

Interstitial pregnancy: insights from a case series and review of the literature

Gravidez intersticial: novas perspetivas a partir de uma série de casos e revisão da literatura

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Abstract

Overview and Aims: Interstitial pregnancy is a rare form of ectopic pregnancy that can lead to serious complications if not promptly diagnosed and managed. This case series aims to describe the clinical variability, diagnostic approaches, and management strategies of interstitial pregnancies in a tertiary-care hospital.

Study Design: This was a retrospective case series conducted between 2014 and 2025.

Population: Ten women diagnosed with interstitial pregnancy were included.

Methods: Data on clinical presentation, obstetric history, ultrasound findings, treatment approaches, and outcomes were collected and analyzed.

Results: Most patients presented between 5 and 8 weeks of gestation with pelvic pain and/or vaginal bleeding. Five patients had identifiable risk factors, including previous salpingectomy, cesarean delivery, or uterine fibroids. Transvaginal ultrasound was the primary diagnostic tool in all cases, with 3D imaging aiding diagnosis in selected patients. Seven patients underwent surgical treatment – laparoscopy in stable cases and laparotomy in complex or severe presentations. Blood loss varied from 50 to 1800 mL. Three patients were managed medically with methotrexate, all with favorable outcomes. No persistent ectopic tissue or recurrence was observed. Three patients achieved subsequent pregnancies after treatment.

Conclusions: Interstitial pregnancy can present with a wide range of clinical features. Early diagnosis and individualized treatment planning are essential to minimize complications and preserve fertility. Both medical and surgical approaches can be effective when selected appropriately based on clinical presentation and resource availability.

Keywords: Pregnancy; Interstitial; Pregnancy, ectopic; Methotrexate; Gynecologic surgical procedures.

Resumo

Introdução e Objetivos: A gravidez intersticial é uma forma rara de gravidez ectópica que pode dar origem a complicações graves se não for diagnosticada e tratada precocemente. Esta série de casos tem como objetivo descrever a variabilidade clínica, as abordagens diagnósticas e as estratégias de tratamento de gravidezes intersticiais tratadas num hospital terciário.

Desenho do Estudo: Estudo retrospectivo baseado na revisão de registos clínicos realizados entre 2014 e 2025.

População: Foram incluídas dez mulheres com diagnóstico confirmado de gravidez intersticial.

Métodos: Foram analisados dados relativos à apresentação clínica, história obstétrica, achados ecográficos, abordagem terapêutica e desfechos clínicos. Todos os dados foram anonimizados antes da análise.

Resultados: A maioria das doentes recorreu ao hospital entre as 5 e 8 semanas de gravidez, com dor pélvica e/ou hemorragia vaginal. Cinco doentes apresentavam fatores de risco identificáveis, incluindo salpingectomia prévia,

cesariana ou miomas uterinos. A ecografia transvaginal foi a principal ferramenta diagnóstica em todos os casos, com recurso a ecografia 3D em casos selecionados. Sete doentes foram submetidas a tratamento cirúrgico (laparoscopia em casos estáveis e laparotomia em apresentações complexas ou graves), com perda hemática estimada entre 50 e 1800 mL. Três doentes foram submetidas a tratamento médico com metotrexato, todas com evolução favorável. Não se registaram casos de persistência ou recorrência, e três doentes obtiveram gravidezes subsequentes após o tratamento.

Conclusão: A gravidez intersticial pode ter múltiplas formas de apresentação clínica. O diagnóstico precoce e a gestão individualizada são fundamentais para minimizar complicações e preservar a fertilidade. Abordagens médicas e cirúrgicas podem ser eficazes quando selecionadas adequadamente, de acordo com a apresentação clínica e os recursos disponíveis.

Palavras-chave: Gravidez intersticial; Gravidez ectópica; Metotrexato; Cirurgia ginecológica.

INTRODUCTION

Ectopic pregnancy is a potentially life-threatening emergency among women of reproductive age¹. Interstitial pregnancies (IP) account for 2-4% of ectopic cases and have a mortality rate of 2-2.5%^{2,3}. They occur in approximately 1 in 2500-5000 pregnancies and, although rare, its rate of incidence is still increasing^{2,4}.

Often used interchangeably, “cornual” and “interstitial” refer to distinct locations: cornual pregnancies develop in the upper-lateral uterus, typically in a bicornuate or unicornuate uterus, whereas IP implant within the proximal, tortuous intramyometrial segment of the tube⁵⁻⁸.

Risk factors for IP include conditions affecting tubal anatomy, such as previous ectopic pregnancy, congenital uterine anomalies, in vitro fertilization, pelvic surgery, and pelvic inflammatory disease^(1,3,4,6,7,9,10), with ipsilateral salpingectomy being a specific risk factor for IP.

Diagnosis is challenging due to low sensitivity and specificity of symptoms and imaging⁸; only 40% present with the classic triad of abdominal pain, amenorrhea and vaginal bleeding^{4,8}. Key ultrasound criteria include an empty uterine cavity, a gestational sac located >1 cm from the lateral edge of the uterine cavity, and a thin myometrial mantle of less than 5 mm^{1,9}. Furthermore, 3D ultrasonography has emerged as a valuable adjunct, enhancing diagnostic accuracy by clearly demonstrating the external bulging of the uterine wall and the precise eccentric location of the gestational sac^{11,12}. Ben-David A *et al.* reported ultrasound diagnosed IP in 86% of cases¹³ and Tulandi *et al.* found a gestational sac in 40.6% and a hyperechoic cornual mass in 25% of 32

women¹⁴. The “interstitial line sign”, an echogenic line from the endometrium to the sac, improves diagnostic accuracy, with 80% sensitivity and up to 99% specificity^{1,3,12}. Asymmetrically increased low-resistance flow in a uterine horn is an additional diagnostic indicator³.

IP typically present later, between 7-12 weeks, due to myometrial distensibility, although 20% are diagnosed after 12 weeks^{2,3}. Rupture usually occurs after 9 weeks, sometimes as late as 20 weeks³. Because IP carry a high risk of catastrophic hemorrhage and shock, due to delayed diagnosis and the rich myometrial blood supply with vascular anastomoses between the ovarian and uterine arteries^{7,9,10,15}, severe bleeding leads to haemorrhagic shock in nearly a quarter of patients, with mortality rate up to 2%^{3,4}, 2-7 times higher than other ectopic pregnancies^{1,9}.

