

## Diagnosis and Management of ‘Cornual’ Pregnancies from 2002 to 2015 at a Tertiary Referral Centre in South India: Insights from Introspection

Vijaya B. Bayyrapu<sup>1</sup> · Sirisha R. Gundabattula<sup>1</sup>

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### About the Author



**Dr. Vijaya Bharathi Bayyrapu** (MD, FMIS) obtained her MD-OBG degree from PGIMER, Chandigarh, and pursued Fellowship in Minimally Invasive Surgery at Dr. Ramesh Hospital, Bangalore. She worked as senior registrar and consultant at various hospitals in Andhra Pradesh and Kerala from 2000 till date. The present study was carried out at Fernandez Hospital, Hyderabad. Her areas of interest include endoscopy, infertility and reproductive endocrinology. She presented posters and papers at various national conferences (AGOICON, RCOG and ISGE Asian Meeting) and was awarded the Best Paper Presentation for the study on outcomes with interval laparoscopic transcervical cerclage. She also co-authored chapters on safe and effective endoscopy, electrosurgery and single-incision laparoscopic myomectomy and has peer-reviewed publications on cornual pregnancy, bilateral ectopic pregnancy and recurrent adnexal torsion.

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Dr. Vijaya Bharathi Bayyrapu (MD, FMIS) obtained her MD-OBG degree from PGIMER, Chandigarh, and pursued Fellowship in Minimally Invasive Surgery at Dr. Ramesh Hospital, Bangalore. She worked as senior registrar and consultant at various hospitals in Andhra Pradesh and Kerala from 2000 till date. The present study was carried out at Fernandez Hospital, Hyderabad, India. Sirisha R. Gundabattula affiliated to Fernandez Hospital, Hyderabad, India.

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✉ Sirisha R. Gundabattula  
drsirisha.g@fernandezhospital.com;  
drgsirisharao@gmail.com

Vijaya B. Bayyrapu  
bharathi.b2002@gmail.com

<sup>1</sup> Department of Gynaecology, Fernandez Hospital, 4-1-1230, Bogulkunta, Hyderabad, Telangana 500001, India

### Abstract

**Purpose** Interstitial, angular and rudimentary horn pregnancies have all been referred to as cornual pregnancies despite definite diagnostic criteria. Angular pregnancies can be followed up expectantly under close surveillance while interstitial and rudimentary horn pregnancies are terminated by medical or surgical methods. This study aimed to assess accuracy of ultrasound in the diagnosis of ‘cornual pregnancy’ and evaluate management.

**Methods** Data pertaining to clinical features, ultrasound findings and treatment modalities of the aforementioned conditions between January 2002 and December 2015 at a tertiary perinatal centre were retrieved from the medical records. The ultrasound images and surgical videos were reviewed by the authors.

**Results** Of 62 cases, 35 were interstitial, 26 were angular/eccentric intrauterine, and 1 was a rudimentary horn pregnancy. The accuracy of ultrasonography in the diagnosis of interstitial and angular pregnancies was 71.0 and 46.8%, respectively. Medical management was successful in 33.3% of interstitial pregnancies. Fifteen women with interstitial pregnancy had subsequent pregnancies and nine (75.0%) were Caesarean deliveries. Rupture and recurrence rates of interstitial pregnancy were 34.2 and 2.9%, respectively. The rudimentary horn pregnancy was managed by laparoscopic excision followed by a subsequent term delivery.

**Conclusion** This study identified frequent occurrences of imprecise nomenclature that resulted in mismanagement of a few potentially viable angular pregnancies. It is imperative for clinicians and sonologists to use unambiguous nomenclature and avoid the term ‘cornual pregnancy’ altogether.

**Keywords** Cornual pregnancy · Interstitial pregnancy · Angular pregnancy · Rudimentary horn · Transvaginal ultrasound · Methotrexate

