CASE REPORT

HETEROTOPIC PREGNANCY- A REPORT OF 2 CASES IN WOMEN WITHOUT RISK FACTORS

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Two cases of heterotopic pregnancy are reported. The cases emphasize that co incident pregnancies may occur in women who are without risk of ectopic pregnancy or multiple gestation. The cases describe the complexities of diagnosis and management.

INTRODUCTION

Heterotopic pregnancy describes the rare coexistence of intrauterine and extra uterine gestation. Heterotopic pregnancy continues to be a very unusual and fascinating entity. Due to the relative rare occurrence of this problem, the diagnosis is often made retrospectively. Although it is a comparatively rare condition, recently there has been a steady flow of reports of such cases and the previously quoted incidence of 1: 30,000 pregnancies has recently been challenged[1] The medical literature in the last decade abounds with case reviews and studies detailing the surge in pelvic sepsis rates as well as the increasing use of fertility-enhancing drugs, both well known to greatly increase the rate for the development of heterotopic pregnancy. Even in vitro-fertilization and embryo-transfer (IVF-ET) technique has been implicated in greatly increasing the risk for the development of co-existent gestations. Combined pregnancies can and have occurred in women in the absence of the above mentioned risk factors as is described below.

We report, here, two such pregnancies, which were diagnosed in the department of obstetrics and gynaecology, Nishtar Hospital Multan in the last four years i.e. 1996-2000. Over the same period, there were 12547 deliveries giving a prevalence of 1 in 6273 pregnancies. Pathologic confirmation was obtained in both th eases.

CASE REPORTS

PATIENT 1:

A 25-year old woman, $G_3P_1A_1$ was admitted to the emergency unit of NHM with a history of vomiting, lower abdominal pain and mild vaginal bleeding. Emergency department assessment revealed that she had a vacuum aspiration done, 3 weeks before for a missed abortion diagnosed on ultrasonography (USG). Both the USG and histopathology report of the aspirated tissue confirmed the diagnosis of a missed abortion 3 weeks ago.

On further history taking, it was found that she had her cycles occurring regularly. She was not taking any contraception. Her sexual history was uncomplicated by sexually transmitted diseases (STDs) or any type of pelvic infection. She had never been on fertility enhancing drugs. She had an alive baby girl from the first pregnancy.

She, now, had a continuing feeling of pregnancy and gave history of breast tenderness. Rest everything was unremarkable.

Her physical examination revealed a pulse rate of above 90 beats per minute. She was pale. No other abnormality was detected on general physical examination (GPE). Her abdominal examination showed generalized lower abdominal tenderness. Pelvic examination revealed a pinkish vaginal discharge, a bulky uterus with bilateral adnexal tenderness and an adnexal mass on the left side of approximately 5x6 cm size. There was fullness in Pouch of Douglas

Beta human chorionic gonadotrophin (β-HCG) levels were found to be 600 mlU/ml Sonogram showed a mass in the left adnexa of 6x7 cm with empty uterus. Fluid was seen in the Pouch of Douglas (POD).

A laparotomy confirmed a left tubal ectopic which was ruptured at the ampullary end. There were multiple left tubal adhesions. Left salpingectomy with adhesiolysis was done followed by peritoneal lavage. The histopathological examination of tissue confirmed the presence of chorionic villi. The patient's post-operative period was uneventful and she was discharged on the 5th postoperative day.

PATIENT 2:

29-year old lady, $G_5PIA|$ was admitted to the emergency ward via antenatal clinic. She had a history of 22 days of amenorrhea. She had pain lower abdomen and vaginal bleeding off and on. She had been married for the last 10 years and was mother of 3 alive and healthy children. Her cycle had always been regular and the couple never used any contraception except condoms occasionally. Though she belonged to the low socioeconomic class, she

took care of her hygiene. There was nothing in the history suggestive of STD or pelvic inflammatory disease (PID). She had never used fertility enhancing

drugs. There was nothing remarkable in systematic inquiry.

