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Gehan Farid
Department of Obstetrics and Gynecology, Security Forces Hospital, Riyadh, Saudi Arabia

Ahmed Talal Chamsi
Department of Obstetrics and Gynecology, Security Forces Hospital, Riyadh, Saudi Arabia

Mohamed Swaraldahab
George Masson University, Fairfax, Virginia, USA

Hassan Swaraldahab
KPMG LLP, USA

Corresponding Author:
Ahmed Talal Chamsi
Department of Obstetrics and Gynecology, Security Forces Hospital, Riyadh, Saudi Arabia

Experience in the management of scar ectopic pregnancy in a tertiary center in Saudi Arabia

Gehan Farid, Ahmed Talal Chamsi, Mohamed Swaraldahab and Hassan Swaraldahab

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Abstract
Background: Scar ectopic is a recent rapidly increasing phenomenon complicating pregnancy occurring in previously scarred uteri.
Objective: To study and evaluate the management of this rare abnormal pregnancy.
Setting: A retrospective observational cohort study, conducted in the Department of Obstetrics and Gynecology, Security Forces Hospital, Riyadh, Saudi Arabia, in the period from June 1st 2017 to July 30th 2019.
Results: A total of 7 cases were studied where the patient characteristics revealed an average age of 35 years, Body Mass Index of 36 Kg/ m^2. The Gestational age ranged from 5^{+5} to 12^{+6} weeks. In five patients (71.4%) the gestational sac was seen with fetal poles in the ultrasound done for all and MRI for one case, for clarification of diagnosis. Two cases had positive fetal heart (28.6%). The number of previous c/s done for the patients ranged from 1-4 previous cesarean scars. Almost all patients responded to one dose of intramuscular Methotrexate, except for two cases that needed extra doses, one given intramuscular and the other inside the gestational sac. Medical disorders encountered were in the form of bronchial asthma and hyper -prolactinemia in one case and hypothyroidism in another one. The average time needed for Bhcg to return to normal value was 61 days.
Conclusion: Although the number studied was small in a new emerging pathology, yet, the good outcome clearly showed that high vigilance and rapid directed management and follow-up entailing combined treatment was mandatory. So far, the diversity and the instigation of a combination of methods of treatment should be existent until final standard protocols are set.

Keywords: Ectopic pregnancy, scar ectopic, cesarean delivery, methotrexate

1. Introduction
Scar ectopic is the implantation of pregnancy in the myometrium and fibrous tissue of previous scar of uterus, most frequently cesarean section. The probable pathology could be due to the migration of pregnancy through defects, basically, microscopic tracts between old cesarean scar and endometrial canal.
The incidence of 1:1800-2261 (9), reaching 1:531 women with one previous cesarean section (12) and conforming 6% of all ectopic pregnancy, was recorded.
This is life threatening condition, with a wide range of variable presentation, ranging from asymptomatic cases to those with lower abdominal pain, per vaginal bleeding, shock and collapse (1) Consequently, the cornerstone of treatment is vigilance and early meticulous diagnosis, as well as counseling, accompanied by expedited management to avoid tragic complications leading to maternal mortality and jeopardy of fertility.
Globally, there is no agreed consensus on the management of scar ectopic, being dictated by the available facilities and expertise for initial interpretation of diagnosis and then treatment. Those treatment options range from the, not much recommended, expectant observational option to medical (mainly Methotrexate), surgical and a combination. Surgical options include dilatation &curettage, hysteroscopic, laparoscopic approaches, hysterectomy as well as uterine artery embolization.
The meagre availability of literature on the management of this rare condition, encouraged the conduction of this retrospective study in a Tertiary Centre in Saudi Arabia.

2. Material and Methods

2.1 Ethical Approval

The study was approved by the Research Committee at Security Forces Hospital.

2.2 Settings

A retrospective observational cohort study done from June 1st 2017 to July 30th 2019, on women who have been diagnosed as scar ectopic pregnancy. The study was conducted in the Department of Obstetrics and Gynecology, Security Forces Hospital, Riyadh. Saudi Arabia A 2 D Ultrasound and flow Doppler studies (both trans abdominal and transvaginal routes) were used for all cases for diagnosis. Salient criteria were essential for diagnosis and which included empty uterus, as well as cervical canal, implantation of the pregnancy at the presumed site of scar incision. Further, myometrial thickness measurement between bladder and gestational sac in addition to Doppler study were done. Doppler flow studies entailed observation of low impedance blood flow around the ectopic gestational sac (consistent with normal Pregnancy) [10].