Various surgical and non-surgical treatments exist for IP, but the optimal approach remains undetermined. Expectant management should be reserved for strictly selected, asymptomatic patients with low and spontaneously declining serum hCG levels and a small interstitial lesion; in clinical practice, this approach is generally considered when initial hCG values are very low (often below 1000 IU/L) and the interstitial mass is small (typically <2 cm), under close surveillance. Conservative options include methotrexate (MTX), potassium chloride (KCl), and selective uterine artery embolization. Surgical intervention, via laparotomy or laparoscopy, is selected according to the location and severity of the IP¹³. Large multicenter studies, such as those conducted by the FRANCOGENT group, have compared medical and surgical approaches, highlighting the importance of individualized management based on clinical presentation and treatment response¹⁶.

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MTX can be administered systemically or locally. Systemic MTX is less invasive and operator-independent and is usually administered as a single intramuscular dose of 50 mg/m². If hCG does not decrease by 15% after 4 to 7 days, a second dose is given on day 7¹⁷. Women with initial hCG below 5000 IU/L often respond to one dose; higher levels typically require two^{3,8}. Local MTX injection allows lower doses, fewer systemic side effects, and higher tissue concentrations^{3,7}. Combining mifepristone with MTX can improve success by promoting trophoblast lysis. Deaberti D *et al.* reported a 63.6% success rate with this approach^{17,18}. MTX efficacy varies (failure rates 9%-65%), particularly with delayed diagnosis, high hCG, large gestational sacs (>20 mm), or a history of ectopic pregnancies^{7,8,11,17}. Patients should be advised that surgery may be needed if medical treatment fails or in cases of IP rupture or severe hemorrhage^{3,15}.

When surgery is needed, the right choice of technique is critical, as improper management can cause uterine rupture and reduced fertility. The average blood loss in laparotomy is 1163 mL, against 168 mL in laparoscopy – nearly 10 times lower¹⁵. Moreover, laparoscopy is preferred over laparotomy, even with significant hemoperitoneum, due to its conservative nature and preservation of uterine architecture^{2,8}. Cornuostomy - incision to remove the pregnancy – is increasingly favoured for smaller gestations (<3.5 cm), while larger ones (>4 cm) may require traditional cornual/wedge resection, often with ipsilateral salpingectomy^{3,4}. To minimize rupture risk, normal uterine tissue should be preserved, cornual excision minimized, the wall reinforced, and defects carefully sutured. Excessive electrocautery should be avoided; techniques like tourniquet sutures, staplers, and endoloops help limit blood loss and preserve fertility^{3,6,7,9}.

Close postoperative monitoring of hCG until undetectable is essential⁹, as IP patients often have higher initial levels and may develop persistent ectopic pregnancy from residual trophoblastic tissue^{3,4}.

The myometrial scar poses a risk of uterine rupture, irrespective of surgical or medical treatment, which may reach 30% during labour¹⁹. Thus, caesarean delivery is generally recommended in future pregnancies^{2,4,7}.

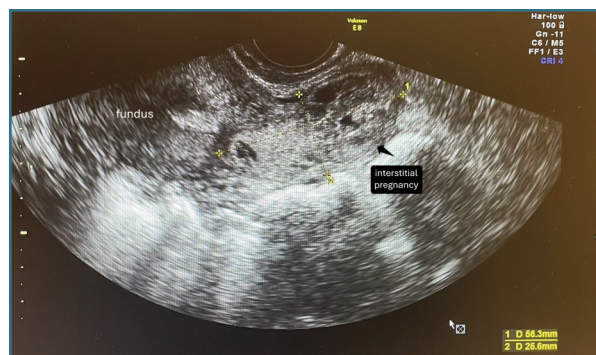


FIGURE 1. Transvaginal ultrasound showing a heterogeneous echogenic mass (56 x 25 mm) in the left cornual region.

METHODS

This article reports a retrospective case series of ten IP managed in a tertiary-care hospital between 2014 and May 2025. Data from electronic medical records included clinical presentation, hCG levels, imaging, treatment modality, surgical details (when applicable), and outcomes. All information was anonymized, and informed consent was obtained. The series aims to provide a comprehensive overview of the clinical variability, risk factors, and management strategies.

RESULTS

Case 1

A 42-year-old multiparous woman developed pelvic pain one week after uterine aspiration for suspected incomplete miscarriage. hCG was 14745 IU/L. Transvaginal ultrasound showed a 56 x 25 mm mass in the left uterine horn with peripheral vascularization and an empty uterine cavity, consistent with IP (Figure 1). Laparoscopic cornual wedge resection and ipsilateral salpingectomy was performed. The patient was discharged on day 2 with hCG reduced by 81%. Histopathology of both the curettage and surgical specimens confirmed a heterotopic pregnancy.

Case 2

A 29-year-old multiparous woman, two months postlaparoscopic salpingectomy for tubal pregnancy, presented with persistent amenorrhea, otherwise asymptomatic.

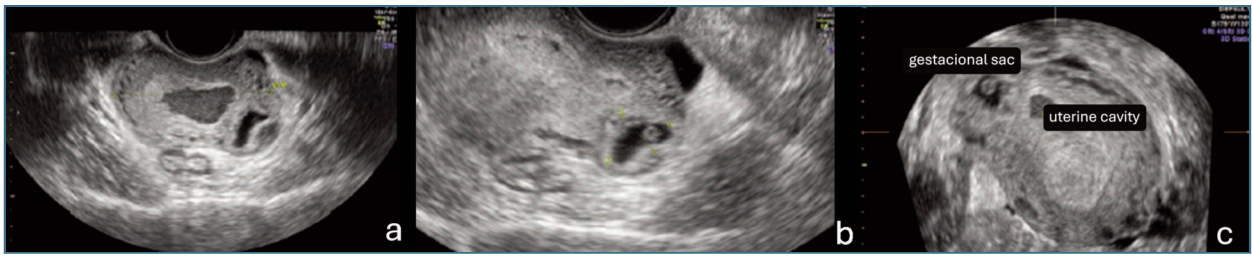


FIGURE 2. Transvaginal ultrasound showing an ectopic mass (1.7 cm) outside the endometrial cavity, with a gestational sac and yolk sac, no embryo, and a thin surrounding myometrial layer (a,b); 3D ultrasound confirming uterine wall bulging (c).

