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CASE REPORT

A Case Report of Retroperitoneal Ectopic Pregnancy and Review of Literature

Liqun Xia, Tongyun Qi, Jianhua Qian

Department of Gynecology, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, 310002, People's Republic of China

Correspondence: Jianhua Qian, Email qianjianhua@zju.edu.cn

Background: Retroperitoneal ectopic pregnancy (REP) is a rare form of ectopic pregnancy, in which fertilised eggs are implanted in the retroperitoneal cavity. Due to its atypical location and non-specific symptoms, REP is often misdiagnosed, leading to delayed treatment. This condition poses serious risks owing to its proximity to the retroperitoneal blood vessels. Limited research and lack of specific guidelines make the management of REP challenging.

Case Report and Literature Review: A 47-year-old woman with REP was initially misdiagnosed as having acute gastroenteritis due to severe abdominal pain and gastrointestinal symptoms. She had amenorrhoea and significant lower abdominal pain, but no vaginal bleeding. After 35 days of amenorrhoea, the patient's serum beta-human chorionic gonadotropin (β-hCG) level was 16111.94 mIU/mL. Imaging revealed no intrauterine gestational sac; however, a mass was detected in the left adnexal area. Emergency laparoscopy identified a 3.0 cm ectopic mass in the retroperitoneal space, adjacent to the lower edge of the left broad ligament and near critical structures, with surface rupture and bleeding. The mass was surgically removed, and the patient's β-hCG levels returned to normal 33 days post-surgery. In addition, we reviewed previously published English literature on REP, highlighting its characteristics, pathogenesis, diagnosis, and treatment with the aim of improving the understanding and management of the condition.

Conclusion: REP is difficult to diagnose because of its rarity and nonspecific symptoms. Early diagnosis relies on serum β-hCG testing, ultrasonography, and radiological examination. When β-hCG is elevated and no gestational sac is found within the uterus or at common ectopic sites, REP should be considered. Surgical resection is the primary treatment for this condition.

Keywords: retroperitoneal ectopic pregnancy, ectopic pregnancy, ultrasonography, laparoscopy, surgery

Introduction

Ectopic pregnancy (EP) involves the implantation of fertilised oocytes outside the uterine cavity. It occurs in 1.3–2% of pregnancies, and 9–13% of all pregnancy-related deaths are associated with EP.[1] In excess of 95% of EPs occur in the fallopian tube.[2] Retroperitoneal ectopic pregnancy (REP) is an extremely rare form of EP, and early diagnosis and treatment are difficult. The risk of death associated with REP is almost seven times that of fallopian tube EPs.[3–5] Because the location of REP is often close to blood vessels or important organs in the abdominal cavity, if diagnosis and treatment are delayed, there is a risk of life-threatening bleeding, which can be fatal. The current study on REP was limited to medical record reports. A PubMed search revealed that Hall et al[6] reported the first case of REPs in 1973. The ectopic gestational sac was located in the space between the left side of the retroperitoneal aorta and upper lateral side of the left iliac artery. By 2023, fewer than 45 cases of REP were reported with the sites of REP mainly involving the retroperitoneum near the aorta, inferior vena cava, iliac blood vessels, renal vein, or in the retroperitoneal space, obturator fossa, uterine ligament, and parapancreas.[7–9]

Here, we report a case of REP that was initially misdiagnosed as acute gastroenteritis with obvious gastrointestinal symptoms. Signs of EP rupture and bleeding appeared in early pregnancy, highlighting that such cases may present challenges in diagnosis and management. The EP was located in the retroperitoneal space of the pelvis, lateral to the left uterosacral ligament, adjacent to the lower edge of the left broad ligament, and near the left ureter and parauterine vessels. According to previous reports, this was an extremely rare case.

