

Simultaneous Tubal Heterotopic Pregnancy with Acute Appendicitis: A Case Report and Literature Review of 5 Cases

Akut Apendisit ile Eş Zamanlı Tubal Heterotopik Gebelik: Bir Olgu Sunumu ve 5 Olgunun Literatür Taraması

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Abstract

Heterotopic pregnancy (HP) is a serious obstetrics phenomenon that occurs when both intrauterine and ectopic pregnancies exist simultaneously. It is an extremely rare condition with potentially life-threatening outcomes. The incidence of acute appendicitis in pregnancy is generally less common compared to the non-gravid population, and its coexistence with HP is exceedingly rare. Herein, we report a case of HP complicated with appendicitis that occurred in a 32-year-old G2P1 female presenting at 12 weeks of gestation with acute severe right lower abdominal pain. She denied any history of assisted reproductive technology or risk factors for ectopic pregnancy. On examination, the patient was conscious, oriented, afebrile, and hemodynamically stable. The abdomen was distended and tender on palpation. Pelvic ultrasonography demonstrated viable intrauterine pregnancy with a heterogenous mass within the right uterine wall with surrounding peripheral vascularity. Fluid collections were also visible in the intraperitoneal cavity. The patient underwent emergency laparotomy with right salpingectomy and appendectomy. Early diagnosis and treatment are correlated with favourable obstetrics outcomes and long-term prognosis. A surgical approach with either laparoscopy or laparotomy is more appropriate compared to medical or conservative management.

Keywords: Appendectomy, appendicitis, ectopic pregnancy, heterotopic pregnancy, salpingectomy

Öz

Heterotopik gebelik (HP), hem intrauterin hem de ektopik gebeliklerin aynı anda var olduğu durumlarda ortaya çıkan ciddi bir obstetrik fenomendir. Potansiyel olarak yaşamı tehdit eden sonuçları olan son derece nadir bir durumdur. Gebelikte akut apandisit insidansı genellikle gebe olmayan popülasyona göre daha az görülür ve HP ile birlikteliği son derece nadirdir. Burada, gebeliğin 12. haftasında akut şiddetli sağ alt karın ağrısı ile başvuran 32 yaşında G2P1 bir kadında ortaya çıkan apandisit ile komplike bir HP olgusu sunuyoruz. Herhangi bir yardımcı üreme teknolojisi öyküsünü veya ektopik gebelik için risk faktörlerini reddetti. Muayenede hastanın bilinci açık, oryante, ateşsiz ve hemodinamik olarak stabildi. Karın palpasyonu ile şişmiş ve hassastı. Pelvik ultrasonografi, sağ uterus duvarında çevreleyen periferik vaskülarite ile heterojen bir kitle ile canlı intrauterin gebelik gösterdi. İntraperitoneal boşlukta sıvı koleksiyonları da görüldü. Hastaya sağ salpenjektomi ve apendektomi ile acil laparotomi uygulandı. Erken tanı ve tedavi, olumlu obstetrik sonuçlar ve uzun vadeli prognoz ile ilişkilidir. Laparoskopi veya laparotomi ile cerrahi bir yaklaşım, tıbbi veya konservatif tedaviye kıyasla daha uygundur.

Anahtar kelimeler: Apendisit, apendektomi, ektopik gebelik, heterotopik gebelik, salpenjektomi



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Cite this article as: Alkouz YB, Jihwaprani MC, Ismirahmadani TD, Abdulmonem MA, Mousa AA. Simultaneous Tubal Heterotopic Pregnancy with Acute Appendicitis: A Case Report and Literature Review of 5 Cases. Bagcilar Med Bull 2023;8(4):386-391

