

# Interstitial Ectopic Pregnancy: The Essential Role of Ultrasound Diagnosis

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## Abstract

Diagnosis of uterine ectopic pregnancy of interstitial or cervical location poses a challenge to the sonographer to assess the exact location and determine the best treatment option.

In the presented case, gray scale ultrasound raised the suspicion of cornual pregnancy. Color Doppler and Pulsed Doppler waveform analysis has identified the typical peritrophoblastic flow. Three-dimensional (3D) ultrasound enabled navigation through multiplanar sections of the uterus and has finally confirmed the diagnosis of interstitial pregnancy.

Due to high human chorionic gonadotropin (hCG) levels, viability of the pregnancy, and impending rupture laparoscopic cornual resection was chosen among different treatment options.

**Keywords:** Interstitial pregnancy, 3D ultrasound, Color Doppler, Trophoblast flow, Laparoscopic cornual resection.

## CASE REPORT

A 35-year-old Caucasian primigravida was referred to our hospital after two cycles of *in vitro* fertilization procedure (IVF/ET). Patient was evaluated 3.5 weeks after embryo-transfer. Serum beta human chorionic gonadotropine (hCG) level was 24,229 IU/ml. Routine ultrasound assessment of early pregnancy in the IVF center had raised suspicion of an interstitial pregnancy. At the time of her admission to our hospital she was clinically stable and had no complaints besides nausea. Her past medical history included endometriosis diagnosed at the age of 19. She had undergone two laparoscopies in United Kingdom, 14 and 8 years ago. Marsupialisation of Bartholinic cyst had been done 4 years back. Two years ago, she had a bilateral salpingectomy in Dubai. The current medication consisted of Cyclogest 400 mg bd per vagina, Folic acid 800 mcg/day, and acetylsalicylic acid 75 mg/day.

Transvaginal ultrasound showed a bulky uterus with an endometrial thickness of 15 mm. An eccentric gestational sac corresponding to 4 weeks gestational age with yolk sac was visualized in the left uterine horn, and was not clearly separated from the endometrium. The serum beta hCG level was above 40,000 mIU/ml. Being aware of the patient's infertility history and, at this moment, inconclusive sonography, we decided in agreement with the couple to

perform expectative treatment. During the following days, there was evidence of serum beta hCG elevation above 100,000 mIU/ml, and embryonal heart action became visible. Repeated transvaginal and transabdominal scans demonstrated an increasing vascularity in the left uterine horn, with thinning of the myometrial mantle around the gestational sac to less than 4 mm. The patient was still completely asymptomatic, with usual signs of early pregnancy. Further conservative management appeared inadequate.

Due to the ultrasound and beta hCG finding, the laparoscopic procedure was performed. Laparoscopy demonstrated cornual pregnancy corresponding to the 8 weeks gestation on the left, which ruptured quasi spontaneously after gentle pressure with the laparoscopic forceps. A resection of the left horn following vasopressin infiltration of the surrounding myometrium was performed and closed by endo-sutures. The embryo and placenta were removed via endo-bag. The patient was discharged 3 days later. The emotional stress for the patient and her husband was considerable, with the ups and downs of hope and disappointment during the course of events in this pregnancy. At all times there was open discussion between the attending physician and the couple regarding the diagnosis and treatment options, which helped to take the rational decision in the management of this potentially life threatening condition.

## DISCUSSION

The use of transvaginal ultrasound (TVS) and human chorionic gonadotropine (hCG) measurements, together with the history of the patient is usually sufficient to establish the diagnosis of a normal intrauterine pregnancy in a primary care facility. When using TVS in normal pregnancy, the gestational sac usually becomes visible, embedded in the endometrium at 4.5 to 5 weeks of gestation. The yolk sac appears at 5 to 6 weeks and remains visible until approximately 10 weeks. In normal pregnancy an embryo with cardiac activity is first detected at 5.5 to 6 weeks.

A complex adnexal mass in the presence of a positive pregnancy test and empty uterus is highly suggestive of an extrauterine gestation and is the most common sonographic abnormality in ectopic pregnancy findings. Visualization of an extrauterine gestational sac containing a yolk sac or embryo is diagnostic of ectopic pregnancy, but this combination of findings is detected in only a small proportion of cases.<sup>1</sup>

Transabdominal US has low sensitivity, specificity, positive and negative predictive values for detection of ectopic pregnancy.<sup>2</sup> However, transabdominal US keeps its special value in detecting a small portion of ectopic pregnancies with bizarre location high in the pelvis in the cornual section of an anteverted uterus, out of reach for high frequency transvaginal probes.<sup>3</sup>

Modern transabdominal 3D probes with color Doppler can deliver excellent and conclusive volumes of just these regions of interest in the pelvis which are too far for TVS. Again, transabdominal power Doppler modality has restrictions due to limited depth.



