

# SPONTANEOUS HETEROTOPIC, ECTOPIC CERVICAL AND ECTOPIC TUBAL PREGNANCY – EVER PRESENT DIAGNOSTIC DIFFICULTY: THREE CASE REPORTS

Ivana Erceg Ivkošić<sup>1</sup>, Renato Bauman<sup>1</sup>, Boris Ujević<sup>1</sup>, Oliver Vasilj<sup>1</sup>, Ivana Petra Kojić<sup>1</sup>, Ante Ivkošić<sup>2</sup>, Darko Vukušić<sup>2</sup> and Tatjana Pavelić Turudić<sup>1</sup>

<sup>1</sup>Clinical Department of Gynecology and Obstetrics; <sup>2</sup>Clinical Department of Surgery, Sveti Duh University Hospital, Zagreb, Croatia

**SUMMARY** – The incidence of heterotopic/ectopic pregnancy in recent times has increased partly due to the increase in assisted reproductive technologies, whereas such medical cases and cervical pregnancy in particular are extremely rare with spontaneous conception. We report on three patients referred to our department in one week: one patient each with spontaneous heterotopic pregnancy, cervical pregnancy and tubal pregnancy. All of them had conceived spontaneously and were properly diagnosed and treated, however, additional care is needed in diagnosing and managing the potentially fatal consequences of ectopic pregnancy if not recognized early and managed properly, despite its low incidence.

**Key words:** *Pregnancy, heterotopic; Fertilization; Pregnancy, tubal; Pregnancy, ectopic; Cervix uteri – pathology; Case reports*

## Introduction

Ectopic pregnancy accounts for only 1% of all pregnancies, and most of them (95%-97%) develop in the fallopian tube<sup>1</sup>, while cervical ectopic pregnancy is very rare and occurs in only 0.15% of all ectopic pregnancies. Heterotopic pregnancy is a condition that encompasses simultaneous occurrence of intrauterine and ectopic pregnancy. Spontaneous heterotopic pregnancy is extremely rare and occurs in approximately 1:30 000 cases<sup>1</sup>, while there is a slightly higher incidence with the use of assisted reproductive technologies (ART), where it rises to 1% to 3%<sup>2</sup>. All of these conditions are potentially life-threatening both for the mother and the fetus. They require early detection and prompt treatment. We report on three cases of

ectopic pregnancy that presented within one week at our Department: spontaneous heterotopic pregnancy, spontaneous cervical pregnancy and spontaneous ectopic tubal pregnancy in one patient each. All three cases were timely diagnosed and successfully treated.

## Case Report 1: Spontaneous Heterotopic Pregnancy

A 32-year-old woman, para 1, gravida 2, was admitted to the Clinical Department of Gynecology and Obstetrics in the 10th week of amenorrhea due to abdominal pain that had begun 5 hours earlier, with no bleeding, in good general condition. She had conceived spontaneously, and had one miscarriage without curettage one year before in her medical history. She had been on progestin therapy for two weeks due to the symptoms of pain and mild vaginal bleeding, when the diagnosis of threatened miscarriage was suspected. Upon clinical examination, the abdomen was diffusely painful, more pronounced in the lower right quadrant, but without signs of significant rigid-

Correspondence to: *Ivana Erceg Ivkošić, MD, PhD*, Clinical Department of Gynecology and Obstetrics, Sveti Duh University Hospital, Sveti Duh 64, HR-10000 Zagreb, Croatia  
E-mail: [ivanaercegivkovic@gmail.com](mailto:ivanaercegivkovic@gmail.com)

