

DOI: <https://dx.doi.org/10.18203/2319-2003.ijbcp20214508>

## Case Report

# Heterotopic pregnancy: a common masquerade than ever thought?

Ayodele A. Olaleye, Boniface N. Ejikeme, Eziaha E. S. Ede, Nwabunike E. Okeke,  
Bartholomew I. Olinya, Charles N. Edene, John C. Obasi,  
Emmanuel O. Onyekelu, Amuchechukwu V. Nwafor

Department of Obstetrics and Gynecology, Alex Ekwueme Federal University Teaching Hospital, Abakaliki, Nigeria

**Received:** 28 September 2021

**Revised:** 23 October 2021

**Accepted:** 29 October 2021

### \*Correspondence:

Dr. Ayodele A. Olaleye,

Email: [ayodele\\_olaleye@yahoo.com](mailto:ayodele_olaleye@yahoo.com)

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## ABSTRACT

Heterotopic pregnancy, coexistence of living or dead intrauterine pregnancy, single or multiple, with extra-uterine pregnancy located in the oviduct, ovary, uterine cornua, cervix or rarely peritoneal cavity. Heterotopic pregnancy is relatively uncommon in spontaneous conception with 1 in 30,000 cases reported, the incidence of heterotopic pregnancy increases to 1 in 3900 when conception is enhanced with various assisted reproduction techniques (ART). It is an ectopic pregnancy coexisting with intrauterine pregnancy. But is the incidence of heterotopic pregnancy rising? A case was reported from our centre in 2018 by Ejikeme et al, and we have recorded another two cases in the period of one year. Ectopic pregnancy has been described as a great masquerader, which makes diagnosis and management of heterotopic pregnancy a dilemma to attending physician. We present a case of an unbooked 26 years old G4P3+0 who has no family history of multiple gestation and presented at gestational age of 8 weeks and 5 days with 2 days history of abdominal pain and vaginal bleeding and 2 hours history of loss of consciousness. She later had exploratory laparotomy with left salpingectomy and manual vacuum aspiration of Retained Products of Conception with good outcome. In conclusion, spontaneous heterotopic pregnancy is a rare occurrence, however with advent of artificial reproductive technology and increase incidence of pelvic inflammatory disease, the incidence could be higher than earlier suspected.

**Keywords:** Intra-uterine, Extra-uterine, Ectopic, Pregnancy, Heterotopic, Pelvic inflammatory disease

## INTRODUCTION

Heterotopic pregnancy is the coexistence of living or dead intrauterine pregnancy, single or multiple, and extra-uterine pregnancy located in the oviduct, ovary, uterine cornua, cervix or rarely peritoneal cavity.<sup>1</sup> More than 90% of ectopic pregnancies are localized in the fallopian tubes. Heterotopic pregnancy is relatively uncommon in spontaneous conception with 1 in 30,000 cases reported, the incidence of heterotopic pregnancy increases to 1 in 3900 when conception is enhanced with various assisted reproduction techniques (ART) including in vitro fertilization, super ovulation, and intrauterine

insemination.<sup>2,3</sup> Heterotopic pregnancy has also been reported with clomiphene citrate ovulation induction.<sup>4</sup> However, with rising incidence of undiagnosed or poorly treated pelvic inflammatory disease in low resource settings, the incidence of heterotopic pregnancy may be on the rise. Chlamydia infections are characterized by a high proportion of asymptomatic infections (up to 70% in women) and has been associated with increased incidence of pelvic inflammatory disease and increase risk of ectopic pregnancy.<sup>5,6</sup>

The risk factors for heterotopic pregnancy includes, assisted reproductive technology, tubal damage (by

endometriosis and tubal surgeries), pharmacological ovulation induction, previous ectopic pregnancy, family history of multiple pregnancy and pelvic inflammatory disease.<sup>1</sup> Other factors that increased the risk of ectopic pregnancy in general include tubal ligation, tubal pathology, in-utero DES exposure, current IUD use, infertility, previous cervicitis (gonorrhoea, chlamydia), multiple sexual partners, smoking, previous pelvic/abdominal surgery, vaginal douching and early age of intercourse (<18 years).<sup>5-7</sup>

## CASE REPORT

Our informant was the patient's sister. Patient is a 26 years old multiparous woman with LMP of 27 January 2021 and EGA of 8 weeks and 5 days, who presented at Gynecology Emergency Unit of our facility with 2 days history of lower abdominal pain and bleeding per vaginal, and 2 hours history of sudden loss of consciousness. Pain was sudden in onset and localized to the left side of her abdomen. It was non-colicky but radiate to her back. There was no known aggravating or relieving factor. No associated shoulder tip pains, no nausea or vomiting but there was progressive abdominal distention. She started passage of scanty altered blood per vaginal which contained no fleshy materials or vesicles 2 days prior to presentation. There was associated dizziness, fainting spell and unconsciousness 2 hours prior to presentation. She had symptoms suggestive of pelvic inflammatory disease to which she took medicines prescribed by a chemist a year prior to presentation. She had no history of pelvic surgery or instrumentation in the past. She did not smoke or used tobacco in any form. There was no prior history of ectopic pregnancy and no family history of twinning. She was not a known hypertensive or diabetic patient and was not on any medication. Pregnancy was conceived spontaneously but has not been booked in any facility. At the onset of the symptoms, she presented at a primary health care centre where intravenous access was established and she was given intravenous fluid and medications. However, patient's condition continued to deteriorate and she was subsequently referred to our facility for expert care.

