Heterotopic Pregnancy: Case Report and Literature Review

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Abstract

Objective: To report for the first time in medical literature a case of multiple and heterotopic pregnancy, without previous use of ovulation induction drugs, ovarian hyperstimulation or in vitro fertilization, in order to contribute to new knowledge on this topic recently described in national and international medical literature.

Materials and Methods: A case of a multiple and heterotopic pregnancy diagnosed by transvaginal sonography, where a right salpingectomy performed laparoscopically and continuity of its twin-diamniotic dichorionic intrauterine gestation is presented. A review and analysis of the clinical case and literature report about cases of heterotopic pregnancy available on multiple databases was conducted: PubMed, Medline, Ovid.

Settings: University Medical School.

Patient: 35-years-old with spontaneous heterotopic multiple pregnancy.

Intervention: Emergency Laparoscopy.

Results: About 23 reported cases of multiple heterotopic pregnancies, of which 11 were by spontaneous conception, 6 after use of ovulation inducers and 9 by in vitro fertilization (IVF) were found, including three cases of multiple heterotopic pregnancies due to the use of ovulation inducers and two cases of in vitro fertilization. In found cases, none of them showed multiple spontaneous heterotopic pregnancy.

Conclusion: In literature, this case becomes the first specific reported case of heterotopic pregnancy without the use of ovulation induction and/or controlled ovarian hyperstimulation. It is known that the application of assisted reproduction techniques or controlled ovarian hyperstimulation is a clear risk factor for the occurrence of this obstetric event. The etiology of its spontaneous emergence is a clinical event to be studied.

Keywords: Heterotopic Pregnancy; Ectopic Pregnancy; Multiple Pregnancy; Laparoscopy

Introduction

Heterotopic pregnancy is defined as the presence of simultaneous pregnancies at two sites of different implantation. The most frequently observed manifestation is the presence of an intrauterine pregnancy and an ectopic pregnancy usually located in the uterine tube, most commonly in the ampullary portion (80%) [1]. It was first described in 1708 on the findings of an autopsy of a patient who died of an ectopic pregnancy [2]. Its incidence has increased since the implementation of assisted reproductive technologies (ART), in the context of in vitro fertilization (IVF), for transfer of multiple embryos [3]. The estimated incidence is one case per 30,000 - 50,000 live births. Intrauterine product survival is around 60 to 70%. Based on this assumption, the incidence of survival of a product of spontaneous heterotopic pregnancy is, on average, 1:46.153 to 1:76.923 live births. By reviewing a case report, the ultrasonographic diagnosis of this type of pregnancy is difficult, striking described that approximately 40% was detected by vaginal study and up to 50% of cases by abdominal study. Usually, ectopic pregnancy is complicated and almost in all cases it needs to be finished with an emergency surgery due to maternal hemodynamic instability. The minimally invasive surgery is the most recommended treatment option when there is hemodynamic compromise [4]. The heterotopic pregnancy is diagnosed in the presence of multiple pregnancies, with one or more coexisting intrauterine

pregnancies with an ectopic pregnancy. The most common factors that predispose to ectopic pregnancy are tubal surgery and pelvic inflammatory disease (PID) [5]. For the diagnosis of heterotopic pregnancy quantifying the beta fraction of human chorionic gonadotropin (hCG) and transvaginal ultrasound are used; the latter has proven to be an invaluable tool since BHCG levels in these cases have erratic behavior. Despite the above, there remains confusion during its implementation because the ectopic pregnancy can be confused with a broken hemorrhagic cyst, hemorrhagic corpus luteum or other adrenal mass. The data of importance that physicians should consider for ultrasonographic differentiation, depend on the duration of pregnancy; when they are less than five weeks, it would be necessary to look for the possible gestational sac, between the fifth and seventh week, a gestational sac and yolk sac can be found and, after the seventh week an embryo of between 5 and 10 mm, with cardiac activity may be distinguished [6].

General Objective

Report a case of multiple and heterotopic pregnancy without a history of use of ovulation induction or ovarian hyperstimulation by in vitro fertilization (IVF), in order to contribute to new knowledge about this medical condition rarely described in national and international literature.

Specific Objectives

- Determine the risk factors that influence multiple heterotopic pregnancies.
- Know the available case reports in the medical literature.
- Identify the etiology, diagnosis and treatment of multiple heterotopic pregnancies.
- To report a case of multiple spontaneous heterotopic pregnancy.