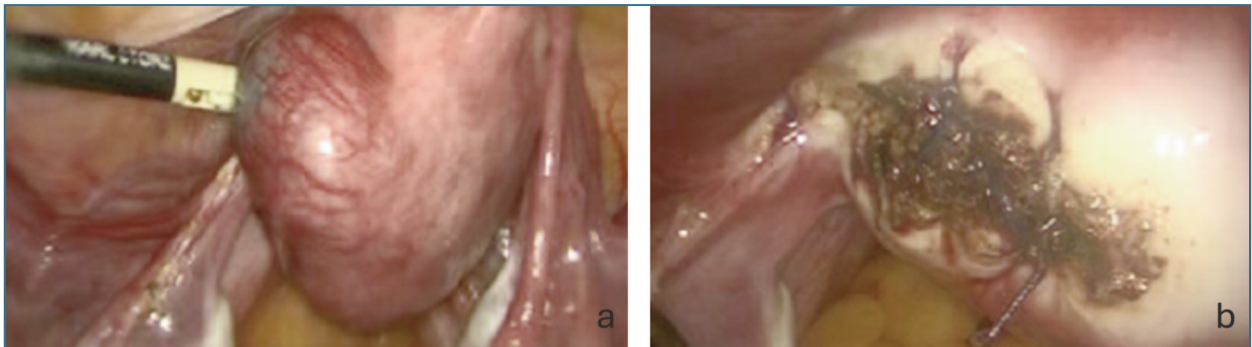


FIGURE 3. Laparoscopic images of an IP in the left cornual region (a) and cornual suture following wedge resection (b).

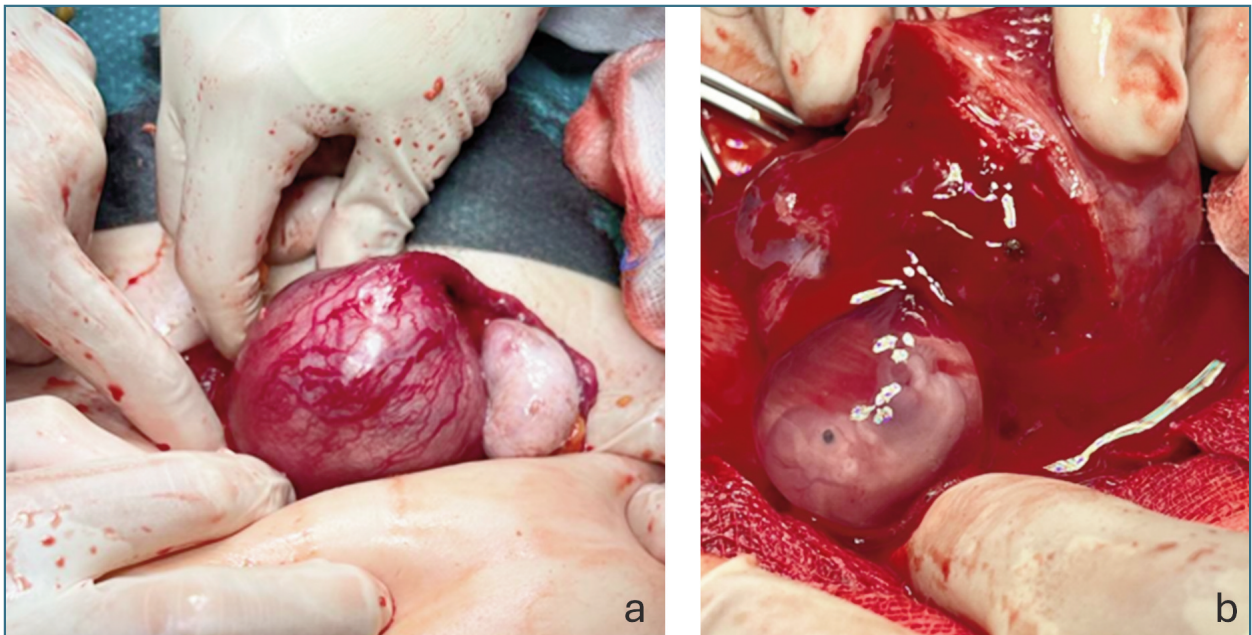


FIGURE 4. Laparotomic images showing an unruptured IP (a) and wedge resection exposing the gestational sac and embryo (b).

hCG was 17013 IU/L. Transvaginal ultrasound revealed a 17 mm interstitial mass with yolk sac, no embryo, thin myometrial layer, and peripheral vascularization (Figure 2). 3D ultrasound further supported the suspicion re-

vealing an external bulging of the uterine wall. Laparoscopic cornuostomy was performed (Figure 3). The patient was discharged on day 3 with hCG reduced by 73%. Histopathology confirmed IP (5-6 weeks).

Case 3

A 35-year-old nulliparous woman with obesity and Antiphospholipid Antibody Syndrome (APS) presented with 8 weeks amenorrhea and lower back pain. hCG was 59311 IU/L. Transvaginal ultrasound revealed a right IP with embryo, cardiac activity, and a crown-rump length (CRL) corresponding to 8 weeks, with a

thin myometrial mantle of 3 mm. Laparotomy with wedge resection and right salpingectomy was performed (Figure 4). Although no rupture was observed, the estimated blood loss was 400 mL, with a hemoglobin drop of 1.8 g/dL (final hemoglobin level of 9.3 g/dL); intravenous (IV) ferric carboxymaltose was given. The patient was discharged on day 4 and enjoyed an uneventful recovery. Twenty months later, she had an urgent preterm cesarean due to non-reassuring fetal status, without uterine rupture.

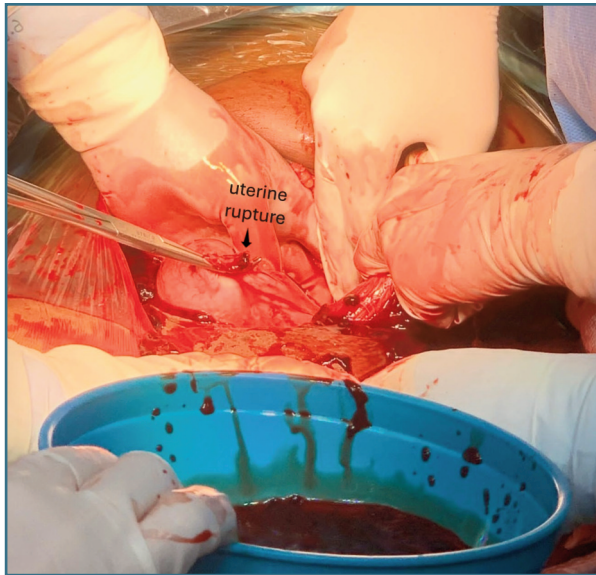


FIGURE 5. Laparotomic image showing cornual rupture with massive hemoperitoneum.