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Case Presentation

A 47-year-old woman presented to the internal medicine department of a local hospital three days ago with a history of lower abdominal pain. The pain was colicky and unbearable, accompanied by profuse sweating, and lasted for half an hour before becoming a persistent, dull ache throughout the abdomen. The patient was initially diagnosed with gastroenteritis and was treated with levofloxacin, an anti-inflammatory agent. The abdominal pain did not subside and intensified to severe colic in the lower abdomen the following day, accompanied by nausea, vomiting, and mild diarrhoea. The pain eased after two episodes of vomiting and passing a small amount of loose stool. This episode lasted for approximately two hours before transitioning to a persistent dull ache throughout the abdomen. No vaginal bleeding, dizziness, fatigue, fever, urinary frequency, urgency, or other discomforts were reported. The patient was then transferred to the First Affiliated Hospital of Zhejiang University School of Medicine. She was gravida 7, para 3, with a history of 2 vaginal deliveries, 1 caesarean section (three years ago), and 4 induced abortions (the last one was more than four years ago). She had no plans of having more children. Her menstrual cycles were regular, occurring every 23–25 days, with moderate flow, and no dysmenorrhoea. She had been experiencing amenorrhoea for 35 days upon admission. Physical examination revealed a soft abdomen with no tenderness, rebound tenderness, or McBurney point tenderness. Routine stool analysis, blood biochemistry, and blood amylase levels were normal with a haemoglobin level of 104 g/L. The quantitative serum beta-human chorionic gonadotropin (β-hCG) titre was 16,111.94 mIU/mL. Computed tomography (CT) of the abdomen revealed a round, mixed-density lesion with clear borders in the left appendage area, measuring approximately 4.3 cm × 2.7 cm (Figure 1). Blood accumulation was observed in the pelvis and paracolic gutters on both sides. Transvaginal ultrasonography (TVS) combined with transabdominal ultrasonography (TAS) revealed a uterine size of 5.7 cm × 5.6 cm × 6.2 cm, with an endometrial thickness of approximately 0.6 cm (Figure 2A). No gestational sacs in the uterine cavity or bilateral uterine horns were observed. Approximately 2.0 cm of pelvic effusion was reported with multiple hypoechoic masses inside, most likely blood clots (Figure 2B). An irregular echo mass in the left appendage area measured approximately 3.7 cm × 2.5 cm and showed no significant blood flow (Figure 2C and D). The left ovary was of normal size and the mass was adjacent to but not connected to the left ovary (Figure 2E and F). Gynaecological examination revealed a medium-volume, clear vaginal secretion with no cervical tenderness or tenderness of the uterus. The left adnexal area was slightly thickened, whereas the right adnexal area appeared unremarkable, with no tenderness in either adnexal region. The patient was diagnosed with EP and underwent emergency laparoscopy. The operative findings revealed approximately 500 mL of hemoperitoneum in the pelvic and abdominal cavities. The uterus was positioned anteriorly, slightly enlarged, and smooth (Figure 3A). A cyst, measuring about 0.6 cm × 0.5 cm, was identified in the mesosalpinx on the left side. The fallopian tubes and ovaries appeared normal bilaterally (Figure 3B). A mass approximately measuring 3.0 cm × 3.0 cm was observed in the retroperitoneal space of the pelvis, adjacent to the lower edge of the posterior leaf of the left broad ligament. The mass had a surface break with active bleeding (Figure 3C). Careful exploration of the omentum, intestinal canal, and mesenteric surface revealed the absence of embryonic tissue.

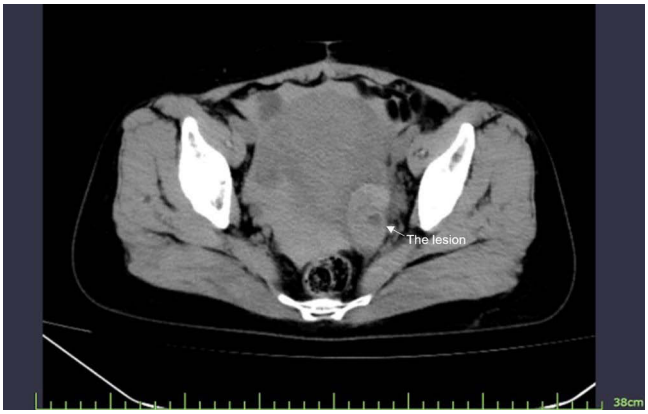

Figure 1 A round, mixed-density lesion was observed in the left adnexal region, measuring approximately 4.3×2.7 cm (as indicated by the arrow).

