

# Caesarean section scar pregnancy: a case series at a single tertiary centre

Yi Ping Cindy Pang<sup>1</sup>, MBBS, MRCOG, Wei Ching Tan<sup>1</sup>, MBBS, MRCOG, Tze Tein Yong<sup>1</sup>, MBBS, MRCOG, Poh Kim Elisa Koh<sup>1</sup>, MBBS, MRCOG, Hak Koon Tan<sup>1</sup>, MBBS, MRCOG, Tew Hong Ho<sup>1</sup>, MBBS, FRCOG

**ABSTRACT** We present a case series of four patients with Caesarean scar pregnancies (CSPs) managed at our gynaecological unit between October 2008 and May 2009. Three patients were detected while asymptomatic, and were treated with elective intragastric sac methotrexate injections. The last patient had presented following complications from a termination of pregnancy for a CSP that was misdiagnosed as intrauterine. Following treatment, this patient and another developed arteriovenous malformation, which responded to bilateral uterine artery embolisations and gonadotropin releasing hormone (GnRH)-agonist treatment.

*Keywords:* Caesarean section, ectopic, methotrexate, pregnancy  
*Singapore Med J 2012; 53(10): 638–642*

## INTRODUCTION

Caesarean scar pregnancy (CSP) is a very rare form of ectopic pregnancy, with an estimated incidence ranging from 1:1,800 to 1:2,226 pregnancies.<sup>(1)</sup> In a CSP, the gestational sac is embedded in the myometrium and fibrous tissue of the Caesarean scar, separate from the endometrial cavity. CSP is a rare iatrogenic complication<sup>(2,3)</sup> that is increasing in numbers worldwide, in line with the rising rate of Caesarean sections. It is potentially life-threatening, and if undetected or misdiagnosed, can cause serious maternal morbidity from uterine rupture and massive haemorrhage, even maternal death.<sup>(1)</sup>

Evidence-based guidelines for the treatment of CSP are few, with treatment options ranging from systemic or local injections of embryocides and surgical sac aspiration to surgical techniques, such as wedge resection of the ectopic pregnancy via laparotomy or laparoscopy, or hysteroscopic excision.<sup>(4)</sup> We retrospectively reviewed four women with first-trimester CSP managed at our hospital and discuss the clinical presentations, diagnosis, management strategies and outcome in these patients. This study was exempted from the institutional review board's purview.

## CASE REPORTS

### Patient profile

Three patients (Patients 1, 2 and 3) were referred to the Department of Obstetrics and Gynaecology at Singapore General Hospital, Singapore, in November and December of 2008 with a suspected diagnosis of CSP. The patients were asymptomatic at presentation. However, routine antenatal ultrasonography findings were compatible with CSP according to the criteria proposed by Jurkovic et al<sup>(3)</sup> and Vial et al,<sup>(5)</sup> which are as follows: (a) an empty uterine cavity; (b) anterior location of the gestational sac at the level of the internal os covering the visible or presumed site of the previous lower segment Caesarean section (LSCS) scar; (c) evidence of functional trophoblastic circulation on Doppler

scans; and (d) the presence of trophoblast between the bladder and the anterior uterine wall as a sign of deep implantation. Patient 4 was referred in May 2009 following persistent bleeding after a termination of pregnancy (TOP) at another hospital. No histological confirmation was performed of the termination. Both ultrasonography and magnetic resonance (MR) imaging findings of the pelvis performed after admission confirmed a complex, solid, cystic hypervascular mass in the myometrium over the LSCS scar site in close contact with the bladder dome. The clinical histories of all four patients are summarised in Table I.

### Management

Clinical management for Patients 1, 2 and 3 were discussed at a multidisciplinary meeting comprising gynaecologists, urologists, anaesthetists and sonographers. Transvaginal sac aspiration was performed and local methotrexate (MTX) injection was administered under general anaesthetic and antibiotic cover. As the pregnancies were early, the transvaginal approach permitted easy access with minimal risk of bladder injury. An intragastric injection of MTX rather than a systemic one was considered to be more efficacious and with less systemic side effects. Cystoscopy was performed to exclude bladder invasion. Using a 16-gauge double lumen oocyte-retrieval *in vitro* fertilisation (IVF) needle, the sac contents (7–10 mL) were aspirated under transvaginal ultrasonography guidance, followed by an intrasac injection of 50 mg MTX (Fig. 1). The treatment objective was to perform foeticide as well as to avoid morbidity from hysterectomy in these patients. The patients were monitored with serial transvaginal colour flow Doppler scans at regular intervals (weekly to once in three weeks) and counselled for the risks of uterine rupture and internal bleeding.

