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E. T. Dassah, MBChB, MPH, Resident, A. T. Odoi, MBChB, FWACS, FGCS, Senior Lecturer, D. E. Darkey, MBChB, Resident, C. M. Senaya, MBChB, MSc, Resident and R. M. Djokoto, MBChB, Resident, Department of Obstetrics and Gynaecology, Komfo Anokye Teaching Hospital, P. O. Box 1934, Kumasi, Ghana

Request for reprints to: Dr. E. T. Dassah, Department of Obstetrics and Gynaecology, Komfo Anokye Teaching Hospital, P.O. Box 1934, Kumasi, Ghana

## SPONTANEOUS HETEROTOPIC PREGNANCY WITH LIVE INFANT: REPORT OF TWO CASES

E. T. DASSAH, A. T. ODOI, D. E. DARKEY, C. M. SENAYA and R. M. DJOKOTO

### SUMMARY

**Heterotopic pregnancy is a potentially fatal condition that rarely occurs in natural conception cycles. We report two cases diagnosed within one month in a 20 year old gravida 3, para 0+2 without any known risk factor and a 38 year old gravida 12, para 6+5 with risk factors. The ectopic pregnancies were diagnosed after rupturing at 10 and 17 weeks respectively and resected via laparotomies. The courses of the intrauterine pregnancies were uneventful and both clients delivered vaginally at term. Heterotopic pregnancy is an important differential diagnosis to consider in clients with intrauterine pregnancies presenting with acute abdominal pain and haemoperitoneum.**

### INTRODUCTION

Heterotopic pregnancy (HP) is the coexistence of an intrauterine and an extrauterine pregnancy (1, 2) and was first reported by Duvemey in 1708 as an autopsy finding (1). The incidence was estimated to be 1: 30,000 spontaneous pregnancies in 1948 (1). More recently, the reported incidence varies from 1: 2,600 to 1: 8,000 in the general population (3 - 6) and may be as high as 1: 100 to 1:500 during assisted reproductive technologies (ART) (7,8). HP is now not as rare as once thought, and may be higher in areas with a high incidence of multiple pregnancies such as Nigeria (9). Though very difficult to diagnose particularly in a natural conception cycle, it is an important differential diagnosis to consider, especially when acute abdominal pain and haemoperitoneum occur in the presence of an intrauterine pregnancy. We report two cases of heterotopic pregnancies in a natural conception cycle within one month, which were only diagnosed after rupture of the ectopic pregnancies, with favourable obstetric outcomes. A brief literature review highlights the diagnostic challenges and the current management options.

### CASE REPORTS

*Case report 1:* A 20 year old gravida 3, para 0+2 client presented to the Obstetrics and Gynaecology Department with a day's history of sudden lower

abdominal pains, dizziness and palpitations. She stated that she was three months pregnant but had not been to an antenatal clinic. Her first pregnancy was four years prior for which she had an elective surgical abortion at one month gestation without any complication. The second pregnancy which was a year prior resulted in a spontaneous miscarriage at two months followed by evacuation of retained products of conception with no post abortion complications. Antibiotics were taken following both abortions. She had never had any other surgery or pelvic inflammatory disease (PID) and was not using contraception. She had no family history of multiple pregnancies.

On clinical examination she was moderately pale with a pulse of 100 beats / min, blood pressure 90/60 mmHg and a respiratory rate of 18 breaths / min. The abdomen was tender all over with lower abdominal guarding. Cervical motion tenderness was present and no cervical bleeding was noted. Bimanual pelvic examination was not possible due to the guarding and tenderness. Urine pregnancy test was positive, haemoglobin of 8.4g/dl, haematocrit of 26.0% and WBC count of  $7.5 \times 10^9/L$ . Intravenous (IV) fluids were started and an urgent abdominal ultrasound showed a live intrauterine foetus of ten weeks gestation with significant free fluid in the peritoneal cavity and normal-looking adnexae. An impression of a ruptured corpus luteum cyst was formed. An emergency laparotomy via a pfannenstiell incision

revealed a haemoperitoneum of about 1.0L, a ruptured left ampullary gestation, and a bulky soft uterus of about ten weeks pregnancy. A left total salpingectomy was performed and the peritoneal cavity lavaged with ringer's lactate. She was haemotransfused 2 units of donor whole blood postoperatively. An abdominal ultrasound done on the sixth postoperative day showed an active intrauterine foetus.