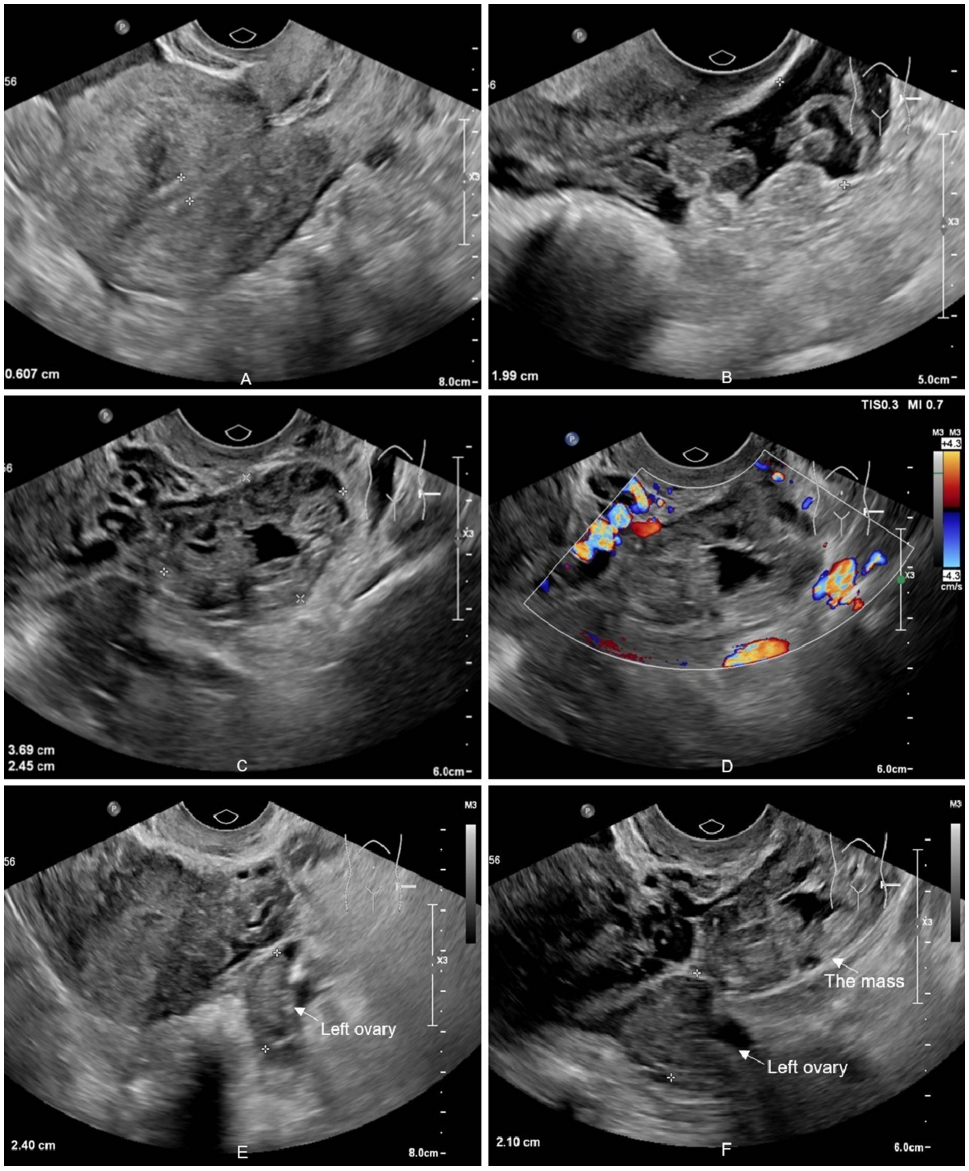

Figure 2 (**A**) The double-layered endometrial lining measured 0.6 cm in thickness. (**B**) Approximately 2.0 cm of pelvic fluid with multiple hypoechoic masses, likely blood clots, was detected. (**C**) An uneven echogenic mass, approximately 3.7×2.5 cm in size, was found in the left adnexal region. (**D**) No obvious blood flow signal was detected in this mass. (**E** and **F**) The mass was not connected to the left ovary.

The retroperitoneal space was meticulously opened, and the gestational tissue was removed. The bleeding was controlled using bipolar coagulation. The retroperitoneal space was located anterior to the left ovarian fossa, next to the lower edge of the left broad ligament, and lateral to the left sacrocervical ligament, ureter, and parauterine blood vessels (Figure 3D). The patient lost approximately 100 mL of blood during surgery but did not require a transfusion. One day post-surgery, the β-hCG level decreased