



## SILENT RUPTURE OF ECTOPIC PREGNANCY: A CASE REPORT AND LITERATURE REVIEW

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### ABSTRACT

Ectopic pregnancy is a major cause of morbidity among the women of reproductive age group worldwide. Ectopic pregnancy is the leading cause of maternal mortality in first trimester of pregnancy. Though this clinical condition is identified with clinical trial of amenorrhoea, vaginal bleeding and abdominal pain; but rarely the patient presents without these alarming symptoms. [Approximately half of patients present atypically and may in fact be asymptomatic at earlier gestations] At times ectopic pregnancy ruptures without any symptom, making the diagnosis difficult in absence of risk factors. This rare condition of silent rupture of ectopic pregnancy occurred with the case presented here. A 32 years old mangolian primigravida with spontaneous conception reported occasional spotting for few days with no pain abdomen at 6 weeks of gestation. She was apparently all well and the ultrasound report showing intrauterine gestational sac almost kept the patient out of suspicion for ectopic pregnancy. After four days of spotting, the abdominal distension with marked pallor compelled to repeat abdominal ultrasound, though it was suggested after 2 weeks. The ultrasound report showed intraperitoneal haemorrhage and ruptured ectopic pregnancy was suspected. Emergency exploratory laparotomy revealed left tubal rupture due to ectopic pregnancy and left salpingectomy was done. Ectopic pregnancy can be initially missed and remains a significant contributor to pregnancy-related deaths and decreased fertility. This case report suggests that ectopic pregnancy can rupture in absence of pain abdomen and significant vaginal bleeding and is expected to increase the awareness regarding atypical presentation of ectopic pregnancy.

**Key words:** asymptomatic; rupture; ectopic pregnancy; vaginal bleeding.

## INTRODUCTION

Ectopic pregnancy (EP) is a relatively common and potentially life threatening condition significantly affecting the fertility. [1] Ectopic pregnancy occurs when a fertilized ovum abnormally implants outside the endometrium of the uterus. [1,2,3]

The incidence of ectopic pregnancy has increased from 0.37% of pregnancies in 1948 to approximately 2% of pregnancies in 1992.

Although mortality due to ectopic pregnancy has decreased by nearly 90% from 1979 to 1992, yet it remains the leading cause of death during the first trimester of pregnancy, with a 9%–14% mortality rate. [2,3,4]

Although the exact aetiology of ectopic pregnancy is unknown; it is supposed that tubal implantation occurs as a result of a combination of arrest of the embryo in the fallopian tube and changes in the tubal microenvironment that facilitate early implantation of fertilized ovum before it could reach the uterine cavity. This defect in the transport of the fertilized ovum through the fallopian tube is controlled by a combination of smooth muscle contractions and ciliary beating. Conditions that damage the integrity of the tubal smooth muscle contractility and impair ciliary beating functions are the risk factors for ectopic pregnancy. [5,6] Inflammation within the tube, due to infection or smoking or toxic stimuli immunologic and hormonal alterations, may affect embryo-tubal transport by disrupting smooth muscle contractility and ciliary beat activity and may also provide pro-implantation signals. [2,5,6]

Although the incidence in the developed world has remained relatively static in recent years, between 1972 and 1992 there was an estimated six-fold rise in the incidence of ectopic pregnancy; and it is supposed that the problem is in increasing trend in developing country though the exact data are not available. [6]

This increase was attributed to three factors: an increase in risk factors such as pelvic inflammatory disease and smoking in women of reproductive age, the increased use of assisted reproductive technology (ART) and increased awareness of the condition, facilitated by the development of specialised early pregnancy units (EPUs)[2,6] Over 98% of ectopic pregnancies implant in the Fallopian tube, in its ampullary region (70%), isthmus (12%) or fimbria (11.1%). Interstitial or cornual ectopics, where the pregnancy implants in the intramyometrial portion of the Fallopian tube, are less common (2.4%) but have a mortality twice than that of any other type of fallopian tube ectopic pregnancy. Rarely, an ectopic pregnancy implants at an extratubal location, such as the cervix, ovary, abdomen, liver, spleen or Caesarean section scar.[1,6]As an ectopic pregnancy enlarges, its risk for rupture increases.[2] Typically, tubal ectopic pregnancies in the isthmus rupture within the first few weeks of gestation, with the ampulla being slightly more expandable, the pregnancy could continue beyond first trimester.[1]

Classic presenting symptoms include lower quadrant abdominal pain, vaginal bleeding, and amenorrhea.[1,2]

Although pelvic pain is the common clinical presentation, the severity of pelvic pain does not necessarily correlate with the size of an ectopic pregnancy, and pain may even decrease or disappear following tubal rupture[1]

As observed in the presented case vaginal bleeding may be insufficient to indicate rupture of ectopic pregnancy.

