CASE REPORT

Successful management of caesarean scar live ectopic pregnancies with local KCL and systemic methotrexate

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SUMMARY

Two cases of live caesarean scar ectopic pregnancies are presented. Beta human chorionic gonadotropin (b-hCG) values in both patients at presentation were 50 099 mIU and 297 969 mIU, respectively. Both were managed with intrasac potassium chloride injection to induce fetal demise and multiple dose methotrexate therapy. The time for b-hCG to become negative in both patients was 91 days and 119 days, respectively. Successful management of live caesarean scar pregnancies even with very high b-hCG is possible with minimally invasive approach.

BACKGROUND

Caesarean scar ectopic pregnancy (CSP) is a relatively new and rare type of ectopic pregnancy with recent rise in incidence due to increasing caesarean section rates since the first reported case in 1978.¹ It is a life-threatening condition with grave maternal complications. Two types of caesarean scar pregnancies have been described in literature. Type 1 or endogenic type is the one with progression towards the uterine cavity and type 2 or exogenic type deeply invades the scar and progresses towards the abdominal cavity or bladder.² Type 1 can progress to viability, although associated with increase risk of bleeding from the placental site. Type 2 is a serious type with risk of uterine rupture and bleeding in early pregnancy. The diagnosis and management of caesarean scar ectopic presents a challenge to the clinician in view of scarcity in literature regarding optimum management. Early diagnosis and management is imperative to avoid fatal complication and preserve fertility. Advances in imaging and early access to serum beta human chorionic gonadotropin (b-hCG) has enabled early detection and non-surgical management before the patient becomes symptomatic. Treatment options include medical or surgical with additional haemostatic measures. Surgical management is inevitable if patient presents with rupture and haemodynamic instability. Cases diagnosed at early gestation can be managed medically and with minimally invasive approach. We report two cases of live CSP with high initial b-hCG which were successfully treated by combined intrasac potassium chloride (KCL) instillation and systemic methotrexate.

CASE PRESENTATION

The first patient was 31-year-old woman (gravid 3, parity 1, living 1, miscarriage 1) who presented to us at 6-week period of amenorrhoea with mild pain in abdomen and bleeding. She had undergone a full-term lower segment caesarean section 3 years back for breech presentation. The second patient was a 34-year-old woman (gravid 6, parity 2, living 1, miscarriage 3) who presented at 7-week period of gestation (POG) with a provisional ultrasound diagnosis of CSP which was reconfirmed on transvaginal sonography (TVS). She gave history of mild pain in abdomen and spotting 2 days back. There was history of two lower segment caesarean sections (one full-term caesarean section 13 years back and one preterm section 11 years back).

INVESTIGATIONS

TVS in first patient revealed single intrauterine gestational sac 40mm cephalad to external os at level of lower uterine segment scar which contained single live fetus with crown rump length (CRL) equivalent to 6 weeks and 2 days POG. The endometrial cavity and cervical canal was empty with endometrial thickness (ET) measuring 11mm double layered (figure 1). Her baseline b-hCG was 50 099 mIU/mL. Other baseline investigations were within normal limits.

The second patient's baseline investigations including haemoglobin was 11.5 g/dL, blood counts as well as liver and renal functions were within normal limits. Baseline b-hCG at presentation was 297 969 mIU/mL. TVS revealed single intrauterine gestational sac at level of lower uterine segment. Caesarean scar was at level of upper end of gestational sac and sac contained an intrauterine live fetus with CRL equivalent to 6 weeks and 6 days POG. Remaining ET was 10mm and double layered. Cervical canal was empty and bilateral adnexa were normal (figure 2).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of CSP include aborting intrauterine pregnancy and cervical ectopic pregnancy. Diagnosis is made when on ultrasound the gestational sac is seen implanted at previous caesarean scar site with empty uterine and cervical canal and thin myometrium between the sac and bladder. On Doppler, vascular flow is seen around the gestational sac in CSP but no flow is seen

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Figure 1 (A) Gestational sac implanted at scar site with empty uterine cavity and cervix. (B) Caesarean scar pregnancy with fetal heart activity.

around aborting intrauterine pregnancy. A positive sliding sign where the sac slides when slight pressure is applied to cervix with endovaginal probe is seen in case of aborting pregnancy suggesting no intimate attachment of sac to uterus.

TREATMENT

As both patients were haemodynamically stable so plan was made for medical management despite high baseline b-hCG levels as the patients desired fertility preservation. Both the patients were counselled regarding treatment alternatives, risks and benefits, need for prolonged follow-up and in case of failure of medical management need of surgery including hysterectomy in the event of rupture and haemodynamic instability. In view of very high b-hCG values and live ectopic pregnancy, we planned combined medical management with intrasac KCL and systemic methotrexate. After informed consent, transvaginal ultrasound-guided intrasac KCL 2–4 mL (20 mEq/10 mL, 15% w/v) instillation was done with 17-gauge double lumen ovum aspiration needle (Cook,

Brisbane, Australia) and fetal heart cessation was observed. This was followed by multiple dose regimen of methotrexate 1 mg/kg slow intravenous four doses alternating with intravenous leucovorin 0.1 mg/kg.