to 3286.79 mIU/mL (Figure 4). Postoperative histopathological analysis confirmed the presence of villous tissues in the retroperitoneal mass. The patient recovered well, and 33 days after surgery, the follow-up β-hCG level was normal (Figure 4).

Literature Review

Case reports and review articles published in English from inception to September 30, 2024 were obtained from the PubMed electronic database, using search term "Retroperitoneal ectopic pregnancy[*all fields*]", including articles or review articles of relevant case reports and references. The inclusion criteria of this study are English report, clear diagnosis criteria for REP and

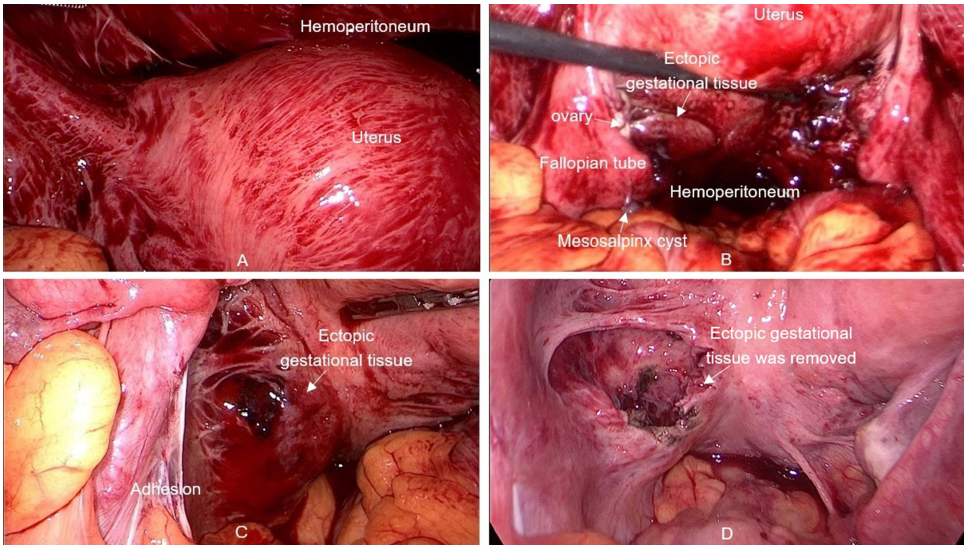

Figure 3 (**A**) Hemoperitoneum was observed in the pelvic cavity. The uterus appeared enlarged with a smooth surface. (**B** and **C**) Pregnancy tissue, measuring approximately 3.0×3.0 cm, was located in the retroperitoneal space. (**D**) The ectopic pregnancy tissue was successfully removed.