## Introduction

Cornual ectopic pregnancy (CEP) by definition refers to the implantation and development of a gestation in a rudimentary horn (rudimentary horn pregnancy, RHP) or in one horn of a septate or bicornuate uterus. However, this term has also been used for pregnancies in the interstitial portion of the fallopian tube (interstitial pregnancy, IP) and those in the lateral angle of the uterine cavity (angular pregnancy, AP) [1, 2]. An IP (incidence: 16/1000 pregnancies) is diagnosed by the presence of a gestational sac separate from the cavity and >1 cm from the lateral most edge of the cavity with continuation of the myometrial mantle around the sac and an interstitial line joining the sac and the uterine cavity. In an RHP [incidence: 1:76,000 to 1:140,000], only a single interstitial portion of the fallopian tube is visualized with the absence of continuity between the cervical canal and the lumen of the pregnant horn. An AP is always intrauterine characterized by asymmetric uterine enlargement and a markedly eccentric gestational sac surrounded by endometrium. IPs account for 2–4% of all ectopic pregnancies and up to 7.3% with the advent of assisted reproductive technologies. Although the exact reason for the higher incidence of IP with assisted reproductive technology is not clear, previous salpingectomy and tubal infertility appear to be significant risk factors probably due to non-migration of embryos beyond the interstitial portion of the fallopian tube [3]. The incidence

of AP has not been clearly determined because of controversies not just in diagnosis but on its very existence.

CEPs can be diagnosed by meticulous 2D transvaginal ultrasonography (USG) in the sagittal and transverse planes by experienced operators; in difficult cases, 3D multiplanar USG facilitates visualization of the interstitial tube helping to differentiate between intrauterine pregnancy (IUP) and IP. Early diagnosis and treatment are important because the risk of rupture increases beyond 12-week gestation. Notwithstanding the reluctance to acknowledge AP as an ‘ectopic’ gestation by some experts, there have been reports describing APs complicated by uterine rupture. Conversely, these pregnancies can also progress to term [4]. Arleo and DeFilippis [2] clarified the terminology and also reviewed the literature with respect to diagnosis and prognosis; this is important because an IP is a non-viable ectopic while an AP is a potentially viable IUP.

Considering these challenges in diagnosis and management, the rarity of these entities and the arbitrary interchange of names, a study of such cases managed at the institute was carried out in order to (1) evaluate accuracy of USG in the diagnosis and (2) reflect on management of CEPs.

## Materials and methods

The study included all cases labelled as CEP, IP, RHP and AP between January 2002 and December 2015 at Fernandez Hospital, a tertiary referral perinatal centre at Hyderabad, India, with an annual delivery rate exceeding 8000. Data pertaining to obstetric history, clinical presentation, USG findings, treatment modalities and surgical details were retrieved from the medical records. The ultrasound images and surgical videos were reviewed by the authors together. Information on subsequent pregnancies was also enquired over telephone. The study protocol adhered to the tenets of the Declaration of Helsinki.

At the study institute, the medical management of all ectopic pregnancies was in accordance with the American Society for Reproductive Medicine (ASRM) guideline [5]. A candidate for medical management with methotrexate had to be haemodynamically stable, have no severe or persistent abdominal pain, be willing for follow-up until resolution and have normal baseline liver and renal function tests. Embryonic cardiac activity, pregnancy size >4 cm by transvaginal USG and the initial serum human chorionic gonadotropin (hCG) >5000 mIU/ml constituted relative contraindications to medical management. Single-dose regime consisted of intramuscular methotrexate 50 mg/m<sup>2</sup> with or without 600 mg of oral mifepristone. A second dose of methotrexate was considered if the fall in serum hCG was <15% between days four and seven of the

initial dose. In the multidose regime, methotrexate (1 mg/kg) and folic acid (0.1 mg/kg) were administered intramuscularly on alternate days until hCG dropped by 15% in 48 h or up to a maximum of four doses. The decision about the regime of medical management was an arbitrary one. Once a satisfactory drop in hCG titres was recorded, the levels were checked every week until they became negative. Surgical intervention was advised to women with features suggestive of rupture, those unsuitable or unwilling for medical management or after failed medical management (no decline in hCG levels or persistent cardiac activity in the mass).

Laparoscopy was the preferred route of surgery; laparotomy was resorted to when endoscopic management was not possible (discussed later) or the woman presented in haemorrhagic shock. Unruptured IPs were managed by cornuostomy or cornual wedge resection, whereas haemostasis was achieved in ruptured IPs using a combination of suturing and electrosurgery. Vasopressin (20 units diluted in 200 ml of normal saline) was injected at the base of the ectopic pregnancy. Cornuostomy involved incising the greatest protrusion of the IP and expelling the products via hydrodissection, whereas cornual wedge resection was carried out by incising the IP circumferentially midway between its base and the top, excising the wedge and repairing the cornua using polyglactin 910 [6]. There was no consensus at the study institute on concurrent ipsilateral salpingectomy.