For Patient 4, the MR imaging findings presented a diagnostic dilemma, as the differential diagnoses included CSP, arteriovenous malformation (AVM) or dehiscence of the scar

<sup>1</sup>Department of Obstetrics and Gynaecology, Singapore General Hospital, Singapore

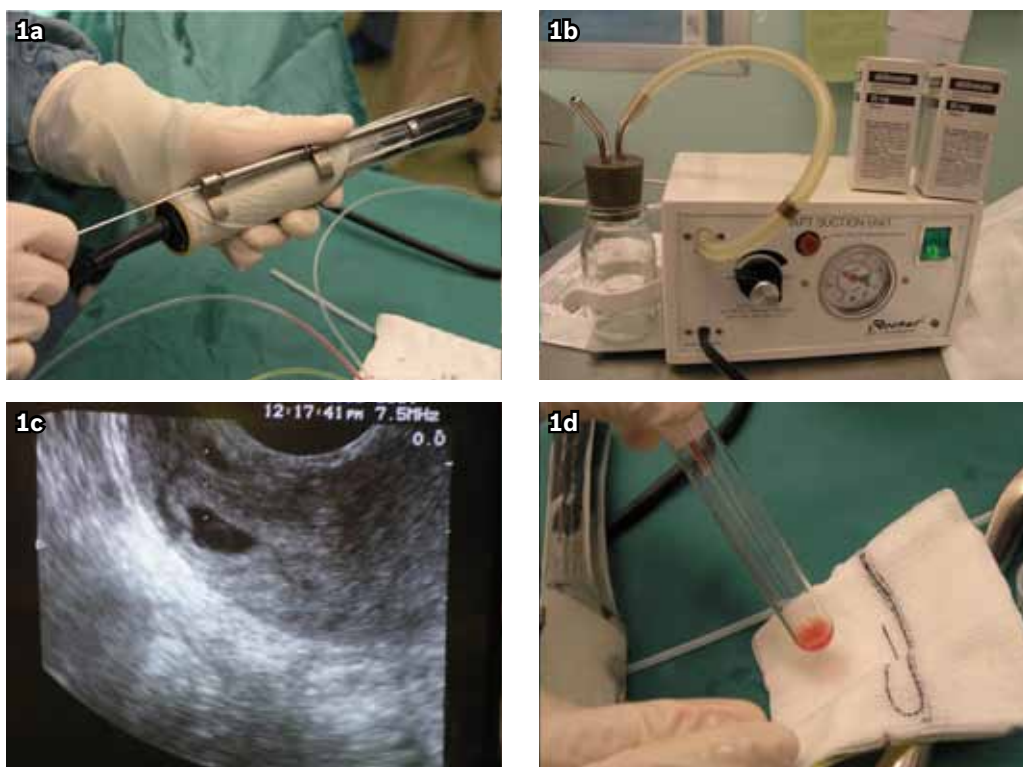
**Correspondence:** Dr Pang Yi Ping Cindy, Associate Consultant, Department of Obstetrics and Gynaecology, Singapore General Hospital, Outram Road, Singapore 169608. cindypang@yahoo.com

**Table 1. Clinical history of the patients with Caesarean scar pregnancies.**

Clinical history	Patient 1	Patient 2	Patient 3	Patient 4
Maternal age (years)	30	42	38	41
Gravidity/parity	G4P2	G3P2	G2P1	G3P2
Obstetric history	2 previous LSCSs; 1 uterine evacuation	2 previous LSCSs	1 previous LSCS	2 previous LSCSs
Gestational age at diagnosis (wks)	8	6	8	11 days after vacuum evacuation
Crown rump length at surgery (mm)	30	2	21	-
Foetal heartbeat at surgery	Positive	Positive	Negative*	NA
Pretreatment $\beta$ -hCG level (IU/L)	63,352	22,305	205,321	9,893
Size of intrauterine gestational sac/ gestational mass (cm)	5.0 $\times$ 3.0 $\times$ 3.0	1.6 $\times$ 1.0 $\times$ 0.5	7.1 $\times$ 6.4 $\times$ 5.5	4.8 $\times$ 4.5 $\times$ 3.3

\*Foetal heartbeat was positive on scan four days before surgery.