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Introduction

Heterotopic pregnancy (HP) is a condition characterized by the coexistence of intrauterine pregnancy (IUP) with ectopic pregnancy (EP). Acute appendicitis, although relatively uncommon during pregnancy, is the most common non-obstetrics cause of acute abdomen in a pregnant woman. The simultaneous occurrence of HP with acute appendicitis poses an extremely difficult diagnostic challenge as both conditions are rare in the pregnancy setting. Delayed diagnosis and management can result in dreaded complications, including intraperitoneal hemorrhage, peritonitis, sepsis, shock, and death. Similar to EP, the majority of HPs occur in the fallopian tube. There is growing evidence of the rise in the incidence of HP with the widespread use of assisted reproductive technology (ART). Its application also increases the risk for more atypical sites and the complexity of the condition (1). Radiological studies have become increasingly reliable in accurately diagnosing HP (2,3). The aim of the management of HPs with concurrent acute appendicitis is to resolve the pathology of the appendix and EP while attempting to preserve the IUP. Our center experienced a rare case of HPs with concurrent acute appendicitis in a 32-year-old G2P1, presenting at 12 weeks of gestation with severe recurrent abdominal pain, nausea, and vomiting. Radiological studies with transabdominal pelvic ultrasonography (TAUS) confirmed the diagnosis of HP while acute appendicitis was found to be inflamed during laparotomy. Subsequent management with appendectomy and right salpingectomy was performed and the patient was able to continue her pregnancy with routine antenatal follow-up.

Case Report

We present the case of a 32-year-old G2P1 female at 12 weeks of gestation. She was a known case of spontaneous conception without prior ART. Her last pregnancy was 11 years ago and was delivered via vaginal delivery. She presented to the emergency department (ED) with a 1-day history of severe lower abdominal pain. The abdominal pain started abruptly and was described as stabbing pain in the right iliac fossa (RIF). The pain has progressively worsened since the onset. The pain was associated with nausea and several bouts of non-bilious vomiting. She denied the presence of urinary symptoms and vaginal spotting. The past medical history includes a history of irritable bowel syndrome.

She has had 2 previous hospital admissions since the start of her pregnancy. Her initial admission was 7.5 weeks ago

for evaluation of pregnancy of unknown location. Her initial β -hCG was 5.851 mIU/mL 48 hours before admission, with a follow-up β -hCG of 7.622 mIU/mL. The patient strictly refused transvaginal pelvic ultrasonography (TVUS). A TAUS was then performed, revealing a normal uterus size and a small echo lucent area in the endometrial cavity that could indicate an early intrauterine gestational sac (IUGS). The fetal pole could not be visualized, and the right and left ovaries were normal in size. There was no visible free fluid in the pelvic cavity. The plan was for an outpatient department (OPD) antenatal follow-up after 4 weeks.

The patient presented to the ED 3 days prior to her OPD appointment with lower abdominal pain and vaginal spotting. A bedside US showed a single viable fetus consistent with 10 weeks of gestation and positive fetal cardiac activity (FCA). The patient was diagnosed with threatened abortion and was discharged on analgesics and progesterone support. One week later, she presented again to the ED with severe lower abdominal pain and worsening dizziness. Laboratory investigation showed anemia and normal leukocyte counts. Initial TAUS showed moderate fluid collection seen in Morison's pouch and left splenorenal region (Figure 1). She was admitted for further investigation and observation. A subsequent follow-up TAUS revealed a localized tender oval-shaped heterogeneous soft tissue mass located adjacent to the right wall of the uterus. The mass could not be delineated from the right ovary, measuring 4.6x3.4x3.6 cm with mild peripheral vascularity. Additionally, the mass displayed neither demonstrable calcification nor mesenteric lymphadenopathy. An initial diagnosis of HP was confirmed. The decision was made by a multidisciplinary team for surgical management. However, the patient refused and insisted on non-surgical management. Consequently, the patient was treated conservatively with analgesics, hydration, broad-spectrum antibiotics, and observation with serial TAUS. She was eventually discharged after 9 days of conservative treatment.

On physical examination, the patient was conscious and oriented. The patient's vital signs were stable. She was afebrile. Abdominal examination revealed rebound tenderness over the RIF region and a moderately distended abdomen. Laboratory evaluation showed Hb of 11.3 g/dL, leukocytes of $9.8 \times 10^3/\mu\text{L}$ (n=4-10), and neutrophils of $7.9 \times 10^3/\mu\text{L}$ (n=2-7.5). TAUS revealed a single viable fetus with a crown-rump length consistent with 12^{3/7} weeks gestation. The previously seen heterogeneous mass was visible within the right uterine wall measuring 3.2x4.1 cm

with unclear peripheral vascularity (Figure 2). Severe fluid was detected in both sides of the pelvic cavity measuring 5.9x5.6x5 cm. Moderate fluid collections were also visible in Morison's pouch. Other abdominal structures, including the appendix, could not be visualized clearly. The scanning process was notably difficult due to obstructed fields by bowel, gas, and probe tenderness throughout the scanning examination.

