

The general surgeon facing a ruptured heterotopic pregnancy. Case presentation and literature review

*El cirujano general frente al embarazo heterotópico roto.
Presentación de un caso y revisión de la literatura*

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Palabras clave:

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ABSTRACT

Heterotopic pregnancy has a low prevalence, but has increased in recent years due to assisted reproduction techniques. Clinical symptoms can be wide, so physicians must have in mind the complications, the most frequent of which is the rupture of the ectopic component, which leads to hemodynamic instability with a high rate of fetal and maternal mortality. We report the case of a patient previously treated with ovarian stimulation, diagnosed with heterotopic pregnancy with a twin intrauterine component; she had been diagnosed with acute appendicitis previous to the surgical resolution, and was treated with salpingectomy for the extrauterine product, without postsurgical complications and a good outcome for both the intrauterine product and the mother.

RESUMEN

El embarazo heterotópico tiene una prevalencia baja, aunque en los últimos años —debido a las técnicas de reproducción asistida— se ha incrementado su ocurrencia. La presentación clínica variable de esta patología obliga a considerar sus complicaciones finales; la más frecuente es la ruptura del componente ectópico con inestabilidad hemodinámica, asociada a un alto índice de mortalidad materna y del componente intrauterino. Se reporta el caso de una paciente con antecedente de estimulación ovárica, con embarazo heterotópico provocado con un componente intrauterino gemelar. Antes de la resolución quirúrgica, se le había diagnosticado con apendicitis aguda; se trató con una salpingectomía para el producto extrauterino, sin complicaciones postquirúrgicas, con evolución favorable de la madre y los productos intrauterinos.

INTRODUCTION

Heterotopic pregnancy is an exceptional event in which an intrauterine and an extrauterine pregnancy coexist.¹

Since it is so rare, cases are underreported.² Incidence among the general population was 1:10,000 to 1:30,000 pregnancies in 1948.³ Overall, current incidence of heterotopic pregnancy is estimated at around 1:7,000 to 1:15,000; 1:50,000 are considered spontaneous, having no relation to assisted fertilization,^{2,3} 1:3,889 are related to inflammatory pelvic disease, and 1:100-119 are associated with assisted reproduction techniques,^{1,4-6} almost as high as 1% in some series;^{3,5} the latter are termed “provoked heterotopic pregnancy”.²

Average survival rate of the intrauterine fetus in spontaneous heterotopic pregnancy ranges from 1:46,153 to 1:76,923 live births,² around 60 to 70% of cases.² Heterotopic pregnancy has a mortality rate six- to seven-fold higher than ectopic pregnancies overall.⁶

Risk factors for heterotopic pregnancy are the same as for ectopic pregnancy, including a history of ectopic pregnancy, tubal or pelvic surgery, assisted reproduction techniques with a large number of transferred embryos, ovarian hyperstimulation techniques, transfer close to the uterine tube, deep catheter insertion during transfer, quality of the embryos, hormonal milieu at the time of transfer, the use of gonadotropins, the amount of fluid used as medium for the embryos, as well as adhesions, related or not to endometriosis and pelvic inflammatory disease.³

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Implantation of an embryo on the wall of the uterine tube involves a high risk of rupture, because of the rich vascularity and local trophoblastic invasion, even with no fetal heart activity.³

Intrauterine and extrauterine pregnancy can coexist in different forms, i.e., intrauterine pregnancy and tubal, abdominal (1.3%), cornual, cervical or ovarian pregnancy (3.2%). A previous review showed that most extrauterine pregnancies were located in the fallopian tube (95%),^{1,7} most often the right one and its ampulla (80%).³

Clinical features of heterotopic pregnancy may vary widely.⁶ Patients present with abdominal pain in 83% of cases and hypovolemic shock with abdominal pain in 13%,⁴ with or without an adnexal mass.³ Vaginal bleeding occurs in 50% of cases. Likewise, there is an increasing number of heterotopic pregnancies with atypical features, such as epigastric pain and vomit.²

