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# **Diagnostic Challenges in Ectopic Pregnancy: Identifying Pseudo Sacs in Suspected Heterotopic** Cases

Authors' Contribution: Study Design A Data Collection B Statistical Analysis C Data Interpretation D Manuscript Preparation E Literature Search F Funds Collection G

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None declared Conflict of interest: None declared

**Patient:** 

Female, 28-year-old

**Final Diagnosis:** Extrauterine ectopic pregnancy with a pseudogestational sac

**Symptoms:** Abdominal pain for four days before admission • vaginal bleeding 10 hours before admission

**Clinical Procedure:** Bilateral salpingectomy • exploratory laparotomy

> Specialty: **Obstetrics and Gynecology**

Objective:

Challenging differential diagnosis

**Background:** 

A pseudo-gestational sac (pseudo sac), or intracavitary fluid, occurs in up to 10% of ectopic tubal pregnancies and can mimic an intrauterine gestational sac, posing a diagnostic challenge. Distinguishing a pseudo sac from a true gestational sac or an ovarian cyst is critical to avoid misdiagnosis. This report describes the case of a 28-year-old woman presenting at 6 weeks of pregnancy with hydrosalpinx, hemosalpinx, and a pseudo sac due to tubal ectopic pregnancy.

Case Report:

A 28-year-old woman, G3P1A1 at 6 weeks of pregnancy, presented with right lower quadrant abdominal pain lasting 4 days and vaginal bleeding that began 10 h before admission. Physical examination revealed cervical motion tenderness and bulging of the Douglas pouch. Ultrasonography showed a suspected heterotopic pregnancy, with a gestational sac in the right adnexa measuring 1.0×7.4×1.9 cm and a "ring of fire" sign, alongside free fluid in the Douglas and Morrison pouches. Intraoperative findings confirmed a ruptured ectopic pregnancy in the interstitial portion of the fallopian tube, with approximately 400 cc of blood clots. Bilateral salpingectomy was performed, owing to the ruptured ectopic pregnancy and contralateral hydrosalpinx. Histopathological analysis confirmed the intrauterine finding as a pseudo sac with no conception tissue.

**Conclusions:** 

This report highlights the importance of distinguishing between true intrauterine pregnancy and a pseudo-gestational sac, to avoid unnecessary interventions. It emphasizes the role of early and precise transvaginal ultrasonography combined with histopathological confirmation in diagnosing ectopic pregnancies, particularly in cases mimicking heterotopic pregnancy.

**Keywords:** 

Diagnosis • Pregnancy, Ectopic • Ultrasonography • Salpingectomy

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### Introduction

Heterotopic pregnancy is a pathological form of biovular dizygotic pregnancy in which implantation occurs on 2 sides, causing extra and intrauterine gestation [1,2]. The incidence in spontaneous pregnancies is about 1 in 30 000 worldwide. In recent years, it has increased to 1.5 in 1000, but some areas have reached 1 in 100 because of the availability of assisted reproductive technology [3]. Heterotopic pregnancies are usually incidentally found during routine antenatal care examinations [1,4]. Ultrasonography is an essential assessment for detecting heterotopic pregnancy, even in women lacking risk factors; hence, following the identification of an intrauterine pregnancy, it should be conducted to ascertain the likelihood of an extrauterine gestational sac [5].

Ectopic pregnancies predominantly occur in the fallopian tubes, comprising approximately 97% of cases [6]. Heterotopic pregnancy can involve an ectopic pregnancy in any of the previously mentioned locations, with a rare case of a triplet heterotopic pregnancy, including both a tubal and cervical ectopic pregnancy, having been reported [7]. Most heterotopic pregnancy cases are tubal, as evidenced by a review of 80 cases in the literature, which found that 66 (72.5%) were situated in the ampullary or interstitial regions of the fallopian tube, 7 were cervical, and 3 were implanted in a cesarean scar [8]. The classic triad of amenorrhea, vaginal bleeding, and abdominal pain is the most common presentation of an ectopic pregnancy [9]. Effective management of a tubal ectopic pregnancy necessitates early presentation, a heightened index of suspicion, comprehensive ultrasound examination, meticulous intraoperative assessment of the contralateral tube, histological validation, and suitable patient counseling, irrespective of the nature being spontaneous or induced [10].