The decision was made for emergency exploratory laparotomy with the attendance of a general surgeon. Informed consent was received from the patient. An infraumbilical midline skin incision was made. Ruptured right fallopian tubal pregnancy was confirmed Figure 3, and the appendix was found to be grossly inflamed. There was no active bleeding at the ruptured tube and sealed with a clot. The left fallopian tube was intact. Both the right and left ovaries looked intact. Hemoperitoneum was seen and

evacuated by scooping and suction. Right salpingectomy and appendectomy were performed. The excised appendix and right fallopian tube were sent for histopathology. Hemostasis was secured and a drain was subsequently placed. Histopathology report of the appendix revealed lymphoid tissue hyperplasia, sheets of macrophages, and giant cells confirming acute appendicitis, whereas the right fallopian tube confirmed the diagnosis of tubal ectopic pregnancy.

Postoperatively, the patient made an excellent recovery. The drain was removed on postoperative day 2. The wound healed without any problem. The patient was discharged on postoperative day 4. OPD follow-up was scheduled after 10 days and she showed progressive recovery and reassuring IUP. The patient underwent routine antenatal checkups in our hospital until 41 weeks of gestation when she insisted to deliver at another hospital. Her delivery outcome is unknown.

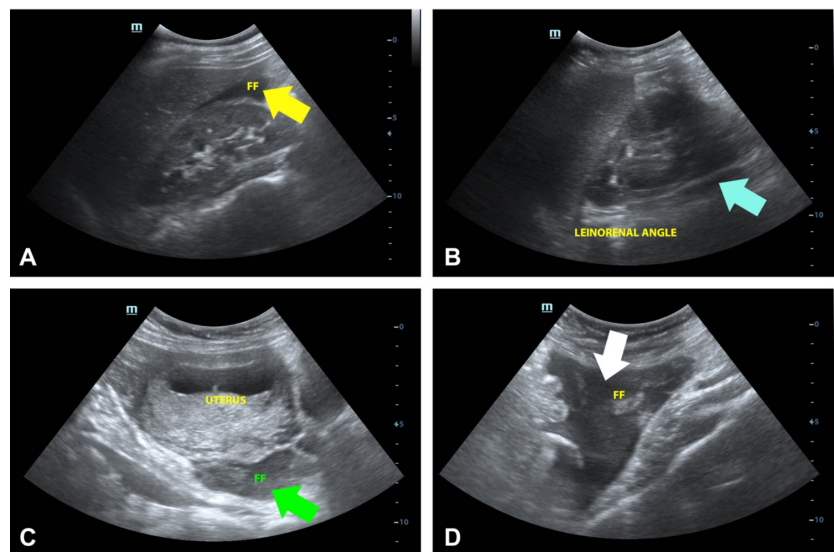


Figure 1. TAUS of the patient demonstrated moderate fluid collection in hepatorenal angle (A, yellow arrow), splenorenal angle (B, blue arrow), pouch of Douglas (C, green arrow), and Morison's pouch (D, white arrow)

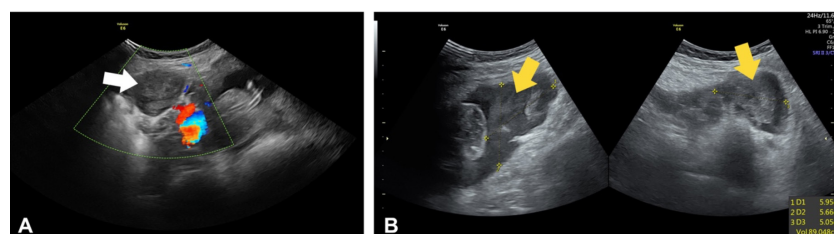


Figure 2. TAUS of the patient at 12^{3/7} weeks of gestation showed a heterogenous mass within the right uterine wall measuring 3.2x4.1 cm (A, white arrow) with peripheral vascularity observed around the mass. Severe fluid collections were visible on both sides of the pelvic cavity measuring approximately 5.9x5.6x5.0 cm (B, yellow arrows). Fluid collection was also observed in Morison's pouch and splenorenal recess

