

Heterotopic Pregnancy: Tubal Ectopic Pregnancy And Monochorionic Monoamniotic Twin Pregnancy: A Case Report

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Abstract

Background: Heterotopic pregnancy, simultaneous presence of intrauterine and extrauterine pregnancies is a very rare condition. In recent years, however, the widespread use of assisted reproductive technologies has dramatically increased the incidence of this condition. Early diagnosis of heterotopic pregnancy is important to decrease mortality and morbidity and to preserve future fertility.

Case: This report describes a 35-year-old female at 10 weeks' gestation with an intrauterine monochorionic monoamniotic twin pregnancy after ovulation stimulation with clomiphene citrate and intrauterine insemination who presented complaining of left lower quadrant abdominal pain. After physical and transvaginal ultrasonographic examinations monochorionic monoamniotic twin pregnancy and intra abdominal bleeding was diagnosed which led us to the decision of performing a emergency laparotomy. The right fallopian tube was found to be ruptured due to extrauterine pregnancy localized in the ampullary region and right salpingectomy was performed.

Conclusion: Heterotopic pregnancy must be considered in the differential diagnosis of abdominal pain in the first trimester, especially in patients who conceived by means of assisted reproductive technology.

Keywords: Heterotopic pregnancy, twin pregnancy.

Monokoryonik monoamniotik ikiz gebelikle birlikte görülen heterotopik gebelik olgusu

Amaç: Heterotopik gebelik, intrauterin ve ekstrauterin gebeliğin birlikte bulunduğu, özellikle risk faktörleri yoksa oldukça nadir rastlanan bir durumdur. Son yıllarda yardımla üreme teknolojilerindeki gelişme sonucu heterotopik gebelik insidansında artış meydana gelmiştir. Heterotopik gebeliklerin erken tanı ve uygun tedavisi mortalite, morbidite ve gelecekteki fertilitate açısından önemlidir.

Olgu: Klomifen sitrat ile ovulasyon indüksiyonu sonrası yapılan IUI uygulaması ile gebe kalan hasta, ani başlayan kasık ağrısı şikayeti ile müracaat etti. Muayene ve transvajinal ultrasonografi ile değerlendirime sonucunda monokoryonik monoamniotik ikiz gebelik ve batin içine kanama ile uyumlu bulgular saptandı. Acil olarak opere edilen hastada rüptüre sağ ektopik gebelik saptandı ve sağ salpenjektomi operasyonu uygulandı. Halen onaltıncı gebelik haftasında monokoryonik monoamniotik ikiz gebelik sağlıklı olarak devam etmektedir.

Sonuç: Özellikle yardımla üreme teknikleri sonucu oluşan gebeliklerde birinci trimesterde karın ağrısı şikayeti ile başvuran hastaların ayırıcı tanısında heterotopik gebelik de akılda tutulmalı ve zamanında uygun şekilde tedavi edilmelidir.

Anahtar Sözcükler: Heterotopik gebelik, ikiz gebelik.

Background

Heterotopic pregnancy is the name of simultaneous presence of intrauterine and extrauterine pregnancies and seen in at 1/30000 to 1/7963 of all pregnancies.¹ It is first defined by Duverney in the year of 1708, as an autopsy finding in a patient died because of ectopic pregnancy and also simultaneously having intrauterine pregnancy.¹ However, its incidence is increasing in women having past pelvic inflammatory disease, tubal surgery, ectopic pregnancy history and women conceived with assisted reproductive techniques (ART) and incidence raises up to 1/100.² There is heterotopic pregnancy cases seen with intrauterine twin pregnancy defined at the end of first trimester in literature.³ Here a tubal heterotopic pregnancy case seen with intrauterine monoamniotic monoamniotic twin pregnancy conceived with an application of intrauterine insemination (IUI) made after ovulation induction with clomiphene citrate (CC) is reviewed.