Case 4

A 33-year-old multiparous woman with four previous cesarean sections presented with 5 weeks amenorrhea and pelvic pain. hCG was 3790 IU/L. An ultrasound identified a 66 x 30 mm adnexal mass, consistent with hematosalpinx or a hematoma, and a 22 x 17 mm nodular mass hinted at an ectopic pregnancy. During evaluation, the patient developed severe pain and hemodynamic instability. An exploratory laparotomy was performed, which revealed cornual rupture with massive hemoperitoneum (1500 mL) and a free mass suspected of being an ectopic pregnancy, which was later confirmed histologically (Figure 5). The cornual area was sutured. Hemoglobin dropped 4.5 g/dL; the patient received one unit of red blood cells (RBC) and IV ferric carboxymaltose. She was discharged on day 4

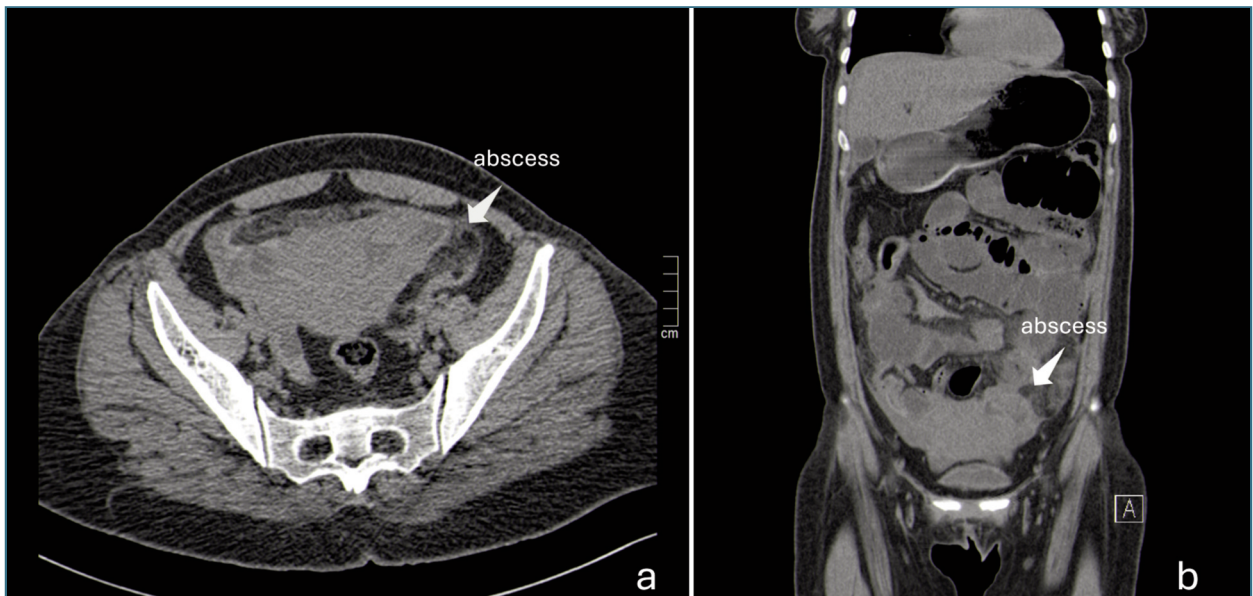


FIGURE 6. Contrast-enhanced CT scan showing an intra-abdominal abscess (arrow): axial (a) and coronal (b) views.

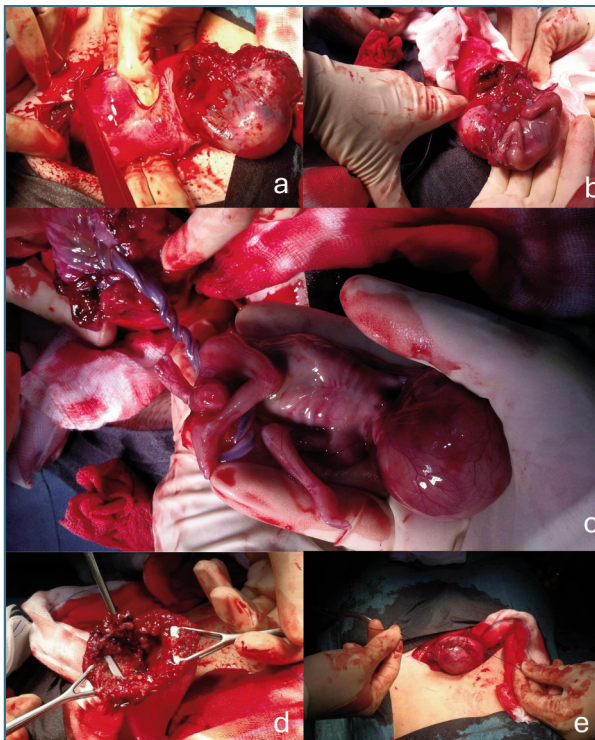


FIGURE 7. Laparoscopic images showing a cornual rupture with partial expulsion of the gestational sac (a); a 15-week fetus (b,c); uterus after removal of the gestational sac and fetus (d); and cornuostomy site (e).

with hCG reduced by 76%. Fifteen months later, elective cesarean was complicated by extensive adhesions.

Case 5

A 38-year-old multiparous woman with 5 weeks amenorrhea presented with acute abdominal pain. hCG was 30491 IU/L. Ultrasound showed a thickened endometrium, right submucosal fibroid (FIGO type 1), and a 45 x 42 mm vascularized mass adjacent to the left uterine body, suggestive of a subserosal fibroid undergoing degeneration or an IP. Echogenic fluid was seen in the right para-ovarian fossa, and guarding was observed on clinical examination. Laparotomy revealed a ruptured left IP, and wedge resection and salpingectomy were performed. Blood loss was 1200 mL, Hb fell to 7.6 g/dL, treated with IV ferric carboxymaltose. Post-op hCG dropped 85%. On day 5, an intra-abdominal abscess with small bowel subocclusion required a second exploratory laparotomy for drainage (Figures 6A,

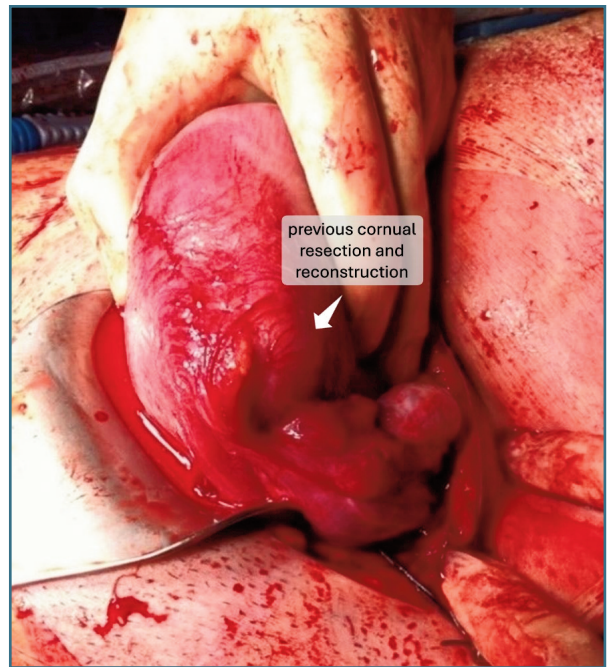


FIGURE 8. Uterine appearance during cesarean section performed 20 months postoperatively.