She was discharged on the seventh postoperative day and followed-up regularly at the antenatal clinic. The pathologic examination confirmed degenerated chorionic villi consistent with an ectopic gestation. The intrauterine pregnancy progressed without complications and the client had a spontaneous vaginal delivery of a healthy baby girl weighing 2.7 kg at term.

*Case report 2:* A 38 year old woman, gravida 12, para 6+5 in her third month of pregnancy presented to the Obstetrics and Gynaecology Department with a three day history of progressive right lower quadrant pain, worst that morning. The pain was aggravated by movement. She had been to the antenatal clinic once during this pregnancy. All her previous deliveries were vaginal with primary postpartum haemorrhages in her last two deliveries. Her gynaecological history was significant for five elective terminations of pregnancy and multiple episodes of PID. On examination, her temperature was 36.8°C, she was neither pale nor dehydrated, the pulse was 82 beats/min and her blood pressure was 110/70mmHg. She had a tender firm mass in the right lower quadrant. Vaginal examination revealed a 12 week uterine size and a tender right adnexal mass of about 10cm. Her haemoglobin was 10.8g/dl and the WBC count  $6.1 \times 10^9/L$ . Abdominal ultrasound scan revealed a single live intrauterine foetus of eleven weeks gestation, a large complex right adnexal (ovarian) mass 9.5x5.2cm, and no evidence of fluid in the pouch of Douglas. An impression of a normal intrauterine pregnancy with a right ovarian mass was made. Her pain was relieved by oral analgesics (tramadol) and she was discharged after three days observation. She was given an appointment a week later but never reported for review. Six weeks later, the client reported to the Department again with sudden onset of severe right lower quadrant pain associated with nausea and vomiting. On examination, the client was obviously in pain, her temperature was 37.0°C, pulse was 90 beats/min and the blood pressure was 100/70mmHg. The right lower quadrant mass was very tender and the haemoglobin was 9.8g/dl. An impression of a right ovarian torsion in pregnancy with differential diagnosis of chronic leaking ectopic gestation was made. A laparotomy via an extended sub-umbilical midline incision revealed a haemoperitoneum (with clots) of about 1.0L. There was a right adnexal conglomerate mass of

papyraceous gestation, right pyosalpinx, right ovary and omentum, and an enlarged soft uterus of about 18 weeks gestation. The left tube and ovary appeared normal. Right adnexectomy up to the isthmic region was done and she was haemotransfused 2 units of donor whole blood postoperatively. An ultrasound scan on the tenth postoperative day confirmed a live intrauterine pregnancy and she was discharged on the twelfth postoperative day. She continued care at the antenatal clinic.

The course of the intrauterine pregnancy was uneventful and at 40 weeks she had a spontaneous vaginal delivery of a live female infant weighing 3.9 kg, without postpartum haemorrhage. Both mother and baby were discharged on the second day postpartum to go to the child welfare clinic and family planning centre.

## DISCUSSION

Heterotopic pregnancy (HP) occurs in various combinations: abdominal and intrauterine pregnancy, twin tubal and intrauterine pregnancy, and intrauterine pregnancy coexisting with tubal, cornual, cervical or ovarian pregnancy (10). The ectopic component of HP is commonly tubal with the most common site being the ampullary region (11,12). The ectopic components in our cases were tubal (ampullary) and an ill-defined conglomerate in the adnexum.

Although a precise aetiology of HP is not known, factors predisposing to HP appear to be identical to those predisposing to ectopic pregnancy (12,13). Assisted reproduction increases the risk of HP because of the highly associated multiple and ectopic pregnancy rates (9,12). Other risk factors for ectopic (and likely heterotopic) pregnancy include PID, treatment with super ovulation medication (such as clomiphene citrate), previous ectopic pregnancy, tubal surgery, tubal malformation, tubal ligation, diethylstilbesterol exposure before birth, endometriosis, use of intrauterine device, dizygotic twins, and possibly cigarette smoking and multiparity, (9,12,14,15). The relationship between ectopic pregnancy and previous pregnancy termination has been a subject of much debate (4,16). While our first client had no obvious risk factors, the multiple episodes of PID and multiparity in the second client possibly contributed to the HP in this client. In patients presenting with risk factors, particularly those undergoing ART, HP should not be ignored as diagnostic consideration (17).