Serial levels of serum βhcg were used to follow the management of cases. Methotrexate was the cornerstone of treatment of all such patients. The dose given was as per the protocol of 50mgs/m^2.

MRI use was reverted to in non-clear cases.

2.3 Subjects

A total of 10 cases were analyzed

The inclusion criteria for this study were:

1. Amenorrhoea with positive βhcg.
2. Abnormal ultrasound findings +/- MRI
3. Women with previous scar on the uterus.

The exclusion criteria were:

1. Women who did not meet the above criteria.
2. If there was possibility of viable intrauterine pregnancy or missed abortion, heterotopic and cervical pregnancy.

The maternal demographic characteristics included previous obstetric history, mode of delivery as well as associated medical disorders. Data was collected from the Medical Record Viewer database of the concerned hospital.

2.4 Statistical analysis: Microsoft Excel 2017 was used to analyze the data collected and entered in it.

3. Results

Out of 10 cases studied, 3 were excluded because they didn't meet the inclusion criteria.

Table (1) illustrates the demographic aspects of the remaining 7 patients, where the average age was 35 years, mean BMI was 36kg/m^2. The number of previous c/s varied between 1-4 scars. The average interval from last pregnancy was 2.4 years and mean Gestational age was 7^{+3} weeks and the average parity was 4. The ultrasound findings of the two cases with lowest values of βhcg revealed masses with cystic degeneration (cases1&2). The other 5 cases had gestational sacs seen, two of which with visible viable cardiac activities (cases 6 & 7).

Table (2) shows the initial levels of βhcg that ranged from 318-16,016 IU/ml. Follow-up was done by serial βhcg values over a period of three months and the average time taken to revert to normal values was 61 days.

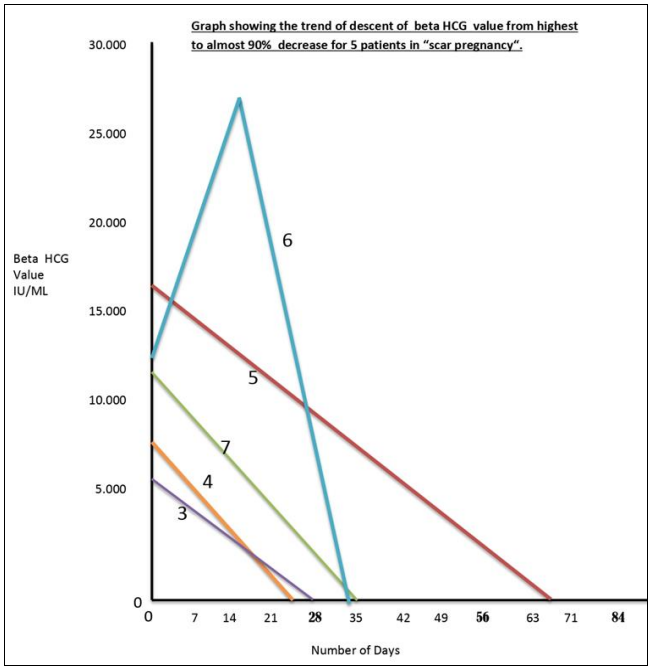

Fig 1: Shows a graphical illustration of the trend in descent of βhcg values for 5 demonstrable.

All cases were hospitalized & responded to one dose of intramuscular Methotrexate, except for two cases where one received an additional intramuscular dose and the other given in the gestational sac. The latter was done using 22 gauge long needle, under ultrasound guidance through the abdominal route and with no anesthesia. All patients had no complications. Prophylactic antibiotics in the form of one gram of 1.5 gram of Cefuroxime was given to one patient only, who had the intragestational injection of Methotrexate.

The clinical presentation of patients ranged from lower abdominal pain in one patient (14%) and per vaginal spotting in another (14%). Otherwise all the other cases were asymptomatic and solely diagnosed at routine booking ultrasound.

Fig (2) shows tranvaginal image of scar ectopic.

Table 1: Shows patient characteristics, time interval from last c/s number of scars as well as G.A and HCG levels.