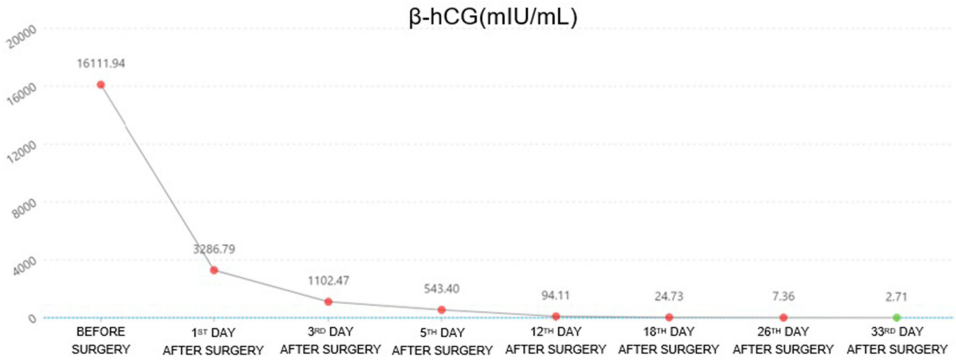

Figure 4 Postoperative β-hCG levels during follow-up.

relatively complete clinical data. The exclusion criteria are duplicate reports of the same case, unclear diagnosis or incomplete clinical data. After a title and abstract review, those studies that met the inclusion criteria were subjected to full-text review.

The preliminary screening and rescreening processes ultimately retrieved 46 cases (including the present case) from 44 studies (Table 1).

Table 1 Summary of All Reported Cases of REP in the English Literature (n=46)

Authors	Years	Country of Authors	Treatment of the REP
This case	2024	China	Laparoscopy
Hall[6]	1973	Jamaica	Laparotomy
Sotus[10]	1977	USA	Diagnostic laparoscopy and laparotomy
Ferland[11]	1991	USA	Laparotomy
Lazarov[12]	1993	Bulgaria	Laparotomy

(*Continued*)

Table 1 (Continued).

Authors	Years	Country of Authors	Treatment of the REP
Dmowski[13]	2002	USA	Laparotomy
Reid[14]	2003	UK	Diagnostic laparoscopy and laparotomy
Lee[15]	2005	South Korea	Laparotomy
Meire[16]	2007	Belgium	Laparotomy
Iwama[17]	2008	Japan	Twice single-dose MTX and laparotomy
Chang[18]	2008	China	Laparoscopy
Lin[19]	2008	China	Diagnostic laparoscopy and laparotomy
Bae[20]	2009	Korea	Laparoscopy
Persson[21]	2010	Sweden	Twice laparoscopy, then robot-assisted laparoscopy
Okorie[22]	2010	Cameroon	MTX (100mg) and laparotomy
Martínez-Varea[5]	2011	Spain	Laparoscopy and MTX (50 mg/m^2) administered the day after surgery
Protopapas[23]	2014	Greece	Laparoscopy, under ultrasound guidance
Jiang[24]	2014	China	MTX (20-mg intramuscular injection daily for 5 consecutive days) and laparotomy
Liang[25]	2014	China	Diagnostic laparoscopy and laparotomy
Yang[26]	2017	China	Laparoscopy
Ouassour[27]	2017	Morocco	Laparotomy
Pak[28]	2018	USA	Laparotomy
Yang[29]	2018	China	Laparotomy
Zhang[30]	2018	China	MTX and selective arterial embolization, then laparotomy
Veleminsky[31]	2018	Czech Republic	Diagnostic laparoscopy and laparotomy
Huang[32] (*two cases*)	2019	China	CT-guided MTX injection in the gestational sac
Lu[33]	2019	China	Laparoscopy
Le[34]	2020	Vietnam	Laparotomy with a multidisciplinary team
Wang[35]	2020	China	Laparotomy and local injection of 10 mg of MTX in the psoas major muscle
Anh[36]	2021	Vietnam	Laparoscopy, then laparotomy
Lorenzo[37]	2021	Italy	Twice MTX (50 mg/m2) administered, then laparoscopy
Wen[38]	2021	China	Laparoscopy and MTX (50 mg/m2) locally injected
Hou[39]	2021	China	Diagnostic laparoscopy and laparotomy
Yuan[40]	2022	China	Laparoscopy
Xu[41]	2022	China	Systemic MTX (intramuscular 20 mg daily for 5 consecutive days) combined with ultrasound-guided local potassium chloride solution injection into the gestational sac and laparotomy
Ren[42]	2022	China	Twice laparoscopy
Tong[43]	2022	China	Laparoscopy

(*Continued*)

Table 1 (Continued).