Around 15 to 50% of heterotopic pregnancies are asymptomatic before rupture and its complications happen. Some pregnancies may solve spontaneously,⁷ progressing to anembryonic pregnancy or fetal death.²

Complications of the uterine pregnancy are the same as those for a normal pregnancy, and their treatment may be surgical, including curettage or manual aspiration.²

Early diagnosis reduces maternal morbidity and mortality and preserves reproductive function.⁷

General surgeons should maintain a high level of suspicion in order to diagnose a heterotopic pregnancy early, that is, before rupture;^{1,4} it is worth noting the importance of multidisciplinary teamwork (gynecologists, general surgeons) before the diagnosis is confirmed. In 1878, Spiegelberg set the criteria for diagnosing ovarian pregnancy (*Table I*).

Clinicians should be suspicious of all female patients presenting with amenorrhea, abdominal pain, peritoneal irritation and enlarged uterus, even if an intrauterine pregnancy has been confirmed. Suspicion should be higher in women with risk factors for an ectopic pregnancy and in low risk women who have free fluid with or without an adnexal mass with an intrauterine pregnancy.¹

The presence of an intrauterine pregnancy, whether viable or not, may mask the ectopic component of a heterotopic pregnancy.¹ Seventy percent of ectopic pregnancies are diagnosed between 5 and 8 weeks of pregnancy, 20%, between 9 and 10 weeks, and 10% after 11 weeks.^{3,4}

Only in 57% of cases in literature the presence of heterotopic triplets was diagnosed before surgery. Around 78% are diagnosed after tubal rupture, with symptoms of acute abdomen.³

Ultrasound location of an intrauterine pregnancy does not effectively rule out an ectopic pregnancy. Identification of ectopic pregnancy using transvaginal ultrasound has a low sensitivity (26%); published reports show diagnosis is made in around 40% of cases with transvaginal sonography and 50% with abdominal sonography, mainly in patients under follow-up after the use of assisted reproduction techniques.² Ultrasound visualization of heart activity in both intrauterine and extrauterine pregnancies is important for diagnosis, but rare; other signs include empty gestational sac, gestational sac with a fetal pole, gestational sac containing a yolk sac or embryo, or an adnexal mass (cyst).⁷ During an ultrasound examination, an ovarian pregnancy is easily misdiagnosed as a corpus luteum.^{1,5} It is important to emphasize the need for systematic examination of the pelvis in the first ultrasound during the first trimester, even if an intrauterine gestational sac is already confirmed and there are no apparent risk factors.¹

There are isolated reports from around the world of spontaneous heterotopic ectopic

Table I. Spiegelberg criteria for ovarian ectopic pregnancy.

- The ipsilateral fallopian tube should be intact and clearly separate from the ovary.
- The gestational sac should occupy the anatomical site of the ovary.
- The gestational sac should be connected to the uterus by the ovarian ligament.
- Histological techniques must document ovarian tissue in the walls of the gestational sac.⁸

pregnancies, most of them not diagnosed during the first ultrasound.⁶ The use of Doppler ultrasound may improve the likelihood of diagnosis.⁶

β -HCG in itself is not useful for the diagnosis of heterotopic pregnancy; neither are serial tests of the hormone. The intrauterine pregnancy masks the changes in β -HCG of the extrauterine pregnancy and vice versa. Often the diagnosis is made during surgery or after the pathology report.¹

Abdominal paracentesis may reveal hemoperitoneum, but even if it is negative, a heterotopic pregnancy cannot be ruled out.⁴

The diagnosis in cases of pelvic pain in women is challenging because of the number of presenting symptoms and signs, which are unspecific. Conditions such as ectopic pregnancy, appendicitis, ruptured ovarian cyst, pelvic inflammatory disease, and ovarian torsion should be considered. Adequate assessment of the pain and its features, as well as a gynecological exam and reproductive history will help in reaching a differential diagnosis.^{2,7}

