



Therapeutic Approaches in Cases with Heterotopic Pregnancy: A Retrospective Analysis of Six Patients

Heterotopik Gebelik Olgularında Tedavi Yaklaşımları: Altı Hastanın Retrospektif Analizi

Heterotopik Gebelik ve Tedavi / Heterotopic Pregnancy and Treatment

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Özet

Amaç: Kliniđimizde takip edilen heterotopik gebelik (HG) olgularının hastaneye başvuru řikâyetleri, uygulanan tanı ve tedavi yöntemleri ile gebelik sonuçlarını deđerlendirmek. **Gereç ve Yöntem:** Hastanemiz elektronik kayıt sisteminden 1 Ocak 2010 ile 30 Haziran 2013 tarihleri arasında gebelik durumu ve diř gebelik tanı kodları ile kliniđimize yatışı yapılan hastalar tarandı. HG tespit edilen, cerrahi veya medikal tedavi uygulanan 6 hasta çalışmaya dâhil edildi. **Bulgular:** Üç yıllık dönem içerisinde kliniđimizde tedavi edilen 6 HG olgusu saptandı. Hastaneye başvuru řikâyetleri arasında 3 hastada karın ağrısı ve vajinal kanama, 2 hastada hemoperitoneuma bađlı akut batin tablosu saptanırken, 1 hastanın ise rutin kontrol amacıyla hastaneye başvurduđu ve transvajinal ultrasonografi ile heterotopik gebeliđinin tespit edildiđi görüldü. Akut batin tablosu ile başvuran 2 hastaya laparotomi ile salpenjektomi, tubal rüptür saptanmayan ve hemodinamik açıdan stabil olan 2 olguya laparoskopisi ile konservatif cerrahi uygulanırken kalan 2 olguya ise ultrasonografi eřliđinde diř gebelik kesesi içerisine uygulanan potasyum klorür ve metotreksat ile tedavi edildiđi saptandı. HG nedeniyle tedavi uygulanan 6 gebemizden üçünün canlı dođum yaptıđı, diđer üçünde ise gebelik kaybı yaşandıđı tespit edildi. **Tartışma:** Özellikle üremeye yardımcı yöntemlerle gebe kalan hastalarda intrauterin gebelik kesesi tespit edilse dahi HG yönünden dikkatli bir pelvik muayene yapılması hem maternal hem de fetal mortaliteyi azaltmada önemli bir rol oynar.

Anahtar Kelimeler

Diř Gebelik; Heterotopik Gebelik; İnfertilite

Abstract

Aim: To assess presenting complaints, diagnostic and therapeutic approaches and outcomes of pregnancy in cases with heterotopic pregnancy managed in our clinic. **Material and Method:** We screened the electronic database of our hospital for patients admitted to our clinic between January 1, 2010, and June 30, 2013, using diagnostic codes of pregnancy and ectopic pregnancy. Six patients with a heterotopic pregnancy who underwent either surgical or medical therapy were included in the study. **Results:** Six cases with a heterotopic pregnancy were detected who had been managed at the clinic during a 3-year period. The presenting complaints in 3 cases were abdominal pain and vaginal bleeding and in 2 case an acute abdomen due to a haemoperitoneum. A heterotopic pregnancy was detected by transvaginal sonography in one patient who presented to the clinic for routine control. Salpingectomy via laparotomy was performed in the 2 patients who presented with acute abdomen, and conservative surgery via laparoscopy was performed in 2 patients without haemodynamic instability and tubal rupture. The remaining 2 patients were treated with potassium chloride and methotrexate instillation into the gestational sac via ultrasound guidance. Of the 6 patients treated for heterotopic pregnancy, there were 3 live births and 3 foetal losses. **Discussion:** A careful pelvic examination for heterotopic pregnancy plays an important role in reducing both maternal and foetal mortality, particularly in cases in which pregnancy is achieved by assisted reproductive techniques, even in cases of detection of intrauterine pregnancy.

Keywords

Ectopic Pregnancy; Hp; Infertility

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Introduction

Heterotopic pregnancy (HP) is defined as the simultaneous occurrence of intrauterine and extrauterine pregnancy [1]. Ectopic pregnancy is generally observed at tubes, but it may also occur at a caesarean scar or have a cervical, ovarian or abdominal localisation in rare instances [2]. Although it is rarely seen during natural conception cycles, the incidence has raised to 1:100 due to the increasing use of assisted reproduction techniques in infertile patients [2, 3]. It has been suggested that tubal injury is the most important risk factor for the development of HP. Other potential reasons include tubal surgery, pelvic inflammatory disease, a history of ectopic pregnancy, endometriosis and in vitro fertilisation [2-4]. The most frequent symptoms of HP are abdominal pain and vaginal bleeding, but patients can occasionally present with acute abdomen resulting from a haemoperitoneum [1]. High-resolution transvaginal sonography (TVUS) is the primary diagnostic method, and management may vary depending on the patient's haemodynamic status, localisation of the ectopic pregnancy and desire of the family for a child [2].