Authors	Years	Country of Authors	Treatment of the REP
Munzar[44]	2022	Pakistan	Laparotomy
Liu[7]	2023	China	Laparoscopy
Le[8]	2023	Vietnam	Expectant management
Huang[9]	2023	China	Twice diagnostic laparoscopy and twice local MTX injection (50 mg) under real-time ultrasound guidance, and systemic MTX administration (1 mg/kg every 2 days) for 8 days
Solomon[45]	2024	Israel	Laparoscopy
Ryu[46]	2024	Korea	MTX treatment and twice laparoscopy
Mizutani[47]	2024	Japan	Laparoscopy
Yan[48]	2024	China	Laparoscopy

Abbreviations: REP, retroperitoneal ectopic pregnancy; MTX, methotrexate; CT, computed tomography.

Discussion

Characteristics

Liu et al[7] reviewed the case characteristics of 35 patients with REP until 2022. The clinical manifestations of REP lack specificity and are influenced by the location of pregnancy. It has been reported that these locations can involve various structures, including the kidney, pancreas, para-aortic area, iliac artery, and obturator fossa.[7–9] Abdominal pain is more common than vaginal bleeding is less frequent. If pregnancy stimulates the surrounding organs, symptoms may occur, or there may be no clinical manifestations. In severe cases, REP rupture can lead to immediate hypovolemic shock.[28,29] The duration of amenorrhoea in the REP cases ranged from 35 to 161 days, with an average of 55.8 days. The β-hCG levels vary from 267 to 99,286 mIU/mL, with an average of 31,192.5 mIU/mL.[7] It is speculated that this difference is related to gestational age, embryonic development, and EP location. Our patient was initially diagnosed with gastroenteritis and treated accordingly at a local hospital because of abdominal pain and obvious gastrointestinal symptoms. This case highlights a crucial lesson: Nonspecific clinical symptoms of REP can easily lead to misdiagnosis or oversight. At such times, obtaining a comprehensive and detailed medical history, particularly regarding the menstrual cycle, and timely checking β-hCG levels are crucial. The patient typically had a short menstrual cycle (23–25 days). EP rupture and bleeding occurred 32 days after amenorrhoea, with corresponding symptoms emerging. By 35 days after amenorrhoea, β-hCG was 16,111.94 mIU/mL. The relatively large retroperitoneal space facilitates the invasion of ectopically pregnant embryos. When β-hCG levels are elevated and no gestational sac is observed in the uterus or adnexal areas, one should consider the possibility of an REP. This case began with abdominal pain accompanied by diarrhoea and vomiting, which was later relieved. EP rupture and bleeding are believed to cause loose rectal stools and other gastrointestinal symptoms. The absence of typical vaginal bleeding is thought to be related to the location of pregnancy. During physical examination, the left adnexal area was thickened but non-tender, likely due to local abdominal muscle tension.