$\beta$ -hCG:  $\beta$ -human chorionic gonadotropin; LSCS: lower segment Caesarean section; NA: not available



**Fig. 1** Photographs of the aspiration of the gestational sac show (a) the use of a 16-gauge double lumen needle; (b) the suction unit; (c) the visualisation of the gestational sac during methotrexate injection; and (d) the aspirated contents.

following the vacuum aspiration at TOP. As the patient's  $\beta$ -human chorionic gonadotropin (hCG) levels remained markedly elevated two weeks after TOP and MR imaging showed likely bladder dome involvement of the mass, a diagnosis of CSP was made (Fig. 2). Intralesional MTX injection was not performed, as there was no gestational sac and a risk of haemorrhage from the vascular mass was perceived. Angiography and embolisation of both uterine arteries using gelfoam slurries were performed, and a subsequent reduction in per vaginal (PV) bleeding was observed.

### Outcome and follow-up

Patient 1 remained well postoperatively and resumed regular menstruation after three months. Patients 2 and 3 required readmission for heavy PV bleeding. Patient 2 soaked two sanitary

pads with clots despite  $\beta$ -hCG being undetectable at  $< 0.3$  U/L at 106 days after initial treatment. On ultrasonography, the scar pregnancy had decreased in size to 1.2 cm  $\times$  0.8 cm  $\times$  1.2 cm, with moderate impedance flow. The bleeding resolved spontaneously after one day and was postulated to be menstruation due to resumption of ovarian activity.

Patient 3 presented with sudden heavy PV bleeding (estimated at about 500 mL) with hypotension 102 days following treatment. She was resuscitated and treated with tranexamic acid. Ultrasonography on Day 96 post treatment showed large arterial and venous vessels with turbulent flow supplying a mass that measured 8.0 cm  $\times$  5.6 cm  $\times$  9.5 cm (Fig. 3). A provisional diagnosis of AVM was made. The patient had a second episode of massive PV bleeding three days later. Angiography showed a

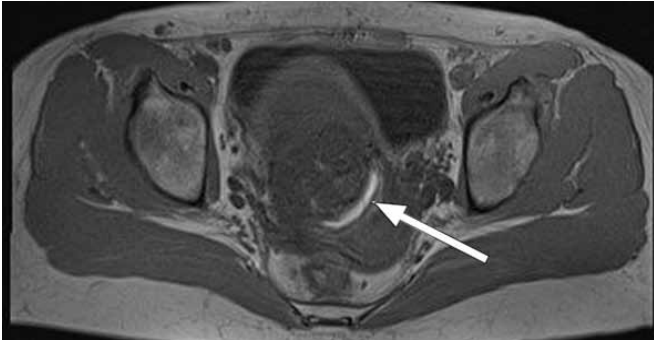


Fig. 2 MR image of Patient 4 shows an abnormal vessel (arrow) in the gestational mass.

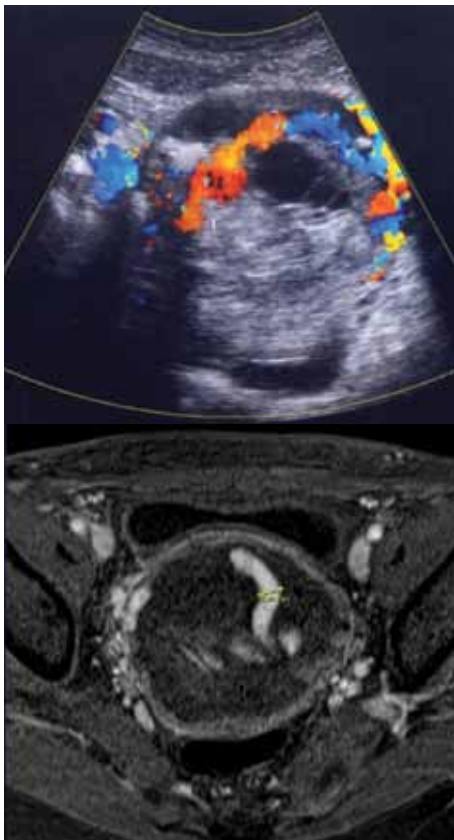


Fig. 3 Ultrasonography and MR images five days post-embolisation in Patient 3 show an arteriovenous malformation.