Here, we discuss the presenting complaints, diagnostic and therapeutic approaches and pregnancy outcomes of 6 patients with HP managed in our clinic.

Material and Method

This retrospective study was carried out at the Department of Gynecology and Obstetrics at our university, was planned in accordance with the Second Declaration of Helsinki (revised in 2008) and was approved by the local ethics committee.

Screening the electronic database of the hospital identified records of 113 cases admitted to the clinic with an ectopic pregnancy (ICD codes; O00.0, O00.2, O00.8 and O00.9) and pregnancy (Z33) between January 1, 2010, and June 30, 2013. Of these, 6 patients with a diagnosis of HP who underwent either surgical or medical therapy were included in the study, and 107 patients with ectopic pregnancy alone were excluded. In all the patients, age at treatment, gestational age, presenting complaints, results of pretreatment evaluations, such as sonography, therapeutic approaches employed and pregnancy outcome were reviewed.

TVUS was employed as a preoperative imaging modality. The size of the mass was calculated by measuring the largest 2 diameters in cases in which a gestational sac or an adnexal mass was detected.

The treatment methods employed were classified into 2 groups: surgical and medical. Surgical treatment was further subclassified as follows: radical surgery via laparotomy or laparoscopy and organ-sparing surgery. The medical treatments were injection of either potassium chloride or methotrexate into the gestational sac.

Results

During the 3-year period, 113 patients with ectopic pregnancy were followed in our clinic. Of these, HP was detected in 6 of the patients (5.31%).

The mean age of the patients was 30.83±5.41 (24–38) years, and the mean number of pregnancies was 1.67±1.63 (0–4) in patients diagnosed with HP. As predisposing reasons for HP, one patient had a history of pelvic inflammatory disease, and another patient had a history of tubal factor infertility. Pregnancy was achieved by in vitro fertilisation in 2 patients (unexplained infertility and male factor), by recombinant gonadotropin stimulation in one patient. As far as we detected, only last case that having pregnancy in spontaneous cycle has no risk factor. The presenting complaints in 3 cases were abdominal pain and vaginal bleeding and acute abdomen due to a haemoperitoneum in 2 cases. HP was detected by TVUS in one patient who presented to the clinic for routine control.

Table 1 summarises the demographic and clinical characteristics of the patients. Medical therapy was achieved by visualization of foetal heart pulse cessation through either injection of 5 ml (2 mEq/mL) of potassium chloride or 25 mg methotrexate into gestational sac. These interventions in two patients are performed via transabdominal route by using a 20 G spinal needle. For visualization purpose, transabdominal ultrasonography was used. We applied single dose intramuscular injection of 500 mg OH-progesterone prophylactically for patients who had surgery.

Discussion

HP, which has an increasing incidence due to widespread use of assisted reproduction techniques in infertile patients, is an important obstetric problem that can cause maternal and foetal mortality if not diagnosed at an early stage [5, 6]. It has been suggested that a delay in diagnosis can cause maternal mortality of 1% and foetal mortality of 45–65% [2]. It is important to perform a meticulous pelvic sonography evaluation to detect HP even in cases with a positive pregnancy test and an intrauterine gestational sac on sonography after infertility treatment [1]. Diagnosis of a HP can be challenging and a high index of suspicion is mandatory for early diagnosis and appropriate treatment. High-resolution TVUS is the primary diagnostic method in HP [2]. The findings of a complex cyst in the adnexal area, a haematosalpinx, a tubal ring and a foetal heart rate and free fluid in the Douglas space should raise the suspicion of a HP [7]. The serum beta-human chorionic gonadotropin (β -hCG) level, which is an important laboratory tool for the diagnosis of an ectopic pregnancy, is not considered as a useful marker in HP due to the presence of intrauterine pregnancy. In HP, the β -hCG level can be detected as normal or elevated [3]. In the present study, all the cases were diagnosed using TVUS. However, the β -hCG levels were not evaluated. Therefore, the β -hCG levels cannot be

Table 1. Gestational age, findings of transvaginal sonography, treatment modalities used and outcomes of pregnancy in cases.

	Gestational week	Mass finding on TVUS (FHR)	Treatment Employed	Surgical Method	Prognosis of pregnancy
Case 1	7	Right adnexal 18x36 mm (+)	KCl	None	C/S on week 37
Case 2	8	Left adnexal 20x40 mm (+)	MTX	None	Abortion
Case 3	8	Right adnexal 21x42 mm and free fluid (-)	L/T	Salpingectomy	Abortion
Case 4	7	Right adnexal 18x38 mm (+)	L/S	Salpingostomy	C/S on week 39
Case 5	9	Left adnexal 23x44 mm and free fluid (-)	L/T	Salpingectomy	C/S on week 38
Case 6	8	Right adnexal 16x38 mm (+)	L/S	Salpingostomy	Abortion

Abbreviations: C/S: Cesarean section; KCl: Potassium chloride; L/T: Laparotomy, L/S: Laparoscopy; MTX; Methotrexate; TVUG: Transvaginal sonography; FHR: Fetal heart rate

used in the differential diagnosis.