Pathogenesis

However, the cause of REP remains unclear. Some reports have suggested that in vitro fertilisation (IVF) may increase the risk of certain types of EP.[7,11,13,17,34–36,40,45] However, the patient in this case conceived naturally. The exact cause of REP in this case is unknown. Previous studies have suggested several possible mechanisms of REP: 1. The blastocyst may have initially been implanted in a peritoneal defect (Figure 3C), with peritoneal regeneration covering most of the area except for the defect. Alternatively, the defect could have been caused by the erosion and rupture of the peritoneum by the initially covering pregnancy tissue.[26] 2. A complete miscarriage of a fallopian tube pregnancy might have occurred, with fresh villi invading the peritoneum and reaching the retroperitoneal space. However, this scenario is

extremely rare.[12] 3. Some researchers have proposed that fertilised eggs can reach the retroperitoneal space via the lymphatic system.[21,40] 4. Other researchers speculate that the presence of an endometriotic lesion in the pelvis may facilitate the retroperitoneal implantation of pregnancy tissue.[45] Endometriosis may have represented the access route for the fertilised ovum, which implanted on endometriotic superficial tissue and then moved toward the retroperitoneal vascularised structures.[37] Considering that this patient had no history of using assisted reproductive technology as well as no previous ectopic pregnancies, endometriosis, or high-risk factors such as smoking or intrauterine device use, it is noteworthy that she had undergone a caesarean section 3 years prior and had a history of four artificial abortions. These factors may have led to pelvic infections and/or inflammation, creating conditions that facilitate the invasion of fertilised eggs into the peritoneum through trophoblasts. A review of published reports on REP revealed that the location in this case was similar to that reported by Yang et al[26] in 2017.

Diagnosis

The accurate diagnosis of REP is often challenging owing to its specific location, nonspecific symptoms, low incidence, and insidious nature. Consequently, the misdiagnosis rate of REP was notably high (62.9%).[7] Diagnosis is typically made only after ruling out other common sites. TAS and TVS are the primary tools used to evaluate REP.[23,30] If an intrauterine pregnancy is present, the gestational sac should be visible on TVS when the serum β-hCG level exceeds a certain threshold. This threshold, known as the β-hCG ultrasound threshold, is generally set at 3510 mIU/mL to minimise the risk of misdiagnosis and avoid premature termination of a potentially normal intrauterine pregnancy.[49] The patient had 35 days of amenorrhoea and a β-hCG level of 16,111.94 mIU/mL. However, B-mode ultrasound revealed that the thickness of the double-layered endometrium was only 0.6 cm, and no gestational sac was present in the uterine cavity, effectively excluding the possibility of intrauterine pregnancy. Both ultrasonography and CT tomography identified abnormalities in the left adnexal area. Ultrasonography revealed 2 cm of pelvic fluid. The patient experienced abdominal pain for three days, and the bleeding spread throughout the abdomen. CT imaging revealed blood accumulation in the pelvis and bilateral paracolic gutters, indicating that the pelvic fluid observed on ultrasonography did not accurately reflect the true volume of bleeding. Additional imaging studies, such as magnetic resonace imaging (MRI) and CT scans, may be necessary for some EPs, particularly those located in the upper abdomen, to ensure the diagnosis is not missed. Unlike ultrasound, which has inherent limitations in the field of view, CT and MRI provide a comprehensive view of the entire abdominopelvic cavity, enabling accurate assessment of the location of the gestational sac and its relationship with the surrounding structures. A recent REP case report involved a patient who was first misdiagnosed with fallopian tube pregnancy and received systemic methotrexate (MTX) medication and bilateral salpingectomy, and was later found with REP lesions in the retroperitoneal vena cava through CT.[46] It is recommended that patients with unstable vital signs or intrauterine pregnancy be clearly ruled out, and CT examination be performed to assist in diagnoses.[46,47,50,51] Additionally, MRI is advised to evaluate the peripheral vasculature after ultrasound examination in suspected cases.[36,38,50,51]