The primary outcome measure was the accuracy of ultrasonography in the diagnosis of IP and AP. The success rate with medical management in IP was the secondary outcome measure. The data were entered into a Microsoft Excel 2007 spread sheet and frequency, mean, median, standard deviation and interquartile range calculated. The diagnostic accuracy of USG in the diagnosis of IP and AP was presented as sensitivity, specificity, positive and negative predictive values, calculated by OpenEpi software version 3.01 ([https://www.openepi.com/Menu/OE\\_Menu.htm/](https://www.openepi.com/Menu/OE_Menu.htm/)).

## Results

A total of 62 cases were included (Table 1); the ratio of IP:RHP was 35:1. The diagnosis of AP versus an eccentrically located IUP could not be ascertained because asymmetrical painful enlargement of the uterus, a characteristic finding in AP, was not recorded in the case files, and radiologically, there was/is no anatomic boundary to distinguish the two. In 41 patients, the USG images were available for review by the authors (Fig. 1); the initial USG findings were compared with the image review as well as with the final diagnosis (Fig. 2). The sensitivity, specificity, positive

and negative predictive values, and accuracy of USG in the diagnosis of IP (14.3, 88.9, 62.5, 44.4%, 0.468) and AP (30.8, 100.0, 100.0, 66.7%, 0.710) were largely a reflection of incorrect nomenclature rather than missed diagnosis.

Expectant, primary medical or primary surgical management was offered in almost equal proportions (Fig. 3). Expectant management was offered only to APs/IUPs while IPs were managed medically or surgically. Medical management was successful in a third of the 15 IPs that were managed medically with normalization of hCG in 5.5 (SD 2.9) weeks; three were lost to follow-up, one required uterine artery embolization, and the rest required surgical intervention. In the six women who had surgery following medical management, three were for high hCG titres (>25,000 mIU/ml), two were for pain, and one was for persistent embryonic cardiac activity. Most (19, 67.9%) surgeries were accomplished laparoscopically. Concurrent ipsilateral salpingectomy was performed in 14 (36.8%) cases. There was one heterotopic pregnancy diagnosed at eight weeks of amenorrhoea in a primigravida who conceived with ovulation induction. Emergency laparoscopy for suspected ectopic gestation disclosed a ruptured IP. The intrauterine pregnancy continued uneventfully, and she delivered at term by Caesarean section. Two other ruptured IPs presented at 18 weeks of gestation (Fig. 4), but did not necessitate hysterectomy, and there were no major intraoperative complications.

The future pregnancy details were not known in 15 women with IP who were lost to follow-up. Fifteen (93.8%) women with IPs desiring pregnancy conceived with 70.6% pregnancies resulting in live births; three of 12 births were spontaneous vaginal deliveries (elsewhere); and the Caesarean rate was 75.0%. There were no instances of uterine rupture, and recurrence was observed in one case (2.9%). The woman with RHP had a Caesarean delivery at term in the subsequent pregnancy.

## Discussion

The aims of the present study were to review the diagnosis and management of CEPs: these were fulfilled within the context of the inherent limitations posed by a retrospective study, but a precise assessment of outcomes of medical management was hindered by the percentage lost to follow-up. The substandard (46.8%) accuracy of USG in the diagnosis of IP was predominantly due to incorrect nomenclature and lower than the literature-reported accuracy of 71.4%.

The RHP in the present study was managed by laparoscopic excision of the unruptured (120 × 80 × 80 mm) gravid horn which is the recommended treatment because of the continuing risk of sudden rupture and haemorrhage.