left uterine arteriovenous fistula feeding a 6-cm venous aneurysm. Embolisation was performed with three platinum coils and gelfoam slurries. Repeat MR imaging of the pelvis five days post-embolisation showed a large serpiginous vessel of up to 9 mm in diameter within the mass (Fig. 3). The patient declined hysterectomy, which was offered in view of recurrent PV bleeding and the presence of turbulent flow within the mass. As she had continued PV spotting, repeat embolisation using polyvinyl alcohol particles was performed on day 119 post-treatment for the numerous small serpiginous arterial feeders from the bilateral internal iliac arteries. PV bleeding reduced thereafter and the patient was treated with gonadotropin releasing hormone-agonist (GnRH-agonist) for four months to reduce uterine vascularity. At 250 days post-treatment and 9 weeks after the last GnRH-agonist injection, ultrasonography showed an avascular mass that had regressed to 3.9 cm in size.

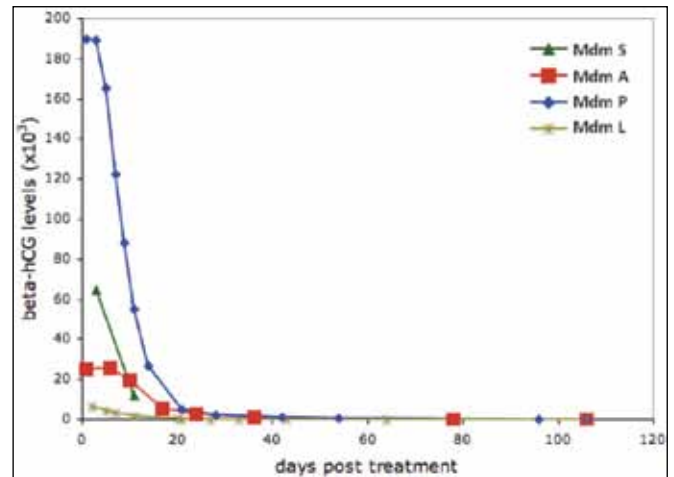


Fig. 4 Graph shows the regressive pattern of  $\beta$ -hCG in the four patients with Caesarean scar pregnancies.

Ultrasonography of Patient 4, who was reviewed on Day 20 post-treatment, showed a vessel within the 4.5-cm mass that was suggestive of recanalisation. As her  $\beta$ -hCG levels had reduced to 313 U/L, GnRH-agonist was given. When the patient presented with PV bleeding of 500 mL a day later, she was treated with tranexamic acid and repeat embolisation, which successfully arrested the bleeding. Fig. 4 summarises the regressive pattern of  $\beta$ -hCG seen in all four patients during the post-treatment period.

## DISCUSSION

The first patient with CSP was reported by Larsen and Solomon in 1978.<sup>(6)</sup> The number of patients with CSP reported in the literature has since increased from 18 in 2002<sup>(7)</sup> to 161 in 2007.<sup>(3)</sup> One of the reasons for this increase in number is the rising rate of Caesarean sections and the availability of ultrasonography for early pregnancy assessment. The natural history of such pregnancies is unclear, as most pregnancies are terminated once CSP is detected due to an associated risk of rupture. As with many non-tubal ectopic pregnancies, a large proportion of CSPs are non-viable. In the largest case series of CSPs reported, 44% of 18 pregnancies were found to have ended in spontaneous first-trimester miscarriages.<sup>(3)</sup> Only one report has documented a CSP developing to term, albeit with the development of placenta accreta.<sup>(8)</sup>

Although a CSP is similar to abnormal placentation in terms of pathophysiology, the incidence of CSP does not correlate with the number of LSCSs a patient has undergone previously. Quite to the contrary, the risk of placenta accreta is known to increase from 0.03% after one LSCS to 0.8% after four LSCSs for non-*praevia* women, and from 3.3% to 61% in patients with placenta *praevia*.<sup>(9)</sup> In comparison, a systematic review in 2006 by Rotas et al highlighted that a majority of CSPs (52%) occurred in women following one previous LSCS.<sup>(10)</sup> This is of importance when counselling patients on the impact of LSCS on future fertility.