Approximately half of patients present atypically and may in fact be asymptomatic at earlier gestations .[1,2] Such asymptomatic patients suspected to have ectopic pregnancy are to be monitored with serum  $\beta$ -hCG levels . In ectopic pregnancies are often characterized with slower rise of serum  $\beta$ -hCG levels . If  $\beta$ -hCG levels increase by less than 50% during a 48-hour period, there is almost always a nonviable pregnancy, may it be associated with intra- or extrauterine pregnancy; this gives a clue to suspect ectopic pregnancy. Eighty-five percent of viable intrauterine pregnancies reflect an increase in  $\beta$ -hCG levels of 66% or more during a 48-hour period . However, up to 21% of ectopic pregnancies demonstrate a  $\beta$ -hCG doubling time identical to that of intrauterine pregnancies . Arriving at a  $\beta$ -hCG plateau early in the pregnancy is highly suggestive of an ectopic pregnancy, though not diagnostic.[2,5]

A normal serum progesterone level in viable pregnancies is typically more than 25 ng/mL. Ninety-nine percent of nonviable pregnancies have a progesterone level of less than 5 ng/mL. The combination of a low serum progesterone level and an abnormal rise in serum  $\beta$ -hCG is nearly diagnostic of a nonviable pregnancy although not exact indicator of ectopic pregnancy.[5,6]

Diagnosis can be straightforward when a transvaginal ultrasound scan (TVS) positively identifies an IUP or ectopic pregnancy. However, TVS fails to identify the location of a pregnancy in a significant number of women and such women are currently diagnosed as having a 'pregnancy of unknown location' (PUL).[6]

The 2006–2008 CMACE report drew attention to a maternal death secondary to ruptured ectopic pregnancy where a diagnosis of PUL had been made. Although most patients with a PUL will subsequently be diagnosed with either a failed IUP (a spontaneous abortion) or viable IUP, the report highlights that 7-20% will be diagnosed with an ectopic pregnancy. It is therefore very important that a diagnosis of PUL should trigger further diagnostic pathways and follow-up until the final outcome of the pregnancy is known.[3,6]

Despite modern advances in diagnostic technologies during the last 20 years , around half of the women with an eventual diagnosis of ectopic pregnancy are not diagnosed at their first presentation. [6] Early diagnosis reduces the risk of tubal rupture and allows more conservative medical treatments to be employed. Ectopic pregnancy is one of the few medical conditions that can be managed expectantly, medically or surgically depending on how early the diagnosis can be made.[2,6]

## CASE REPORTS

A 32 years old mangolian primigravida with history of spontaneous conception after five years of marriage presented to the outpatient department with complain of occasional spotting for 2 days at 6 weeks 0/7 day of pregnancy and denied history of pain abdomen .She was having normal menstruation every 32-