No.	Age/year	BMI (Kg/m^2)	Parity (p)	No of previous C/S	Time interval from last delivery (year)	initial HCG level (IU/L)	GA (weeks)
1	38	34	4	3	3	318	7 (0)
2	26	34	1	1	2	5534	9^{+2} (0)
3	36	41	4	4	2	6446	8^{+5}
4	35	32	3	2	3	11,976	5^{+5}
5	40	38	6	3	2	16,016	12^{+0}
6	39	39	4	4	3	13,022	6^{+4} (+)
7	31	36	4	4	1	13,122	8^{+2} (+)

C/S: Cesarean section BMI: Body Mass Index
G.A: Getational age (O): Only Multicystic Mass
+: positive fetal heart

Table 2: Shows the trend in βhcg value, till normal values and the number of doses of Methotrexate used and route

No.	First month (BH)CG	Second month (βHCG)	Third month (BHCG)	Recorded time to normal BHCG value (days)	No of I.M. MXT and Route
1	318 → 155	121 → 44	● — ●	57	1
2	302 → 92	92 → 25	22 — ●	66	1
3	6446 → 381	197 → ●	● — ●	56	1
4	11976 → 118	● — ●	● — ●	43	2
5	16016 → 701	207 → 68	41 → 9	67	1
6	13,022 → 24,056	255 → 28	22 — ●	77	2 *
7	12, 022 → 9218	720 — ●	25 — ●	62	1

MXT: Methotrexate
*: intra gestational sac injection
I.M: intramuscular route

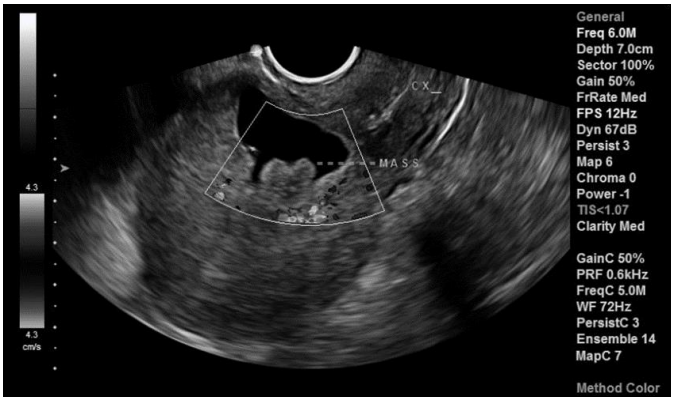

Fig 2: Transvaginal image done showing gestational sac at the isthmical region between uterus and cervix.

Cefuroxime was given to one patient only who had intragestational injection of Methotrexate. The clinical presentation of patients ranged from lower abdominal pain in one patient (14%) and per vaginal spotting in another (14%). Otherwise all the other cases were asymptomatic and solely diagnosed at routine booking ultrasound. Fig (1) shows the of scar ectopic in one patient

4. Discussion

This rapidly emerging occurrence of scar ectopic pregnancy resulting from the embedding of pregnancy into the myometrium and fibrous tissue at the site of preexisting uterine scar, pose an enigma.

The difficulties encountered in this phenomenon encompass many aspects. To start with is the presentation which varies widely from asymptomatic cases, as was seen in 71% of cases in our study and which is more than 45% reported by Yu *et al.* [13]. Comparison with above mentioned study, there were 55% of cases that presented by per vaginal bleeding unlike 14% encountered in our cases. Whereas, 7% only had abdominal pain unlike 14% in our studied population. Further, patient counseling is not easy because of the difficulty in reaching a definitive diagnosis by Doppler Ultrasound and hence need for Magnetic Resonance Imaging in complicated cases, as was reverted to, in one of the patients in our study.

Treatment options is a challenge being dependent on the presenting symptoms, experience of attendants, available facilities and expertise. The role of observational expectant management is not satisfactory, in view of its association with high morbidity and mortality due to rupture uterus, hemorrhage, hysterectomy and even maternal death.

Other available options include medical, surgical treatment and a combination if the need arise. Medical treatment in the form of systemic Methotrexate +/- intra gestational injection is the commonest form of treatment and is accompanied by high success rate where only 28% of the cases in our study needed only one extra dose, systemic for one patient and local for the other.Our results agree with Timor- Tritsh [9] and is also associated with one of the least complications compared to other modes of treatment.