Various theories have been proposed to explain why a developing embryo would implant in the LSCS scar.<sup>(11,12)</sup> Most describe the embryo entering the myometrium through microscopic tracts from small uterine scar dehiscences, with the absence of decidua basalis over the scar. This would explain

why the gestational sac in a CSP is completely embedded in the myometrium, surrounded by fibrous scar tissue and separate from the endometrial cavity. Another study by Ben-Nagi et al, which described endometrial changes after LSCS, found that fewer leucocytes and less vascularisation was seen at the scar site than in the endometrium of the unscarred uterus.<sup>(13)</sup> However, no definite conclusions could be made regarding the molecular factors that led to an embryo implanting in the scar. A key observation of our series was that CSPs can be asymptomatic in the early weeks of pregnancy and thus misdiagnosis can occur, leading to inappropriate management of such women, with potentially catastrophic outcomes. For instance, a diagnosis of CSP was made in Patient 4 in our series only due to a high index of suspicion following our experience with the three earlier patients with CSPs.

According to a study by Michener and Dickinson of 13 patients with CSP,<sup>(14)</sup> PV bleeding was the commonest presenting symptom in nine patients. The median gestation at diagnosis in this series was 6.8 weeks. Meanwhile, a literature review of presenting symptoms in 57 women with CSPs by Silver et al<sup>(9)</sup> found that 37% were asymptomatic, 38% had painless PV bleeding, 16% had painful PV bleeding and 9% experienced abdominal pain without PV bleeding. PV bleeding during early pregnancy was a common event according to Harville et al<sup>(15)</sup>, and Ananth and Savitz<sup>(16)</sup>, occurring in about 9%–15% of normal pregnancies. Bleeding has also been associated with miscarriages, ectopic pregnancy and perineal lesions or infections,<sup>(17)</sup> which are much more common than CSPs.

As outcomes and treatments differ, a CSP must be distinguished from other differential diagnoses, including cervicoisthmic pregnancy and the different types of miscarriages. Differentiation from a cervicoisthmic pregnancy is especially crucial, as expectant management is justified for a cervicoisthmic pregnancy since it may progress to a viable foetus. Ultrasonography combined with Doppler flow imaging using the four sonographic criteria proposed by Jurkovic et al has been suggested as a reliable diagnostic tool in this scenario.<sup>(3)</sup> When in doubt, MR imaging may be a useful adjunct that aids evaluation. MTX (either local or systemic), hysterectomy or wedge resection of the prior scar and pregnancy has each been used in the treatment of CSP.<sup>(3)</sup> Optimal treatment options, however, depend on factors such as pregnancy size, patient profile, absence or presence of scar rupture,  $\beta$ -hCG levels, desire for future fertility, and the haemodynamic status of the patient.

Complications are commonly reported in patients with CSPs after treatment, with reports suggesting persistent gestational sac, severe bleeding during the procedure,<sup>(2)</sup> scar rupture and heavy PV bleeding for up to 15 days post-treatment.<sup>(18)</sup> Yet, with compliant patients, highly trained sonographers and rapid access to emergency services, we did not encounter any complications with our approach of treating CSPs with intragastric MTX injections. If compliance or prompt access to emergency services cannot be achieved, a safer treatment option may be elective

laparotomy with excision of the gestational mass, in spite of there being an attendant risk of hysterectomy in the event of massive haemorrhage due to the vascularity of the gestational mass. Although surgery would enable excision of the mass and repair of the defect, no treatment modality can ensure uterine integrity.<sup>(3)</sup> Repair of the myometrium may result in focal weakened areas that may potentially increase the risk of rupture during future pregnancies. In patients who do not desire future fertility, hysterectomy may be taken as the best option.

Following the diagnosis of CSPs in Patients 1, 2 and 3 in our series, a management guideline was initiated at our unit whereby the high-risk pregnancy team, comprising maternal foetal medicine specialists, would be notified if CSP was suspected on ultrasonography, and MR imaging would be ordered if there was any doubt. We agree with previously published papers<sup>(3,19,20)</sup> that have supported the use of transvaginal ultrasonography for diagnosis and the double lumen needle for oocyte retrievals during treatment, as familiarity with the equipment does increase the success rates. Intracardiac injections of the foetus were not attempted in our series so as to reduce both manipulation time and the risk of bleeding.