According to a study by Lee et al, the incidence of ectopic pregnancy was significantly reduced in the presence of intrauterine fluid collection. Intrauterine fluid accumulation in a woman with a pregnancy of indeterminate location cannot differentiate between a gestational sac and a pseudogestational sac [11] Their analysis of 1236 women with pregnancies of unknown location revealed that 36.6% had intrauterine fluid collection on ultrasound. Among these, the rate of ectopic pregnancy was only 2.2%, compared with 26.7% in those without intrauterine fluid collection. Furthermore, the presence of intrauterine fluid collection was associated with a markedly reduced adjusted relative risk of ectopic pregnancy (0.09; 95% CI, 0.05-0.19) after accounting for factors such as age and bleeding. However, intrauterine fluid collections could not reliably differentiate between a true gestational sac and a pseudogestational sac, as evidenced by the study's findings that the mean sac diameter did not differ significantly between ectopic and intrauterine pregnancies. This underscores the need for careful clinical evaluation and consideration of additional sonographic findings, to avoid misdiagnosis or delays in diagnosis [11].

A pseudogestational sac is a rare ultrasonographic finding typically observed in women with ectopic pregnancy. The American College of Obstetricians and Gynecologists defines it as a collection of fluid or blood within the uterine cavity, which can mimic a gestational sac but lacks the features of a developing embryo or yolk sac [12]. On ultrasound, a true gestational sac within the uterus is characterized by a dense, highly reflective border surrounding a centrally dark area, while a pseudogestational sac often appears elongated with tapering borders and lacks the double decidual sac or intradecidual sac sign [13]. If a patient is suspected to have an intrauterine pregnancy, it is necessary to perform further examinations to identify the presence of a developing yolk sac, embryo, or both [14,15].

The double decidual sac describes the presence of 2 concentric hyperechoic rings representing parietal and capsular decidua. The intradecidual sac is an eccentrically located sac embedded within a thickened decidua on one side of the uterine cavity. In a recent study of intrauterine sac-like structures confirmed to be intrauterine pregnancy, only 30.5% had a double decidual sac, and 53.5% had an intradecidual sac [11]. An intradecidual sac could be seen at 4.5 weeks of gestation or when human chorionic gonadotrophin (hCG) >1500 IU/L and mean sac diameter >3 mm by transvaginal ultrasonography. As an alternative, a double decidual sac can be seen at 6 to 6.5 weeks of gestation by transabdominal ultrasonography [13].

Transvaginal ultrasonography is the first line of examination that can be used to diagnose pregnancies and determine the location of ectopic pregnancy, as well as the vitality of an intrauterine pregnancy. Nevertheless, ultrasonography sensitivity ranges from 26.3% to 92.4%, with the expertise of the ultrasound user, in diagnosing ectopic pregnancy [16,17]. In a pregnancy of unclear location, intrauterine fluid collection can signify either the early gestational sac of an intrauterine pregnancy or, as documented in prior literature, the pseudogestational sac of an ectopic pregnancy. Multiple sonographic characteristics have been used to differentiate between these 2 entities; however, the clinical significance of the pseudogestational sac remains ambiguous [18-20].

The present case reports the clinical signs or symptoms and ultrasonography findings, which suggested a hemorrhagic process in ectopic pregnancy and the presence of an echogenic structure within the fluid-filled endometrial cavity mimicking an embryo of a pseudo-gestational sac. In a case report by Puttagunta et al, a similar clinical observation was made involving a pseudogestational sac, which had been previously misdiagnosed as an intrauterine pregnancy [15]. Although pseudogestational sacs are rare, their clinical significance remains ambiguous. Studies indicate that

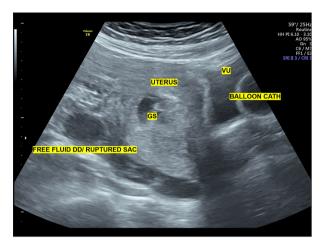


Figure 1. Transabdominal ultrasound showing free fluid suggestive of ruptured ectopic pregnancy and a gestational sac (GS) within the uterus, indicative of a heterotopic pregnancy. Additional annotations include the uterus, balloon catheter (for bladder visualization), and urinary bladder (VU).

there is no specific cutoff for intra-fluid collection, to reliably differentiate between true gestational sacs and pseudogestational sacs. This highlights the need for careful clinical and sonographic evaluation in cases of pregnancies with unclear location [11].