Case Report

A 35-year-old woman who is in her second pregnancy with a history of previous abortion, controlled rheumatoid arthritis and Sjogren’s syndrome, who consulted on May-29-2012 to a medical center for reproductive desire, and was handled without inducing ovulation to regulate her cycles and study of signs of hyperandrogenism. A month later, on July-10-2012 she presented an early pregnancy status with gestational age of 5 weeks 4 days according to last menstrual period (LMP) of June 1, 2012 for an expected delivery date on March 10, 2013. On July 18, 2012 the patient presented to a third level hospital with a clinical picture of pelvic pain of 8 days of evolution with increased intensity with little vaginal bleeding. Obstetric transvaginal ultrasound was performed, and intrauterine twin pregnancy of 6 weeks plus 5 days was detected and also a right ectopic pregnancy (heterotopic multiple gestation). Therefore it was decided to hospitalize and schedule the patient for emergency laparoscopy. A full right salpingectomy with resection of ectopic pregnancy was performed with continuity of its twin-diamniotic dichorionic intrauterine pregnancy. The patient continued with their normal gestation attending prenatal care. On January-11-2013 the patient presented to an emergency department with 32 weeks 1 day of gestation, presenting vaginal bleeding and spontaneous rupture of membranes, with a regular uterine activity of good intensity. Diagnosis of twin preterm labor, premature rupture of membranes. Initial treatment of uterine inhibition with nifedipine, lung maturation with betamethasone and magnesium sulfate for neuroprotection. Since regular uterine contractions and cervical dilation continued, it was decided to schedule a cesarean section. Newborn one: male with Apgar 7/10 and newborn 2 female with Apgar 6/10.

Figure 1: Ectopic pregnancy.
Methodology

This is a descriptive study in which it is reported a clinical case which helps to give information on multiple heterotopic pregnancy, a condition little reported in literature. A review and analysis of the case and literature that reports and informs about these types of cases in the database was made: Pubmed, Medline, Ovid; terms relating to "Multiple Heterotopic Pregnancy" and "Multiple Heterotopic Pregnancy" were used in the period from the first half of 2014, where, case reports and review articles in which there were selected and reviewed a total of 627 related titles, of which a total of 23 items in full text were reviewed, identifying etiology, diagnosis and treatment methods thereof. In this case the informed consent for review and publication of the patient and his partner was obtained, as well as the compliance with current legislation on confidentiality with ethical principles of research.

Results

As shown, there are approximately 23 reported cases of heterotopic pregnancies, of which 11 were in spontaneous conception, 6 after the introduction of ovulation inducers and 9 by in-vitro fertilization, including three cases of multiple heterotopic pregnancy, one reported by use of ovulation induction, and, two by in vitro fertilization. In the cases found, there was no evidence of any spontaneous multiple heterotopic pregnancy reported. In the literature this becomes the first report of a specific case without the use of inducing ovulation and/or controlled ovarian hyperstimulation.

Mancera R and Arredondo M in their article Spontaneous Heterotopic Pregnancy: A 28-years old Patient, with seven weeks of gestation according to LMP date. No history of PID, abortions, intrauterine device use, surgeries or ART, presented to hospital due to a throbbing type in the abdomen, intensity 8/10, continuous, in hypogastrium and both iliac fossa, that increased with movement. Pain increased during hours. On admission to the emergency department: BP: 100/60 mmHg, heart rate of 78 bpm, respiratory rate of 20 per/minute and temperature: 36.4°C. Unaltered cardiopulmonary system, hyperalgesic soft abdomen, superficial pain, predominance in the right iliac fossa; vaginal touch, antverted uterus, painful to mobilization, closed cervix, and plastron is felt towards the posterior fornix and annex law, no bleeding or vaginal discharge. Transvaginal ultrasound revealed an uterus 8 x 7 x 5 cm, with an image inside the uterine cavity suggesting a corresponding gestational sac of seven weeks of gestation with live embryo inside, a cystic image on the right tube, the another embryo with cardiac activity. It was concluded that this was a heterotopic pregnancy: a viable intrauterine seven weeks of pregnancy and an ectopic tubal law [6].