**Fig. 1:** Transvaginal gray scale ultrasound (US), fundal coronal plane. Topography of endometrium and GS: is it just an excentric or could it be an interstitial GS?

Interstitial pregnancy accounts for up to 1 to 3 percent of ectopic pregnancies.<sup>4</sup> Interstitial portion of the fallopian tube is the section of the tube which is surrounded by the myometrium in the cornual area. If pregnancy implants to this area it is called interstitial or cornual ectopic pregnancy. The term interstitial pregnancy is often used interchangeably with cornual pregnancy. However, cornual pregnancy specifically refers to pregnancy in the horn of a bicornuate uterus. Angular pregnancies with implantation medial of the round ligament, intrauterine, and medial to the insertion of the Fallopian tube, have been considered as an own clinical entity.<sup>5</sup> Implantation of the fertilized ovum is more likely to occur in the interstitial part of the Fallopian tube following *in vitro* fertilization (IVF/ET) and previous salpingectomy.<sup>3</sup> Both of these risk factors were evident in our patient. Other risk factors could be: previous ectopic pregnancy, uterine anomalies, ovulation induction, and history of sexually transmitted infections.<sup>6</sup>

Interstitial pregnancy can reach higher gestational age than tubal ectopic pregnancy because of greater compliance of the surrounding myometrium. Because they are intrauterine, interstitial pregnancies are more likely to be mistaken for normal intrauterine pregnancy. With increasing gestational age, the threshold for surgical intervention becomes higher, both for the patient and the physician. Ultrasound examination of an interstitial pregnancy shows a gestational sac or hyper/hypoechoic mass in the cornua, with myometrial thinning. However, an interstitial pregnancy can be difficult to distinguish from an eccentrically positioned intrauterine pregnancy (Fig. 1).

Several reports suggest that the use of three-dimensional US is helpful in the diagnosis of interstitial pregnancy, because 3D ultrasound allows accessibility of the planes that are not accessible by 2D US. Earlier and accurate diagnosis of ectopic pregnancy also permits appropriate therapeutic planning.<sup>7</sup>

Two-dimensional sonographic examination may reveal a gestational sac located outside the uterine cavity, but may not be able to define its exact anatomic position. The use of 3D sonography enables correct depiction of the sac and its location where the fallopian tube crosses the uterine horn.<sup>8</sup>

Typical signs of cornual pregnancy are the following:

1. The eccentric location of the intrauterine GS and its separation from the endometrium by a thin rim of myometrial tissue surrounding the GS;<sup>9</sup> and
2. Thin myometrial mantle of less than 5 mm between GS and abdominal cavity.

**Table 1:** Sonocriteria of interstitial pregnancy

- Empty uterine cavity
- Gestational sac is visualized separately and more than 1 cm away from the most lateral edge of the uterine cavity and is surrounded by a thin myometrial layer of less than 5 mm.

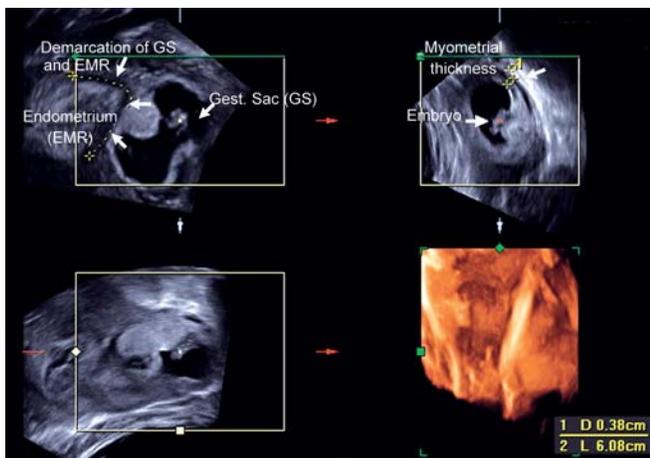
These findings confirm interstitial location of the pregnancy (Table 1).<sup>3</sup>

The interstitial line has been described as an echogenic line extending from the cornual side of the endometrium into the cornual region reaching the gestational sac, and is believed to be highly specific sign for interstitial pregnancy.<sup>10</sup> Once the interstitial section of the tube is completely occupied by an advanced interstitial pregnancy, this sign is no longer evident.