Although there are no established guidelines on the frequency of monitoring for patients with CSP, an extrapolation of the guidelines for medical management of ectopic pregnancies<sup>(21,22)</sup> suggests that it would be prudent to monitor these patients with weekly  $\beta$ -hCG measurement until the levels are undetectable, and with monthly ultrasonography until no products of conception are visualised. Patients should be counselled that compliance with regular monitoring is mandatory, as it may take as much as 4–16 weeks for  $\beta$ -hCG levels to normalise after treatment.<sup>(3)</sup>

In our series, Patients 3 and 4 developed AVM – one following treatment for CSP and the other after a failed TOP. In a first report of AVM in a patient, Rygh et al<sup>(23)</sup> described a woman who presented with repeated episodes of heavy PV bleeding following curettage for presumed first-trimester pregnancy loss. The patient, who subsequently underwent uterine artery embolisations that failed, required resection of the LSCS scar. Clinicians should, therefore, be mindful of iatrogenic or pathological conditions that can lead to communications between the uterine arteries and myometrial veins, leading to malformations that may present as sudden severe haemorrhages.<sup>(24)</sup> Close surveillance of potentially rare complications is thus essential to ensure good outcomes in patients being treated for CSP. We used GnRH-agonists in patients 3 and 4 as an adjunct to embolisation to reduce uterine vascularity, as such treatment has been reported to successfully reduce the size of the lesion where embolisation of the AVM has failed.<sup>(25)</sup>

Expectant management of a viable CSP, once the diagnosis is certain, is unacceptable due to the risk of life-threatening haemorrhage that may result from uterine scar ruptures. The patient must, therefore, be counselled on the dismal prognosis and possible complications should pregnancy be allowed to

progress, and be offered a termination of pregnancy.<sup>(26-28)</sup> The primary aim of treatment in our case series was to avoid a laparotomy and its inherent morbidities. It has been reported that preservation of the uterus exposes patients to an increased risk of ectopic pregnancies and placental pathologies, such as placenta praevia, placenta abruption or placenta accreta, in subsequent pregnancies.<sup>(29)</sup> Data on pregnancy outcomes for women with treated CSPs is limited. Some authors have recommended surgical repair of the scar either as a primary treatment or as a secondary operation after initial treatment for patients desiring future pregnancies.<sup>(30)</sup>

In a literature review, Rotas et al found 22 patients who conceived following conservative treatment for CSP.<sup>(10)</sup> 16 patients delivered via elective LSCS and one experienced recurrent miscarriage. Five women had severe complications, including two who had recurrence of CSP – one with uterine rupture at 38 weeks resulting in maternal death and foetal stillbirth, and the other with placenta accreta complicated by disseminated intravascular coagulation.<sup>(29)</sup> One patient conceived a heterotopic triplet pregnancy via IVF and underwent TOP of the perceived intrauterine sac, with the pregnancy ending in the premature delivery of twins at 32 weeks and a hysterectomy.<sup>(28)</sup> These findings draw attention to the fact that effective contraception is essential in these women in view of the potential risk of severe complications in future pregnancies.

Our case series highlights the importance of multidisciplinary management and the need for guidelines based on the best available literature to manage a rare, potentially life-threatening condition that presents a diagnostic challenge to clinicians in maternity clinics. It also emphasises the importance of entertaining a high index of suspicion when faced with atypical presentations in complications during the first trimester of pregnancy. Due to the risk of late complications, such as AVM formation and recurrent PV bleeding, in patients treated for CSPs, close vigilance must be maintained and emphasis on compliance strictly enforced long after the initial postoperative period in these patients.