TAUS: *Transabdominal pelvic ultrasonography*

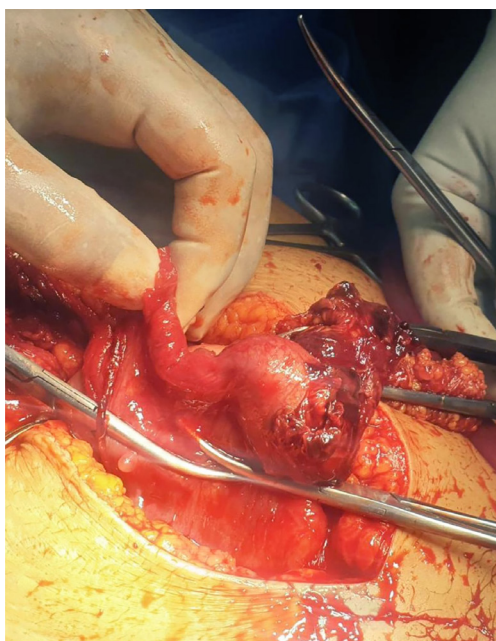


Figure 3. Intraoperative image of the ruptured ampullary part of the right Fallopian tube

Discussion

Here, we described the case of spontaneous HP with coexisting acute appendicitis. HP is exceedingly rare. Its incidence is approximated to be 1/30,000 spontaneous pregnancies (2). However, the risk increases in pregnant women following successful ART, with an estimated incidence of 0.1-1.0% (4). In addition, the incidence rate of acute appendicitis during pregnancy is reported to be between 1/1,250 and 1/1,500 (5). Currently, the incidence of concurrent appendicitis with HP is unknown, with only limited cases have been reported in the literature. We conducted a literature search on Medline/PubMed and Google Scholar using the following keywords: [heterotopic pregnancy (Title/Abstract)] AND [appendicitis (Title/Abstract)]. Our literature search as of February 2023 has yielded only 7 relevant available case reports. Two articles were excluded for unavailable full text. A literature review of the topic is summarized in Table 1. Our case report is also included in the analysis.

Table 1. Characteristics of the included case reports

Authors	Year	Country	Age/GP	GA (w)	PMH	Clinical presentation	Diagnosis confirmation/ Site of EP	Intervention	Obstetric outcome
Murewanhema et al. (6)	2020	Zimbabwe	34/G3P2+0	11	No significant PMH/PSH	Abdominal pain, poorly localized vaginal bleeding backache WBC: 18.3	Radiological diagnosis (US) fallopian tube (left)	Laparotomy with midline incision appendectomy and left salpingectomy	Pregnancy continues Delivery outcome: N/A
Downes (7)	2015	Bahamas	36/G3P1+1	6	Unruptured ectopic pregnancy with salpingostomy	Abdominal pain, periumbilical migrating to RIF nausea, vomiting WBC: 17.1	Surgical diagnosis fallopian tube (right)	Single-port laparoscopy appendectomy and right salpingectomy	Pregnancy continues LSCS
Barnett et al. (8)	2009	UK	32/G1P0+0	9	Primary infertility due to tubal damage Prior IVF	Abdominal pain RIF vomiting, diarrhea WBC: 8.1	Surgical diagnosis fallopian tube (left)	Laparotomy Pfannenstiel's incision appendectomy and right salpingectomy	Twin pregnancy continues multiple admissions for HG CS at 37 th week
Daponte et al. (9)	2006	Greece	31/G1P0+0	6	Prior IVF 6 times	Abdominal pain RIF nausea, anorexia WBC: 15.9	Radiological diagnosis (US) fallopian tube (right)	Laparotomy appendectomy and right salpingectomy	Pregnancy continues CS at 38 th week
Radwan et al. (10)	2006	Poland	35/G4P0+4	7	N/A	Lower abdominal pain	Radiological diagnosis (US) fallopian tube (right)	Laparoscopy appendectomy and right salpingectomy	Pregnancy continues delivery at 39 th week

US: Ultrasonography, WBC: White blood cell, RIF: Right iliac fossa, EP: Ectopic pregnancy

The median age of the patients is 33 years (range between 31-36 years old). The majority of cases were diagnosed in the first trimester, with the median gestational age at the presentation of 8 weeks of gestation (range between 6-12 weeks). A total of 33.3% (2 in 6 women) were in their first pregnancy. In addition, as many as 50% of women have preceding risk factors for HP (2), including ART (33.3%), tubal damage including salpingostomy (33.3%), and a previous history of EP (16.7%). Our patient has no identifiable risk factor.