Received July 2, 2014, accepted February 2, 2015

ity at that time. Pelvic examination showed signs of recent uterine bleeding, normal cervix, and anteverted, enlarged and soft uterus. Transvaginal sonography (TVS) revealed a vital ten-week intrauterine embryo and a small amount of free fluid in Douglas space, with both ovaries appearing normal. The patient was then referred to the emergency surgical service for additional examination. Ultrasound showed a substantial amount of free fluid in the abdomen, surgical workup excluded the possibility of an acute surgical event and the patient was referred for further observation to the gynecological department. Repeated complete blood counts showed a significant red blood cell (RBC) decline (hemoglobin 86 g/L, RBC 2.81x10<sup>12</sup>/L). Informed consent was obtained from the patient and diagnostic laparoscopy was performed: the exploration discovered a rupture in the middle third of the left fallopian tube (Fig. 1). Salpingectomy on the left side was subsequently performed with removal of hemoperitoneum and peritoneal lavage. The surgical procedure was uneventful. The postoperative course was without incident, and normal intrauterine pregnancy continued. The patient was discharged after six day hospital stay.

### Case Report 2: Spontaneous Cervical Pregnancy

A 28-year-old patient, para 0, gravida 1, with six weeks of amenorrhea but without earlier TVS pregnancy confirmation was admitted to the emergency department because of sparse vaginal bleeding with

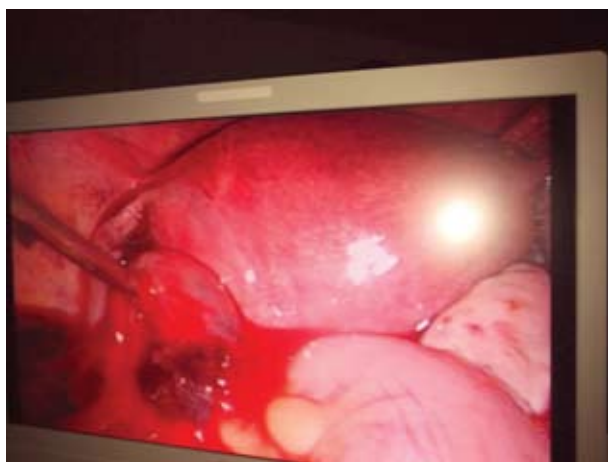


Fig. 1. Rupture in the middle third of the left fallopian tube.

an unremarkable previous medical history. Genital examination revealed a normal cervical finding with a small amount of dark blood in the vagina, and anteverted uterus of normal size. TVS examination showed an endometrium 15 mm thick and a clearly separated gestational sac measuring 15 mm in diameter situated in the cervix, with a visible yolk sac measuring 3.3 mm in diameter. A vital embryo with a crown-rump length (crl) of 2 mm was seen without free fluid in cul-de-sac space, with normal appearance of both ovaries.

The value of beta-chain of human chorionic gonadotropin ( $\beta$ -hCG) at admission was 6850 IU/L. Ultrasound guided gestational sac suction was performed and 75 mg of methotrexate was applied locally. Repetitive TVS of cervical pregnancy and serial monitoring of  $\beta$ -hCG showed an increase to 10042 IU/L at 72 h, followed by marked drop over every 48 hours from 3794 to 350, respectively, until no traces of  $\beta$ -hCG could be measured. There was no need of systemic administration of methotrexate and the patient was discharged after 15 days with normal ultrasound and gynecological findings.

### Case Report 3: Spontaneous Tubal Pregnancy

A 32-year-old patient, para 0, gravida 0, with six weeks of amenorrhea, referred by her primary gynecologist who suspected miscarriage, was admitted to the emergency department with unremarkable medical history. On the previous day, she felt mild pain in the central lower abdomen, accompanied by sparse bleeding. On the day of admission, she was completely without bleeding. Ultrasound examination on admission revealed an endometrium measuring 20 mm in thickness, with no free fluid, and ovaries of normal size and appearance.  $\beta$ -hCG was 3448 UI/L and repeated value 48 h later was 6110 IU/L. The patient remained asymptomatic, with no signs of intrauterine pregnancy. TVS then revealed a 10 mm gestational sac in the left fallopian tube, with a 2 mm yolk sac and vital embryo with crl 1 mm.

Laparoscopy was performed, and a thickened left fallopian tube was found with signs of tubal pregnancy. Left salpingectomy was performed. The postoperative course was uneventful, and the next day the patient was discharged in good general condition.

