

Case Report

# Management of the Ectopic Pregnancy Located at the Level of the Uterine Scar

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## Abstract

The ectopic pregnancy located on an uterine scar is basically defined as implantation of the gestational sac at the level of the fibrous tissue of a uterine scar. The incidence of this pathology varies a lot, it can reach up to 1 case in 2000 ectopic pregnancies. It is expected that the incidence will increase. In the case of ectopic pregnancy, there were many therapeutic, medications or surgical (radical or conservative) options.

**Case report:** We are presenting a prospective study conducted over a period of 26 months from July 2012 to September 2014 in Craiova Emergency County Hospital. This article reports 2 cases diagnosed with ectopic Pregnancy Located at the Level of the Uterine scar. The first case is of a 26 year old patient, 4 pregnancies, 1 birth, who came to the Gynaecology practice due to a 6 week amenorrhoea, pelvic pain, low vaginal bleeding. Following the discussion with the patient, the conservative drug therapy was initiated, namely she was given methotrexate 50 mg/m<sup>2</sup>. The patient showed no side effects after the methotrexate. The second case is of a 31 year old patient, 2 pregnancies, 1 birth, who came to the gynaecology practice due to a 4-5 week amenorrhoea, pelvic pain, vaginal bleeding. Following the discussion with the patient, the decision was made to conduct the haemostatic and evacuation uterine curettage under transrectal ultrasound control in order to minimise the risk of perforation. The uterine curettage was performed in the classic way. No complications were reported during the procedure or in the recovery period.

**Conclusion:** Ectopic pregnancy located in the uterine tranche can be successfully treated with medicine, but it is preferable that in the case of patients who still want to have a baby, the tranche to be repaired by means of surgery to minimize the risks and a recurrence of this pathology.

**Keywords:** Ectopic; Pregnancy; Uterine tranche; Surgery

## Introduction

The ectopic pregnancy located on an uterine scar is basically defined as implantation of the gestational sac at the level of the fibrous tissue of a uterine scar [1]. This clinical situation arises because there is a micro-niche at the level of the uterine suture line, the area in which the new gestational sac will grow [2].

The first case reported on an ectopic Pregnancy Located at the Level of the Uterine scar was in 1978 [3]. Over 850 cases of pregnancies located at the level of the uterine suture line after Caesarean sections were published worldwide in 2015 [1].

The incidence of this pathology varies a lot, it can reach up to 1 case in 2000 ectopic pregnancies and it occurs in about 0.15% of patients who have a caesarean section in history [2]. It is expected that the incidence will increase greatly due to increasing caesarean operations and the increase in the number of *in vitro* fertilization techniques on a cicatricial uterus, clinical situations that foster the occurrence of this pathology [4].

The average gestational age when this pathology is diagnosed is generally about 7.5 ± 2.5 weeks [5].

Risk factors incriminated in the development of this form of ectopic pregnancy are represented by a history of caesarean section, placental pathology, patients who have experienced myomectomy, therapeutic hysteroscopy uterine curettage and manual extraction of the placenta [6].

The patient's initial symptomatology may be dramatic with signs of hypovolemic shock, but it may also be poor or even absent. Still, in most cases, patients complain of abdominal pain and vaginal bleeding [7].

The paraclinical diagnosis is done using transvaginal ultrasound (it is the most widely used method and the cheapest at the same time),

transrectal ultrasound, MRI (by coronary, transverse and sagittal sections at T1 and T2 levels, information can be obtained on the size of the gestational sac and the degree of myometrial invasion), diagnostic laparoscopy [8,9].

In the case of ectopic pregnancy, there were many therapeutic, medications, or surgical (radical or conservative) options [10].

Drug therapy is based on the use of methotrexate or potassium chloride intramuscularly or intraamniotically [11]. Depending on the severity of the case, surgical treatment can be chosen, from the minimally invasive one, such as uterine artery embolization or uterine curettage to laparotomy or laparoscopy with hysterectomy or emergency hysterectomy in extremely serious cases [12,13].

## Study Design

We are presenting a prospective study conducted over a period of 26 months from July 2012 to September 2014 in Craiova Emergency County Hospital, Department of Obstetrics and Gynecology. This article reports 2 cases diagnosed with ectopic Pregnancy Located at the Level of the Uterine suture line. Both patients gave their consent to the use of the data for scientific purposes. We will detail the diagnosis

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methods used and the treatment conducted as well as the patients' subsequent evolution.