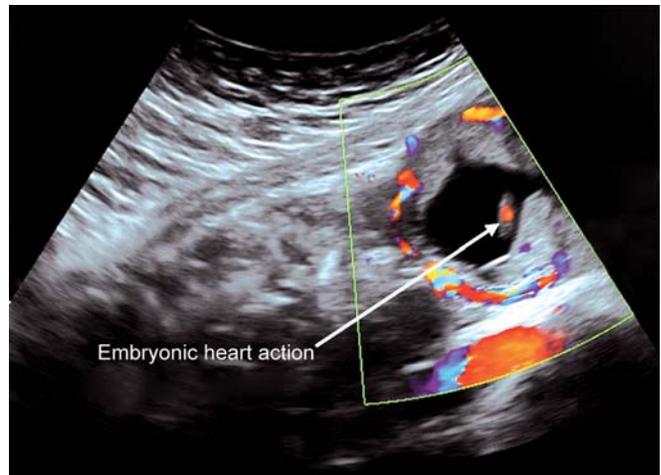
Three-dimensional ultrasound obtains an unlimited number of sections in a stored volume, which are then processed without probe manipulations, and without the presence of a patient. Such an approach facilitates the meticulous work-up of the region of interest (ROI) exactly according to these sonocriteria. Navigating through multiplanar sections, sonographer can identify the thickness of the myometrial mantle over the cornual ectopic pregnancy, and visualize the separating myometrial layer between the endometrium and trophoblast (Fig. 2).

Color Doppler ultrasound is an excellent guide for blood flow signals in the entire pelvis (Fig. 3).

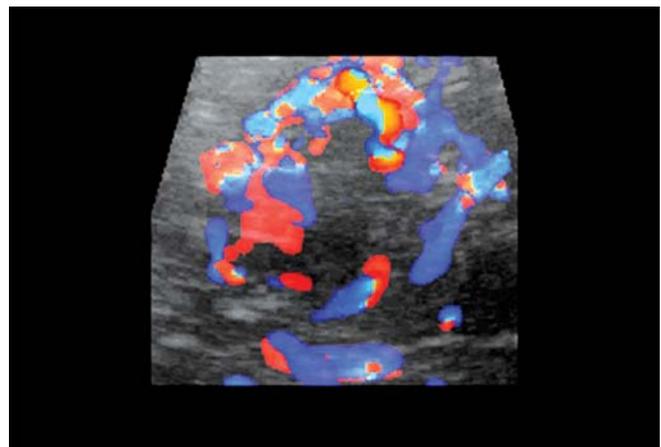
Color Doppler flow pattern in ectopic pregnancy usually presents randomly dispersed multiple small vessels with low resistance indices around 0.42, and higher, if pregnancy is non-viable. In viable ectopic pregnancies (only up to 8% of



**Fig. 2:** Three-dimensional study of the region of interest (ROI) at 7 weeks demonstrate endometrium, marked as EMR, and a gestational sac (GS). The endometrium and GS are separated by a thin layer of myometrium, meaning that GS is outside the endometrial cavity. The thickness of the uterine mantle encircling the GS is only 3.8 mm, suggesting a risk of impending rupture



**Fig. 3:** Eccentric gestational sac with a “ring of fire”; trophoblastic flow and embryonic cardiac activity in cornual pregnancy were demonstrated by transabdominal ultrasound