## REFERENCES

- Seow KM, Huang LW, Lin YH, et al. Caesarean scar pregnancy: issues in management. *Ultrasound Obstet Gynecol* 2004; 23:247-53.
- Herman A, Weinraub Z, Avrech O, et al. Follow up and outcome of isthmic pregnancy located in a previous caesarean section scar. *Br J Obstet Gynaecol* 1995; 102:839-41.
- Jurkovic D, Hillaby K, Woelfer B, et al. First-trimester diagnosis and management of pregnancies implanted into the lower uterine segment Caesarean section scar. *Ultrasound Obstet Gynecol* 2003; 21:220-7.
- Ash A, Smith A, Maxwell D. Caesarean scar pregnancy. *BJOG* 2007; 114:253-63.
- Vial Y, Petignat P, Hohlfield P. Pregnancy in a cesarean scar. *Ultrasound Obstet Gynecol* 2000; 16:592-3.
- Larsen JV, Solomon MH. Pregnancy in a uterine scar sacculus--an unusual cause of postabortal haemorrhage. A case report. *S Afr Med J* 1978; 53:142-3.
- Fylstra DL. Ectopic pregnancy within a cesarean scar: a review. *Obstet Gynecol Surv* 2002; 57: 537-43.
- Ben Nagi J, Ofili-Yebovi D, Marsh M, Jurkovic D. First-trimester cesarean scar pregnancy evolving into placenta previa/accreta at term. *J Ultrasound Med* 2005; 24:1569-73.
- Silver RM, Landon MB, Rouse DJ, et al. Maternal morbidity associated with multiple repeat cesarean deliveries. *Obstet Gynecol* 2006; 107:1226-32.
- Rotas MA, Haberman S, Levgur M. Cesarean scar ectopic pregnancies: etiology, diagnosis, and management. *Obstet Gynecol* 2006; 107:1373-81.
- Godin PA, Bassil S, Donnez J. An ectopic pregnancy developing in a previous caesarian section scar. *Fertil Steril* 1997; 67:398-400.
- Frank H, Kaufmann P. Non-villous parts and trophoblast invasion. In: Benirschke K, Kaufmann P, editors. *Pathology of the Human Placenta*. New York: Springer-Verlag, 2000: 229-32.
- Ben-Nagi J, Walker A, Jurkovic D, Yazbek J, Aplin JD. Effect of cesarean delivery on the endometrium. *Int J Gynaecol Obstet* 2009; 106:30-4.
- Michener C, Dickinson JE. Caesarean scar ectopic pregnancy: a single centre case series. *Aust N Z J Obstet Gynaecol* 2009; 49:451-5.
- Harville EW, Wilcox AJ, Baird DD, Weinberg CR. Vaginal bleeding in very early pregnancy. *Hum Reprod* 2003; 18:1944-7.
- Ananth CV, Savitz DA. Vaginal bleeding and adverse reproductive outcomes: a meta-analysis. *Paediatr Perinat Epidemiol* 1994; 8:62-78.
- Promes SB, Nobay F. Pitfalls in first-trimester bleeding. *Emerg Med Clin North Am* 2010; 28:219-34.
- Lai YM, Lee JD, Lee CL, Chen TC, Soong YK. An ectopic pregnancy embedded in the myometrium of a previous cesarean section scar. *Acta Obstet Gynecol Scand* 1995; 74:573-6.
- Hwu YM, Hsu CY, Yang HY. Conservative treatment of caesarean scar pregnancy with transvaginal needle aspiration of the embryo. *BJOG* 2005; 112:841-2.
- Schiff E, Shalev E, Bustan M, et al. Pharmacokinetics of methotrexate after local tubal injection for conservative treatment of ectopic pregnancy. *Fertil Steril* 1992; 57:688-90.
- Royal College of Obstetricians and Gynaecologists (RCOG). The management of tubal pregnancy. Green-top Guideline No. 21. May 2004.
- American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 94: Medical management of ectopic pregnancy. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2008; 111:1479-85.
- Rygh AB, Greve OJ, Fjetland L, Berland JM, Eggebø TM. Arteriovenous malformation as a consequence of a scar pregnancy. *Acta Obstet Gynecol Scand* 2009; 88:853-5.
- Cura M, Martinez N, Cura A, Dalsaso TJ, Elmerhi F. Arteriovenous malformations of the uterus. *Acta Radiol* 2009; 50:823-9.
- Morikawa M, Yamada T, Yamada H, Minakami H. Effect of gonadotropin-releasing hormone agonist on a uterine arteriovenous malformation. *Obstet Gynecol* 2006; 108:751-3.
- Einenkel J, Stumpp P, Kösling S, Horn LC, Höckel M. A misdiagnosed case of caesarean scar pregnancy. *Arch Gynecol Obstet* 2005; 271:178-81.
- Herman A, Weinraub Z, Avrech O, et al. Follow up and outcome of isthmic pregnancy located in a previous caesarean section scar. *Br J Obstet Gynaecol* 1995; 102:839-41.
- Maymon R, Halperin R, Mendlovic S, Schneider D, Herman A. Ectopic pregnancies in a caesarean scar: review of the medical approach to an iatrogenic complication. *Hum Reprod Update* 2004; 10:515-23.
- Seow KM, Hwang JL, Tsai YL. Subsequent pregnancy outcome after conservative treatment of a previous cesarean scar pregnancy. *Acta Obstet Gynecol Scand* 2004; 83:1167-72.
- Hasegawa J, Ichizuka K, Matsuoka R, et al. Limitations of conservative treatment for repeat cesarean scar pregnancy. *Ultrasound Obstet Gynecol* 2005; 25:310-1.