Factors influencing the treatment of heterotopic pregnancy include certainty of diagnosis, site of implantation and clinical features.¹ Most heterotopic pregnancies (72%) are surgically treated, while 27% receive conservative treatment.¹

In patients with no intrauterine pregnancy, conservative treatment involves the use of methotrexate. The following criteria must be met for its use: hemodynamic stability, no signs of hemoperitoneum or active bleeding, the ability and willingness to come for frequent office visits, a pregnancy no larger than 3.5 cm with no heart activity, and concentrations of β fraction of hCG lower than 5,000 mUI/ml.¹ Injection of potassium chloride has also been advocated as another form of treatment in case of non-ruptured ectopic pregnancy.⁴ Local treatment with KCl or hyperosmolar glucose is an option, especially in cases of pregnancy in the cervix.¹

Traditionally, laparoscopic treatment has been used for non-ruptured ectopic pregnancies at an early gestational age, whereas laparotomy has been used for ruptured ectopic pregnancies.³

Laparoscopic treatment is used most often, since it has demonstrated its effectiveness; besides, reports show that a minimally invasive approach improves the prognosis for intrauterine fetuses. It is currently considered the standard therapy,⁴ having both a diagnostic and a therapeutic role in stable patients.⁷

Bruhat et al. (1980) were the first to describe a laparoscopic method to preserve the uterine tube in ectopic pregnancy.⁷ The usual approach for an ovarian pregnancy is a wedge resection or ipsilateral oophorectomy. Manipulation of the uterus during surgery should be kept to a minimum, in order to prevent intra- or postoperative contractions. Particular attention should be paid to preserving blood flow to the ovary, especially to the corpus luteum. Salpingectomy is indicated in patients with irreparable damage or recurrent ectopic pregnancy, as well as concentrations of β -hCG over 5,000 mUI/ml, indicating possible obstruction of the fallopian tube. Salpingostomy is indicated in cases where women wish to become pregnant again. Theoretically, salpingostomy intends to preserve tubal integrity, unlike salpingectomy.⁷

Early diagnosis and laparoscopic treatment offer a favorable outcome without the postoperative inconveniences of laparotomy, and with the advantage over medical treatment of achieving immediate results. Besides avoiding the risk of manipulation of the uterus and open exposure, which may lead to uterine irritability and postoperative spontaneous pregnancy loss, this provides a definitive solution to the ectopic pregnancy and, at the same time, is safe for the intrauterine pregnancy.^{1,5}

Some reports suggest that, in patients undergoing laparotomy, there may be a 40% risk of loss of the intrauterine pregnancy.³ It is worth noticing that 27% of operations may end in a laparotomy due to unstoppable bleeding.¹

After treating the heterotopic pregnancy, most intrauterine pregnancies lead to the term delivery of healthy infants, whereas 26% end up in spontaneous miscarriage.²

The type of delivery depends on the characteristics of each patient; no specific indication exists for either vaginal delivery or cesarean section, unless there is an obstetrical indication. Usually, only one infant is born.²

CASE REPORT

This was a 37-year-old female patient with no personal history of surgery, chronic or degenerative disease; her mother suffered from hypertension. Menarche at the age of 13, 30 x 3; G1P0. History of ovarian stimulation treatment with unspecified drug for 6 months until her current pregnancy started. History of ovarian hyperstimulation syndrome three months before admittance; no complications reported. Eleven-week twin pregnancy (ultrasound gestational age).