Treatment

REP lesions are so rare that there are no specific treatment guidelines for surgeons. As with most EPs, treatment should be individualised, taking into account factors such as the gestational age, size of the gestational sac, location of the EP, clinical features, β-hCG levels, foetal cardiac activity, and the patient's preferences.[1,3] Previously reported treatments for REP include surgical intervention, MTX therapy, expectant management, or a combination of these approaches. The treatments for the 46 patients with REP are presented in Table 1. For example, in 2023, an REP was detected adherent to the para-aortic area in a patient at 7–9 weeks of gestation.[8] Since the pregnancy stopped spontaneously without clinical symptoms, expectant treatment was performed after careful evaluation and follow-up for 1 month later, the ectopic mass degenerated naturally without complications, and the β-hCG levels returned to negative values. Additionally, the MTX regimen can be used under appropriate conditions to target trophoblast cells, either as part of conservative treatment or to reduce intraoperative bleeding.[9] Systemic administration of MTX to patients with an unruptured REP prior to surgery may be beneficial. Preoperative treatment with systemic MTX followed by surgical resection of the mass can minimise potential blood loss and is a reasonable approach for treating patients with unruptured REP.[24,37,41] Postoperative systemic MTX therapy is also recommended to prevent the persistence of trophoblastic tissue.[5] Local injection of MTX into the REP (gestational sac),

guided by ultrasound or CT has also been recommended.[30,32,35,38] Several patients with REP initially underwent unsuccessful MTX treatment, which led to a subsequent switch to surgical intervention.[17,22,30,37,41] In addition, side effects should be monitored during MTX administration. Surgery, including laparoscopy, laparotomy, and robotic surgery, remains the main treatment option for REP. For patients with stable haemodynamics, laparoscopy is typically preferred over laparotomy because of its shorter operation time and reduced blood loss.[7,18,20,33,40,42,43,48] Persson et al[21] conducted robot-assisted laparoscopic resection of an REP mass located in the right obturator fossa and concluded that robot-assisted laparoscopic surgery is a feasible and safe approach for treating REP. However, because REP ectopic blastocysts are often located near major blood vessels and vital organs, some researchers believe that laparotomy may be safer than laparoscopy for patients with REP experiencing shock, blastocyst rupture, or massive bleeding.[16,27–29,44] Additionally, the choice of the surgical method is related to the experience of the surgeon. In our case, laparoscopic surgery provided a clear field of vision, allowed for complete resection of the lesion, resulted in minimal intraoperative bleeding and trauma, achieved an ideal postoperative β-hCG drop, and was free of complications. The importance of multidisciplinary team consultations was emphasised in the selection of appropriate treatment options for REP cases.[34,36,41] Such collaborative evaluation can significantly reduce surgical complications and improve patient survival rates. Due to the high rate of preoperative misdiagnosis, some patients with REP have undergone two or more treatments, including both drug and surgical interventions,[24] or require two or more surgical procedures.[9,14,19,21,25,31,36,39,42,46] These cases underscore the critical importance of accurate initial treatment of REP, and to improve outcomes, it is crucial to enhance preoperative evaluation and conduct thorough intraoperative exploration. During surgery, resected specimens should be meticulously examined for suspected ectopic gestational tissue and the presence of villous tissue to avoid unnecessary reoperation and postoperative complications. Additionally, because of the specific location of the ectopic gestational sac, surgeons must have a thorough understanding of the anatomical structures of the pelvic and abdominal cavities. In the present case, the EP was located within the retroperitoneal space adjacent to the left ureter, left uterine artery, and vein. If the mass had continued to grow, it could have invaded the surrounding structures and led to serious complications. During surgical resection of an REP mass, it is crucial to carefully identify and preserve the surrounding organs and blood vessels to avoid damage and additional complications.

Conclusion

The rare incidence, nonspecific clinical manifestations, and unique location of REP present significant challenges for its diagnosis and treatment. In cases of suspected EP where common sites are ruled out, clinicians should consider the possibility of REP. Treatment should be individualised, with surgery being the primary method for managing REP. For complex cases, a multidisciplinary team is recommended to thoroughly evaluate the situation and mitigate the potential risk.

Data Sharing Statement

All data used and/or analyzed during the current study are available from the corresponding author.

Ethics Approval and Consent to Participate

This study was approved for publication by the Clinical Research Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine.

Consent for Publication

Written informed consent was obtained from the patient for the publication of this report.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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