OUTCOME AND FOLLOW-UP

B-hCG was measured on alternate days during methotrexate injection until a fall of more than 15% and then was measured weekly until it was negative. In the first patient, we observed a slight rise in b-hCG initially and it started declining after third dose. In the second patient, it started declining immediately but a fall of more than 15% was seen after second dose. [Figure 3](#) shows the trend of b-hCG levels during treatment and follow-up. Follow-up scan done after 3 weeks showed an empty sac in first patient and a heterogeneous mass at site of ectopic in second patient. There was no free fluid in abdomen of both patients. The duration for b-hCG to become negative in first

Figure 2 (A) Gestational sac at caesarean section scar site with empty cervical canal. (B) Empty uterine cavity.

Figure 3 Trend of beta human chorionic gonadotropin (b-hCG) in both patients during treatment and follow-up.

patient was 91 days and in second patient was 119 days. The follow-up period was uneventful in both the patients.

DISCUSSION

CSP is implantation of gestational sac in the uterine scar and is a recently increasingly recognised complication of pregnancy following previous caesarean delivery. The incidence of CSP ranges from 1/1800 to 1/2500 of all caesarean deliveries.³ A variety of treatment modalities have been proposed but optimal management is yet to be determined. If patient presents with uterine rupture and

haemodynamic instability, surgical management becomes imperative and radical surgery in form of hysterectomy is often needed as a life-saving procedure. Management of patients presenting early and who are stable present a challenge to the clinician and range from medical methods including systemic methotrexate to surgically assisted medical management and intrasac instillation of methotrexate or KCL, minimally invasive surgery—dilatation curettage (D&C), hysteroscopy-guided resection, laparotomy or laparoscopic-guided excision and repair.⁴

Management of CSP carries a significant complication rate with around 44.1% patients treated (331 out of 751) ending up in complications like hysterectomy, laparotomy and uterine artery embolisation in emergency. The highest complication rate was seen with singular treatment modalities like systemic methotrexate, D&C and uterine artery embolisation. The least complication was observed when systemic treatment was combined with local intragestational methotrexate or KCL instillation and additional haemostatic measures used with hysteroscopy management.⁴ Systemic methotrexate alone has been used for the treatment of tubal ectopic pregnancies with defined risk factors for failure of medical management like presence of fetal cardiac activity, b-hCG more than 3000 mIU/mL and gestational sac diameter more than 4 cm.⁵ No such risk factors have been defined for CSP in view of rarity of cases. But, since all of these risk factors were present in our case, we used combined local and systemic treatment and multiple doses of methotrexate. Schufreider *et al* have reported a similar case of CSP with live ectopic pregnancy and b-hCG of 58 641 mIU/mL. They initially used systemic methotrexate alone but in view of rising b-hCG and persistence of fetal heart activity they also did intrasac KCL instillation followed by sac aspiration and two more repeat doses of methotrexate were administered.⁶ Following this, the patient had successful resolution of ectopic gestation and mean duration for b-hCG to become negative was 5 weeks. Roy *et al* also reported a similar case in which they used 5 doses of methotrexate alternating with folinic acid and intrasac KCL and methotrexate injection.⁷

Timor-Tritsch *et al* in their retrospective series of 26 patients, used local as well as systemic methotrexate in 19 patients with live CSP and had successful outcome with no complications in any patient.⁸ The maximum b-hCG in their series was 101 000 mIU/mL but our second patient had values 297 969 mIU/mL. We used both local KCL and systemic methotrexate in both patients and had similarly no complications. Mean duration for b-hCG to become negative in their series was 41–100 days which was almost similar to ours. Our first patient had an initial transient increase in b-hCG followed by steady decline, whereas in the second patient the decline was seen from the start of treatment. The initial increase in b-hCG prompts many clinicians for secondary treatment modalities which seems unnecessary and we also adopted a multiple dose protocol wherein a significant fall of more than 15% was observed at least after two doses which could also be a reason for successful outcome in our case.

Both our patients had endogenic (type 1) type of CSP. The success rate of medical management is not differentiated on the basis of type of CSP in the cases reported in literature. There are case series of successful laparoscopic resection of exogenic (type 2) type of CSP.^{9 10} However, medical management may be beneficial in both types if the patient presents early and in haemodynamically stable condition.

The most common side effect seen with systemic methotrexate treatment was oral ulcers seen in 26% (7/27) patients which responded to local treatment in a retrospective cohort of CSP treated with either local or systemic methotrexate.¹¹ In another systematic review, side effects seen in various studies with methotrexate treatment were elevated liver enzymes (2%), suppression of bone marrow (2%), fever (1%) and oral ulcers (1%).¹² Our patients did not report any side effects following treatment.

There is limited data on reproductive outcome following treatment of CSP. One case series reports good pregnancy rate

of approximately 87% following various treatment modalities, most commonly a combination of systemic methotrexate and D&C. The miscarriage rate was 25% and one patient each had recurrent CSP and placenta accreta.¹³ Both our patients have not yet conceived during follow-up period.

Learning points

- Caesarean scar ectopic pregnancy is a serious and life-threatening condition with recent rise in incidence due to increasing caesarean section rates.
- No optimal treatment strategy can be proposed due to scarcity of cases in literature.
- Combined medical management, which includes local feticidal agent and systemic methotrexate, is an effective treatment modality in cases diagnosed early even with very high beta human chorionic gonadotropin and live ectopic pregnancy.
- Medical management is applicable to patients who are desirous of avoiding surgery, haemodynamically stable, have no contraindications to methotrexate and are willing for follow-up.
- This treatment modality is minimally invasive, with no requirement of anaesthesia and has very low risk to patient.

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