All patients who came during this period to the Emergency County Hospital of Craiova, Department of Obstetrics and Gynecology underwent a transvaginal ultrasound, with a 7.5 MHz Voluson E8 ultrasound.

The ultrasound diagnosis criteria used for the ectopic pregnancy located at the level of the suture line were:

1. Empty uterine cavity and free cervical canal
2. Gestational sac located in the anterior part of the uterine cavity at the isthmus level
3. The width reduction of the myometrium at the level of the isthmic wall, from the level of the urinary bladder up to the gestational sac (the differential diagnosis with the cervico-isthmic pregnancy is thus done). The absence or reduction of the myometrium located between the gestational sac and the urinary bladder by less than 5 mm are deemed as defining elements [14]
4. Trophoblastic movement showed via Doppler examination [15], pulsatility index <1, resistance index less than 0.5, a high-velocity flow >20 cm/s, peak systolic in diastoles less than 3 [12,13]. Using Doppler ultrasound has greatly helped in differentiating viable pregnancies from unviable pregnancies.
5. An image of a "double ring" located at the level of the uterine anterior part.

The first case is of a 26 year old patient, 4 pregnancies, 1 birth, who came to the gynecology practice due to a 6 week amenorrhoea, pelvic and abdominal pain, low vaginal bleeding. The pregnancy test came out positive. The patient has a history of a birth by cesarean section about 24 months ago at 39 weeks of gestation for fetal macrosomia and 2 induced abortions conducted about 1 year and 6 months ago, respectively, these abortions were practically made after delivery by Caesarean section. The previous birth showed no subsequent complications. The transvaginal ultrasound showed an embryonic sac located on the anterior uterine wall (Figure 1), measuring 11/9 mm in diameter without viable embryo, an image meeting all the previously mentioned criteria for the diagnosis of an ectopic Pregnancy Located at the Level of the Uterine suture line.

No liquid was found in the peritoneal cavity. When diagnosed, the patient was in a stable condition and she was recommended to conduct a betaHCG test which had a result of 1963 mU/ml. After 24 h it was 2370 mU/ml and after 36 h it was 2760 mU/ml.

Following the discussion with the patient and after getting her informed consent, the conservative drug therapy was initiated, namely she was given methotrexate 50 mg/m<sup>2</sup>, namely 86 mg for her body size. The patient is 174 cm tall and she weighs 62 kg, so a body size of 1.72 m<sup>2</sup>. The subsequent management consisted in serial beta-hCG tests and serial ultrasounds. The patient needed 4 days of hospitalisation. She no longer needed to be given another dose of methotrexate. Seven days after the administration of methotrexate, the beta-hCG dosing was 150.70 and 3 weeks later, it was minimum. The patient showed no side effects after the methotrexate.

After about 6 weeks, the embryonic sac was no longer viewed in the ultrasound and the dosing was negative. About 3 months after the administration of the methotrexate, the ultrasound examination showed a suture line disorder. The patient wanted to undergo a laparoscopy for the restoration of the suture line for future pregnancies. After the laparoscopy, the patient showed no complications or menstrual cycle disorders. Until the publication of this article, the patient has not become pregnant anymore.

The second case is of a 31 year old patient, 2 pregnancies, 1 birth, who came to the gynecology practice due to a 4-5 week amenorrhoea, pelvic and abdominal pain, intermittent vaginal bleeding. The patient has a history of a birth by cesarean section about 36 months ago for foetal malposition, 37-38 weeks of gestation and one induced abortion conducted 9 months ago. The previous birth showed no subsequent complications. The transvaginal ultrasound showed an embryonic sac measuring 15/8 mm in diameter without viable embryo located at the level of the anterior uterine wall (Figure 2), an image meeting all the previously mentioned criteria for the diagnosis of ectopic Pregnancy Located at the Level of the Uterine suture line. No liquid was found in the uterine cavity.

Following the discussion with the patient and after obtaining the informed consent, the decision was made to conduct the haemostatic and evacuation uterine curettage under transrectal ultrasound control in order to minimise the risk of perforation. The uterine curettage was performed in the classic way. For better safety, a blood unit and a



Figure 1: The transvaginal ultrasound showing an embryonic sac located on the anterior uterine wall in first case.



Figure 2: The transvaginal ultrasound showing an embryonic sac at the level of the anterior uterine wall in second case.

complex surgical team were prepared. No complications were reported during the procedure or in the recovery period. The patient had normal menstruation during the following period and she had no complaints of pain or abnormal bleeding.