**Table 1** Characteristics of the study population with cornual pregnancy

Characteristic	Interstitial pregnancy (IP) = 35	Angular pregnancy (AP)/intrauterine pregnancy (IUP) = 26	Rudimentary horn pregnancy = 1
Mean (SD) age in years	28.9 (4.1)	29.1 (3.6)	26
Primigravidae	13 (37.1%)	7 (26.9%)	1
Prior ectopic pregnancy	8 (22.9%)	5 (19.2%)	0
Prior ipsilateral salpingectomy	8 (22.9%)	0 (0.0%)	0
Assisted conception	6 (17.1%)	9 (34.6%)	0
Asymptomatic	13 (37.1%)	18 (69.2%)	1
Abdominal pain	19 (54.3%)	5 (19.2%)	0
Vaginal bleeding	6 (17.1%)	5 (19.2%)	0
Syncope	8 (22.8%)	0 (0.0%)	0
Mean (SD) gestational age in weeks	8.0 (3.8) <sup>a</sup>	6.7 (1.3)	11
Detection in first trimester	31 (88.6%) <sup>a</sup>	26 (100.0%)	1
Ultrasound (USG): mean (SD) mass size in mm	29.6 (11.8)	Not applicable	Not applicable
USG: mean (SD) sac diameter in mm	17.9 (10.8)	10.0 (7.3)	Not applicable
USG: visualization of embryo	7 (20.0%)	8 (30.8%)	1
USG: free fluid in upper abdomen	8 (22.9%)	0 (0.0%)	0
Serum beta-human chorionic gonadotropin (hCG) at diagnosis (mIU/ml) <sup>b</sup> : mean (SD); median (IQR)	13,241.7 (22,720.4); 6066.5 (12,349.5)	16,267.8 (29,980.4); 4930.0 (7180.0);	86,540 (actual value of hCG)
Mullerian anomaly	1 (2.9%)—septate uterus	0 (0.0%)	1—unicornuate with rudimentary horn
Rupture	13 (37.1%)	0 (0.0%)	0
Blood transfusion	7 (18.4%)	0 (0.0%)	0

<sup>a</sup> Gestational age was not recorded in two cases and no amenorrhoea in two women

<sup>b</sup> Data of hCG were available for 26 cases of IP and 13 cases of AP/IUP; one IP was diagnosed incidentally during hysterolaparoscopy; hCG was negative, but histological examination confirmed products of conception

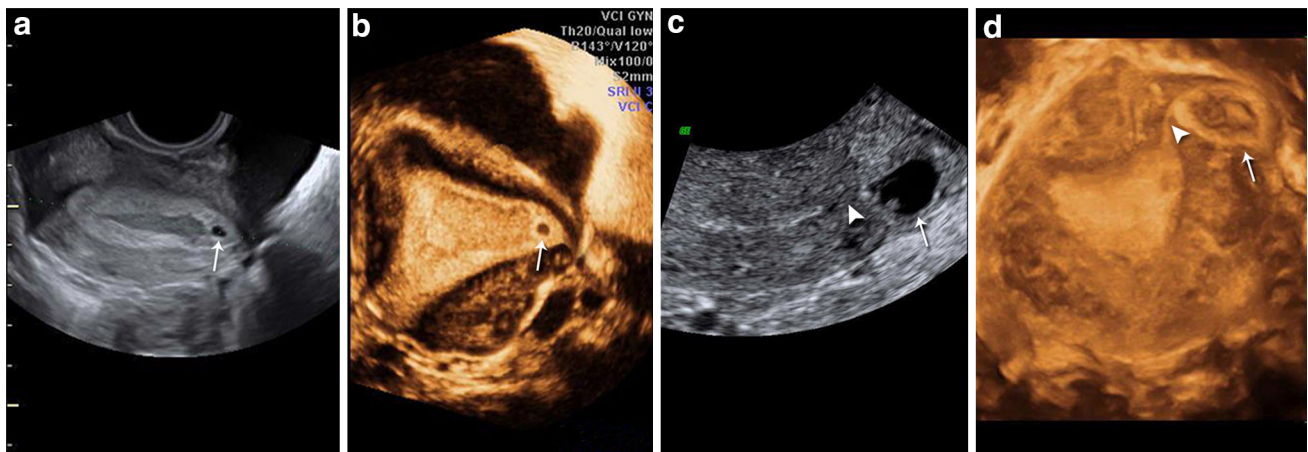
A high (50.0%) miscarriage rate among the 26 APs/IUPs was observed in the present study, comparable to 38.5% in a previous meta-analysis of 38 APs; in contrast to the estimated uterine rupture rate of 13.6%, none in the present study were complicated by rupture, possibly because prior uterotubal implantation, found to be associated with rupture, was not noted in this study.

