A rare case of spontaneous heterotopic pregnancy with intrauterine gestational trophoblastic neoplasia and tubal ectopic pregnancy at a remote secondary care hospital

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ABSTRACT

A simultaneous presence of intrauterine and extrauterine gestation is called as heterotopic pregnancy (HP). The incidence of spontaneous HP is 1:30000, which is very rare. In this case report, we are reporting a rare case of spontaneous HP in a 40-year-old lady with intrauterine gestational trophoblastic neoplasia (GTN) and ruptured tubal ectopic pregnancy in a remotely located secondary care hospital. The lesson learnt from our case report is that detection of intrauterine gestation does not rule out the possibility of the presence of ectopic pregnancy. Also, HP can occur without any obvious risk factors like in our case. It should be always kept in mind that HP can occur in any woman of reproductive age group. In the end, our patient was fortunate that she presented to us in a stable haemodynamic condition in spite of having ruptured tubal ectopic with spontaneous stoppage of bleeding from the ruptured tube. Hence, to achieve a great chance of favourable obstetric outcome, all treating doctors including family physicians should have a high index of suspicion to have accuracy in early diagnosis and treatment of a various variety of HP as these can occur with or without predisposing risk factors.

Keywords: Ectopic pregnancy, gestational trophoblastic neoplasia, heterotopic pregnancy

Introduction

A simultaneous presence of intrauterine and extrauterine gestation is called as heterotopic pregnancy (HP). The incidence of spontaneous HP is 1:30000, which is very rare. Although it has come down to 1:100–500 in the recent past due to increased successful pregnancies post assisted reproductive technologies.¹⁰ Most common site for ectopic gestation is the fallopian tube followed by the cornual region of the uterus, other rare sites are the ovary, cervix and abdomen.¹⁰ HP is a life-threatening complication of pregnancy, and early diagnosis and definitive management are very essential to avoid maternal morbidity or mortality.¹¹ Hence, it is important to keep the possibilities of HP in mind by obstetricians while treating patients reporting to emergency with complications of early pregnancy. Many times diagnosis is difficult due to intrauterine pregnancy masking the ectopic pregnancy.¹³ Transvaginal sonography can help in differentiating between intrauterine and extrauterine pregnancy in almost 90% of cases and if there is doubt about the diagnosis, diagnostic ovarian stimulation associated with HP. Many cases in the literature are found without any risk factor.¹²-¹⁴

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laparoscopy is ideal to perform to avoid delay in diagnosis and management of HP.\textsuperscript{[3]} In this case report, we are reporting a rare case of spontaneous HP in a 40-year-old lady with intrauterine gestational trophoblastic neoplasia (GTN) and ruptured tubal ectopic pregnancy in a remotely located secondary care hospital.

**Case Presentation**

A 40-year-old multigravida lady reported with secondary amenorrhoea of 3 months (last menstrual period (LMP) not known) and pain in the abdomen since a few days. The pain was intermittent in nature without nausea, vomiting or any other gastrointestinal symptoms. There was no history of vaginal bleeding and she refused any previous history of illness or allergies. She was not tubectomised. The patient was found to have a urine pregnancy test positive.

On examination, she was afebrile, arterial blood pressure was 100/70 mm Hg, heart rate was 90/min and uterus was abdominally palpable (16-week gravid size). Transvaginal sonography was showing echogenic contents inside a bulky uterus with snow storm appearance, no foetal parts were appreciated and bilateral adnexa could not be visualised clearly. On admission, haemoglobin was 10 gm%. Her serum beta-human chorionic gonadotropin (HCG) was 1254.385.20 mIU/ml and thyroid-stimulating hormone (TSH) was 0.01 mIU/L (both reports were available on the third postoperative day).

A provisional diagnosis of GTN (complete mole) was done and she was planned for suction and evacuation, and laparoscopic ligation of tubes after informed consent. Pre-operative informed consent was taken for blood transfusion and emergency perioperative hysterectomy in view of the large size of the uterus and expected blood loss due to gestational trophoblastic disease (GTD). She underwent suction and evacuation under general anaesthesia and the procedure was uneventful with average bleeding. Primary 10 mm umbilical port was placed for laparoscopic ligation. An incidental finding of haemoperitoneum with 200 ml of blood in the pouch of Douglas and right haematosalpinx was seen with ruptured tubal ectopic. However, there was no active bleeding. Flimsy adhesions were found around haematosalpinx. Aspiration of haemoperitoneum and laparoscopic right salpingectomy was carried out and left tubal ligation was done using Falope's ring.

The pathology report of salpingectomy specimen showed a right fallopian tube with chorionic villi with a blood clot and decidua along with benign squamous mucosa, which confirmed tubal ectopic pregnancy. The pathology report of intrauterine product of conception showed variably preserved fibromuscular tissue with cells showing eosinophilic and mild to moderate atypia. No mitotic activity was noted. Few syncytiotrophoblasts were noted. No villi were observed. No evidence of granuloma or malignancy was seen. Features suggestive of placental site trophoblastic reaction, which was suggestive of GTN with no malignant potential. Two postoperative beta-HCG samples sent were having values of 19405.10 and 3154.92 mIU/ml showing a decreasing trend of hormonal value. The patient was discharged on the seventh postoperative day with the advice of weekly beta-HCG and follow-up in the outpatient department (OPD) after 2 weeks.