34days with bleeding for 3-4days until 6 weeks back when she had her last menstrual period. Pregnancy was confirmed after 8 days of her missed period by urine pregnancy test done at local healthcare centre. She was advised to continue taking Folic acid tablet and follow up in the hospital after two weeks for ultrasound scan. Her past medical and surgical history was not relevant. She was non alcoholic and non smoker. She had normal appetite, sleep, bladder and bowel habits. Her vital signs were within normal range with Pulse-68/minute, Blood pressure- 120/70 mm of Hg, Respiratory rate-18/minute and Temperature-98.2 F. She was afebrile with no abnormality detected on systemic examination. On per abdomen examination no abnormality was detected with soft, non-tender abdomen. On per speculum examination –normal cervix with no evidence of bleeding was seen. Bimanual examination was avoided and abdominal ultrasound examination was advised, along with complete blood count and routine urine examination. Her blood count was within normal range with Haemoglobin -12.6 gm/ dl and routine urine examination showed no abnormality. The first ultrasound done at 6 weeks of pregnancy showed intrauterine gestational sac appropriate for the period of amenorrhoea. Since fetal pole was not clearly visualized, she was advised to repeat ultrasound after 2 weeks for better interpretation of fetal development. Since she had conceived five years after marriage and was over concerned about the fetal wellbeing; she was admitted to the hospital on request, for observation with provisional diagnosis of threatened abortion, though the clinical finding was not significant enough to diagnose threatened abortion. She was advised bed rest and to keep her activity limited to basic self care. Everyday on rounds her vitals were stable and abdomen soft and non tender. After two days of her hospital stay, on third day morning round she had said she did not feel like eating anything and had some abdominal discomfort while walking; not otherwise. On examination she was apparently pale though her vitals were within normal range with blood pressure 90/60 mm of Hg and pulse 94 beats per minute, Respiratory rate-20/minute and temperature-98.4 F. Abdomen was distended with mild tenderness and guarding, there was no rigidity. Vaginal spotting was minimal, just one small spot on undergarment. Except obvious pallor and abdominal distension there was no any sign or symptom to indicate the possible pathology. Blood was sent for complete blood count and cross-match. Emergency ultrasound was advised to seek for the cause of abdominal distension. The ultrasound report showed intraperitoneal haemorrhage with suspected rupture of ectopic pregnancy. Emergency exploratory laparotomy was done under general anaesthesia. Intraoperatively –about 1400ml of blood and clots were removed, bleeding from the rupture at the isthmus of left fallopian tube was noted and left salpingectomy was done. The patient was transfused four units of whole blood in post operative period, then she had smooth recovery and was discharged after four days.

## DISCUSSION

In context of ectopic pregnancy clinical suspicion is the key to identifying the women who need prompt and careful evaluation. The risk of EP increases 2-fold for infertility, 3-fold for tubal pathology and 4-fold for documented salpingitis. [3,7] Chlamydia trachomatis has been linked to 30-50% of all ectopic pregnancies. The exact mechanism of this association is not known but it has been proposed that in addition to distortion of tubal

architecture, it may alter the tubal microenvironment. [3,6] One third of pregnancies in women who have been sterilised and one half in women with a LNG-IUS (intrauterine contraceptive device) are likely to have ectopic. [7] One third of all cases of ectopic pregnancy are thought to be associated with smoking. In vitro fertilisation (IVF) is associated with 2-5% risk for an ectopic pregnancy. The risk of ectopic pregnancy increases with advancing maternal age, with age over 35 years being a significant risk factor.[3,6] The risk of recurrence is approximately 10% for women with one previous EP and at least 25% for women having two or more previous EP's. This suggests that Women with a history of EP should be given early access to an EPAU in a future pregnancy.[3,7]

According to one retrospective, descriptive study of ectopic pregnancies (conducted by Osaheni LLawani et.al) managed in EBSUTH (a state tertiary health facility in Abakaliki, Ebonyi State, Nigeria) over the 10-year study period (June 1, 2002 to May 31, 2012) analysis of total 205 cases were done of which more than half had a past history of induced abortion, while (43.4%) had pelvic inflammatory disease, as risk factors for ectopic gestation. Other associated risk factors were previous history of abdominopelvic surgery (8.8%), puerperal sepsis (8.3%), previous ectopic pregnancy (3.4%), and use of intrauterine contraceptive devices. It was observed in the study that the significant proportion (67 of 205, 32.68%) of these were nulliparous, while only six of 205 (2.93%) were grand multiparous. This data suggests strong association of ectopic pregnancy with infertility. The mean age of the patients was observed to be  $27 \pm 3$  years and this was supposed to be due to risky sexual behavior in this age group, in the concerned area of study. [8]

Although the literature mentions that the women with ectopic pregnancy frequently have no identifiable risk factors, like the patient in the presented case; a prospective case-controlled study has shown that increased awareness of ectopic pregnancy and a knowledge of the associated risk factors helps identify women at higher risk in order to facilitate early and more accurate diagnosis.[6] Patients with an ectopic pregnancy commonly present with abdomino-pelvic pain and vaginal bleeding between 6 and 10 weeks' gestation. However, these symptoms are common in early pregnancy, with one third of women experiencing some pain and/or bleeding, even in normal intrauterine pregnancy and most of the time it is self-limiting though at times may indicate spontaneous abortion.[5,6] The pain can be persistent and severe and is often unilateral. However, unilateral pain is not always indicative of ectopic pregnancy as, in early pregnancy, a prominent painful ovarian corpus luteum cyst is common. [6]