The patient presented to the emergency department with sudden-onset continuous abdominal pain in the right iliac fossa (RIF) lasting for nearly 7 hours (visual analogue scale, 7/10), radiating to the ipsilateral lumbar region. She referred nausea, one episode of vomiting of gastric content, and no fever. Transvaginal bleeding occurred, approximately 15 ml. No medication had been taken and she referred no aggravating or relieving factors. Heart rate, 80 bpm; breathing rate, 21 bpm; blood pressure, 120/80, temperature, 37 °C. Physical examination revealed a globose abdomen with thick abdominal pannus and

decreased peristalsis in the RIF. Soft abdomen with guarding and both superficial and deep tenderness in the RIF. Uncertain hyperesthesia, mainly in the RIF. No uterine growth was palpable. McBurney's point tenderness, positive Von Blumberg sign, negative Rovsing sign, positive heel tap test. Blood tests: hemoglobin 13.2 g/100 ml, hematocrit 38%; leukocytes 26,900/mm³, segmented neutrophils 95%, BUN 10.2 mg/dl, urea 22.1 mg/dl, creatinine 0.58 mg/dl. Gynecological ultrasound reported pregnant uterus measuring 12.0 x 8.2 x 7.4 cm in its longitudinal, AP and transverse axes. The endometrial cavity contained two gestational sacs with normal location that appeared viable; pouch of Douglas with free fluid; right iliac fossa at the caecum location showed bowel loop with slightly thickened walls and no peristalsis; free fluid in the area. Appendix inflammation could not be ruled out (*Figure 1*). Laparoscopic appendectomy was scheduled. Intraoperatively, a 250-ml hemoperitoneum was found, together with an enlarged, ruptured right fallopian tube, consistent with ruptured ectopic pregnancy, plus an organized blood clot in the RIF, besides an enlarged pregnant uterus, normal left annex and right ovary with corpus luteum. Right salpingectomy, evacuation of hemoperitoneum, and peritoneal lavage were performed. A 19 French Blake drain was placed (*Figure 2*). The postoperative diagnosis was ruptured right heterotopic pregnancy (*Figure 3*). The patient was transferred to the postoperative care unit in a compensated state. On the first postoperative day, serous bloody drainage was 85 ml. A gynecological ultrasound was performed, reporting vitality and viability of both intrauterine fetuses (*Figure 4*). Forty-eight hours after surgery, the drainage was removed and the patient was discharged by the Ob/Gyn and general surgery departments. Pregnancy ended with the birth by cesarean section of two infants, male and female, at 35 weeks gestational age; indication for surgery was pre-eclampsia. No complications occurred during the procedure.

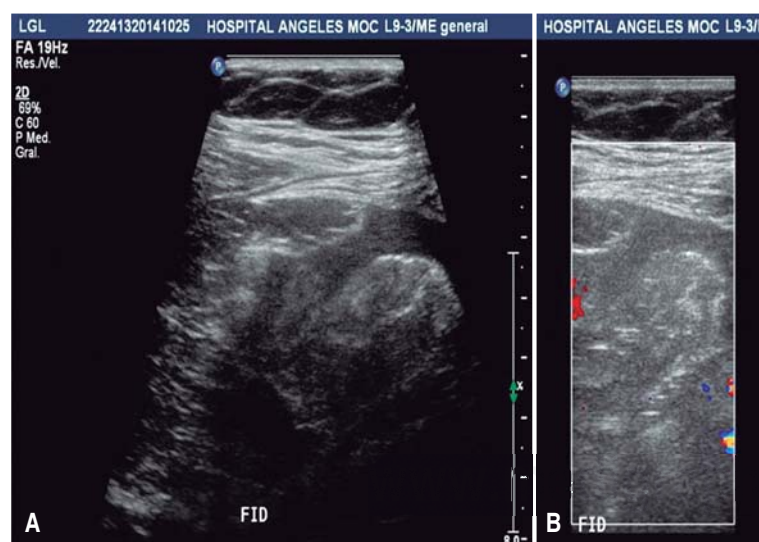


Figure 1. A. Abdominal ultrasound. In the RIF, at the caecum location, a bowel loop with slightly thickened walls and no peristalsis is visualized, as well as free fluid. B. With the use of color Doppler, no abnormal reinforcements are seen; inflammation of the appendix cannot be ruled out. Right ovary with an approximate volume of 18 cm³.