6B). The patient recovered and was discharged on day 15.

Case 6

An 18-year-old nulliparous woman at 15 weeks of gestation presented with acute abdomen and hemodynamic instability. First-trimester ultrasound had described a viable 11-week intrauterine pregnancy (Figure 7A), but emergency scan revealed an extrauterine fetal mass without cardiac activity near and severe hemoperitoneum (>500 mL). hCG was 3908 IU/L, hemoglobin 12.5 g/dL. Laparotomy identified a ruptured left IP (Figures 7B-7C); continuous sutures and hemostatic reinforcement were done (Figures 7D, 7E). Blood loss was 1800 mL, hemoglobin fell to 7.6 g/dL. The patient received 2 RBC units and Intensive Care Unit (ICU) monitoring for hypovolemic shock. Post-op hCG dropped 83%, and she was discharged on day 4. Weekly follow-up confirmed resolution. Twenty months later, she had an uncomplicated elective cesarean delivery of a healthy infant (Figure 8).

Case 7

A 34-year-old multiparous woman with a history of

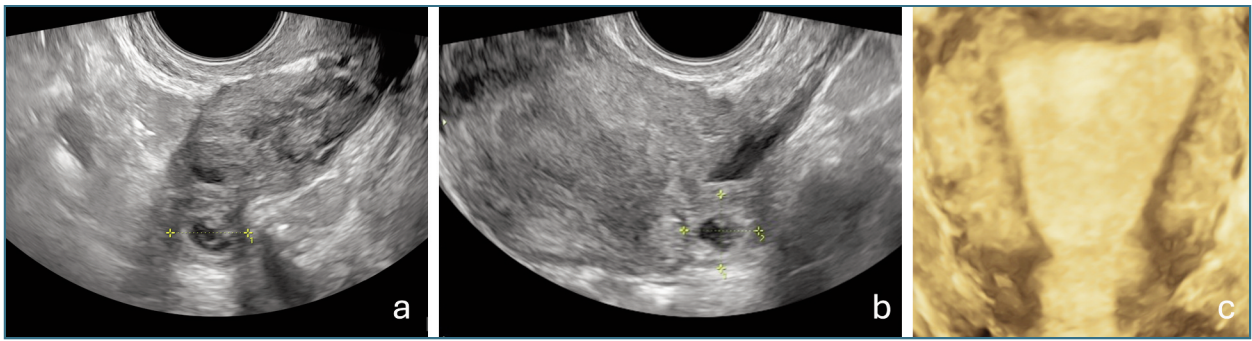


FIGURE 9. Transvaginal ultrasound showing an ectopic mass outside the endometrial cavity, surrounded by a thin myometrial mantle (a,b); and 3D ultrasound confirming an empty uterine cavity (c).

cesarean section, two ectopic pregnancies (one right-sided, laparoscopically treated), one abortion, and six miscarriages, presented with light vaginal bleeding and 6 weeks of amenorrhea. Initial transvaginal ultrasound revealed thickened endometrium without intrauterine

gestation. hCG showed an initial rise up to 2130 IU/L and two days later repeat scan identified a left IP with an embryo and cardiac activity (Figure 9). Due to limited laparoscopic expertise, laparotomy with left cornuostomy, salpingectomy, and cornual suturing was performed (Figure 10). The patient was discharged on day 2 with hCG reduced by 90%.

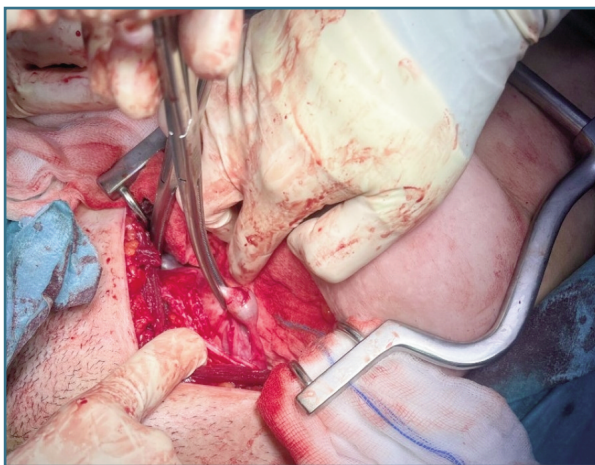


FIGURE 10. Cornuostomy performed by laparotomy.

Case 8

A 22-year-old nulliparous woman with 5 weeks amenorrhea presented with vaginal bleeding and pelvic pain. hCG was 3733 IU/L. Transvaginal ultrasound findings were consistent with a right IP, showing an eccentrically located gestational sac without communication with the endometrium, surrounded by a thin myometrial layer and peripheral ring vascularization (Figure 11). She was treated conservatively with intramuscular MTX (80 mg). Serial hCG demonstrated a 17% decline between days 4-7, and levels became undetectable within one month. The patient remained stable and asymptomatic throughout follow-up.

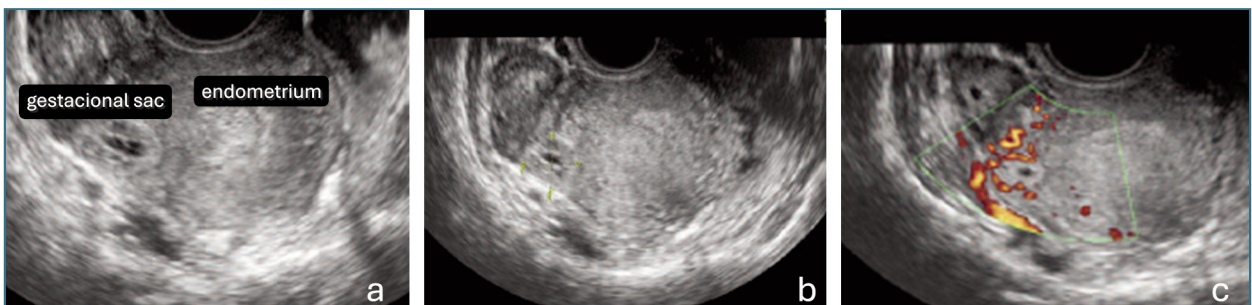


FIGURE 11. Transvaginal ultrasound showing an eccentrically located gestational sac bulging beyond the uterine contour, with no communication with the endometrium (a,b) and mild peripheral vascularization (c).