According to the retrospective, descriptive study of ectopic pregnancies (conducted by Osaheni LLawani et.al) managed in EBSUTH during the study period (June 1, 2002 to May 31, 2012) showed that the incidence of ectopic pregnancy in the study was 2.1% out of which (95.6%) had ruptured ectopic pregnancies, while (4.4%) were unruptured. The observation also concluded that the commonest clinical presentation was abdominal pain (80.0%), amenorrhoea (79%), vaginal bleeding (65.4%), followed by dizziness/fainting attack (37.1%), and shock (10.2%). The majority of the patients (79%) presented with amenorrhoea of which 99.1% of which was 12 weeks. [8] The similar data correlating the findings in above study has been mentioned in the literature as well.[6]

Among the various presentation shoulder tip pain, syncope and shock occur in up to 20% of women and abdominal tenderness in more than 75% indicate ruptured ectopic.[2,6] Although Cervical motion tenderness can be elicited in up to 67% of cases, and a palpable adnexal mass in about 50%. Bimanual examination, is usually avoided due to fear of aggravating haemorrhage. [6]

According to the literature up to 50% of patients who have an ectopic pregnancy could be asymptomatic this causes delay in diagnosis and predispose the patient to risk of rupture.[1,2] More recently, it has been reported that one third of women with ectopic pregnancy have no clinical signs and 9% have no symptoms.[6]

The presented case in her early pregnancy had spotting now and then only, no frank vaginal bleeding and no pain abdomen at all.All of the above studies indicate that the classic symptoms may not always be the presenting feature of ectopic pregnancy.

In contrast to the above condition ,it is also important to remember that a woman may present with abdominal pain without knowledge of her pregnancy status. For this reason, any woman of childbearing age who presents with abdominal pain or abnormal vaginal bleeding should be evaluated for pregnancy as part of the initial examination.[5]

When the patient falls in clinical suspicion for ectopic pregnancy the serum markers like  $\beta$ -hCG and progesterone can give clue to the diagnosis of ectopic pregnancy, yet ultrasound remains the cornerstone modality of the diagnosis with greater accuracy being achieved by transvaginal sonography compared to abdominal sonography.In such a clinical condition,one of the key elements in the diagnosis is the exclusion of a viable or non-viable IUP[6] The identification of an IUP can rule out ectopic pregnancy in most settings unless a heterotopic pregnancy is suspected, where an ectopic pregnancy coexists with an IUP. They are rare (1 in 40,000), although more common after assisted conception, and difficult to diagnose. [5,6,9] In the absence of an intrauterine gestation sac, an ectopic pregnancy can be diagnosed by the presence of an adnexal mass, often visible within the Fallopian tube. The positive identification of a non-cystic adnexal mass with an empty uterus has a sensitivity of 84-90% and a specificity of 94-99% for the diagnosis of an ectopic gestation. [6]

Moreover, it is recognised radiographic practice that an IUP is only definitively diagnosed by ultrasound visualisation of a yolk sac or embryo in addition to a gestational sac.[5,6] This is because an ectopic pregnancy can be accompanied by a 'pseudosac', a collection of fluid within the endometrial cavity that may be the result of localised breakdown of the decidualised endometrium ' pseudosac' which is estimated to be seen in 10% of patients with ectopic pregnancies. [6,9]

In a very early normal pregnancy below the detection threshold for US visualisation of IUP gestational sac even in absence of yolk sac or embryo with normal-appearing adnexa suggests normal IUP. In such cases, clinical and US follow-up are recommended.[9]

This was the exact clinical scenario of the case presented here.