DISCUSSION

Heterotopic pregnancy is also related to the implantation and survival of two or more

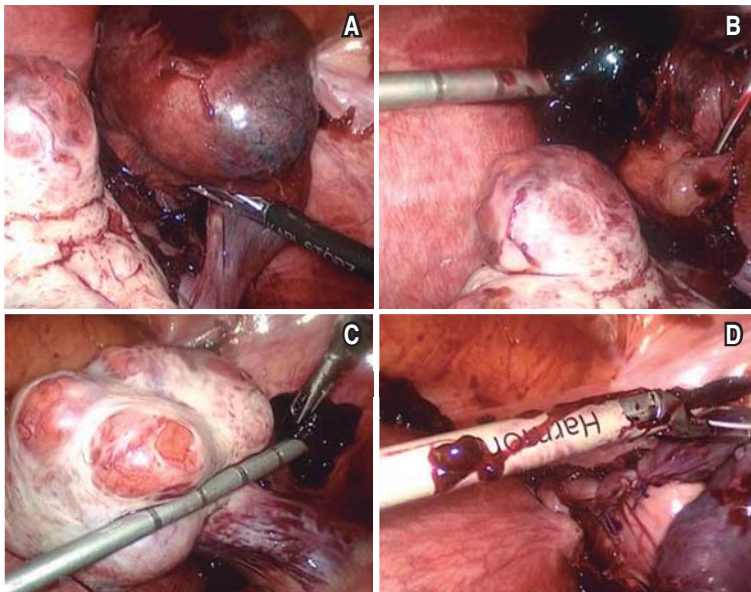


Figure 2. A. Right fallopian tube and ectopic component of the pregnancy. B. Rupture site of the ectopic component. Enlarged uterus and right ovary can be seen. C. Normal right ovary. D. Section of the fallopian tube and the ectopic component with Harmonic scalpel®.

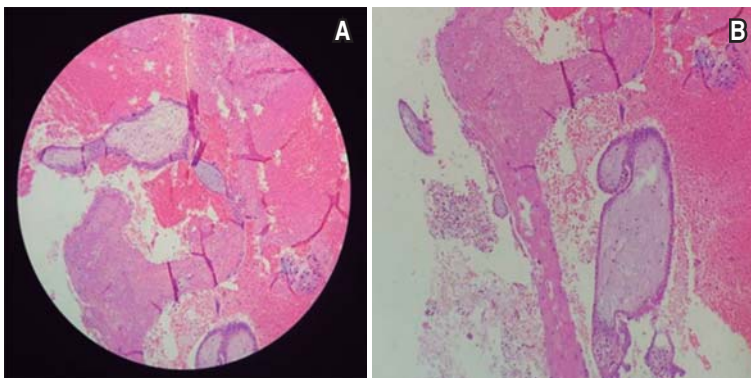


Figure 3. A. First-trimester villi inside the tubal lumen. B. Villi and decidua attached to the tubal wall.

intrauterine embryos that may reach an adequate gestational age for survival.⁹

The limited number of case reports of heterotopic pregnancy with a twin intrauterine component and an insidious evolution highlights our case report as an important reminder of the atypical presenting symptoms of this condition. It is also useful to point out the difficulty in diagnosing internal hemorrhage, as well as the role of the general surgeon confronting the

complications of conditions rarely seen in the emergency department.

Luna et al. (Mexico, 2011) reported 40 cases worldwide during 1982-2010, of which 8 were in Mexico. Out of the 40 cases, 9 were spontaneous and 3 were provoked heterotopic pregnancies; no case of twin intrauterine pregnancy associated to an ectopic pregnancy is mentioned.²

The diagnosis of heterotopic pregnancy requires a high level of suspicion, especially in patients with no history of assisted reproductive techniques or pelvic inflammatory disease.