**Discussion**

HP is coexisting presence of intrauterine and extraterine pregnancy. The incidence of HP has increased since the advent of assisted reproductive techniques up to 1% although spontaneous HP is still rare with an incidence of almost 1:30000.\textsuperscript{[1,3]} Other risk factors are found to be a pelvic inflammatory disease, previous tubal surgeries or pathologies, endometriosis, an increasing number of embryos transferred.\textsuperscript{[3,7]} Our patient had spontaneous HP with no risk factor observed, indicating yet unknown tubal causes predisposing patients to developing HP, making this case rare. Also, there was the presence of intrauterine GTD and extraterine tubal ectopic, which is not documented in any literature we could find making it an extremely rare and unique case of spontaneous HP.

Most of the cases (95%) of ectopic pregnancy in HP are found in the fallopian tube and rarely in other places like the cervix, caesarean scar, interstitial part of the tube, ovary or abdominal cavity. In our case, it was in the right fallopian tube.\textsuperscript{[1,7]}

In spite of advancements in medical knowledge, sophisticated ultrasound facilities and sensitive hormonal assays, diagnosis of HP has been challenging to emergency room consultants and obstetricians due to its very low incidence. Abdominal pain, adnexal mass, signs of peritoneal irritation and enlarged uterus are defined as signs and symptoms of HP, but these symptoms are generalised and are seen with ectopic and intrauterine pregnancies too. Almost 50% of ectopic pregnancies are asymptomatic; hence, its early diagnosis is difficult due to the absence of symptoms and simultaneous presence of intrauterine gestation. About 50% of HP are detected during emergency laparotomies due to tubal rupture.\textsuperscript{[7]} In our case, the patient had a history of secondary amenorrhoea and only symptom of intermittent moderate-intensity pain in the abdomen. She was haemodynamically stable, no symptoms of peritoneal irritation were there in spite of ruptured tubal ectopic with haemoperitoneum, which was incidentally found subsequently during laparoscopy.

As per the literature, 70% of HP are diagnosed very early, between 5 and 8 weeks of pregnancy and only 10% of cases are reported after 10 weeks of gestation.\textsuperscript{[8,4]} Our patient presented to OPD after almost 14–16 weeks of amenorrhoea with ultra-sonography (USG) suggestive of suspected intrauterine GTD with the abdominally palpable uterus of 16-week size. Transvaginal sonography was done in OPD, showing snow storm appearance of intrauterine contents, no foetal parts were visible. Both adnexa could not be visualised and neither organised haematoma in cul de sac was appreciated by the observer, probably due to the large size of the uterus and non-availability of sonologist at peripheral setup. Hence, ectopic pregnancy was missed when the patient was admitted for therapeutic
management of intrauterine GTDs. Although transvaginal ultrasound is the most important tool for the diagnosis of HP, its sensitivity remains variable ranging from 26% to 92% resulting in the diagnosis of 26–41% of total such cases. In a few centres, magnetic resonance imaging is being done to differentiate HP from other pregnancies. Beta-HCG testing is recommended for detecting intrauterine pregnancies and ectopic pregnancies, but its value is debatable in cases of HP due to the simultaneous presence of both pregnancies. Abnormal hormonal values are masked by beta-HCG produced by intrauterine pregnancy. In the reported case, intrauterine pregnancy was GTD. The beta-HCG report was available to us after 48 h and which was very high (1254385.20 mIU/ml) favouring the diagnosis of GTD.

In the presented case, management was clear in the form of suction and evacuation of intrauterine contents, right salpingectomy and tubal ligation of the left fallopian tube and awaiting histopathological diagnosis of the product of conception. Histopathological examination showed placental site trophoblastic reaction without evidence of malignancy. The patient was suggested follow-up in the form of weekly beta-HCG, which was showing decreasing values.

Moamar et al recently in 2021, reported a case of heterotrophic intrauterine complete molar pregnancy with coincidental un-ruptured tubal ectopic pregnancy wherein the authors had challenges to offer best treatment modalities as there were no such cases mentioned in literature. Finally, surgical evacuation for intrauterine complete mole and medical methotrexate therapy for un-ruptured ectopic pregnancy was done. Soares et al also reported a spontaneous HP which was diagnosed very early and successfully treated with laparoscopic surgery in 2020. The tubal ectopic pregnancy was managed by left salpingectomy on confirmation of trophoblastic tissue on exploratory laparoscopy. The remaining pregnancy was uneventful and the lady delivered a healthy live baby girl at 39 weeks through spontaneous vaginal delivery. Basile et al also reported a spontaneous HP, an ovarian and intrauterine, in 28 years lady detected early and managed laparoscopically. All these authors suggested that since cases are rare, to achieve a great chance of favourable obstetric outcome, all treating doctors including family physicians should have a high index of suspicion to have accuracy in early diagnosis and treatment of a various variety of HP as these can occur with or without predisposing risk factors.

Conclusion

Detection of intrauterine gestation does not rule out the possibility of the presence of ectopic pregnancy. Also, HP can occur without any obvious risk factors like in our case. It should be always kept in mind that HP can occur in any woman of reproductive age group. The authors were unable to find any case of HP with intrauterine GTD and ruptured tubal ectopic making our case unique and rare. In the end, our patient was fortunate that she presented to us in a stable haemodynamic condition in spite of having ruptured tubal ectopic with spontaneous stoppage of bleeding from the ruptured tube. Nevertheless, the possibility of HP should always be kept in mind of a pregnant woman presenting with pain in the abdomen.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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