Scholars Journal of Medical Case Reports
Sch J Med Case Rep 2014; 2(9):635-638
ISSN 2347-6559 (Online)
ISSN 2347-9507 (Print)

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com
DOI: 10.36347/sjmcr.2014.v02i09.018

Heterotopic multiple pregnancy: report of a case with bilateral ectopic pregnancy and triplet intrauterine pregnancy

Dr Smita Sinha*[1], Dr Harkiran Kaur Khaira[2], Dr Manjot Kaur[3], Dr Arun Kumar Maria[4]
[1]Assistant Professor, [2]Professor, Department of Obstetrics & Gynaecology, [3]Associate Professor, Department of Radiodiagnosis, [4]Professor, Department of Medicine, Adesh Institute of Medical Sciences & Research, Bhatinda-151101, Punjab, India

***Corresponding Author:**
Name: Dr Smita Sinha
Email: obsusg@gmail.com

Abstract: Literature is replete with case reports of heterotopic pregnancy (HP). With IVF, incidence of heterotopic pregnancy increased. Although bilateral ectopic with an intrauterine pregnancy has been reported, there is no report of bilateral ectopic with triplet intrauterine pregnancy in literature so far. Here we report a 25 year old gravida 2 para 1 with previous premature preterm delivery. Present pregnancy was conceived following ovulation induction with 150 mg/day clomiphene citrate. Ultrasonography revealed bilateral ectopic with three intrauterine viable foetuses. An expectant approach was considered appropriate. Five weeks after diagnosis, intrauterine foetuses continued to grow at normal pace while left tubal ectopic resolved. Right tubal ectopic resolved by 20 weeks gestation. The pregnancy was strictly followed up with optimal progesterone support, timely steroid prophylaxis and managed several times for threatened preterm labour. At 33 weeks 3 days, three live babies were delivered by emergency caesarean.
Keywords: heterotopic pregnancy, bilateral ectopic, expectant management, preterm labour

INTRODUCTION

Spontaneously occurring heterotopic pregnancy (HP) was first described by Duverney in 1708 at autopsy of a woman who had died of ruptured ectopic [1]. The risk of HP significantly increases after ovulation induction [2]. It is 1:900 in clomiphene citrate induced pregnancy and rises to 1% in assisted reproduction [3].

Successful outcome of a twin intrauterine pregnancy where the tubal ectopic had been managed by laparoscopic salpingostomy at 7 weeks has been reported[4]. Here we report a triplet intrauterine pregnancy with bilateral ectopic managed expectantly.

CASE REPORT

A 25 year old (gravida 2, para 1) presented to us with history of preterm premature delivery 5 months ago. The baby died due to extreme prematurity. Anxious to conceive again she took treatment from a local practitioner. She had been given tablet clomiphene citrate 150 mg from day 2 to day 6 of cycle. Follicular imaging was not done and she conceived following timed intercourse in the same cycle. Urine pregnancy test was positive at 42 days of amenorrhoea and she had come to our outpatient department for antenatal care. An ultrasound evaluation of pregnancy was done at the first visit.

Ultrasonography revealed ongoing viable triplet intrauterine pregnancies each of about 9 weeks gestation (Figure 1). A more diligent search also showed a right tubal pregnancy of 5 weeks 4 days with absent cardiac activity , as also a left tubal gestational sac of 5 weeks (Figure 2). Ring of fire sign was seen around the ectopic pregnancies.

Fig-1: Ultrasonography showing triplet intrauterine pregnancies

Fig-2 : Ultrasonography showing a right tubal pregnancy of 5 weeks 4 days & a left tubal gestational sac of 5 weeks

The patient was admitted and kept under observation in hospital. An expectant approach was followed keeping preparation ready for immediate laparotomy in event of tubal rupture. Progesterone support given and weekly ultrasonography was done to follow up the pregnancies. The intrauterine triplets continued to grow. Nuchal translucencies of intrauterine fetuses were within normal limits at 11 weeks. Both ectopic pregnancies did not show any further growth or regression till 11 weeks. The left ectopic completely regressed at 13 weeks. In view of previous preterm delivery, cervical length was monitored which was 4 cm at 13 weeks. Right tubal ectopic disappeared by 20 weeks.

Glucose tolerance test at 24 weeks was within normal limits. The patient had threatened preterm at 26 weeks, managed with parentral followed by oral isoxsuprine. Steroid prophylaxis (betamethasone) was given. Intramuscular 17α hydroxy progesterone caproate was given biweekly. She developed iron deficiency anaemia (Hb 7.5 g%) inspite of oral iron supplementation but responded well to parenteral iron therapy.

Again at 31 weeks she started having uterine contractions. The cervix dilated to 2cm and its length was shortened to 2.5 cm. She received parentral isoxsuprine for 4 days, followed by oral doses. Rescue dose of betamethasone was given. Considering tachyphylaxis on continued usage of isoxsuprine she was switched over to oral nifedipine. The pregnancy continued on oral nifedipine as tocolytic. At 33 weeks 3 days she went into preterm labour; cervix dilated to 6 cm. Emergency cesarean was done as the first triplet was in shoulder presentation. She delivered three live babies; the first male baby weighing 1.2 kg, second male baby 1.4 kg and the third baby is female 995 g. Per operatively bilateral tubes were seen to be normal, with no evidence of ectopic pregnancies. The first born received surfactant and all the babies are doing well in the neonatal period.