The preoperative diagnosis of HP particularly in natural conception cycles remains a major challenge for modern reproductive medicine (18). Early diagnosis is often difficult either because clinical symptoms are lacking or are non-specific. Even with a high index of suspicion, most cases are missed on initial presentation, and only diagnosed after rupture

of the ectopic pregnancies (17,18). Tal *et al.* (8) reported that 70% of HPs were diagnosed between five and eight weeks of gestation, 20% between nine and ten weeks gestation and 10% after the 11<sup>th</sup> week. Diagnosis beyond the ninth week represents a risk of tubal rupture with subsequent blood transfusion (18). Our cases were diagnosed at 10 and 17 weeks respectively when the ectopic pregnancies had ruptured, and both clients were haemotransfused.

Reece *et al.* (11) defined four common presenting signs and symptoms of HP as; abdominal pain, adnexal mass, peritoneal irritation and an enlarged uterus. Our clients presented with signs and symptoms of peritonism due to haemoperitoneum from the ruptured ectopic gestations. Bimanual examination was not possible in the first case but the second case showed an enlarged uterus with a tender right adnexal mass.

Transvaginal ultrasound has been shown to be superior to transabdominal ultrasound in the diagnosis of ectopic pregnancy, and the diagnosis can be made in up to 80% of cases with meticulous sonographic evaluation of the adnexae using Doppler ultrasound (15). Interestingly however, improved ultrasound technology has not reflected in improved early diagnosis of HP (18). A suspicious adnexal finding on pelvic ultrasound is frequently misdiagnosed as corpus luteum cyst (6). Ultrasound visualisation of cardiac activity in both intrauterine and extrauterine gestations though helpful for diagnosis is very rare (12). The presence of moderate or large amounts of intraperitoneal fluid can raise a suspicion of ectopic pregnancy (8,10,18). A concomitant finding of free fluid in the pelvis has been observed in the vast majority of reported cases of HP, whether identified by ultrasound, culdocentesis or at surgery (17). Serial measurement of serum  $\beta$  human chorionic gonadotropin ( $\beta$ -HCG) is of limited value in the diagnosis of HP as the intrauterine pregnancy masks any underlying  $\beta$ -HCG changes from the extrauterine pregnancy (12,15).

Surgery by laparoscopy or laparotomy with minimal manipulation of the uterus remains the mainstay of treatment despite the anaesthetic and surgical risks to both the mother and the intrauterine foetus (12,15,19). Laparotomy is reserved for life-threatening cases with haemoperitoneum and haemorrhagic shock or for cases that cannot be treated laparoscopically (9,15). Early diagnosis and laparoscopic treatment provide good outcome without the postoperative inconvenience of laparotomy, and the advantage of an immediate result over medical management (18). Fifty per cent and 62.5% of coexistent intrauterine pregnancies will proceed to term after open and laparoscopic surgery respectively (15). In our cases, laparotomy was done due to the suspicion of considerable haemoperitoneum, and ovarian torsion in the second case.

Medical management is only considered when the diagnosis is certain and the extrauterine pregnancy remains unruptured (15). Transvaginal ultrasound or laparoscopic guided aspiration and/or injection of potassium chloride, methotrexate, mifepristone (RU486), prostaglandin or hyper osmolar glucose has been described (12,13,15,18,19). While potassium chloride is nonteratogenic and commonly used, methotrexate, RU486 and prostaglandin are potentially teratogenic and should not be used (12,15).

The survival rate of the intrauterine pregnancy has risen from 35-54% in 1970 (20) to 66% of live intrauterine pregnancies mainly treated by surgery in recent times (8). This improvement is probably due to diagnostic and treatment developments and the closer follow-up of women conceiving after ART (12,15).

We presented two cases of spontaneous HPs that were diagnosed within one month. Only one of the cases had obvious risk factors for ectopic pregnancy and both were diagnosed intraoperatively after rupture of the ectopic pregnancies illustrating the diagnostic difficulties of this condition. Moreover, the increasing incidence of HP even in natural conception cycles emphasises the need for a high index of suspicion and extreme vigilance in symptomatic patients with/without risk factors for ectopic pregnancy. It is reassuring that both cases achieved live deliveries of the intrauterine pregnancies at term.

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