Case

The patient (35 age, gravida: 0, parity: 0) who had pre-diagnose of infertility due to male mate had ovulation induction with CC and subsequently IUI applied to our clinic for routine antenatal examination at eighth week of the pregnancy for the first time. After resulting of physical examination and ultrasonographic evaluation, monoamniotic monoamniotic twin pregnancy is determined and antenatal routine tests are prompted. In the patient applying to our clinic after two weeks with inguinal pain acute abdominal findings and in transvaginal ultrasonography monoamniotic monoamniotic double vital fetus inside the smooth contoured regular single gestational sac, hyperechoic solid mass in size 30x45 mm at the right adnexial region and findings related to intraabdominal bleeding observed and withthat decided for operation. In laparotomy finding compatible with ruptured ectopic pregnancy is determined at right tubal ampullar region (Figure 1). Right salphengectomy is performed in patient and taken to her bed. It is reported tubal ectopic pregnancy in pathology report. At the same day, after opera-

tion it is observed that both fetuses are vital by ultrasonography. No complication occurred and the patient discharged in third day after operation with cure to come back for routine pregnancy controls. The patient is still in 16th gestational week and her pregnancy is lasting without any problem.



Figure 1. Intraoperative viewing of heterotopic pregnancy at right tuba. (EG: ectopic pregnancy).

Discussion

While spontaneous ectopic pregnancy is seen in 1-2% of all of the pregnancies,⁴ it is seen as 5% of the pregnancies after ART.² Risk factors increasing the frequency of ectopic pregnancy are, past pelvic inflammatory disease (PID), intrauterine device (IUD), assisted reproductive techniques, endometriosis, past abdominal surgery, tubal surgery and sexually transmitted diseases and these risk factors seem similar to the heterotopic pregnancies. The accused mechanism in ectopic and heterotopic pregnancies especially seen after ART is immigration of transferred embryo to damaged tuba and unrejection from tuba by peristalsism.^{1,5}

Early diagnose of heterotopic pregnancy is hard because of insufficient clinic symptoms. Reece et al¹ defined four widespread symptoms and findings. These are; abdominal pain, adnexial mass, peritoneal irritation and increasing in the size of uterus. While Tal et al² reported abdominal pain in 83% and abdominal tenderness with hipovolemic shock in 13% of the heterotopic pregnancy cases also reported vaginal bleeding in

half of the patients. Finding of vaginal bleeding that can be coincided in ectopic pregnancies is rarely seen in heterotopic pregnancies because of intact endometrium of intrauterine pregnancy.⁶ In our case too no clinical finding is seen until developing of tubal rupture related to heterotopic pregnancy but, patient applied to our clinic with peritoneal irritation findings occurring because of intraabdominal bleeding as a conclusion of rupture.

The most important diagnose method in diagnosing heterotopic pregnancy is high-resolution transvaginal ultrasonography. In high risk patients, especially the ones that ART is applied 4-6 weeks after embryo transfer it is offered to make ultrasonographic evaluation for diagnose of both intrauterine pregnancy and for differential diagnose of ectopic and heterotopic pregnancy routinely.⁷ But, especially the diagnose of heterotopic pregnancy is very hard even with ultrasonography and only 10% of cases can be diagnosed in preoperative period and it is known that sensitivity of sonography is only 56 %.⁸ In our case too, routine antenatal physical examination was made before 2 weeks of her admittance to our clinic with acute table, intrauterine monoamniotic, monochorionic pregnancy was determined but did not find any finding compatible with heterotopic pregnancy.

Intrauterine pregnancy diagnose with ultrasonography, is very easy if it is made by an experienced physician. But, in ectopic pregnancies monitoring of gestational sac at adnexial region or fetal cardiac activity is a rarely seen finding.^{7,8} Furthermore, determining of intrauterine pregnancy does not frequently bring to mind the ectopic pregnancy and heterotopic pregnancy diagnose can be missed. For this reason, especially in the presence of intrauterine pregnancy more than one, it must be considered that there can be an ectopic pregnancy simultaneously and to make differential diagnose adnexial regions must examined with ultrasonography carefully. In pregnancies developing especially after ART probability of heterotopic pregnancy increases and even if these pregnancies are evaluated with ultrasonography, its diagnose is very hard in early period. In the differential diagnosis of the patients admitting with the complaint of abdominal pain

and especially the ones having acute abdomen and peritoneal irritation findings in first trimester heterotopic pregnancy must not be forgotten. Because, majority of heterotopic pregnancies, also as in our case, are diagnosed in emergency laparotomy performed after it came symptomatic.

Although majority of heterotopic pregnancies case is placed at tubae, abdominal, cervical, cornual and ovarian heterotopic pregnancies are also reported,⁹ even bilateral tubal heterotopic pregnancy with intrauterine pregnancy is presented.¹⁰ For this reason, if suspected from heterotopic pregnancy it is required to evaluate fallopian tubes bilaterally, abdomen and pelvis before surgery.