## Discussion

Heterotopic pregnancy is a condition that encompasses simultaneous occurrence of intrauterine and ectopic pregnancy, usually localized in the fallopian tube, with rare incidents occurring in the abdomen, cervix or ovaries. This situation is extremely rare and occurs in 0.08% of patients<sup>3</sup>, while its incidence increases with the use of ART. Risk factors for ectopic pregnancy include tubal pathology, pelvic inflammatory disease, the use of methods of assisted conception, endometriosis, previous abdominal or gynecological surgical procedures, patient age, smoking tobacco products, intrauterine device, and previous spontaneous abortions<sup>2,4</sup>. This is a potentially life-threatening condition, and undiagnosed ectopic pregnancy can lead to serious complications such as rupture of the fallopian tubes, hemoperitoneum, oophorectomy, salpingectomy, hysterectomy, and even death. Ectopic pregnancy can occur in the absence of any predisposing risk factors and it must always be included in the differential diagnoses<sup>5</sup>. Early diagnosis of ectopic pregnancy is sometimes difficult. Clinical findings are not specific. Ectopic pregnancy shows irregular increase in  $\beta$ -hCG values, but, for example, not in heterotopic pregnancy<sup>6</sup>. A detailed ultrasound examination of the patient must be an integral part of the examination<sup>7</sup>; however, it should be emphasized that ectopic pregnancy can be overlooked, especially in early pregnancy. In heterotopic pregnancy, the signs of intrauterine pregnancy may be misleading. Heterotopic pregnancy is nowadays more common in the wake of ART, and has been diagnosed as an asymptomatic occurrence in 54% of ART cases due to regular serial ultrasound controls and monitoring for possible heterotopic pregnancy<sup>8</sup>. Some patients present with symptoms of tubal rupture and hemorrhagic shock. Laparoscopy is then often both a diagnostic and therapeutic intervention, as was in our cases. About 70% of heterotopic pregnancy cases are diagnosed between the 5<sup>th</sup> and 8<sup>th</sup> week, 20% in the 9<sup>th</sup> and 10<sup>th</sup> week, and 10% in the 12<sup>th</sup> week of pregnancy<sup>8</sup>.

The etiology of cervical pregnancy, a particularly rare entity of ectopic pregnancy, as well as of other ectopic pregnancies remains unknown; alongside the predisposing factors mentioned earlier, it has additional predisposing factors such as uterocervical anomalies, cervical stenosis, and previous curettage.

Advanced cervical pregnancy can cause life-threatening bleeding and very often requires hysterectomy. It is considered a high risk ectopic pregnancy and early diagnosis is important. Ultrasound is the gold standard for diagnosing cervical pregnancy, as it is for all other ectopic pregnancies.

Treatment of ectopic pregnancy can be conservative or surgical and depends primarily on the severity of the patient's clinical condition. Obstetric medical history and the desire to maintain a possible pregnancy and planning future pregnancies should be considered. Heterotopic pregnancy requires a minimally invasive approach if possible in order not to jeopardize the existing intrauterine pregnancies. Conservative treatment includes an expectative approach or pharmacological therapy. Pharmacological therapy includes instillation of hypertonic solutions or pharmacologically active substances, with methotrexate being most common, administered directly in the gestational sac<sup>4</sup>. Methotrexate treatment can be administered systemically as well. In heterotopic pregnancy, the use of methotrexate is limited due to intrauterine pregnancy. Contraindications to the pharmacological approach include a ruptured fallopian tube, hemorrhagic shock, and size of ectopic pregnancy over 4 cm in diameter<sup>4</sup>. Surgical treatment consists of laparoscopy, which is the gold standard, and possible conversion to laparotomy<sup>9</sup>. Laparoscopic surgical methods are linear salpingotomy and extrusion (milking) of gestational sac, and partial and total salpingectomy. After treatment of heterotopic pregnancy, intrauterine pregnancy has a successful outcome in 50%-66% of cases<sup>7</sup>.