DISCUSSION

Heterotopic pregnancy is the simultaneous occurrence of intrauterine and extra uterine pregnancies with an incidence of 1/30000 of all spontaneously occurring pregnancies[1]. With use of ovulation induction and assisted reproduction the incidence has increased significantly[5].

This patient in focus was an otherwise healthy patient with short married life and no history of infertility. Having lost a baby to extreme prematurity she was too anxious to conceive. She had resorted to unguided ovulation induction with high dose clomiphene citrate. Clomiphene citrate blocks the negative feedback mechanism of rising estradiol levels that normally reduce the FSH (follicle stimulating hormone). Thus continuous flow of FSH encourages multiple follicle development which is relatively common[6]. The risk of multiple gestation is therefore increased and is estimated at 8- 13% [7-10]. The vast majority of these are twin pregnancies, but the risk may be reduced considerably by ultrasound monitoring and withholding hCG (human chorionic gonadotrophin), IUI (intrauterine insemination) or intercourse if more than 2 follicles of more than 15 mm are seen[11]. Most of these data however pertain to cases that have had infertility of some duration. It is known that clomiphene citrate causes more than 50% increase in endogenous FSH in infertile patients[9]. It can be argued that there was hyper responsiveness in this patient resulting in too many follicles. Moreover, no more than 100 mg/day of clomiphene is used in the hope of preventing multiple pregnancy and hyper stimulation[12]. This patient had been given 150 mg/day. The occurrence of pentaplet in this patient can be accounted for by the administration of not indicated, unmonitored, high dose clomiphene. It has also been demonstrated by studies that clomiphene alters the local progesterone to estradiol ratio,

disturbing oviductal peristalsis[13]. Early rising of progesterone would favour opening of isthmus and myorelaxation of the tube [14] and account for tubal pregnancy.

In almost all cases of heterotopic pregnancy patients have presented with symptoms varying from subtle to shock. This patient who presented with no symptoms, the diagnosis of the coexistence of ectopic pregnancy with intrauterine pregnancy required diligent search. Many patients are minimally symptomatic and careful ultrasound survey of pelvis is required especially in the face of documented intrauterine pregnancy to identify ectopic[15]. Transvaginal ultrasonography has revolutionized the assessment of early pregnancy problems allowing clearer visualization of both normal and abnormal gestations [16]. Ectopic pregnancy can be identified by the presence of a gestational sac with foetal pole with or without cardiac activity, a mass with hyper echoic ring around gestational sac i.e. an empty tubal ring sign, with a positive predictive value of 100% [17]. An inhomogeneous adnexal mass or blob sign has 99.6% positive predictive value for diagnosing ectopic [18]. In this patient right tubal ectopic was diagnosed by presence of gestational sac with foetal pole but no cardiac activity, and left tubal ectopic was diagnosed by empty tubal ring sign.

The problem that arose was that of management of the ectopic. Most case reports as well as textbooks [19-21] described surgical management for heterotopic pregnancy. Surgical therapy has been the traditional mainstay, but involves surgical and anaesthetic risks to both the mother and intrauterine pregnancy[15]. A 40 precent loss of intrauterine pregnancy after laparoscopy has been reported [22]. Recently medical management of heterotopic pregnancy has gained popularity. Injection of potassium chloride to reduce ectopic pregnancy has been used. Several case reports of successful resolution of ectopic at tubal and interstitial sites after administration of potassium chloride injection exist [23- 25]. In a series of twenty heterotopic pregnancies reported after IVF and embryo transfer, tubal pregnancy in one patient resolved spontaneously, two cases were treated by an injection of potassium chloride into the gestational sac and the remaining 17 cases were treated by salpingectomy[26]. However this case was exceptional as we were faced with bilateral ectopic and triplet intrauterine pregnancy with the background of a previous preterm delivery. This young woman with no living child and was extremely desirous of saving the intrauterine pregnancies. With a consistent, albeit small (in certain cases) chance of loss of intrauterine pregnancy any kind of intervention to remove the ectopic pregnancies was ruled out. The patient was intensively counseled regarding the outcomes. Expectant management of ectopic pregnancy is an acceptable method but it depends on the finding of a falling beta hCG level. With the concurrent presence of intrauterine pregnancy such monitoring of expectant management is not possible. Ectopic pregnancy size, the presence of embryonal elements, vascularity and peak systolic velocity of the extra ovarian mass does not predict the outcome of the pregnancy [27] . With limited literature on successful expectant management of heterotopic, this patient was strictly observed in the hospital. In view of precious pregnancy and questionable reproductive life after this pregnancy, we preferred expectant management for this patient. At 13 weeks with the resolution of one ectopic sac, the future prognosis seems promising.