This report describes the case of a 28-year-old woman presenting at 6 weeks of pregnancy with hydrosalpinx, hemosalpinx, and a pseudo gestational sac, or pseudo sac, due to tubal ectopic pregnancy. The authors aim to provide educational awareness concerning the potential misidentification of an intrauterine gestational sac. This example underscores the importance of early identification, especially using transvaginal ultrasound, despite the necessity for bilateral salpingectomy, owing to a hydrosalpinx in the contralateral fallopian tube.

## **Case Report**

A 28-year-old woman, G3P1A1, at 6 weeks of pregnancy, experienced abdominal pain for 4 days before admission, which increased in severity, and had vaginal bleeding 10 h prior. She reported soaking 1 pad with reddish blood but without clots resembling fish eggs. She had not taken any medications or herbal remedies and denied any history of trauma. There was no history of autoimmune or chronic diseases. Her last menstrual period was 3 months prior to admission.

On physical examination, her vital signs were as follows: blood pressure of 106/68 mmHg, heart rate of 102 beats/min, respiratory rate of 20 breaths/min, and body temperature of 36.6°C. Abdominal pain was localized to the right lower quadrant, without peritoneal signs. Bimanual examination revealed cervical motion tenderness with bulging in the Douglas pouch. Transabdominal ultrasound (Figure 1) showed a free fluid suggestive of ruptured ectopic pregnancy and a gestational sac within the uterus, indicative of a heterotopic pregnancy. Further confirmation with transvaginal ultrasonography was conducted. Transvaginal ultrasonography showed a suspected heterotopic pregnancy, with 1 intrauterine gestational sac and 1 extrauterine gestational sac. The uterus was anteflexed with a homogeneous density measuring 4.57×4.84×5.80 cm, and the endometrial line was not visible. A gestational sac measuring 1.0×7.4×1.9 cm with a "ring of fire" sign was observed in the right adnexa, along with free fluid in the Douglas pouch and Morrison pouch (Figure 2). Laboratory findings (Table 1) were unremarkable, except for a positive pregnancy test and a  $\beta$ -hCG level of 107.5 mIU/mL.

The patient, G3P1A1 at 6 weeks and 4 days of pregnancy, received a diagnosis of a heterotopic pregnancy. Surgery was deemed necessary owing to worsening abdominal pain,

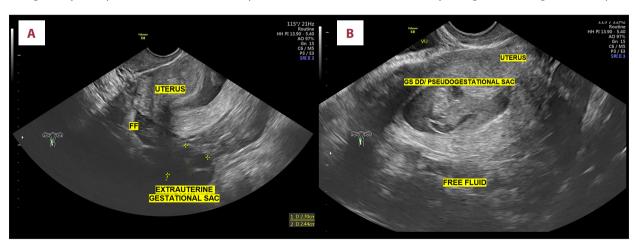


Figure 2. Transvaginal ultrasonography reveals gestational sac with free fluid. (A) shows a gestational sac in right adnexal volume 1.0×7.4×1.9 cm with ring of fire. (B) Suspected intrauterine gestational sac with probable pseudo-gestational sac. FF – free fluid; GS – gestational sac.

**Table 1.** Laboratory findings before and after surgery in a 28-year-old woman presenting at 6 weeks of pregnancy with tubal ectopic pregnancy.

Findings	Muhammadiyah Hospital (Nov 5, 2023)	Margono Soekardjo Hospital (Nov 6, 2023)	Normal values (6 weeks' gestation)
Hemoglobin (g/dL)	10.3	9.9	11.0-14.0
Hematocrit (%)	33.4	30.4	33-42
Leucocyte (/µL)	16 820	12 270	6000-15 000
Thrombocyte (/μL)	242 000	292 000	150 000-400 000
Random glucose (mg/dL)	109	100	70-110 (fasting)
Anti-HIV	Negative	Negative	Negative
HBsAg	Non-reactive	Non-reactive	Non-reactive
Albumin (g/dL)	-	4.32	3.0-5.0
PT/aPTT (s)	-	13/23.7	PT: 11-14, aPTT: 25-35
SGOT/SGPT (U/L)	_	15/8	SGOT: 5-40, SGPT: 5-35
Urea/Creatinine (mg/dL)	_	27.3/0.68	Urea: 15-40, Creatinine: 0.5-1.1
LDH (U/L)	_	155	140-280
Pregnancy test	Positive	Positive	Positive