The diagnosis of HP is especially challenging and is sometimes missed due to the paradoxically reassuring presence of IUGS on the ultrasonography (US) (2). The presence of IUGS sometimes, and frequently, distracts physicians from the suspicion of possible extrauterine pregnancy. The clinical manifestations are generally non-specific and overlap with other more common obstetrics problems. In this review, all patients presented with abdominal pain, which is mostly right lower abdominal pain (66.7%). Nausea and vomiting are typical, occurring in 66.7% of women. Other symptoms include vaginal spotting, backache, and anorexia. Fever is unexpectedly not observed in any of the patients. This, compounded by low suspicion of intraabdominal non-obstetrics pathologies such as appendicitis, makes the diagnosis of concurrent HP with acute appendicitis frequently delayed. Delayed diagnosis may subsequently lead to complications such as rupture with peritonitis, intraperitoneal hemorrhage, sepsis, shock, and even death.

Historically, the majority of HPs were diagnosed surgically (3). However, the definitive diagnosis of HP has mostly shifted toward radiological diagnosis, mostly by US (2). This is primarily due to the improved quality of sonographic imaging in addition to the increased awareness following the rising popularity of ART in recent years. Importantly, TVUS is preferred since it provides better accuracy in diagnosing EP compared to TAUS and permits earlier detection. In this review, HP was diagnosed radiologically in 66.7% of cases. In the case of acute appendicitis in pregnancy, the diagnosis is particularly challenging, as clinical diagnosis using the Alvarado score may be unreliable during pregnancy (6). Many obstetrics conditions can also mimic acute appendicitis, such as miscarriage, ectopic pregnancy, round ligament pain, adnexal torsion, and placental abruption. Visualization of the appendix by the US, as in our case, can be difficult, especially when EP has ruptured and the view becomes obstructed by increased intraperitoneal and bowel gas.

Although the management of HP may include medical management by either methotrexate or US-guided potassium chloride injection, the management of HP with concurrent acute appendicitis should primarily be surgical (4). Methotrexate should not be used if IUP is viable and continuation of pregnancy is desirable. The surgical approach is generally preferable, with options being either laparoscopy or laparotomy. The laparoscopic approach is generally safe in pregnancy and is desirable in hemodynamically stable patients. Alternatively, laparotomy is frequently done in the emergency setting when the patient is hemodynamically unstable. Other indications may include the surgeon's expertise, preference, and available modalities. In this review, the majority of cases (66.7%) were managed by laparotomy with subsequent salpingectomy and appendectomy. The authors recommend against conservative management in the case of HP with concurrent acute appendicitis as it has proven ineffective to treat the patient's condition in our case.

Conclusion

HP is rare, and its coexistence with acute appendicitis is exceedingly uncommon. However, with the more widespread use of ART, the condition may become more frequently encountered in the clinical setting. Misdiagnosis can occur owing to its rarity, however delay in diagnosis may potentially be fatal. The presence of IUP doesn't exclude the possibility of coexisting EP. Therefore, a low threshold of suspicion for HP should be applied even in the presence of an established IUP. The clinicians should get detailed clues and focus on narrowing the possible differential diagnosis. In our case, there were no identifiable risk factors that could be obtained, therefore, a trained clinical judgment is necessary. Early surgical management with either laparotomy or laparoscopy is the mainstay of therapy and is associated with good outcomes.

Ethics

Informed Consent: Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Concept: Y.B.A., M.C.J., T.D.I., M.A.A., Design: Y.B.A., M.C.J., T.D.I., M.A.A., Data Collection or Processing: Y.B.A., M.A.A., Analysis or Interpretation: M.C.J., T.D.I., Drafting Manuscript: M.C.J., T.D.I., Critical Revision of Manuscript: Y.B.A., M.C.J., T.D.I., M.A.A., Final Approval

and Accountability: Y.B.A., M.C.J., T.D.I., M.A.A., Technical or Material Support: Y.B.A., M.A.A., Writing: Y.B.A., M.C.J., T.D.I., M.A.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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