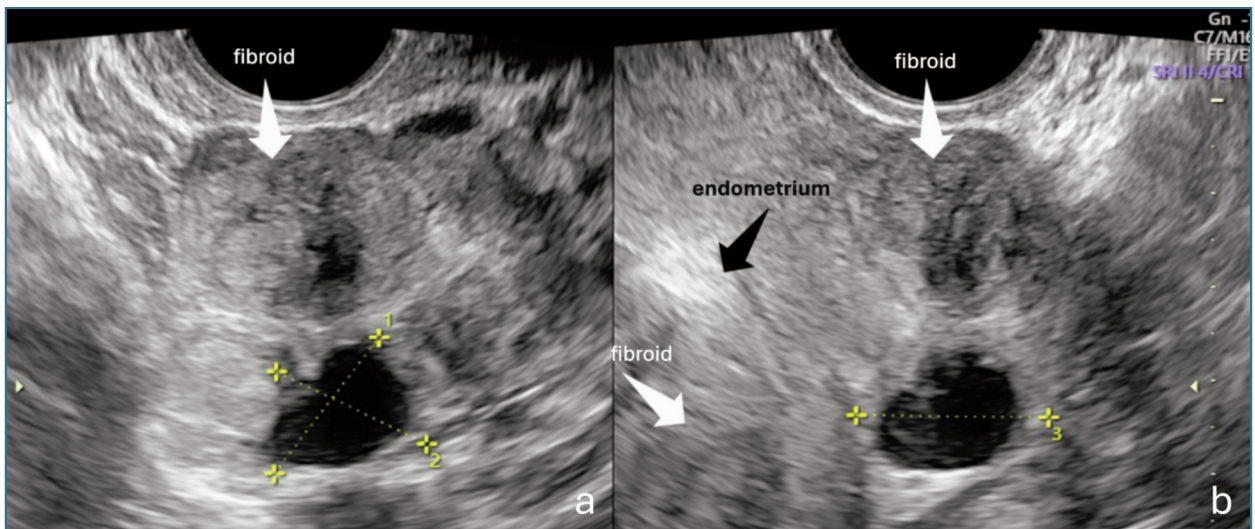


FIGURE 12. Transvaginal ultrasound showing a saccular, anechoic structure with regular borders in the left cornual region, adjacent to two fibroids.

Case 9

A 31-year-old nulliparous woman with a history of a myomatous uterus and 5 weeks amenorrhea presented with vaginal bleeding. Initial hCG was 1144 IU/L; transvaginal ultrasound revealed a pregnancy of unknown location. Serial hCG showed a plateau. Three days later, repeat ultrasound showed a saccular, anechoic structure in the left cornual region, separate from the endometrium and adjacent to a type 6 fundal fibroid, consistent with a left IP (Figure 12). She was treated with intramuscular MTX (93 mg). hCG increased from 1144 IU/L to 1935 IU/L between days 4 and 7, a second dose (93 mg) was required, after which levels declined by 20% and became undetectable within one month. The patient remained stable and asymptomatic throughout follow-up.

Case 10

A 37-year-old multiparous woman with no relevant medical or surgical history, asymptomatic, was referred for a suspected right interstitial pregnancy diagnosed abroad earlier that day. Her last menstrual period was three months earlier, and hCG abroad was 2000 IU/L. Transvaginal ultrasound confirmed a right IP (18 x 12 x 12 mm) and a right ovarian teratoma; 3D ultrasound further demonstrated an empty uterine cavity and a saccular structure in the right cornual region

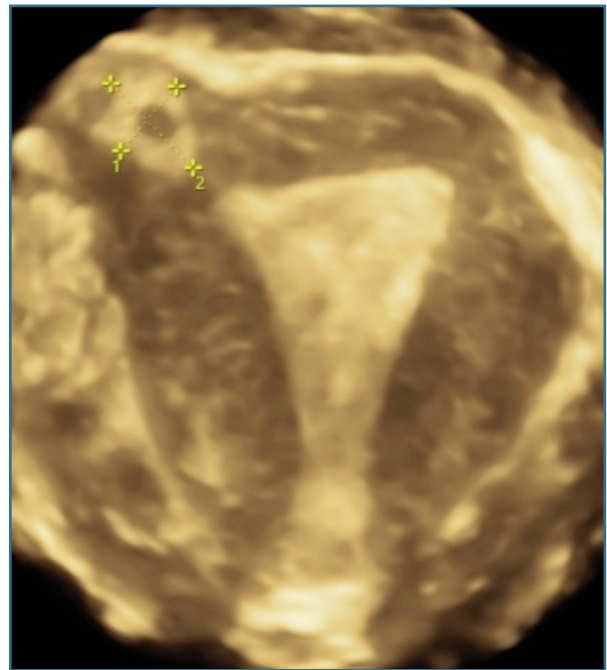


FIGURE 13. 3D transvaginal ultrasound showing a right IP, completely separated from the endometrial cavity.

(Figure 13). She was managed conservatively with intramuscular MTX (75 mg). hCG declined initially by 43% and then steadily, becoming undetectable within one month. She reported only mild, non-progressive abdominal pain, with no signs of rupture or free fluid. The clinical course remained stable throughout.

Tables I and II summarize ten cases of IP, illustrating diverse clinical presentations, management approaches, and outcomes.

All pregnancies were spontaneous. The mean gestational age at diagnosis was 7 weeks, with most cases presenting between 5-8 weeks, except one at 15 weeks and another with unquantified amenorrhea. Pelvic pain was the most common symptom, and three patients were hemodynamically unstable, all of whom experienced IP rupture.

Initial hCG levels ranged widely (mean 13948 IU/L; SD 17512 IU/L). In the seven surgically managed cases, final hCG averaged 2671 IU/L, decreasing 80% on average (range: 73%-90%). Medically managed cases showed gradual declines consistent with MTX treatment. An embryo was visualized in three cases. Risk factors were present in five patients, including previous uterine surgery (curettage, caesarean, salpingectomy) and myomatous uterus.