Acute pain in the right iliac fossa makes it necessary to rule out certain conditions within the scope of general surgery.

Our case was a patient with a diagnosis of intrauterine twin pregnancy and a history of assisted reproductive techniques leading to complications (ovarian hyperstimulation syndrome). Low sensitivity of the transvaginal ultrasound (26%)² in these cases was apparent in our patient since, in spite of an adequate prenatal care, an early imaging diagnosis was missed.

Clinical features made it necessary to rule out obstetric complications such as threatened miscarriage, leading to the involvement of the Ob/Gyn department and the use of imaging studies to search for an etiology. Hemodynamic stability together with such clinical features as nausea, vomiting, anorexia and pain in the RIF, as well as the patient's evolution, all suggested a diagnosis of acute appendicitis. After ruling out obstetric complications and confirming this presumed diagnosis, it was decided to operate. It is worth noting that appendicitis is the most common non-obstetrical emergency during pregnancy.¹⁰

This is a clear example of the various presenting features of patients with heterotopic pregnancy, especially after obstetric complications have been ruled out and the general surgeon has considered the conditions most common during pregnancy.

Thanks to the advances in technology, the role of laparoscopy as both a diagnostic and a therapeutic tool in abdominal diseases is well known. This case was no exception, and a laparoscopic approach was decided. As in most reported cases, the diagnosis of heterotopic

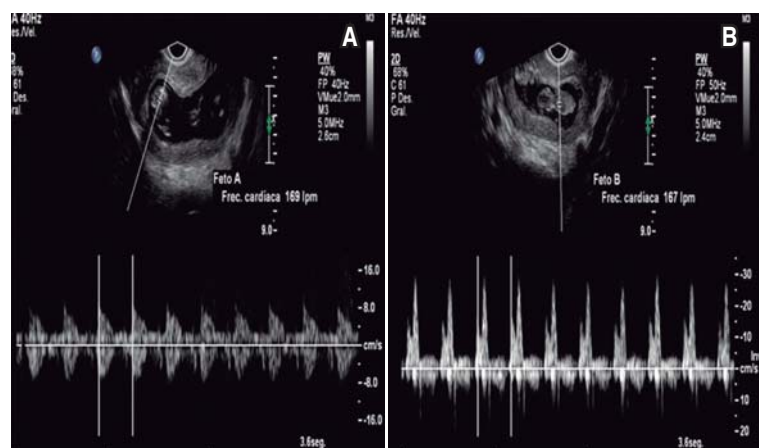


Figure 4. Obstetric ultrasound. **A.** Fetus A. Heart rate, 169 bpm. Gestational age: 11.3 weeks. Gestational sac diameter: 4.48 cm. Crown-rump length: 4.7 cm. Yolk sac diameter, 7 mm. Multiple musculoskeletal movements. No abnormalities. **B.** Fetus B. Heart rate, 169 bpm. Gestational age: 11.2 weeks. Gestational sac diameter: 4.0 cm. Crown-rump length: 3.7 cm. Yolk sac diameter, 7 mm. Multiple musculoskeletal movements. No abnormalities.

pregnancy was intraoperative, given that the ectopic component in the right fallopian tube was ruptured.

CONCLUSION

Heterotopic pregnancy is rare; most cases are associated with the use of assisted reproductive techniques, where there may be more than one intrauterine fetus.

Presentation is highly variable, from asymptomatic cases to hemodynamic disturbances with a high mortality rate. It is difficult to make a diagnosis before complications arise, and as for imaging studies, great technical ability is necessary.

Careful history taking and physical examination are important for the differential diagnosis from other conditions in the area of general surgery. The risk of death for the mother and the intrauterine fetus requires surgical treatment for the extrauterine pregnancy when there is hemodynamic instability.

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