On examination, her GPE and systemic examination were unremarkable. Pelvic examination revealed bleeding per vaginum, a bulky uterus with cervical os, which was 2 finger open. After 4 hours of fasting, evacuation was done for inevitable (incomplete) abortion. The histopathology confirmed the removed tissue to be products of conception (POCs). Post operatively, the patient kept on complaining of lower abdominal pain. B-HCG, a couple of days later was found to be 600mIU/ml. A transvaginal scan was done to rule out incomplete removal of POCs. It showed the uterus to be empty but a complex mass of mixed echogenicity was observed in the right adnexa measuring 4x4 cm. Pelvic examination had failed to reveal it because the examination had to be abandoned because of marked tenderness in the fornices.

Ectopic was suspected and consents for laparotomy and tubal ligation were taken. Per operatively, there was right tubal incomplete abortion with old blood in the peritoneal cavity. There were 2 corpora lutea with a slightly bulky uterus and left tubal congestion.

Right salpingectomy with left tubal ligation was done. Histopathology report confirmed the presence of placental villi.

Post-operative period was uneventful.

DISCUSSION

Heterotopic pregnancy is an exceedingly rare phenomenon. Since the first description of a heterotopic pregnancy by Duverney in 1708, over a thousand cases have been reported in the literature [6] In contrast to the quoted incidence of 1: 30,000pregnancies, Richards et al reached the conclusion that the actual incidence is higher, some or most of the cases not being reported. Estimates made in the last 2 decades place the true figure at twice that[7] [8]. Areas with a greatly increased risk of ectopic pregnancy have reported rates of heterotopic pregnancy as high as 1:2600[1,6]. The 2 cases described here constitute a prevalence of 1:6273 in out Department.

Several factors have been mentioned as instrumental in putting a female at risk for incurring a combined pregnancy. Multiple gestations have increased greatly with the use of ovulation-inducing agents such as clomiphene[9]. Berger and Taymore cite an incidence of coincident gestation as high as one in 100 patients on fertility agents, increasing chances by 300-fold[10]. Their review looked at 204 pregnancies

resulting from fertility drugs, with two cases of combined pregnancy, clomiphene in one case and human chorionic gonadotrophin in the other. Others have maintained that rate may be as low as 1 in 8000 patients[6]. Devoe and Pratt estimated in 1948 that coexistent intrauterine and extrauterine pregnancies occur in 0.8% of all ectopic pregnancies[11].

Increased rates of PID secondary to STD have also contributed to combined gestations. Upwards of a 7-10-fold increase in risk for ectopic pregnancy has been cited for those women with a documented case of PID as compared to women whose tubes have never been infected[12,13], Westrom et al cited an ectopic rate of I in 200 earlier in the century, presumably reflecting more rate as infection was not nearly as prevalent at tat time[712]. Another confirmed risk factor for ectopic pregnancy would include tubal ligation, with a resultant pregnancy inspite of the procedure having a 16% chance of being ectopic[17].

Lund et al reported a case of a woman who had undergone IVF-ET with a resultant combined pregnancy.[14] This was the 5th reported case of this relationship. Estimates of heterotopic pregnancy in patients undergoing successful implantation via IVF-ET put the rate at 1 in 500[l4]. This occurs because most centers transfer more than one fertilized ovum into the uterus to increase the likelihood of successful implantation and the transfer is done in large amounts of culture medium which increases the likelihood of their being refluxed into the fallopian tubes.

Attempts to explain the increased risk for ectopic pregnancy and multiple gestation as an important cause for heterotopic pregnancy have all but discounted the fact that coincident pregnancies may occur in women without risk factors. There exists no information with respect to the incidence of coincident pregnancies in women without risk factors. In many cases, the simultaneous existence of a co-incident gestation is not entertained, and no further search is made for via ultrasound since an IUP has been found. Lund and colleagues reported that a woman who was ultimately found to have a combined pregnancy had had serial ultrasounds during the prenatal visits with no evidence of ectopic pregnancy reported[14].