Generally it is not easy to differentiate anembryonic adnexial ectopic pregnancy from hemorrhagic corpus luteum cyst in ultrasonography. Morphologic ultrasonography findings help in differential diagnose. These are; seeing a loop around the gestational sac in 2-6 mm thickness, following of trophoblastic invasion into wall of tuba and typically, following of echogenity at around of the ovarian tissue which is more intense than the echogenity rounding corpus luteum.⁹ Monitorization of both intrauterine and extrauterine cardiac activity in ultrasonography helps in diagnose but, it is a rarely determined finding. Additionally fetal cardiac activity beginnings can be at different times. Hirsch et al¹¹ reported intrauterine fetal cardiac activity observed 6 days after the extrauterine cardiac activity. Tal et al² reported that 70% of heterotopic pregnancies are diagnosed at 5-8th week of pregnancy, 20% of them at 9-10th week and 10% after 11th week.

As intrauterine pregnancy can go on without problem in heterotopic pregnancies, sometimes ectopic pregnancy forms hematoma itself and causes deterioration of the pregnancy in a way. As told here, a heterotopic pregnancy case is reported which the intrauterine pregnancy resulted with missed abortus.¹²

In diagnose and following of heterotopic pregnancies, it is thinkable that β -hCG and progesteron levels can be useful beside the ultrasonography. But, placental excessive production of β -hCG in intrauterine pregnancy can cause a

false in diagnosing the heterotopic pregnancy by masking subnormal β -hCG production that is produced in ectopic pregnancy. Because of this reason, serial β -hCG following is not useful in heterotopic pregnancies.⁹

There is not a standart follow method for heterotopic pregnancy because it is a rare event. Generally, there is a thought that laparoscopy is the most successful method in diagnose and treatment of heterotopic pregnancy.^{3,13} But, there are also publications that reports laparotomy is more successful.^{1,2} Even it carries surgical and anesthetic risks both for mother and fetus, surgical approach is fundamental especially in acute cases. In laparotomy requiring acute cases, operation must be ended with minimal trauma and minimal anaesthesia for continuation of healthy intrauterine pregnancy. Error or delay in diagnose leads to increase in mortality, major blood losses and on the same time conservative tubal surgery can not be done in tubal heterotopic pregnancies.^{3,14} Although it is reported that more than 40% of intrauterine vital pregnancies are resulted with loss after surgery,¹⁵ there are also publications reporting that pregnancy is not deteriorated and continued healthy and resulted with healthy deliveries.² In the literature other treatment methods are described except surgical treatment. In studies including a few cases some methods are reported like ultrasonography guided local methotrexate, an antiprogesterone called RU 486 (mifepriston), injection of prostaglandins or potassium chloride and also aspiration of heterotopic pregnancy via transvaginal tract.¹⁶ But, generally methotrexate, RU 486 and prostaglandins are not used because of their teratogen effects on intrauterine pregnancy.⁹ For that reason in cases suspected from diffuse hemoperitoneum and in conditions that patient's hemodynamic impaired laparotomy must be considered primarily. Besides this in patients with stable hemodynamic and suspected heterotopic pregnancy, laparoscopy made for diagnose and treatment is a confidential method.^{3,13} In our case intraabdominal bleeding is determined and patient is treated with laparotomy performed in emergency conditions, tubal surgery could not made because tubal damage was severe relating to tubal rupture and it is needed to perform salpingectomy. Early diagnose of hetero-

topic pregnancies carries great importance about patient's mortality, morbidity, continuation of a healthy intrauterine pregnancy and patient's future fertility. In such cases maternal mortality is 1% and intrauterine fetus mortality rate is 45-65%.¹⁷ In the year of 1970 Smith and Siddique reported that 35-54% of intrauterine pregnancies after heterotopic pregnancy are ended in a healthy way.¹⁸ In recent years, in followings of more than 150 cases reported as heterotopic pregnancy after surgery, it is reported that approximately 66% of intrauterine pregnancies are resulted with live deliveries.² This progress is related to developing in diagnose and treatment and also especially to the frequent follow of patients taking infertility treatment. In our case too, although intrauterine pregnancy is mono-chorionic-monoamniotic pregnancy is going on healthy in 16th gestational week.