## Discussion

The ectopic Pregnancy Located at the Level of the Uterine suture line is a rare form of extrauterine pregnancy associated with complications which are even more serious as the diagnosis is made in advanced stages [16]. The peculiarity of this pathology is given both by the atypical location of a pregnancy and the evolution of this pathological situation which is one of extreme emergency [17].

In 1948, Devoe and Pratt reported an incidence of 1 in 30,000 births from ectopic pregnancies localised at the level of the uterine suture line, but given the increasing incidence of caesarean sections and *in vitro* fertilisation techniques, the incidence of this pathology has risen [15].

The diagnosis frequency is still very low, because in some cases, symptomatology is minimum. Cases have been reported of diagnosis decided when a uterine rupture occurred, and the patient showed signs of haemoperitoneum and hypovolemia. In this type of situations, hysterectomy seems to be the only available treatment [18].

Among the first cases reported was the one described by Rempen and Albert in 1990. They reported a case of ectopic pregnancy located on the uterine suture line and the cases was solved by laparotomy [14].

Another case was reported in 1995 by Hermen et al. In this situation, the patient got to 35 weeks of gestation and birth resulted in a living, healthy foetus. However, the location of the uterine scar caused uterine hypotonia and doctors were forced to perform a hysterectomy [18].

We reported 2 cases over a period of about 2 years, the number is quite small due to the fact that our hospital is ranked as Level 2.

Analyzing specialist studies we were unable to determine with certainty whether the increased number of cesareans performed in medical history causes an increased risk but studying both the results of other authors and our cases we observed that a possible risk is the previous curettage and especially the short time from caesarean surgery to an abortion and then to another pregnancy [1].

Most of the time the evolution of an ectopic Pregnancy Located at the Level of the Uterine scar is to progress on the inside of the tranche towards the abdominal cavity [5]. It is the most common evolutionary form of ectopic pregnancy situated in the uterine installment and also the most serious one, because it can result in uterine rupture, massive intraperitoneal hemorrhage and hypovolemic shock or even maternal death.

However, in some cases the ectopic pregnancy located at the uterine scar may progress to uterine cavity [19]. In this case the embryo survival may be possible and the case will be resolved with a viable fetus but this requires constant ultrasound monitoring and it is a pretty rare situation [20].

If the ectopic pregnancy situated on the uterine tranche is diagnosed in an early stage multiple therapeutic options can be chosen and fertility can be maintained [21]. Timing of a pregnancy located on the uterine tranche may endanger the patient and can lead to uterine rupture and needs urgent hysterectomy [22].

In the absence of randomized trials, several factors must be taken into account, such as: the choice of the method of treatment for ectopic pregnancy on the uterine tranche, the age of the patient, the gestational age, the viability of the embryo, the existence of a tranche uterine defect,

the patient's desire about a subsequent fertility, the previous medical history and the doctor's experience [2,3].

Conservative drug therapy is represented by methotrexate administered orally, intramuscularly or intraamniotically [4]. Also KCL can be used [6].

Methotrexate can be administered orally, intramuscularly or intraamniotically. It is recommended to administer 50 mg/m<sup>2</sup> (based on body weight) intraamniotically or 1 mg/kg/day intramuscularly [20]. Methotrexate can be administered both intraembryonic and intracorally [7], solely or in combination with the embolization of the uterine artery or curettage of the uterine cavity [21]. It has the great advantage that it helps the preservation of the fertile function and the conservation of the uterine cavity but sometimes it requires a longer dosing and long-term follow [16]. The administration of this drug should be continued until the disappearance of fetal cardiac activity. Methotrexate may affect the liver and may cause vaginal bleeding [2,14]. The liver function, renal function and blood counts should be assessed before beginning therapy, during treatment and after treatment [5].

In the case of methotrexate administration, the length of time until  $\beta$ hCG values are normalized varies from 30 days to three months and the picture of the gestational sac may persist up to 5-6 months [2,14].

After 2-3 months, the patients who received treatment with methotrexate had normal menstrual cycles [21]. KCL which has been injected transvaginal intraamniotically at a concentration of 40mmol up to a maximum of 150 mmol/day. The injection has to be made slowly and requires monitoring of renal and hepatic activity. The recall can be performed until such time as the cardiac activity is absent. When administering this substance it is necessary that the acid-base balance to be monitored and making EKG permanently due to acute bradycardia and dehydration which frequently occur [1,2,6].