Seven patients underwent surgery: three wedge resections with ipsilateral salpingectomy, two cornuostomies, and two laparotomies with cornual suturing. Estimated blood loss ranged from 50 to 1800 mL (mean 729 mL; SD 695 mL). Preoperative hemoglobin averaged 12.4 g/dL (range 11.0 to 14.5 g/dL), falling to an average of 9.3 g/dL (mean decrease 3.1 g/dL; maximum 4.9 g/dL). Three patients required intravenous iron, and two received RBC transfusion. Operative times ranged from 50-140 minutes; shorter procedures (50-70 minutes) correlated with faster discharge (2-4 days). The longest surgery (140 minutes) was complicated by an intra-abdominal abscess requiring reoperation, extending hospitalization to 15 days. Moreover, two patients with anemia and one with a hypovolemic shock were discharged on day 4. The remaining three medically managed cases resolved successfully with MTX, without surgical intervention or complications.

Fertility outcomes were documented in three patients (cases 3, 4, 6), with successful subsequent pregnancies 15 months to 3 years later. Deliveries were by cesarean: preterm for case 3 (non-reassuring fetal status) and elective for cases 4 and 6.

DISCUSSION

This case series includes both stable, early diagnosed

pregnancies suitable for conservative management and complex or ruptured IP requiring emergency surgical intervention. It provides valuable insights into the diagnostic and therapeutic challenges of IP.

IP carries a higher risk of maternal morbidity and mortality than other ectopic pregnancies, making early and accurate diagnosis critical, yet still challenging. Advanced ultrasonography, including 3D imaging, combined with clinician expertise, played a key role in early detection and optimizing outcomes. The most common presenting symptom in this series was pelvic pain, reported in 4 out of 10 patients, highlighting the often subtle or nonspecific clinical presentation.

Risk factors traditionally associated with IP, such as assisted reproductive technologies, were absent in this series, as all pregnancies were spontaneous. Several cases highlighted diagnostic challenges: Case 1 involved a rare heterotopic pregnancy initially misdiagnosed as an incomplete miscarriage. Case 2 demonstrated the need for strong clinical suspicion even in asymptomatic patients, particularly with specific risk factors like a history of ipsilateral salpingectomy. Case 4, with multiple previous cesareans, emphasizes considering ectopic pregnancy in any patient with amenorrhea and pelvic pain, even without gestational evidence. Case 6 illustrates misdiagnosing intrauterine pregnancies when imaging findings are atypical. Finally, Case 8 underscores challenges posed by fibroids.

Management strategies varied according to patient stability and severity. In hemodynamically stable patients (cases 1 and 2), laparoscopic wedge resections and cornuostomies were effective, resulting in minimal blood loss (50--100 mL) and prompt recovery (discharge within two days). The decision for surgery over medical management was based on specific risks. Both Cases 1 and 2 presented with high hCG level (14745 and 10323 IU/L, respectively), which significantly reduce the success rate of methotrexate and increase the risk of secondary rupture. Additionally, in Case 1, a suspected heterotopic pregnancy added complexity, while in Case 2, the prior ipsilateral salpingectomy and a visible yolk sac favored definitive surgery over uncertain medical follow-up. These choices align with the FRANCOGENT group protocols, which prioritize surgical intervention in cases with high metabolic activity or complex surgical histories¹⁶.

In contrast, cases featuring significant hemorrhage, or

TABLE I. CASES OF IP – DEMOGRAPHIC CHARACTERISTICS, CLINICAL AND ULTRASOUND PRESENTATION, AND CHOICE OF TREATMENT.

Case Report	Age	Obstetric index				GA	Medical history	Symptoms	Ultrasound findings		
									Side	Size (mm)	Embryo/FHR
1	42	1	0	0	1	NA/-	Suction curettage 1 week before	Pelvic pain	Left	56x25	No
2	29	0	1	2	1	5	Previous left laparoscopic salpingectomy	Amenorrhea	Left	17	No
3	35	0	0	0	0	8	Obesity, APS	Pelvic pain	Right	NA/-	Yes/Yes
4	33	4	0	0	4	5	Four prior cesarean sections	Pelvic pain	Left	22x17	No
5	38	2	1	1	3	5	NA/-	Acute abdomen	Left	45x42	No
6	18	0	0	1	0	15	Previous right inguinal hernia repair	Acute abdomen	NA/-	NA/-	Yes/No
7	34	1	0	9	1	6	Previous right laparoscopic salpingectomy	Amenorrhea	Left	12x12x13	Yes/Yes
8	22	0	0	1	0	5	Previous abortion	Vaginal bleeding + Pelvic pain	Right	16	No
9	31	0	0	0	0	5	Myomatous uterus	Vaginal bleeding	Left	18x17x19	No
10	37	1	0	0	1	8	NA/-	Amenorrhea	Right	18x12x12	No

Legend: APS – Antiphospholipid Syndrome; FHR – Fetal Heart Rate; GA – Gestational Age; IP – Interstitial Pregnancy; MTX – Methotrexate; NA/- – Not Available or Not Applicable.

hemodynamic instability (cases 4, 5, 6), laparotomy was necessary to manage IP rupture and extensive hemoperitoneum (up to 1800 mL). Moreover, in case 3, it was the surgical complexity motivated by the extensive adenomyosis, that dictated the need for an open approach; and case 7 emphasized the importance of choosing a surgical technique aligned with the team’s expertise, underscoring how experience is critical for optimizing outcomes.

These more severe presentations were associated with higher blood loss, longer operative times, extended recovery, and more intensive postoperative care. Case 5, for example, required a 140-minute-long pro-

cedure, featuring postoperative intra-abdominal abscess that called for a second laparotomy, prolonging hospitalization to 15 days. Despite the severity of these cases, radical surgery (such as hysterectomy), sometimes needed in cases where bleeding is life threatening²⁰, was avoided in all patients.