However, central location of 'pseudosac' within the endometrial cavity distinguishes it from the very early gestation sac that is typically eccentrically placed.[6] Real-time observation of this phenomenon will often

show a shifting of the fluid as the exam progresses, unlike the fixed position of a true intrauterine gestational sac. [9] In addition, pseudosacs are transient rather than consistent and they do not have a hyperechoic decidual reaction around them. [6] A sonographer with experience in early pregnancy scanning should generally be able to tell the difference between a pseudosac and an empty early intrauterine sac. [6,9]

As observed in one large prospective study of 6621 patients, ectopic pregnancy was correctly diagnosed by TVS with a sensitivity of 90.9% and specificity of 99.9%. False positives can, however, occur if other structures such as the corpus luteum, bowel, a paratubal cyst, a hydrosalpinx or an endometrioma are mistaken for an ectopic pregnancy. False negatives can occur if the ectopic is small or if it is concealed by bowel or uterine anomalies such as fibroids. [6]

As the presence of pseudosac is misleading so is the absence of suspicious adnexal mass indicating ectopic pregnancy. It is estimated that 15%-35% of patients with ectopic pregnancy do not have an extrauterine mass identified on transvaginal US[9] It is therefore possible for an ectopic pregnancy to go unnoticed on an ultrasound scan, especially if the patient is asymptomatic. [6,9]

As ectopic pregnancy affects young, fit women they are often able to mount remarkable haemodynamic compensation [6], as seen in our patient, the presented case. In the presented case, presence of a 'pseudosac' was mistakenly thought to be IUP, this being supported by the absence of suspicious adnexal mass indicating ectopic pregnancy. So, the vaginal spotting was considered to be the symptom of threatened abortion. The absence of pain and vaginal bleeding with vitals within normal range also spared her from being suspected for the actual condition; she had suffered from 'silent rupture of ectopic pregnancy'.

The similar incidents have been reported in the literature. Maternal and Child Enquiries (MACE) report, four of the six women who died from early ectopic pregnancy complained of diarrhoea, dizziness or vomiting as early symptoms, without triggering any consideration of extrauterine pregnancy by their medical attendants. [6]

Similarly, one of the retrospective reviews of women with tubal EP mentioned that a young woman who collapsed on arrival at hospital and died – a differential diagnosis of ectopic pregnancy was provided, but could not be substantiated through documentation of a positive pregnancy test result or autopsy findings. That study also revealed the possibility that EPs causing maternal death may have been missed. [10]

The Confidential Enquiries into Maternal Deaths reports (1997-1999 and 2003-2005) highlighted that most of the women who died from ectopic pregnancy were misdiagnosed in the primary care or accident in the emergency settings. [6] According to a retrospective review of women with tubal EP managed at Modilon General Hospital (MGH), Madang Province, PNG, during 56 months of the period (01/01/2008 – 31/08/2012); 77 women were treated for ectopic pregnancy mentioned that none of the 77 women with confirmed ectopic pregnancy of any type died. In the same study, four cases were not EP: women underwent surgery for clinical suspicion of EP but were subsequently confirmed to have viable intrauterine pregnancies (n = 3) or ruptured luteal cysts (n = 1). Out of those four women with negative findings on laparotomy, two of them had a positive culdocentesis. It has been suggested that the accuracy of diagnostic aids need to be evaluated. [10] Since

ectopic pregnancy may mimic other gynaecological disorders and gastrointestinal or urinary tract disease, including appendicitis, salpingitis, ruptured corpus luteum or follicular cysts, threatened or inevitable spontaneous abortion, ovarian torsion and urinary tract infection; achieving a definitive diagnosis is important for proper management of patient.[6]

Following rupture of EP, salpingectomy has been considered the ideal and commonest life-saving surgical procedure.[6,8]

## CONCLUSION

To establish definitive diagnosis in the setting of atypical clinical presentations of ectopic pregnancy remains a challenge for the clinician.

It is difficult to diagnose an ectopic pregnancy from risk factors, history and examination alone. Ultrasound is an important modality of establishing diagnosis, yet at times confusing the diagnosis; when 'pseudo' gestational sac is mistaken for intrauterine pregnancy and corpus luteum cyst or other adnexal mass is mistaken for ectopic pregnancy. In former condition patient may suffer life-threatening event of ectopic rupture whereas in later condition patient may undergo unnecessary interventions including surgery; ultimately both the conditions contributing to increased morbidity and mortality among the women of reproductive age group. At this stage being aware of the atypical presentation of ectopic pregnancy can be regarded to be of great value.

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