The limits of the drug treatment consist in the fact that total curability is not ensured and there is always the risk of ectopic pregnancy recurrence on the uterus tranche, a situation that has been presented in other articles [5,7].

The surgery is represented by:

- The curettage by D&C. To better perform this maneuver it can be done along with TRUS [10]. It is preferable that this maneuver be performed in combination with the administration of methotrexate. The evacuation of pregnancy using hemostatic uterine and hauler curettage under control of TRUS is a new method that allows the visualization of the uterine cavity during the maneuver with enough space for performing, thus lowering the risk of perforation. This method has also been reported by T. Bignardi and collaborators in 2010 as a major risk free procedure as long as it is performed by a specialist in this technique. It has been observed that patients who received D&C experienced a quicker decrease of BHCG values and a quicker installation of normal menstrual cycles [10,14,23].
- Uterine artery embolization can also be used in combination with the administration of methotrexate and D&C [11,17].
- Hysterectomy - is the final situation, the last method applied. It is performed when the trophoblast crossed the myometrium and the uterine rupture is massive [1,5].
- There is no universal therapeutic treatment protocol the reason being the lack of experienced doctors caused by the relatively low number of cases.

- The protocol that we suggest, based on our own experience and on specialized studies analysis, is as follows:
- BHCG  $\leq$  5000 and patient with good general condition - the administration of methotrexate injection - 1 mg/kg or 50 mg/m<sup>2</sup> is recommended.
- BHCG  $\geq$  5000 UI and patients with good general condition - the administration of methotrexate injection - 1 mg/kg or 50 mg/m<sup>2</sup> in combination with intraamniotically injection of similar amounts of methotrexate is recommended.
- According to the clinician's experience and patient with good general condition one can opt for the intraamniotically administration of potassium chloride with the indication mentioned above.
- According to clinic facilities one can also opt for uterine artery embolization when the BHCG is greater than 5,000 IU.
- Hysterectomy is indicated when a patient presents with abundant vaginal bleeding and an important loss of substance in the uterus. This should be the last therapeutic option.

The follow-up care of patients who presented this pathology lies in the determination of  $\beta$ HCG serial and regular ultrasound examinations for an average of six months or until the normalization of  $\beta$ HCG values and the disappearance of the embryo sac. Otherwise, after 12 weeks, when the sonographic examination is done, it is ideal not to notice any anomaly and the  $\beta$ HCG's be under 2 mU/ml [1,3,10].

Fylstra et al. [18] recommend defect trance surgical resection to minimize the risk of recurrence, resection that can be done during pregnancy or after the drug treatment. Therefore it is recommended that defect trance repair to occur especially for patients who want a new pregnancy [20].

Another issue that deserves further research is the risk genes that might be associated with ectopic pregnancy and its recurrences.

The expression of HOXA10 is up-regulated at the ectopic implantation site in the fallopian tube, which indicates that mis-regulation of HOXA10 might lead to ectopic pregnancy [24]. As lymphoid-specific helicase (Lsh) controls Hox gene silencing during development, including HOXA10 [25], aberrant expression of LSH may cause ectopic pregnancy. Interestingly, since Lsh is able to recruit DNA methyltransferases (DNMTs) and histone methyltransferases G9a/GLP complex at specific loci [26] and the latter is also involved in the maintenance of DNA methylation in mammals [27], abnormal DNA methylation levels at the HOXA10 locus might directly lead to the occurrence of ectopic pregnancy. Therefore, to minimize the risk and recurrence of ectopic pregnancy in women who underwent uterus operation, it is essential to investigate the expression levels of HOXA10 at the uterine suture line before they get pregnant.

There is no consensus about the length of time until a new pregnancy is possible. Some authors recommend a duration of 12-24 months or until complete restoration of the defect trance [1,6,7].

## Conclusion

Because of the many complications that can occur with or without treatment for ectopic pregnancy located in the uterine trance, numerous studies are needed to minimize the risks. The pregnancy located in the uterine trance is a very dangerous clinical procedure which requires intensive monitoring. If the diagnosis is made in time, complications such as bleeding or hysterectomy can be avoided to the maximum. The

rarity of this disease explains the nonexistence of universal diagnosis and therapeutic protocol but still waiting should not be an option because it can lead to catastrophic results. However the protocol should be individualized and reported each time to increase universal experience.

In conclusion, ectopic pregnancy located in the uterine trance can be successfully treated with medicine, but it is preferable that in the case of patients who still want to have a baby, the trance to be repaired by means of surgery to minimize the risks and a recurrence of this pathology.

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