In cases of HP with tubal localisation, patients can present with acute abdomen and hypovolemic shock secondary to tubal rupture [1]. In such cases, the differential diagnosis includes a haemorrhagic corpus luteum cyst, adnexal torsion, a neoplasm and abortion [1, 2]. The use of TVUS and β -hCG should be beneficial in the differential diagnosis of such clinical entities.

The main issue in the treatment of the HP is to be as minimally invasive as possible to preserve the developing intrauterine pregnancy. The management of HP may vary depending on the patient's haemodynamic status, localisation of the ectopic pregnancy, skills of the surgeon and preference of the family regarding intrauterine pregnancy [2]. In general, salpingectomy via laparotomy is the choice of treatment in patients who present with acute abdomen due to tubal rupture. Conservative surgery and medical therapy should be employed in cases without haemodynamic instability and rupture, as well in those who want to have children. Laparoscopic salpingostomy is frequently used in conservative surgery, and injection of potassium chloride and methotrexate into the ectopic gestational sac is used in medical therapy [4, 5, 6, 8]. When a review of the literature, it is obvious that there is no unique attitude in medical treatment of HP. Treatment of KCL, placental tissue continues to develop until birth and it can cause acute bleeding. In the treatment of MTX, there are reports on the varying effects of the drug when used at differing stages of fetal development. The most critical exposure time is between six and eight weeks [5, 6]. Whereas, it is suggested that KCL and MTX is a safe and efficacious treatment method in HP [8]. Salpingectomy via laparotomy was warranted in 2 of the cases in the current study who presented with acute abdomen and excessive free fluid in the Douglas space on the TVUS. Conservative therapy was considered inappropriate in these patients. Foetal reduction was achieved by injections of potassium chloride and methotrexate in 2 cases who had an ectopic gestational sac of 18×36 mm and 20×40 mm in size and a foetal heart beat within the gestational sac but no finding of rupture. Laparoscopic salpinostomy was employed as conservative surgery in 2 other cases who had a tubal foetal heart rate.

One study proposed that the rate of intrauterine pregnancy loss increases 2–3 fold in patients who undergo surgical or medical therapy for a HP compared to those with intrauterine pregnancy alone and that two-thirds of these patients have live births [2]. In the current case series, pregnancy resulted in abortion in 3 cases who underwent surgical and medical therapy, and 3 women had live births. When the outcomes of pregnancy were assessed in the context of the surgical and medical therapy, the rates of healthy pregnancy and abortion were identical in both groups (50%).

In conclusion, a careful pelvic examination for HP plays an important role in reducing both maternal and foetal mortality, particularly in cases in which pregnancy is achieved with treatment of infertility such as assisted reproductive techniques and intrauterine insemination, even in cases of detection of intrauterine pregnancy.

Competing interests

The authors declare that they have no competing interests.

References

1. Sun SY, Araujo JE, Elito JJ, Rolo LC, Campanharo FF, Sarmiento SG, et al. Diagnosis of heterotopic pregnancy using ultrasound and magnetic resonance imaging in the first trimester of pregnancy: a case report. *Case Rep Radiol* 2012;2012:317592. doi: 10.1155/2012/317592.
2. Ercan CM, Keskin U, Coksuer H, Balıkcı E, Ergun A. A case of heterotopic pregnancy in a spontaneous cycle. *Perinatal Journal* 2012;20(2):63-7.
3. Deka D, Bahadur A, Singh A, Malhotra N. Successful management of heterotopic pregnancy after fetal reduction using potassium chloride and methotrexate. *J Hum Reprod* 2012;5(1):57-60.
4. Schroepfel TJ, Kothari SN. Heterotopic pregnancy: a rare cause of hemoperitoneum and the acute abdomen. *Arch Gynecol Obstet* 2006;274(3):138-40.
5. Georgiou EX, Domoney C, Savage P, Stafford M. Heterotopic abdominal pregnancy with persistent trophoblastic tissue. *Acta Obstet Gynecol Scand* 2011;90(5):551-3.
6. Sijanovic S, Vidosavljevic D, Sijanovic I. Methotrexate in local treatment of cervical heterotopic pregnancy with successful perinatal outcome: case report. *J Obstet Gynaecol Res* 2011;37(9):1241-5.
7. Elito JJ, Montenegro NA, Soares RC, Camano L. Unruptured ectopic pregnancy: diagnosis and treatment. State of art. *Rev Bras Ginecol Obstet* 2008;30(3):149-59.
8. Litwicka K, Greco E, Prefumo F, Fratelli N, Scarselli F, Ferrero S, Iammarrone E, Frusca T. Successful management of a triplet heterotopic caesarean scar pregnancy after in vitro fertilization-embryo transfer. *Fertil Steril* 2011;95(1):291-3.