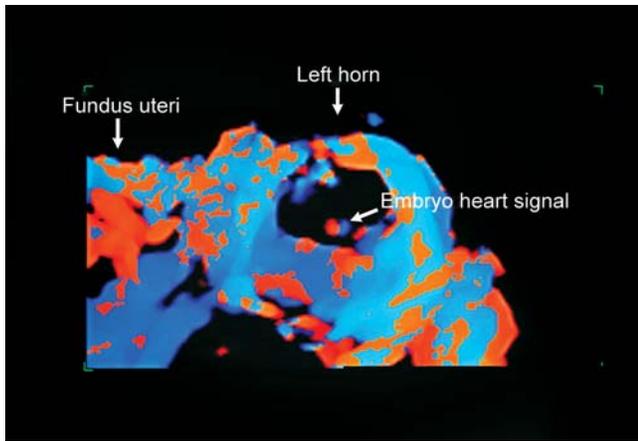


**Fig. 4:** Color Doppler demonstrates intense trophoblastic angiogenesis suggestive of interstitial pregnancy. Note a “vascular net” surrounding the gestational sac

all ectopic pregnancies), the intense ring of vascular signals, so called “ring of fire” in 2D, or “net of fire” in 3D US are visualized<sup>11</sup> (Fig. 4).

Trophoblastic tissue has high velocity systolic flow and low impedance diastolic flow, characteristics that are highlighted with Doppler and are not visible on grey scale US. Interstitial pregnancies are often associated with high serum  $\beta$ -hCG levels and presence of fetal cardiac activity, accompanied by impressive adaptive angiogenesis of the surrounding tissue, easily visible by color Doppler.

The intensity of flow in an area with limited compliance to further growth of the ectopic pregnancy gives an idea of the speed in which hemoperitoneum with hypovolemic shock may develop after the rupture of an ectopic pregnancy (Fig. 5).



**Fig. 5:** Three-dimensional color Doppler demonstrates impressive vascularization of the cornual ectopic, also showing an embryonal heart action

## MANAGEMENT OPTIONS

Indications for surgical rather than medical therapy of an ectopic pregnancy include:

- Impending or ongoing rupture of ectopic mass, and
- Contraindications to use of methotrexate (MTX).

This applies as well to interstitial ectopic pregnancies.

Women with a serum beta human chorionic gonadotropin ( $\beta$ -hCG) concentration greater than 5000 mIU/mL before treatment, or with embryonic cardiac activity on ultrasonographic examination, are more likely to experience treatment failure with Methotrexate. In addition, there is a high probability that in patients following Methotrexate treatment, an ectopic pregnancy may not be visualized or palpated at surgery. Therefore, the patient should be managed conservatively with expectant management, or with Methotrexate if beta-hCG-concentration in mIU/mL is below 5000.

Laparoscopic surgery is the standard surgical approach for ectopic pregnancy. Most ectopic pregnancies, even in the presence of hemoperitoneum, and even interstitial pregnancies may be successfully treated by laparoscopic surgery. Historically, cornual resection and/or hysterectomy was the most common management for treatment of interstitial pregnancy, probably as a result of delayed diagnosis.<sup>12,13</sup>

In recent years, widespread use and availability of transvaginal ultrasound and sensitive beta-hCG assays have allowed diagnosis of these pregnancies at an earlier gestational age and prior to rupture. Treatment options include:

- Open surgery,
- Laparoscopy with cornual incision or resection,

- Low-dose local injection of Methotrexate, and
- Local injection of potassium chloride.

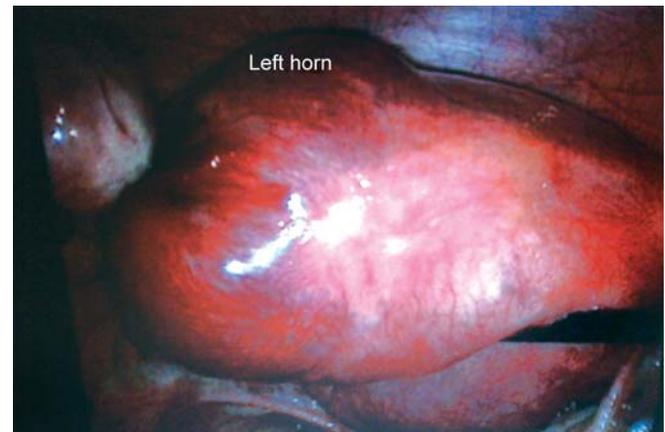
The last two options are color Doppler ultrasound guided procedures.

In our case, we had chosen a laparoscopic approach to verify the sonographic suspicion of impending rupture of interstitial ectopic pregnancy (Figs 6A to E).