Mendivil C., et al. In their article Heterotopic Pregnancy: Ultrasound diagnosis and early laparoscopic management. Case report and review of the literature: 25-year-old G0P0A0, consulted the emergency department for presenting a clinical 15-day history of little genital bleeding that three days ago was associated with cramping abdominal pain in the right lower quadrant. Amenorrhea 8 of weeks. No history of ARTs or previous pelvic infections. Hemodynamically stable, with no signs of peritoneal irritation but with localized pain in right iliac fossa, so her income for study and treatment is decided. Qualitative BHCG positive: 2500 IU/ml. Transvaginal ultrasound described the presence of an intrauterine pregnancy with live embryo, of nine weeks, and, in turn described gestational sac in the right tube with living embryo. It was decided to perform a surgery with laparoscopic salpingectomy which is done with extraction of gestational sac and embryo. Postoperative was satisfactory and micronized progesterone used with normal progression of intrauterine pregnancy [7].
Mendivil C., et al. in their article Heterotopic Pregnancy: Ultrasound diagnosis and early laparoscopic management. Case report and review of the literature: 25-year-old G0P0A0, consulted the emergency department for presenting a clinical 15-day history of little genital bleeding that three days ago was associated with cramping abdominal pain in the right lower quadrant. Amenorrhea 8 of weeks. No history of ARTs or previous pelvic infections. Hemodynamically stable, with no signs of peritoneal irritation but with localized pain in right iliac fossa, so her income for study and treatment is decided. Qualitative BHCG positive: 2500 IU/ml. Transvaginal ultrasound described the presence of an intrauterine pregnancy with live embryo, of nine weeks, and, in turn described gestational sac in the right tube with living embryo. It was decided to perform a surgery with laparoscopic salpingectomy which is done with extraction of gestational sac and embryo. Postoperative was satisfactory and micronized progesterone used with normal progression of intrauterine pregnancy [7].

Alex J Childs, Anthony B Royek., et al. in their triple article Heterotopic Pregnancy after gonadotropin stimulation and intrauterine insemination. Diagnostic laparotomy: 30 year-old patient with 7 weeks of gestation. Intrauterine twin pregnancy after treatment referral. In week 9 of gestation she presented with pain in the left lower quadrant, vomiting and constipation. A urinalysis showed blood, so, a renal ultrasound reported as usual from urological perspective showed attachments without masses. The patient was discharged and readmitted a week later and had to be hospitalized because of persistent symptoms. Handling began with a presumptive diagnosis of diverticulitis; treated for 48 hours with no improvement in symptoms. She was taken to sigmoidoscopy that showed no evidence of colitis or diverticulum, but, a CT-scan revealed a 7.5 cm left adnexal mass compressing the sigmoid colon. Transvaginal ultrasound showed a solid mass of 10.5 cm in the left annex with a differential diagnosis of an ovarian mass or pedunculated fibroid. With this clinical picture it was decided to perform laparoscopic surgery with findings of a hemoperitoneum with an ectopic pregnancy rupture in the left fallopian tube. She was discharged 2 days after the postoperative period. Histological examination of the left fallopian tube and its contents revealed chorionic villi, confirming the diagnosis of triple heterotopic pregnancy [9]. It is worth noting that for these cases, the recommended image study is the MRI without contrast.

Judy Yeh MD, Natali Aziz MD, Jane Chueh MD, in their article Conservative Treatment of Abdominal Heterotopic Pregnancy: Woman 34 years of age, G1PO. 17 weeks of gestation, conceived by ART. Abdominal ultrasound revealed an intrauterine pregnancy with normal amniotic fluid, along with a second viable pregnancy with severe oligohydramnios and separated placenta in the left lower quadrant of the abdomen. These findings were confirmed with a pelvic examination by MRI, which showed the implantation of the placenta in the mesentry of the colon. The patient was advised and decided to undergo selective reduction of abdominal pregnancy. She had vaginal delivery without fetal maternal complications at 40 weeks of gestation. An ultrasound performed 5 months after delivery, showed a 5.3 cm left asymptomatic pelvic mass with visible fetal parts coinciding with a head and limbs. There was still visible color Doppler flow in the part of the placenta. BHCG was negative. Finally it was decided to lead to surgery for removal of abdominal remains of the ectopic pregnancy [10].

According to Salih Tas, Elif Aylin., et al. in their article Heterotopic Pregnancy Scar. How should this be handled?: Patient, 24-years-old, G2P1, vaginal bleeding. Their first child was born by transverse cesarean section three years ago. The transvaginal ultrasound shows two gestational sacs, one located in the fundus and the other in the cesarean scar. Containing both, viable embryo sacs of 8 weeks and 4 days of gestation. Together with the patient and family, selective embryo reduction of cesarean scar pregnancy is planned. The pregnancy continued normally until 34 weeks when the patient’s admission to hospital with preterm labor. A cesarean section was done and during surgery, profuse vascularization was observed in the lower uterine segment extending to the peritoneum of the bladder with residual mass in the cesarean scar; heterotopic pregnancy palpable in the lower uterine segment with the subsequently born of a healthy girl weighs 2,310 grams, through a transverse incision above this mass [11].