The study included 35 women with IP. A prior ipsilateral salpingectomy, a risk factor unique to IP, was observed in a fifth of the IPs. The authors do not have any experience with expectant management. However, this was described by Poon et al. in 17 of 19 non-viable IPs with declining serum hCG levels [7]. The higher median gestational age in the expectant management group (10 weeks) compared to medical (6–8 weeks) and surgical (8 weeks) groups probably implied that those managed expectantly presented later when the trophoblast was regressing naturally. It is, however, impossible to determine whether and when an IP will undergo spontaneous resolution.

In the present series, successful resolution of IPs with systemic methotrexate was achieved in only 33.3% of IPs; multidose regime was successful in 20.0% of cases compared to 40.0% with the single-dose regime, but the numbers were too few to compare. This contrasts with reported

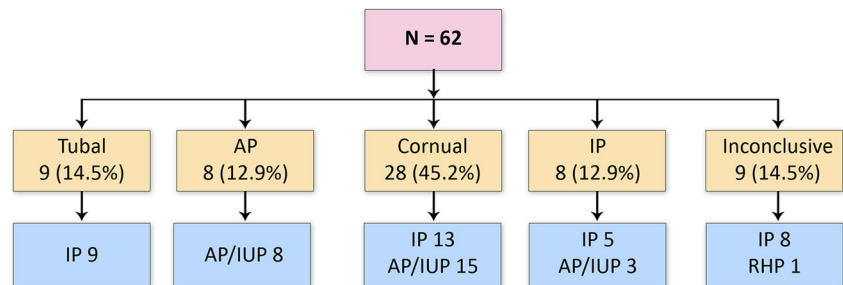
success rates of 64–83% with methotrexate and the concept of multiple doses being more efficient than a single dose [8]. The disparity in results could be because of few numbers and the 20% lost to follow-up in the present study. In agreement with earlier reports [9], one IP resolved successfully following uterine artery embolization after failed medical management.

Although laparoscopy is the preferred route of surgery for IP, laparotomy should not be delayed when expedient laparoscopic services are not available. In this study, laparoscopy was converted to laparotomy in four women with unruptured IP, and four others with ruptured IP had a direct laparotomy to facilitate suturing after cornual resection and expedite the surgery, particularly in haemodynamically unstable patients and/or when the surgeon lacked expertise in endosuturing. Haemostatic techniques at the study institute were limited to vasopressin, bipolar electrosurgery or suturing, singly or in combination, but their effects on blood loss and operative time were not quantified. Although there is no consensus on the best method from among vasopressin, purse-string suture, square suture, encircling suture, Endo-loop<sup>(R)</sup>, electrocoagulation, occlusion of ascending branch of uterine artery, fibrin glue, automatic stapler, uterine artery ligation or



**Fig. 1** Transvaginal ultrasound images. **a** 2D image of eccentric intraendometrial pregnancy; **b** 3D image of eccentric intraendometrial pregnancy; **c** 2D image of interstitial pregnancy; **d** 3D image of interstitial pregnancy. Arrows indicate gestational sac and arrow heads indicate interstitial line

**Fig. 2** Sonographic diagnosis of cornual pregnancy compared to the final diagnosis based on operative findings and image review (AP angular pregnancy, IP interstitial pregnancy, IUP intrauterine pregnancy, RHP rudimentary horn pregnancy)



double-impact devascularization, Cucinella et al. concluded that laparoscopic injection of vasopressin was the preferred approach [10, 11].