At presentation, she was unconscious with a Glasgow Coma Scale of 6/15, she was pale, anicteric, acyanotic, afebrile, with no pedal edema. Her respiratory rate was 46 cycles per minute, she was dyspneic and tachypneic. Air entry was however equal on both lung fields. Pulse rate and blood pressure were not recordable. Abdomen was distended, there was suprapubic fullness with generalized areas of tenderness. Liver and spleen were not palpable and kidneys were not ballotable.

An assessment of suspected ruptured left ectopic pregnancy was made. Resuscitation commenced by ensuring a patent airway and oxygen was given at 6L/min. Another intravenous access was secured on the other arm, blood was collected for laboratory investigations. Intravenous fluid was commenced and she

had an emergency bedside ultrasound done. Her packed cell volume was 18%, Quantitative hCG was 22,300.0 MIU/ML, indicating pregnancy. A transvaginal ultrasound showed one gestational sac with no fetal cardiac activity in the endometrial cavity with mean crown-rump length of 6.7mm, corresponding to 9 weeks 0 days gestational age (Figure 1). A second gestational sac in the left adnexa with a fetal pole but no cardiac motion was also seen with mean crown-rump length of 6.5mm, corresponding to 8 weeks 3 days gestational age (Figure 2). Significant fluid collection was seen in the peritoneal cavity. An ultrasound diagnosis of heterotopic pregnancy was made.



**Figure 1: Intrauterine gestation with no cardiac activities.**



**Figure 2: Complex adnexal mass with peritoneal fluid collection.**

Patient had emergency exploratory laparotomy and the intraoperative findings included haemoperitoneum of 3 litres, bulky uterus of 12 weeks size, ruptured left ampulla ectopic pregnancy, normal right fallopian tube, and left and right ovaries. The findings on manual vacuum aspiration included parous cervical Os, 1cm opened with about 100mls of product of conception. Four units of blood were transfused intra and post-operatively. She has parenteral antibiotics and analgesics for 48 hours

post-operation. Her post-transfusion packed cell volume was 31% on third day post-operation and she was discharged home on day 5 post-operation.

Patient was seen at the Gynecology Clinic two weeks after discharge. She had no complain and her histology report showed portions of necrotic decidua, endometrium and chorionic villi from the sample of manual vacuum aspiration, and specimen sample at laparotomy also confirmed ruptured left tubal ectopic pregnancy.

## DISCUSSION

The diagnosis and management of a heterotopic pregnancy poses unique challenges, as majority of the cases may be missed. Heterotopic pregnancy is relatively uncommon in spontaneous conception with 1 in 30,000 cases reported, the incidence of heterotopic pregnancy increases to 1 in 3900 when conception is enhanced with various assisted reproduction techniques (ART) including in vitro fertilization, super ovulation, and intrauterine insemination.<sup>2</sup> The incidence of heterotopic pregnancy could be rising, especially with advent of ART and use of clomiphene citrate for ovulation induction.<sup>4,8</sup> Also reported is effect of pelvic inflammatory disease on ectopic pregnancy. Increase incidence of untreated or poorly treated pelvic inflammatory disease could be a risk of developing heterotopic pregnancy as seen in our patient.<sup>5-7</sup> Other factors that increase the chance of developing a heterotopic pregnancy include history of previous tubal damage, ectopic pregnancy and family history of multiple gestations.<sup>2</sup> These factors should raise clinical suspicion and warrants further investigation when presenting with symptoms of early pregnancy or ectopic pregnancy.

About 8 months prior to the presentation of the index case, we had a 23 years old nulliparous woman who presented with vaginal spotting after 7 week of absence of menses. She was reviewed and had a pelvic ultrasound that made a diagnosis of viable intrauterine pregnancy with coexisting right tubal ectopic pregnancy. She later had exploratory laparotomy with right salpingectomy. She was placed on intravenous fluid, antibiotics and was commenced on progesterone suppository per vaginum with the aim of keeping the intrauterine gestation. However, the patient developed vaginal bleeding on 3rd day post operation and later had a complete miscarriage of the intrauterine pregnancy. A similar case of heterotrophic pregnancy was reported in our centre by Onoh et al in 2018, but the intrauterine gestation in this case survived and resulted in life birth.<sup>3</sup> The case under discussion was the third case treated or reported in our facility over a short period of time, and this masquerade could be commoner now than we ever thought in the past. It should be suspected in every patient presenting with lower abdominal pain in early cyesis.<sup>8</sup>