In conclusion, although a rare occurrence, ectopic pregnancy can pose a life-threatening condition, and often hinders further reproduction potential. The diagnostic process must be supplemented with detailed ultrasound examination and serial  $\beta$ -hCG measurements. Therapy may be conservative or surgical, with laparoscopy being the gold standard if possible. However, the prognosis differs in each individual case, with early diagnosis and proper treatment reducing the possible consequences for future reproductive life of women.

Although heterotopic pregnancy, ectopic cervical and tubal ectopic pregnancies are rare with spontaneous conception, they can occur without any existing

predisposing factors, and should always be considered in the diagnostic process.

## References

1. Lavanya R, Deepika K, Patil M. Successful pregnancy following medical management of heterotopic pregnancy. *J Hum Reprod Sci.* 2009;2(1):35-40.
2. Kasum M. Unilateral twin tubal pregnancy and subsequent heterotopic pregnancy in a patient following *in vitro* fertilization. *Acta Clin Croat.* 2009;48:451-4.
3. Ljuca Dž, Hudić I, Hadžimehmedović A. Heterotopic pregnancy in natural conception – our initial experience: case report. *Acta Clin Croat.* 2011;50:249-52.
4. Čanić T, Fistončić I. Laparoscopsko liječenje ektopične trudnoće. *Gynaecol Perinatol.* 2008;17(2):73-6. (in Croatian)
5. Brown J, Wittich A. Spontaneous heterotopic pregnancy successfully treated *via* laparoscopic surgery with subsequent viable intrauterine pregnancy: a case report. *Mil Med.* 2012;117(10):1227-30.
6. Neilson JP. Ultrasound for fetal assessment in early pregnancy. *Cochrane Database Syst Rev.* 2000;(2):CD 000182.
7. Louis-Sylvestre C, Morice P, Chapron C, Dubuisson JB. The role of laparoscopy in the diagnosis and management of heterotopic pregnancies. *Hum Reprod.* 1997;12(5):1100-2.
8. Singhal M, Ahuja CK, Saxena AK, Dhaliwal L, Khandelwal N. Sonographic appearance of heterotopic pregnancy with ruptured ectopic tubal pregnancy. *J Clin Ultrasound.* 2010;38(9):509-11.
9. Basile F, Di Cesare C, Quagliozzi L, *et al.* Spontaneous heterotopic pregnancy, simultaneous ovarian, and intrauterine: a case report. *Case Rep Obstet Gynecol.* 2012;2012:509694.

## Sažetak

### SPONTANA HETEROTOPIČNA, EKTOPIČNA CERVICALNA I EKTOPIČNA TUBARNA TRUDNOĆA – UVIJEK PRISUTNA DIJAGNOSTIČKA POTEŠKOĆA: PRIKAZ TRIJU SLUČAJEVA

*I. Erceg Ivkošić, R. Bauman, B. Ujević, O. Vasilj, I. P. Kojić, A. Ivkošić, D. Vukušić i T. Pavelić Turudić*

Incidencija heterotopičnih/ektopičnih trudnoća se u posljednje vrijeme povećava između ostalog i zbog sve veće upotrebe metoda pomognute oplodnje, ali ovi slučajevi, a naročito cervikalna trudnoća, iznimno su rijetki u spontanim zanošenjima. Prikazujemo tri bolesnice koje su se javile u našu Kliniku u tjedan dana: bolesnica sa spontanom heterotopičnom trudnoćom, druga s cervikalnom i treća s tubarnom trudnoćom. Sve su spontano zanijele, pravodobno dijagnosticirane i izliječene, ali naglašavamo da je osobita pozornost potrebna u dijagnozi i liječenju potencijalno fatalnih posljedica izvanmaterničnih trudnoća ako nisu prepoznate i liječene dovoljno rano, unatoč tako iznimno rijetkoj pojavnosti.

**Ključne riječi:** *Trudnoća, heterotopična; Trudnoća, tubalna; Trudnoća, ektopična; Cerviks uterusa – patologija; Prikazi slučaja*