However, Morente *et al.* [13] projected that over 50% of patients, post- methotrexate treatment, needed a second dose.

Fortunately, in our series, we encountered no dramatic presentation that would have necessitated surgical interference which could have been in the form of laparotomy, laparoscopy, hysteroscopy depending on the severity of the case. Other forms of available treatment include hypogastric artery ligation done alone laparoscopically +/- dilatation and curettage. Uterine artery embolization is utilized alone or more often in conjunction with methotrexate and before or after Dilatation & Curretage, as well as in cases with arteriovenous malformation [6]. Dilatation and curettage alone per se is not an option being associated with complications [4].

Wedge resection of scar ectopic is strongly advocated by Davidson *et al.* [10] as a primary treatment in view of reduction of recurrence of scar ectopic. However it's believed that this is a major initial procedure to be done, and would rather be reverted to in case of failed medical treatment. However patient counseling still pose an important issue in management [5].

The average age of this abnormal pregnancy in our series was 7^{+3} weeks and is similar to other reported studies (1 & 4). The interval between the last pregnancy and scar ectopic pregnancy was 2.4 years and which was within the wide range of 6 months to 12 years quoted by Seow *et al.* [4].

Most cases of scar ectopic that occurred in our patients were in those with 4 or more previous sections (79%), much more than 50% reported by Maymon *et al.* [12] of 2 or more previous scars. A possible explanation of more frequency in high order cesarean section scars might be due to the bigger scar surface area created by repeated surgery hence providing ease for implantation of abnormal pregnancy.

In our study all patients were initially managed by intramuscular methotrexate and monitored by serial HCG values. Additional single doses were needed in two cases only, one of which was with a positive fetal heart. This might have been avoided if concomitant systemic and local intragestational sac injection was done from the beginning, as advocated by Timor - Tristsch [9].

Regardless of the type of scar ectopic, whether type I where the pregnancy in the scar progress towards cervical- isthmic space +/-uterine cavity or the more serious type ll with deep filtration into uterine myometrium and uterine serosal surface, concomitant serial Doppler studies with βHCG measurement should be done postmedical treatment because of the continued

growth of trophoblastic tissue in spite of lowering in the hormonal level [11], and this ultrasound is to be continued as per protocol, even after normalization of βHCG. This should definitely be the case with higher risk patients that were equal to or more than 9 weeks, had fetal pole that is 10 mm or more, positive cardiac activity and βHCG equal to or more than 10,000 lU/ l [10].

Accordingly, from the aforementioned discussion, there should be a low threshold of suspicion for scar ectopic, this in addition to the multiple available options of treatment and in the absence of universal protocols and guidelines, the general treatment of choice is to interrupt the pregnancy, once diagnosis is made.

The tragedy of missing or delaying the management could end in uterine rupture, massive hemorrhage ending in hysterectomy with jeopardy of fertility, an issue of great importance in many communities.

In our series we did not have any patients that came back with repeat scar ectopic, where it's known that the risk of recurrence is 3.2 - 5.0% (7 & 8).

This mandates the inclusion in counseling of patients, after treatment, of close surveillance of any new pregnancy with knowledge of complications that could occur including abnormal placentation (eg increta), preterm labor, uterine rupture, hemorrhage, hysterectomy and loss of fertility [6].

5. Conclusions

1. Careful scrutiny of combined Trans - abdominal /trans-vaginal Ultrasound with Doppler flow studies at the time of booking of first trimester of pregnancy with history of previous scar of the uterus.
2. Once scar ectopic is diagnosed the target should be termination of the abnormal pregnancy, with little place for conservative watchful management in view of its association with high morbidity and mortality. So far it's hard to draw robust correlation between parity, number of previous scars, βhcg levels for causation and outcome of this abnormal pregnancy.
3. Single or a combination of different medical and surgical methods of treatment is to be widely adopted to secure a safe outcome, bearing in mind the risks and benefits and after careful patient counseling.
4. Medical treatment so far seems to be the commonest mode of treatment and in particular Methotrexate, where it's advisable to be used concomitantly in systemic and local intragestational route in high risk category of patients mentioned.
5. Counseling of all patients about scar ectopic pregnancy, in particularly those undergoing their first cesarean section. Post successful treatment of scar ectopic, extended follow up is needed with outlook for recurrence.

6. Conflict of interest

The authors state no conflict of interest.

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