Heterotopic pregnancies can be asymptomatic in about half of the cases, otherwise, it can be presented by

variable clinical presentations: mainly abdominal pain, adnexal swelling that may be associated with vaginal bleeding, or even shock due to hypovolemia.<sup>9</sup> Clinically, it manifests non-specifically with abdominal pain, vaginal bleeding, and spotting which presents similarly to both normal pregnancies and abnormal obstetrical complications.<sup>2,9</sup> Our patient presented with sudden onset of left abdominal pain and vaginal bleeding, with 2 hours history of loss of consciousness. This is a common presentation of patient with ectopic pregnancy. Shock is a common presentation in patients with ruptured ectopic pregnancy, and our patient was in shock at presentation.

Diagnosis of heterotopic pregnancy could be challenging as ultrasound demonstration of an intrauterine pregnancy is not a reliable indicator for excluding an ectopic pregnancy.<sup>10</sup> Usually, clinical presentation include history of amenorrhea, abdominal pain, bleeding per vaginum and abdominal tenderness, while cervical motion tenderness was most common.<sup>10</sup> Our patient presented in shock and this is a common presentation in patients with ruptured ectopic pregnancy usually due to haemoperitonium.<sup>11</sup> As a result, she was actively resuscitated while being worked up for emergency exploratory laparotomy.

Laboratory findings done at presentation were full blood count, which showed a packed cell volume of 18%, all other differentials were within normal limits. Also, quantitative hCG was 22,300.0 MIU/ML, indicating pregnancy. A transvaginal ultrasound done showed one gestational sac with no fetal cardiac activity in the endometrial cavity with mean crown-rump length 6.7 mm corresponding to 9 weeks 0 days gestational age. A second gestational sac in the left adnexa with a fetal pole but no fetal cardiac activities was also seen with mean crown-rump length of 6.5 mm, corresponding to 8 weeks 3 days. Ultrasound also showed presence of haemoperitoneum. Unruptured ectopic pregnancy is normally visualized on USS in three forms including “blob” sign, “bagel” (doughnut) sign or a gestational sac with a fetal pole.<sup>12</sup> The findings of complex free fluid and an absent intrauterine gestation sac requires interpretation in conjunction with the beta hCG level. If the beta hCG is greater than 2000 IU, the findings are indicative of a ruptured ectopic pregnancy, in this case likely within the left adnexa.<sup>13</sup> Other investigations that can help in diagnosis of heterotopic pregnancy include magnetic resonance imaging and computer tomography.<sup>1-4</sup>

Management of heterotopic pregnancy with unruptured extra-uterine pregnancy and viable intrauterine fetus includes minimally invasive methods of terminating the extra-uterine sac while taking measures to preserve the intrauterine pregnancy.<sup>2,8,14</sup> Medical treatment options include an ultrasound-guided injection of potassium chloride into the corneal sac or fetal heart and single or multiple doses of methotrexate. Surgical management is necessary when the patients demonstrate any of the following: an indication of intraperitoneal bleeding,

symptoms suggestive of ongoing ruptured ectopic mass, or hemodynamically instability.<sup>15,16</sup> Ruptured ectopic pregnancy require surgical removal i.e. salpingectomy, salpingostomy or salpingotomy, which can be done either laparoscopically or through laparotomy. The gold standard is still laparoscopy.

However, our patient had laparotomy because at presentation, she was haemodynamically unstable and the fastest means of clamping the bleeding vessels was laparotomy. During the procedure, she also had manual vacuum aspiration of the missed miscarriage, and this helped to avoid further anaesthetic risk that could occur if the two surgeries were to be done separately. Samples obtained were sent for histology. The histological report later confirmed our diagnosis. Patient was properly informed about her diagnosis, counselled on her management in the Gynecology Clinic, she was counselled on family planning and asked to present in the hospital immediately she misses her menses.

In conclusion, heterotopic pregnancy poses a diagnosis and management challenge and carries risks of maternal morbidities. Either of the pregnancies may be missed during ultrasonography and during surgical management. Although heterotopic pregnancy in natural conception is a rare event than those as a consequence of assisted reproduction techniques, but the outcomes are the same if heterotopic pregnancy occurs. The incidence of heterotopic pregnancy following natural conception is probably rising which may be due to increased incidence of undiagnosed or poorly treated pelvic inflammatory disease and abuse of over-the-counter antibiotics that may result in antibiotic resistant strains of organisms. Multicenter studies is suggested as this will help in determining the current incidence of heterotopic pregnancy, and also help in allocation and planning of health care resources.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

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**Cite this article as:** Olaleye AA, Ejikeme BN, Ede EES, Okeke NE, Olinya BI, Edene CN, et al. Heterotopic pregnancy: a common masquerade than ever thought? *Int J Basic Clin Pharmacol* 2021;10:1410-3.