Najim Muhammad Khan, Sadaf plot., et al. in their paper: Laparoscopic management of Heterotopic Pregnancy-A rare cause of acute abdomen in women, report: 31-year-old with 22 weeks of gestation, consulted the emergency department for abdominal pain in the lower right side. Tenderness in the right iliac fossa. Inflammatory markers reveal a WBC count of 17000 and C-reactive protein 32. For a presumptive diagnosis of acute appendicitis. An abdominal ultrasound showed the presence of a live intrauterine pregnancy and an ill-defined right adnexal mass closely with the appendix and the right ovary of 35 mm diameter. Through a laparoscopy, a mass in the right uterine tube attached to the appendix and the right ovary with a blood clot in the iliac fossa on the same side was found. The appendix appeared normal. Inspection revealed a mass in the middle of the tube, and a dissection salpingectomy of right fallopian tube was performed. She was discharged two days later. Ectopic pregnancy was confirmed by microscopic anatomy. The patient completed her

intrauterine pregnancy without problems and gave birth to a healthy girl at 37 weeks of gestation [12].

Sun Yazaki Sun, Edward Araujo Junior, Julio Elito Junior, et al. in their article Heterotopic Pregnancy diagnosis using ultrasound and MRI in the first trimester of pregnancy: Case report: 33 years-old patient, in her fifth pregnancy. Transvaginal ultrasound: Pregnancy of 10 weeks and 4 days was diagnosed with irregular presence of heterogeneous mass in the abdominal pelvic region with dimensions of 12.8 × 11 × 10 cm. Ovaries with normal size and texture. Abdomen tense and examination mass extending up to 6cm above the symphysis pubis, painful, with no signs of peritoneal irritation. MRI of the pelvis: Large left adnexal mass measuring 13cm was observed. In view of the clinical characteristics, it was decided to perform an exploratory laparotomy. Bleeding was found in the Pouch of Douglas, and heterotopic pregnancy is confirmed [13].

Thomas J Schroeppel and Shannon Kothari in their article The Heterotopic Pregnancy: a rare cause of hemoperitoneum and acute abdomen report: Patient 35-years-old, G8P4A4 with 13 weeks of gestational age, presented to the emergency department with clinical symptoms of abdominal pain associated with nausea and emesis, aggravated by movement. History of: Multiple episodes of PID, surgical history: appendectomy. On physical examination, temperature: 36.2°C, heart rate of 80 bpm and BP: 105/70 mmHg. On palpation of the right upper quadrant discomfort feeling. Abdominal ultrasound revealed ascites. The patient was admitted to hospital. Transvaginal ultrasound diagnosed ruptured corpus luteum cyst and normal intrauterine pregnancy. The abdominal pain was resolved and the patient was discharged the next day. Twelve days later, pain reappeared in the right upper quadrant and returned to the emergency room. A new ultrasound showed an increased amount of liquid in the Morrison pouch and splenorenal space. The patient was admitted to intensive care unit. The next two controls showed decrease in hemoglobin values, 8.4 g/dl and 7.7 g/dl, respectively. A CT-scan was obtained. A lot of hemoperitoneum was identified and active extravasation in the right pelvis. She was taken to surgery and laparotomy. Ectopic pregnancy in the fallopian right tube was confirmed and a salpingectomy was performed. Pathology confirmed that products of conception were consistent with an ectopic pregnancy. The patient was discharged after 3 days and went on to have an uncomplicated intrauterine pregnancy full-term born vaginally [14].