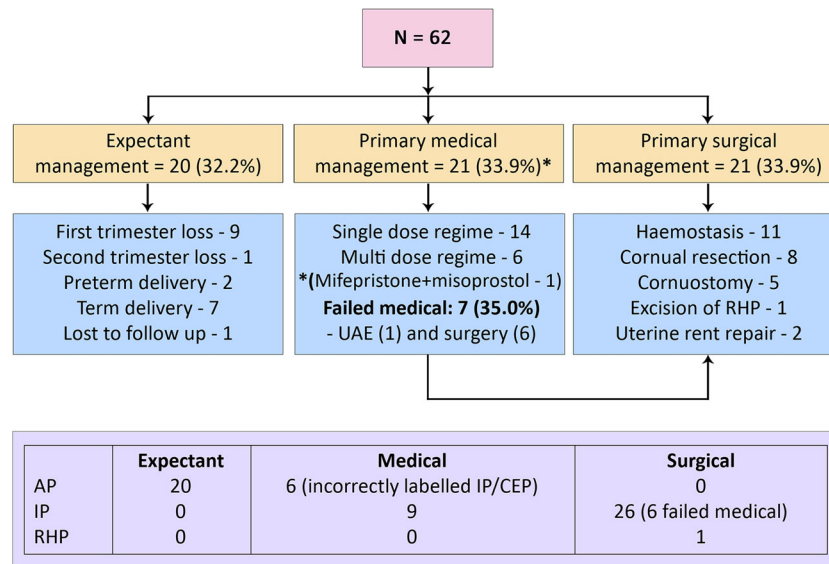
Uterine rupture can occur after IPs that are treated surgically as well as medically, and this may occur in any trimester [12]. Despite reports of successful vaginal births, Caesarean section appears to be the optimum mode of delivery for pregnancies following IP to avoid the risk of intrapartum uterine rupture [3]. There are no definite guidelines on the timing of delivery, but as for prior classical Caesarean delivery (also characterized by a scar on the upper uterine segment), delivery at 36–37 weeks may be applicable [13, 14]. Recurrence of IP is reported in 8.3–9.4% of cases [6]. There was only one recurrence encountered by the authors in a nulliparous woman with septate uterus and recurrent miscarriages. The initial IP was a surprise finding at diagnostic hysterolaparoscopy with no history of preceding amenorrhoea. Following laparoscopic cornuostomy and hysteroscopic septal resection, she presented with a ruptured IP three months later and was managed laparoscopically.

This study identified regular occurrences of imprecise terminology in the ultrasound diagnoses of pregnancies located in the cornual region of the uterus. Inaccurate

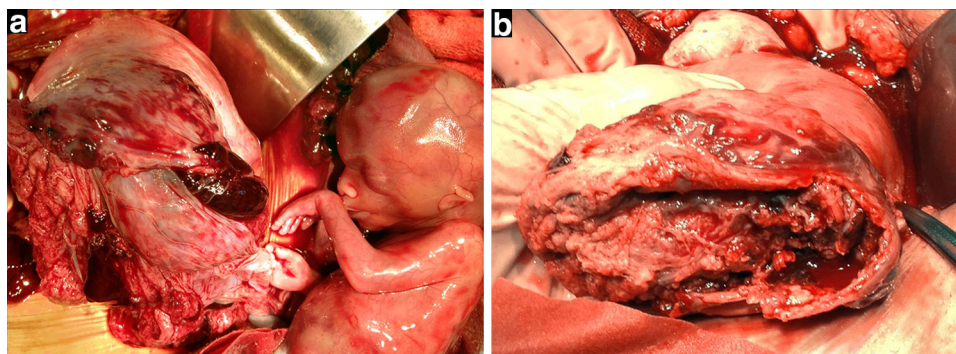
descriptions and nomenclature could have contributed to the early termination of some angular intrauterine pregnancies. The strength of the study was that it created awareness of these pitfalls in diagnosis and the resultant errors in management. Being a retrospective study, incomplete records posed a limitation to data collection. Ambiguous terminology and minor management differences by the individual clinicians were observed. The other drawback was the percentage lost to follow-up.

Clinicians and sonologists facing these challenges in their day to day practice must update their knowledge and skills in order to identify and label these entities precisely. Every institute should audit their cases in order to discern areas for correction and improvement, and strive to improve the diagnostic accuracy of ultrasonography. Future research ought to be directed at prospective studies to assess the efficacy of different modalities of treatment. Further, the feasibility of expectant management in asymptomatic IPs can be explored prior to initiation of therapy. Critical introspection of the technique of salpingectomy, a risk factor for subsequent ipsilateral IP, may be worth pursuing.

To conclude, regular intradepartmental review of all asymptomatic CEPs prior to termination is recommended.



**Fig. 3** Management of and outcomes in women with cornual pregnancy (UAE uterine artery embolization, RHP rudimentary horn pregnancy, AP angular pregnancy, CEP cornual ectopic pregnancy, IP interstitial pregnancy)



**Fig. 4** Ruptured interstitial pregnancy at 18 weeks of gestation

Standardization of nomenclature is essential for better evaluation of management outcomes; ‘cornual ectopic pregnancy’ is a misnomer and should be avoided altogether.

**Compliance with Ethical Standards**

**Conflict of interest** All authors declare that they have no conflict of interest.

**Ethical approval** For this type of study, formal consent is not required.

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