee *et al.*, 1999). This includes hysteroscopy for visualizing the uterine cavity combined with incision and aspiration of the ectopic mass by operative laparoscopy. Currently, no modality appears to be entirely reliable and none can guarantee uterine integrity (Lee *et al.*, 1999; Jurkovic *et al.*, 2003).

It is recognized that a Caesarean section presents one of the risk factors for ectopic pregnancies and placental pathologies (i.e. placenta praevia, placental abruption and placenta percreta) in the subsequent pregnancies (Hemminki and Merilainen, 1996). This was also the case in two of our eight patients. A similar association has also been described in other case reports (Haimov-Kochman *et al.*, 2002; Salomon *et al.*, 2003). Placenta accreta is a catastrophic complication of pregnancy in which trophoblastic tissues invade the myometrial layer and implant on a Caesarean scar (Chazotte and Cohen, 1990). A Caesarean scar pregnancy is, however, considered to be even more aggressive than placenta previa or accreta because of its invasion of the myometrium in the first trimester (Seow *et al.*, 2001).

The high rate of Caesarean section because of breech presentation and the subsequent occurrence of pregnancy in the resultant scar is an intriguing association. Since their concomitant appearance was also described in another four reported cases (Neiger *et al.*, 1998; Vial *et al.*, 2000; Ghezzi *et al.*, 2002; Hartung and Meckies, 2003), this association might not be coincidental. Many of these operations are currently elective procedures performed in a non-developed lower uterine segment, so that the healing processes following the operations might facilitate implantation of the blastocyst within the scar. Jurkovic *et al.* (2003) have found that 72% of their patients underwent multiple (≥ 2) Caesarean sections; and we found this rate in 50% of our patients. This seems to be another risk factor for in-scar implantation of the subsequent

pregnancy because of increased scar surface area (Jurkovic *et al.*, 2003). In addition, the increasing number of Caesarean sections currently performed, together with the changing of the surgical technique, might also have same impact. In the past, the uterus was closed using a double layer of multiple sutures inverting the first layer with the second row. However, a single non-inverting running suture technique is currently more frequently used. Larger series would be needed to further elucidate these issues.

Nowadays, with the advent of transvaginal sonography and with the use of saline infusion, post-Caesarean section uterine wall integrity can be detected even in the non-pregnant state (Monteagudo *et al.*, 2001; Armstrong *et al.*, 2003; Jurkovic *et al.*, 2003). Caesarean section scar defect, defined by the presence of fluid within the incision site (Armstrong *et al.*, 2003), or any filling defect ('niche'), defined as a triangular anechoic structure at the presumed site of the scar (Monteagudo *et al.*, 2001), might alert for uterine scar complication in the subsequent pregnancy (Armstrong *et al.*, 2003; Jurkovic *et al.*, 2003). This might also be important for women at risk for pregnancy in scar, such those with a history of either ectopic pregnancies, placental pathologies, multiple Caesarean sections (Jurkovic *et al.*, 2003) or breech delivery by a Caesarean section. In addition, this will alert the sonographer to look for scars in the pregnant uterus and to verify the integrity of the uterine wall, especially in the presence of an anterior gestational sac closely localized to the Caesarean section scar.

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