The current cases emphasize a major point with respect to intrauterine pregnancies. Ultrasonic diagnosis of ectopic pregnancy has been thought to depend on exclusion of intrauterine pregnancy (IUP) on the basis of absence of intrauterine gestational sac. As an important corollary, the clinician must be careful not to dismiss the possibility of an ectopic pregnancy just because of the presence of an intrauterine sac. An adnexal mass with or without cul-de-sac fluid may occur with or without an IUP and should entail further evaluation[15].

Abbott et al reported on a group of 28 patients who were initially evaluated in the emergency department and discharged, only to subsequently return and have

a second and correct diagnosis of ectopic pregnancy made[16] (extrauterine only).

The cases described above serve to reiterate the difficulty in establishing an accurate prospective diagnosis of a combined pregnancy even with the advent of highly sensitive serum HOG as well as the refinement of USG technology. The importance of high index of suspicion, of the condition as the single most important factor in diagnosing, should always be borne in mind. This is especially true in the presence of risk factors mentioned above but as our cases show, co incident pregnancies may occur in women without risk factors and should be searched for meticulously.

There have been cases where after the treatment of ectopic pregnancy, the I UP has gone to term with the deliveries of healthy babies. Therefore, the routine usage of D and C as prophylaxis against vaginal haemorrhage needs to be condemned specially if the patient desires to maintain a possible IUP or in an infertile patient who has undergone fertility treatment. However, it should be carried out in such cases as the ones described above where the abortion is inevitable, incomplete or missed.

The cases exemplify the need for clinical correlation of patient's history, physical findings with the investigations. This is especially true if abdominal USG is undertaken. An IUP should be meticulously searched for in case of an ectopic gestation and vice versa. One example of limitation of abdominal USG in the diagnosis of combined pregnancy is the visualization of gestational pseudosac seen in association with a tubal ectopic. This is an excellent example of the technology misleading a clinician, if the clinical co-relation of the finding is not entertained: However, this problem has been overcome with the advent of transvaginal USG as well as Doppler flow scanning. Another advantage of transvaginal over abdominal USG is its ability to positively confirm IUP as early as 5-6 weeks' gestation compared to 6-7 weeks with a n abdominal probe. This can be disastrous as delay in the treatment might lead to rupture in case of tubal ectopic with high rate of maternal mortality.

A high index of suspicion is important. Think heterotopic. Once suspected, the set of criteria established by Reece et al. should be followed to allow a better clinical assessment of the possibility of a combined pregnancy. The following precautions should be practiced to minimize the chances of missing the diagnosis of a combined pregnancy:[18]

- In any case of abortion, a thorough vaginal examination must always be carried out. The detection of adnexal tumor can suggest an ovarian cyst, but the possibility of a combined ectopic pregnancy must always be considered specially if there is family history of twins or after ovulation induction.
- In case of ovarian hyperstimulation, the possibility of ectopic plus IUP must be considered.
- Laparoscopy should be done in all dubious cases.
- During a laparotomy for ectopic pregnancy, the uterus must be carefully examined.
- Profuse bleeding after such an operation should be considered as a sign of an abortion.
- Absence of withdrawal bleeding should be taken as a warning sign for possible intrauterine gestation.

These measures would definitely decrease the chances of missing a crucial diagnosis.

CONCLUSION

In conclusion, the two cases along with the literature review suggest that the incidence of previously an uncommon condition i.e. heterotopic pregnancy is rising and is definitely higher than that previously reported. Whatever the pathogenesis, the definitive risk factors predisposing a woman to the potentially fatal condition are PID, fertility drugs, IVF-ET, and tubal ligation. But as the cases show, coincident pregnancies can and do occur in women without risk factors. No high-risk characteristics can be identified to as the typical patient. The presentation can be varied. Women who are suspected of ectopic but who do not bleed or women who after an abortion continue to feel pregnant are the candidates in which a meticulous search for the combined pregnancy should be made. Last but not the least, a high index of suspicion of the condition is of prime importance, otherwise the most advanced technology will be of no help as is evidenced from our cases where a combined pregnancy was overlooked merely because an IUP was seen. Clinicians must be certain that women shown to have an IUP by USG have the presence of simultaneous heterotopic pregnancy excluded as well.

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