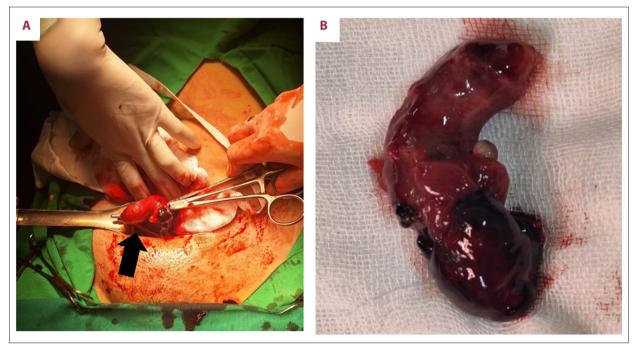


Figure 3. Intraoperative findings. (A) black arrow shows a hydrosalping grade 3 on fallopian tube. (B) Extrauterine product of conception evacuated from this case.

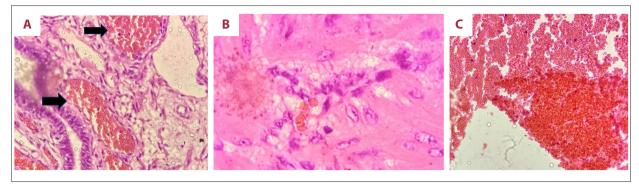


Figure 4. Histopathology result of the specimens. (A) The preparation shows swollen, hyperemic tubal tissue accompanied by bleeding, including chorionic villi, magnification ×100. Black arrow shows a bleeding within tubal tissue. (B) Shows hyperemic tubal tissue, partially cystic dilated lumen with atrophic mucosa, magnification ×100. (C) The preparation shows endometrial tissue with decidual stroma. There are proliferative, winding secreting glands with the appearance of Arias stella, and no signs of malignancy. Magnification ×100.

suggesting a ruptured ectopic pregnancy requiring urgent intervention. Laparotomy exploration was selected as the management strategy.

During the procedure, a thrombus was encountered while carefully separating the peritoneal layer, accompanied by approximately 400 cc of dark-colored blood. The intraoperative findings are depicted in **Figure 3**. Further investigation revealed a ruptured ectopic pregnancy in the interstitial region of the fallopian tube, with active bleeding. The right tube showed evidence of a tubal abortion and grade 3 hydrosalpinx. Additionally, grade 3 hydrosalpinx was detected in the left fallopian tube. The uterus was notably enlarged, comparable to the size of duck eggs. Bilateral salpingectomy was performed due to the hydrosalpinx findings, and the intrauterine gestational sac was evacuated.

Histopathological examination yielded a different diagnosis. The results (Figure 4) indicated that the right fallopian tube contained hyperemic tissues, with bleeding and chorionic villi, consistent with ectopic pregnancy. The left fallopian tube showed hyperemic tissues with cystic dilatation of the lumen and atrophic mucosa, characteristic of hydrosalpinx. The uterine curettage specimen revealed endometrial tissues, with decidual stroma, proliferative glands, and Arias-Stella changes indicative of pregnancy, but no intrauterine products of conception. The definitive histopathological diagnosis was an extrauterine ectopic pregnancy with a pseudogestational sac. When there is diagnostic uncertainty, histopathology remains the criterion standard, as ultrasound findings alone may not always be conclusive.

## **Discussion**

This case report highlights the critical lesson of accurately distinguishing a pseudo-gestational sac from a true intrauterine gestational sac or other pelvic pathologies in the context of a tubal ectopic pregnancy. It underscores the diagnostic challenges posed by overlapping clinical signs and ultrasonographic findings, emphasizing the importance of early and precise transvaginal ultrasonography to prevent misdiagnosis and ensure appropriate management, as demonstrated by the need for bilateral salpingectomy in this case.

Heterotopic pregnancy, the coexistence of intrauterine and ectopic pregnancies, has an incidence of approximately 1 in 3000 in natural conceptions and higher rates with assisted reproductive technologies [21]. In this case, the presence of a suspected intrauterine sac alongside a ruptured tubal ectopic pregnancy highlights the diagnostic challenges of heterotopic pregnancy and emphasizes the importance of maintaining a high level of clinical suspicion, particularly in at-risk patients. However, the final pathology results confirmed that the intrauterine sac was a pseudogestational sac.