CONCLUSION

A high index of suspicion coupled with diligent search is necessary to diagnose a heterotopic pregnancy in time. Though majority literature suggested a surgical or medical approach to its management we continued with watchful expectancy. It may be concluded that when indicated heterotopic pregnancy can be dealt with expectantly.

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. Naki MM, Tekcan C, Uysal A, Güzin K, Yücel N; Heterotopic pregnancy following ovulation induction by clomiphene citrate and timed intercourse: a case report. Arch Gynecol Obstet, 2006; 274(3): 181-183
3. Bhatti KA, Babay ZH, Neyazi SM; Ruptured spontaneous heterotopic pregnancy. Saudi Med J, 2010; 31(4): 445-447
4. Berliner, Mesbah M, Zalaud I, Maulik D; Heterotopic triplet pregnancy. Report of a case with successful twin intrauterine gestation. J Reprod Med. 1998; 43(3): 237-239
5. Callen PW;Ultrasound in Obstetrics and Gynaecology. In: Levine D, editor. Ectopic pregnancy. 5th edition. Philadelphia: Saunders Elsiever; pp 1020-47
6. Homburg R;Clomiphene citrate – end of an era? A mini review. Hum Reprod. 2005 May; 20(8): 2043-2051
7. Schenker JG, Yarkoni S, Granat M; Multiple pregnancies following induction of ovulation. Fertil Steril, 1981; 35: 105- 123
8. Scialli AR. The reproductive toxicity of ovulation induction. Fertil Steril. 1986; 45: 315- 323
9. Kousta E, White DM, Frank S;Modern use of clomiphene citrate in induction of ovulation. Hum Reprod Update. 1997 Jul; 3: 359- 365

10. Eijkemans MJ, Hebbema JD, Fauser BC; Charachteristics of the best prognostic evidence: an example on prediction of outcome after clomiphene citrate induction of ovulation in normogonadotrophic oligoamenorrheic infertility. Semin Reprod Med, 2003; 21: 39- 47
11. Homberg R, Insler V;Ovulation induction in perspective. Hum Reprod Update. 2002; 8: 449-462
12. Richard PD,Dorsey EH;Development, pharmacology and clinical experience with clomiphene citrate. Hum Reprod Update, 1996; 2(6): 483- 506
13. Marcus SF, Macnamec MC, Brineden PR; Heterotopic pregnancies after in-vitro fertilization and embryo transfer. Hum Reprod. 1195; 10: 1232-1236
14. Salat B, J Giacomini P, Cornet D et al. Grossesses extrauterines après fecundation in-vitro don't deux associees a une grossesse intra- uterine ecolutive. J Gynecol Obstet Biol Reprod (Paris). 1985; 14: 601-606
15. Scheiber MI, Cedars MI; Successful non- surgical management of a heterotopic abdominal pregnancy following embryo transfer with cryopreserved-thawed embryos. Hum Reprod, 1999; 14(5): 1375-1377
16. Kirk E, Bourne T; Diagnosis of ectopic pregnancy with ultrasound. Best Prac Res Clin Obstet Gynaecol, 2009; 23: 501- 508
17. Condus G, Emeka O K, Khalid A, Lu C, Huffel SV, Timmernan D et al.; The accuracy of Transvaginal ultrasonography for diagnosis of ectopic pregnancy prior to surgery. Hum Reprod, 2005; 20(5): 1404- 1409
18. Browne DL and Doubilet PM; Transvaginal ultrasonography for diagnosing ectopic pregnancy: positivity criteria and performance characteristics. J Ultrsound Med. 1994; 13: 259- 266
19. Rock JA, Jones III HW; Te Linde's Operative Gynaecology. 10th ed. New Delhi. Wolters Kluwer. 2009; 820- 821
20. Berek and Novak's Gynaecology. 14th Edn, LWW Publication
21. Dewhurst's Text book of Obstetrics & Gynaecology. 7th Edn. Blackwell Publishing
22. Louis Sylvester C, Morice P, Chapron C and Dubbuisson JB; The role of laparoscopy in the diagnosis and management of heterotopic pregnancies. Hum Reprod, 1997; 12: 1100- 1102
23. Fernandez H, Lelaidier C, Doumerr S; Non surgical treatment of heterotopic pregnancy: a report of 6 cases. Fertil Steril, 1993; 60: 428- 432
24. Wright A, Kowalczyk CL, Quintero R, Leach RE; Selective embryo reduction in a heterotopic pregnancy using potassium chloride injection resulting in a hematosalpinx. Fertil Steril, 1996; 66(6): 1028- 1030
25. Benifla JL, Fernandez H, Sebban E; Alternative to surgery in treatment of unruptured interstitial pregnancy: 15 cases of medical treatment. Eur. J Obstet Gynecol Reprod Biol,1996; 70: 151- 156
26. Marcus SF, Macnamee M, Brinsden P; Pregnancy: heterotopic pregnancies after in-vitro fertilization and embryo transfer. Hum Reprod, 1995; 10(5): 1232- 1236
27. Atri M, Chow CM, Kintzen G, Gillet P, Aldis AA, Thibodeau M; Expectant treatment of ectopic pregnancies: Clinical and sonographic predictors. AJR, 2001; 176: 123- 127