In this series, the success of surgical intervention was assessed by the percentage of hCG decline, with an average reduction of 80%. These measurements were consistently collected within the first 24 to 48 hours postoperatively. The sharp initial drop in hCG levels suggests complete removal of trophoblastic tissue and

	Ultrasound findings			IP rupture	Surgery	Procedure
	Ultrasound signs	Free fluid	3D			
	Heterogeneous echogenic mass with peripheral vascularization; empty uterine cavity	No	NA/-	No	Laparoscopy	Wedge resection + left salpingectomy
	Rounded anechoic mass with yolk sac with peripheral vascularization; thin myometrial mantle	No	External bulging of the uterine wall	No	Laparoscopy	Cornuostomy
	IP with a viable embryo; thin myometrial mantle of 3 mm	No	NA/-	No	Laparotomy	Wedge resection + right salpingectomy
	Cornual nodular mass with signs of rupture (hematoma/hemosalpinx); empty uterine cavity; examination extremely painful	No	NA/-	Yes	Laparotomy	Exploratory laparotomy
	Heterogeneous echogenic mass with peripheral vascularization; type 1 right fibroid; extremely painful	Yes	NA/-	Yes	Laparotomy	Wedge resection + left salpingectomy
	Enlarged uterus; massive hemoperitoneum	Yes	NA/-	Yes	Laparotomy	Exploratory laparotomy
	Empty uterine cavity; thickened endometrium; IP with a viable embryo	No	Empty cavity	No	Laparotomy	Cornuostomy + left salpingectomy
	Eccentric anechoic mass with peripheral vascularization; thin myometrial mantle	No	External bulging of the uterine wall	No	NA/-	MTX 50 mg/m ² (total dose: 80mg)
	Cornual saccular anechoic structure; interstitial line sign; adjacent to a type 6 fundal fibroid	No	External bulging of the uterine wall	No	NA/-	MTX 50 mg/m ² (total dose: 93 mg) Twice
	Empty uterine cavity; interstitial line sign	No	Saccular anechoic structure in the right cornual region	No	NA/-	MTX 50 mg/m ² (total dose: 75 mg)

is highly predictive of successful surgical resolution without the need for adjuvant methotrexate, as demonstrated in multicenter studies by the Francogent group and Herondelle *et al*^{16,22}.

Conservative management with MTX is increasingly recognized as an effective and fertility-preserving alternative to surgical management, particularly in young women who have not yet completed their reproductive plans^{3,8,17}. In this series, three cases (8, 9 and 10) illustrate the successful use intramuscular MTX in hemodynamically stable patients with moderate hCG levels, ranging from 1397 and 3733 IU/L. One

patient required a second MTX dose on day 7 despite hCG levels being below 5000 IU/L, highlighting that some patients may benefit from multiple-dose protocol rather than a single-dose regimen. Literature suggests that local MTX administration may reduce systemic side effects, such as transitory peripheral neuropathy, severe constipation, and deterioration in liver function¹¹, although in our cases no adverse effects were reported. These cases highlight that the success of conservative management relies on careful patient selection, thorough serial hCG monitoring, and consistent follow-up, along with precise ultrasound assessment²¹.

TABLE II. CASES OF IP – HCG MONITORING, OUTCOMES, AND FOLLOW-UP.

Case Report	initial hCG	final hCG	hCG ↓	%	initial Hb	final Hb	Hb ↓	Blood loss (mL)	RBC	IV iron	Surgery time (min)	ICU stay	Postoperative complications	Discharge (days post-surgery)	Subsequent pregnancies
1	14745	2768	11977	81%	12.3	NA/-	NA/-	100	0	0	60	No	No	2	NA/-
2	17013	4561	12452	73%	14	12	1.6	50	0	0	50	No	No	3	NA/-
3	59311	NA/-	NA/-	NA/-	11.1	9.3	1.8	400	0	Yes	70	No	Anemia	4	Preterm cesarean section at 20 months postpartum due to non-reassuring fetal status
4	3790	900	2890	76%	11	6.5	4.5	1500	1	Yes	60	No	Anemia	4	Elective cesarean section at 15 months postpartum
5	30491	4468	26023	85%	11.5	7.6	3.9	1200	0	Yes	140	No	Intra-abdominal abscess managed with laparotomic drainage on day 5	15	NA/-
6	3908	659	3249	83%	12.5	7.6	4.9	1800	2	0	60	Yes	Hypovolemic shock	4	Two elective cesarean sections (first at 20 months, second at 3 years postpartum)
7	2130	210	1920	90%	14.5	12.5	2	50	0	0	59	No	No	2	NA/-
8	3733	3098	635	17%	NA/-	NA/-	NA/-	NA/-	0	NA/-	NA/-	NA/-	NA/-	NA/-	NA/-
9	1935	1541	394	20%	NA/-	NA/-	NA/-	NA/-	0	NA/-	NA/-	NA/-	NA/-	NA/-	NA/-
10	2419	1383	1036	43%	NA/-	NA/-	NA/-	NA/-	0	NA/-	NA/-	NA/-	NA/-	NA/-	NA/-

Legend: Hb – Hemoglobin; hCG – Human Chorionic Gonadotropin; ICU – Intensive Care Unit; IV – Intravenous; NA/- – Not Available or Not Applicable; RBC – Red Blood Cell.

Complications varied according to the severity of presentation and the type of management. One patient required ICU admission due to hypovolemic shock, underscoring the potential for rapid deterioration in IP. Three patients developed postoperative anemia requiring intravenous iron supplementation, while two required RBC transfusions. A particularly severe postoperative complication occurred in Case 5, where the patient developed an intra-abdominal abscess that required a second laparotomy for drainage. This complication extended the hospital stay to 15 days, highlighting the potential impact of surgical morbidity on recovery time.

Long-term follow-up, including contraception counselling, serial hCG monitoring, and clinical assessments, proved essential for ensuring complete recovery and preservation of reproductive potential. Notably, there were no cases of persistent or recurrent IP in the cornual resection group, and three patients successfully achieved subsequent pregnancies. Future fertility appeared largely dependent on the patency of the contralateral fallopian tube².

As is common with studies on rare conditions, this analysis is limited by a small sample size and relatively short follow-up period, which restricts generalization and a full assessment of long-term outcomes. Emerging evidence suggests that laparoscopic cornuostomy may provide shorter operating times and better reproductive outcomes compared to wedge resection, but further research is needed to confirm these advantages¹.

Standardized protocols for conservative treatment, including predictive scoring systems, could improve patient selection for non-surgical management.

In conclusion, these cases emphasize the critical need for individualized care, timely diagnosis, tailored surgical or conservative management, and diligent postoperative follow-up in IP. While laparoscopic techniques remain highly effective for stable patients, laparotomy is indispensable in more severe cases. Conservative management with MTX offers a valuable fertility-preserving option for selected patients. Advancements in ultrasound technology and clinical expertise have greatly improved early detection and outcomes, though diagnostic challenges still exist. Therefore, the implementation and compliance with clear guidelines and protocols are essential for standardizing care, reducing diagnostic delays, and optimizing outcomes, while preserving fertility.

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AUTHOR CONTRIBUTIONS

Carolina Mendonça: Information research from clinical records, drafting of the manuscript, and final revision. Inês Lourenço, Njila Amaral, Carlos Verissimo: Critical revision of the manuscript for important intellectual content.

COMPETING INTERESTS

There are no conflicts of interest.

ETHICS APPROVAL

This study was reviewed and approved by the Ethics Committee.

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