The sonographic presentation in this case aligns with findings in the literature, including those by Puttagunta et al, who reported a pseudogestational sac initially misdiagnosed as an intrauterine pregnancy [15]. The pseudogestational sac is characterized by a fluid collection within the endometrial cavity that lacks a yolk sac, fetal pole, or double decidual sac, with an elongated shape and tapered margins [14]. Similar to findings in our case, the largest pseudogestational sac reported in prior studies was 13 mm, smaller than the >16 mm guideline cutoff for suspected early pregnancy failure [11].

Detecting ectopic pregnancies can be difficult because the early ultrasound features of intrauterine pregnancy are often nonspecific [22]. Concern for ectopic pregnancy is raised when a patient with abdominal or vaginal bleeding has  $\beta\text{-hCG}$  levels that are lower than expected for an intrauterine pregnancy, and there is no ultrasound evidence of an intrauterine

pregnancy. Abnormal increases or decreases in  $\beta$ -hCG levels outside the typical range further heighten the suspicion of an ectopic pregnancy [23].

An embryo becoming evident at 6 weeks indicates the presence of a sac structure measuring up to 25 mm. Prior to that time, the intradecidual sign might be observed at 4.5 weeks using transvaginal ultrasonography; alternatively, the double decidual sac could be seen at 6 to 6.5 weeks using transabdominal ultrasonography [13]. This case study demonstrates 2 key aspects. Initially, it is crucial for early indications of pregnancy to be discernible, even for experienced professionals. Furthermore, transvaginal ultrasonography provides the most accurate detection of early pregnancy symptoms.

Initial observations of an intrauterine pregnancy evolve from a basic gestational sac to a double-decidual sign, yolk sac, and fetal pole. This prevents the potential misinterpretation of a pseudogestational sac as an indication for intrauterine pregnancy. The identification of intrauterine pregnancy can rule out ectopic pregnancy only when the likelihood of heterotopic pregnancy is low. The patient in this case did not use assisted reproductive technologies for fertilization; therefore, the chance of a heterotopic pregnancy was low [23].

Ectopic pregnancy diagnosis requires a combination of clinical assessment, β-hCG trends, and ultrasonography. A review article demonstrated that transvaginal ultrasonography has a sensitivity ranging from 74% to 84% and a specificity between 84% and 99% [24]. While transvaginal ultrasonography is the most sensitive method for early detection, findings can still depend on the examiner's expertise. Classic ultrasound features of ectopic pregnancy, such as the "blob sign" or "bagel sign," and the presence of free pelvic fluid or an abnormal adnexal mass should heighten clinical suspicion [24]. Ectopic pregnancy was detected about 70% between 5 and 8 weeks, 20% between 9 and 10 weeks. Less than 10% of patients were diagnosed after 11 weeks of pregnancy due to late signs and symptoms. This may have occurred because the most frequent extrauterine implantation site was the fallopian tube. It showed a heteroechoic mass with peripheral vascularity at the implantation site. Irregular elevation of β-hCG between day 12 and 16 of intrauterine gestation or remained high after the evacuation of intrauterine pregnancy [25,26]. Ideally, heterotopic pregnancies should be diagnosed prior to surgery; however, in this case, the accuracy of the diagnosis remains heavily reliant on the expertise of the examiner, whether it is a general practitioner at a primary healthcare center or an obstetrician at a referral hospital [24].

Management of ectopic pregnancy is guided by the patient's clinical stability and  $\beta$ -hCG levels. Patients with hemodynamic instability require immediate surgical intervention, such as laparotomy or laparoscopy, depending on resource availability.

Conservative management can be considered in select cases, with close monitoring [17]. For patients with hemodynamic stability, expectant care can be advised to prevent surgery and avoid the use of transvaginal ultrasound-guided aspiration, which is still difficult to achieve [27,28]. Surgical intervention is recommended in the following scenarios: (1) detection of yolk sac echo or primitive cardiac duct pulsation in an aberrant echo region; (2) when the diameter of the abnormal echo region exceeds 3 cm; and (3) progressive enlargement of the abnormal echo region, with a diameter greater than 3 cm [29]. Studies indicate that, because laparoscopic management involves less uterine manipulation than laparotomy, it is preferable for patients with a confirmed intrauterine pregnancy and a probable ectopic pregnancy if the facilities support it [27,28]. Women with hydrosalpinx have few options, such as (1) laparoscopy salpingectomy, (2) laparoscopy tubal occlusion, (3) laparoscopy neosalpingostomy, (4) transvaginal aspiration, and (5) antibiotic treatment [30].