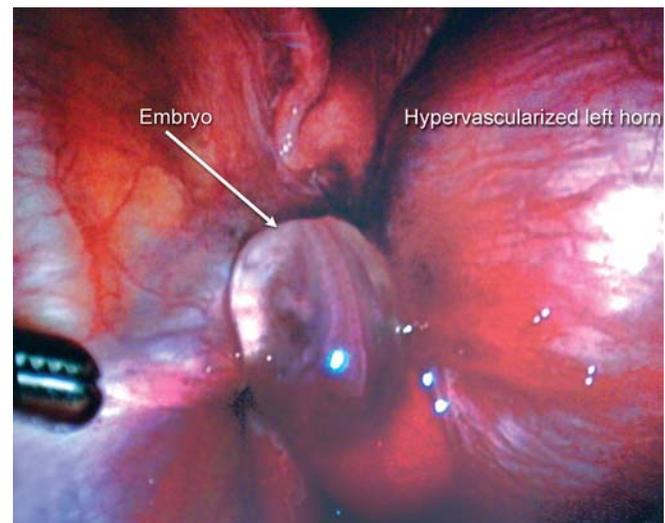
During laparoscopy, interstitial pregnancy appeared as asymmetrical swelling lateral to the insertion of the round ligament (Fig. 6A).

Diluted Vasopressine was injected into the cornual myometrium, with the aim to minimize blood loss and improve visibility.

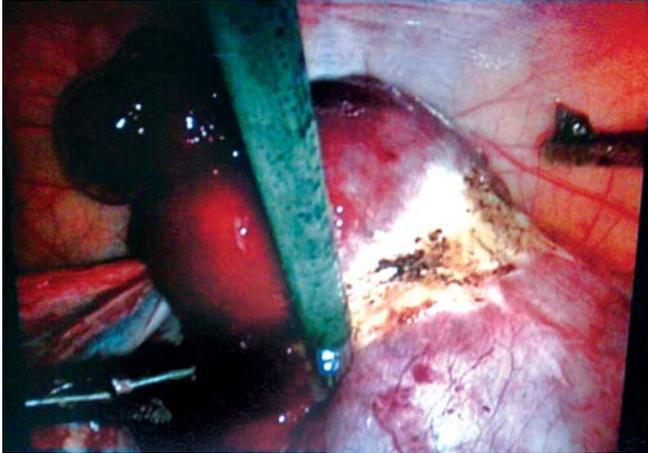
The unique anatomical location of interstitial pregnancy often leads to a delay in diagnosis; thus, rupture of the uterus is a common presentation.



**Fig. 6A:** Laparoscopic view of the left cornual ectopic pregnancy. Note asymmetry of the uterine cornual region, with swelling of the left horn and hypervascularity



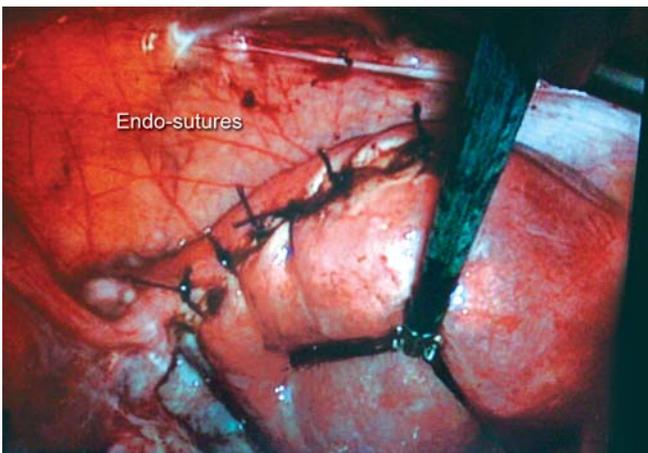
**Fig. 6B:** The gestational sac with an embryo has herniated from the site of the rupture



**Fig. 6C:** Resection of the left horn after infiltration with vasopressine was performed, starting with a coagulation trace for the incision



**Fig. 6D:** Excision almost completed



**Fig. 6E:** Cornual regiona after closure with endosutures

In a survey of 32 cases of interstitial pregnancy, nine required laparotomy for uterine rupture and hemoperitoneum. Although the maternal mortality rate associated with tubal pregnancy is decreasing, the maternal mortality rate of interstitial pregnancies remains at 2 to 2.5 percent because of misdiagnosis of intrauterine pregnancy. As pregnancy grows in the area of the fallopian tube that enters the uterus, surrounding myometrial tissue allows for further development of the pregnancy into the second trimester. Rupture of such an advanced gestation may result in a catastrophic hemorrhage.<sup>6</sup>

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