Rimpy Tandon, Poonam Goel, Pradip Kumar Saha, and Lajya Devi in their paper: Spontaneous heterotopic pregnancy with tubal rupture: case report and literature review. Patient 24-year-old primiparous woman of Indian origin was presented to the emergency department with a history of a brief episode of loss of consciousness and severe abdominal pain four hours of evolution. She was 8 weeks pregnant. It was a spontaneous conception and no history of abortion, infertility, PID or any history of abdominal surgery. She was pale, heart rate of 120 bpm and BP: 80/60 mmHg. On abdominal examination, sensitivity was observed in the lower quadrant with defense and significant stiffness. The pelvic examinations evidenced anteverted uterus and a palpable mass in the right annex; cervical movements were painful, but no bleeding. Her hemoglobin was 4.2 g/dl and BHCG positive. Transvaginal ultrasonography revealed a viable intrauterine pregnancy of 8 weeks and an echogenic mass 3.3 × 2.2 cm near her right ovary with a central anechoic area. A moderate amount of liquid was observed in the pouch of Morrison and heterotopic pregnancy diagnosed with rupture of the tube. An emergency laparotomy revealed a 8 weeks pregnant uterus and right tube rupture with presence of hemoperitoneum. Right salpingectomy was performed. She had a transfusion of four units of blood during and after surgery, and postoperative period was uneventful. The histopathology of the resected specimen showed the presence of chorionic villi that confirmed a viable pregnancy. The patient was discharged and followed up with intrauterine pregnancy. At 38 weeks of gestation the patient had a spontaneous labor and birth of a healthy male baby weighing 2.6kg. Mother and baby were discharged within three days after birth [15].

Ben-Ami MF, Ushakov Panski Vaknin Z, Herman A., et al. in their article Heterotopic Pregnancy recurrent after bilateral salpingectomy in a patient with IVF: Case report: 35-years-old patient with a history of bilateral salpingectomy due to heterotopic pregnancy. A year earlier she had undergone laparoscopy to release serious peridnexal adhesions. The pregnancy was achieved after IVF Five weeks after embryo transfer, she was admitted to the emergency room because of crampy abdominal pain accompanied by an episode of syncope. One day before admission, transvaginal ultrasound revealed a gestational sac with intrauterine pregnancy, a yolk sac and embryonic pole with pulse suitable for seven weeks gestation. Her medical history includes mutation of factor V Leiden, treated with low molecular weight heparin, 40 mg/day, and chronic anemia treated as well. On admission, BP was 90/44 mmHg, and pulse of 120 bpm, diffuse lower abdominal tenderness without signs of peritoneal irritation. Hemoglobin levels of 8.3 mg/dl. Transvaginal ultrasound revealed not only a regular intrauterine sack seven weeks gestation, but also adjacent to the right ovary, a 2 × 2.5 cm mass. Fluid accumulation was also observed in

the sack. Emergency laparoscopy revealed a 2 cm mass located on the right tubal stump, covered with blood clots and hemoperitoneum. After aspiration of clots, a site of active bleeding in the active part of the fallopian tube was found. The stump was resected cautiously in cutting and coagulation avoiding the penetration and damage of the intrauterine pregnancy. The postoperative recovery was successful and the patient was discharged in general good condition. The pathology reported tube resection that confirmed the presence of trophoblastic tissue. The intrauterine pregnancy went smoothly and ended with the birth of a baby to term [16].

Po-Jen Cheng, Chieh Ho-Yen and Qiu Jian-Tai in their article Heterotopic Pregnancy in a Cycle of Natural Conception Presenting as Hematometra, report the case of a young woman, multiparous who consulted the gynecology clinic with vaginal discharge of dark reddish brown fluid with discomfort in the left lower quadrant. The patient had six weeks of amenorrhea. BHCG: 4878 IU/dl. No history of PID, abdominal surgery or ART. A transvaginal ultrasound showed an intrauterine pregnancy with a small gestational sac surrounded by a fluid-filled space. Furthermore, an echogenic mass present in left fallopian tube was observed. Shortly after admission, the patient suddenly worsened her abdominal pain. A repeated transvaginal ultrasound showed increased fluid in the uterine cavity. Emergency laparoscopy confirmed that the patient had an ectopic pregnancy in the ampullary portion of the left tube, and about 650 ml of blood in the peritoneal cavity. Conservative salpingectomy followed by dilation and curettage to remove gestational tissue of the uterine cavity was performed. The pathology report confirmed heterotopic pregnancy [17-28].

Conclusions

It is known that the application of reproduction techniques including use of ovulation induction and/or controlled ovarian hyperstimulation are clear risk factors for the occurrence of this obstetric event. But this report demonstrates the possibility of occurrence of similar symptoms in patients without exposure to this type of treatment. However, the possibility that the underlying pathologies in the patient in case reported to be risk factors for this, is not precluded. One could suggest performing an analytical review of reported cases evaluating additional risk factors to reproductive treatments that may be considered as a risk factor for the occurrence of heterotopic pregnancy.

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Conflict of Interest

It is stated that there is no conflict of interest, and that we did not have any financial help or meetings where this paper work was presented.

Bibliography