In our case, an urgent laparotomy was performed because of intra-abdominal hemorrhage due to right tubal rupture ectopic pregnancy, and bilateral salpingectomy was performed because a hydrosalpinx was present on the other side of the fallopian tube. Curettage due to incomplete abortion of the intrauterine pregnancy was performed.

A dilemma in this case also arose when selecting the surgical method, as the patient wished to preserve her fertility. The management approach should prioritize maintaining fertility while addressing hydrosalpinx. A case-control study showed the re-accumulation of hydrosalpinx 14 days after aspiration. However, advanced hydrosalpinges are unlikely to be effective in aspiration treatment [31]. An alternate method is transvaginal ultrasonography-guided aspiration with sclerotherapy for patients exhibiting significant abdominal cavity adhesions, to prevent complications [32]. A study indicated that salpingectomy adversely affects ovarian reserve; nevertheless, it demonstrated no significant change in anti-mullerian hormone and antral follicle count, compared with transvaginal ultrasonography-guided aspiration [33]. Hydrosalpinx diminishes pregnancy rates for several reasons. Fluid composition can influence implantation and adversely impair ovarian function, including the oocyte quality. We concluded that (1) there is no distinction in in vitro fertilization (IVF) retrieval outcomes between individuals under 35 years and those over 35 years old; (2) an interval exceeding 3 months between surgery and IVF negatively impacts oocyte quantity, pregnancy rates, and live birth rates; and (3) there is no embryonic contamination associated with retrieval prior to surgery in women who have undergone salpingectomy [34].

A pseudogestational sac can pose a significant diagnostic challenge, especially when accompanied by an extrauterine gestational sac mimicking a heterotopic pregnancy [15]. In the present case, the initial diagnosis suggested a heterotopic pregnancy, due to the presence of a suspected intrauterine sac alongside an ectopic pregnancy. However, further investigation revealed no evidence of intrauterine conception, confirming the presence of a pseudogestational sac. Our case highlights the diagnostic complexity of distinguishing between a true intrauterine pregnancy and pseudogestational sac, particularly in cases with concurrent ectopic pregnancies. Accurate diagnosis is crucial to avoid unnecessary intervention and ensure appropriate treatment.

Bilateral salpingectomy is recommended because the presence of hydrosalpinx in fallopian tubes reduces the chances of successful live birth [15]. Even if the patient undergoes IVF in the future, removing the fallopian tubes improves pregnancy outcomes in IVF, compared with those who retain tubes affected by hydrosalpinx [35]. In this case report, we aimed to differentiate between a pseudogestational sac and a true gestational sac. When there is uncertainty, the criterion standard is to confirm the diagnosis with histopathology, as ultrasound alone can be inconclusive. It is important to note the detection rate of ultrasound in such cases, as well as its sensitivity and specificity in accurately identifying a true gestational sac.

## **Conclusions**

This report has highlighted the importance of identifying pregnancy in women of reproductive age who present with acute

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abdominal symptoms or signs and has described the association between pseudo gestational sac, or pseudo sac, and tubal ectopic pregnancy. A pseudogestational sac can pose a significant diagnostic challenge, especially when accompanied by an extrauterine gestational sac mimicking a heterotopic pregnancy. Clinical examination poses a challenge in avoiding delayed diagnosis in heterotopic cases, particularly since no standardized approach has yet been established. A subnormal  $\beta\text{-hCG}$  level can complicate the diagnosis, making precise transvaginal ultrasonography crucial. The simple dictum "think ectopic" when an intrauterine gestational sac is absent should always be kept in mind. Surgery remains the definitive treatment for ectopic pregnancies, especially when rupture occurs.

#### **Informed Consent Statement**

The patient has received a comprehensive explanation regarding the case's particulars and the images to be included in the case report and provided consent in the case report.

#### **Acknowledgements**

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#### **Declaration of Figures' Authenticity**

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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