Conclusion

In recent years, it is seen an increase in heterotopic pregnancy incidence as parallel to increase in ART and early diagnose and treatment of these patients came into prominence. In first trimester pregnancies, especially in ART used pregnancies, patients applying with inguinal pain and peritoneal irritation findings, even if normal pregnancy is followed heterotopic pregnancy must be considered in differential diagnosis. In diagnose transvaginal ultrasonography takes an important place but, it is not an accurately confidential method. Early diagnosing and proper treatment are very important about patient's mortality, morbidity, healthy continuation of intrauterine pregnancy and especially preserving of future fertility. The most frequently used methods in diagnose and treatment of these pregnancies are laparoscopy and laparotomy in proper cases.

References

1. Reece EA, Petrie RH, Sirmans MF, Finster M, Todd WD. Combined intrauterine and extrauterine gestations: a review. *Am J Obstet Gynecol* 1983; 146: 323-30.
2. Tal J, Haddad S, Gordon N, Timor-Tritsch I. Heterotopic pregnancy after ovulation induction and assisted reproductive Technologies: a literature review from 1971 to 1993. *Fertil Steril* 1996; 66:1-12.
3. Alex JC, Anthony BR, Brian L, Pamela GG. Triplet heterotopic pregnancy after gonadotropin stimulation and intrauterine insemination diagnosed at laparoscopy: A case report. *South Med J* 2005; 98: 833-5.

4. Saraiya M, Berg CJ, Shulman H, Green CA, Atrash HK. Estimates of the annual number of clinically recognized pregnancies in the United States, 1981-1991. *Am J Epidemiol* 1999; 149: 1025-9.
5. Oliveria FG, Abdelmassih V, Abdelmassih Oliviera S, Abdelmassih R, Nagy ZP. Heterotopic triplet pregnancy: report and video of a case of a ruptured tubal implantation with living embryo concurrent with an intrauterine twin gestation. *Reprod Biomed Online* 2002; 5: 313-6.
6. Jacobson A, Galen D. Heterotopic pregnancies and IVF. *Fertil Steril* 1990; 54: 179-80.
7. Guirgis RR, Craft IL. Ectopic pregnancy resulting from GIFT and IVF: Role of ultrasonography in diagnosis and treatment. *J Reprod Med* 1991; 36: 793-6.
8. Ankum WM, Van der Veen F, et al. Transvaginal sonography and human chorionic gonadotrophin measurements in suspected ectopic pregnancy: a detailed analysis of a diagnostic approach. *Hum Reprod* 1993; 8: 1307-11.
9. Michael V, Christodoulos A, Grigorios H, Nikolaos A. Heterotopic pregnancy in a natural conception cycle presenting with tubal rupture: a case report and review of the literature. *Eur J Obstet Gynecol Reprod Biol* 2003; 106: 79-82.
10. Hun-Shan P, Jesse Chuang, Su-Fang C, Bih-Chwen H, Yu-Hung L, Yieh-Loong T, Shih-Chia H, et al. Heterotopic triplet pregnancy: report of a case with bilateral tubal pregnancy and an intrauterine pregnancy. *Hum Reprod* 2002; 17: 1363-6.
11. Hirsch E, Cohen L, Hecht BL. Heterotopic pregnancy with discordant ultrasonic appearance of fetal cardiac activity. *Obstet Gynecol* 1992; 79: 824-5.
12. Çepni İ, Öçal P, Benian A, İdil M. Yardımla üreme teknikleri ve heterotopik gebelik; bilateral tubal ve intrauterin gebelik. *Perinatoloji Dergisi* 2004; 12: 50-3.
13. Louis SC, Morice P, Chapron C, Dubuisson JB. The role of laparoscopy in the diagnosis and management of heterotopic pregnancies. *Hum Reprod* 1997; 12: 1100-2.
14. Bhargav MM, Sanjeev B, Ralph S, Satnley AS, Bryan RT. Heterotopic pregnancy presenting as an acute abdomen: a diagnostic masquerader. *Am Surg* 2000; 66: 307-8.
15. Oehninger S, Kreiner D, Bass MJ. Abdominal pregnancy after in vitro fertilization and embryo transfer. *Obstet Gynecol* 1988; 72: 499-502.
16. Fernandez H, Lelaidier C, et al. Nonsurgical treatment of heterotopic pregnancy: a report of six cases. *Fertil Steril* 1993; 60: 428-32.
17. Schenker J, Ezra Y. Complications of assisted reproductive techniques. *Fertil Steril* 1994; 61: 411-22.
18. Smith DJH, Siddique FH. A case of heterotopic pregnancy. *Am J Obstet Gynecol* 1970; 108: 1289-90.