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Case Report

Distinguishing between cornual, angular and interstitial ectopic pregnancy: A case report and a brief literature review ☆,☆☆

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ABSTRACT

For all clinical purposes, cornual, angular, and interstitial pregnancies are considered ectopic pregnancies that can have grave consequences for the patient. In this article, we describe and distinguish 3 types of ectopic pregnancies in the cornual region of the uterus. The authors advocate using the "cornual pregnancy" term only for ectopic pregnancies in malformed uteruses. We describe an ectopic pregnancy in a 25-year-old G2P1 patient in the cornual region of the uterus that was missed twice sonographically in the second trimester and had almost fatal consequences in the patient. Radiologists and sonographers should be aware of the sonographic diagnosis of angular, cornual and interstitial pregnancies. Whenever possible, first-trimester transvaginal ultrasound scanning is crucial for diagnosing these 3 types of ectopic pregnancies in the cornual region. In the second and third trimesters, ultrasound tends to become equivocal; hence alternate imaging, such as MRI, might add additional value to the management of the patient. A case report assessment and a comprehensive literature review comprising 61 case reports of ectopic pregnancy in the second and third trimesters are diligently undertaken in the Medline, Embase and Web

Abbreviations: CT, Computed Tomography; MRI, magnetic resonance imaging; OR, operating room; ED, Emergency Department; POC, products of conception; FF, Free Fluid.

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of Science databases. The major strength of our study is that it is one of the few studies that describe a literature review of ectopic pregnancy in the cornual region exclusively in the second and third trimesters.

Introduction

Implantation of a developing blastocyst outside the endometrial cavity is known as an ectopic pregnancy. Statistically, approximately 2%-5% of these occur in the interstitial or cornual regions of the uterus [1,2]. Clinicians commonly regard all types of ectopic pregnancies in the normal cornual region of the uterus as "Cornual" ectopic pregnancy [3,4,8]. It is essential to understand the terminology surrounding cornual, angular, or interstitial pregnancies because the findings, management, and outcomes are different in each of the 3 ectopic pregnancies [5]. These 3 forms of ectopic pregnancies are often lumped together, and clinicians sometimes have ambiguity in arriving at a correct diagnosis based on history and imaging [6]. Interstitial pregnancies account for 2%-11% of tubal ectopic pregnancies and constitute approximately 20% of deaths [7]. Radiologists and several practitioners have used the term cornual and interstitial ectopic pregnancy interchangeably [7,8]. In the literature, true cornual pregnancy is located in the rudimentary horn of the unicornuate uterus or the rudimentary horn of a septate or bicornuate uterus [9–12]. Therefore, some authors synonymously use the term "cornual" pregnancy with "rudimentary horn" pregnancy [13]. To add to this incertitude, most obstetricians and gynecologists still use the term "cornual pregnancy" to describe any pregnancy in the normal anatomical cornual regions of the uterus [14]. In this article, we chose to use the term "cornual" pregnancy only for pregnancies in the uterus presenting with congenital anomalous presentation, that is, rudimentary, septate, bicornuate, unicornuate, or any other uterine malformation. Regardless of the confusion around the terminology for cornual pregnancy, the sonographic criteria for this type of pregnancy are an empty uterine cavity, a gestational sac located eccentrically (1 cm from the lateral wall of the uterine cavity), and a thin myometrial layer (<5 mm) surrounding the gestational sac [10]. The biggest concern for cornual pregnancy is the potential to rupture due to the lack of myometrial support surrounding the delicate gestational sac [15].

An interstitial pregnancy is an ectopic pregnancy implanted in the interstitial part of the fallopian tube and close to the uterine musculature. Interstitial pregnancies implant lateral to the round ligament and are approximately 1-2 cm within the intra-myometrial region of the tube, with the gestational sac surrounded by less than 5 mm of the myometrium in all scanning planes, a chorionic sac separate (> 1 cm) from the lateral edge of the uterine cavity, and the presence of an interstitial line sign [6,16,17,18]. In the literature, the sensitivity and specificity of the sonographic "interstitial line sign" varies from 80% to 100% [16,11,20]. The interstitial line sign is thought to be a sonographic impression that represents an echogenic line from the mass or gestational/interstitial sac to the endometrial echo complex [11,18,21]. Some authors believe these criteria are more valid in the first trimester and tend to lose sensitivity after this period [19]. The interstitial uterine region is prone to rupture owing to increased distensibility and hypervascularity [6,9]. Therefore, it is vital to diagnose ectopic pregnancy in the first trimester for conservative treatment such as methotrexate to be effective. A delay in the diagnosis of interstitial pregnancy may lead to cornual uterine resection. Some studies have reported a mortality rate of 2%-3% with interstitial pregnancy [22].

Angular pregnancy is the third type of pregnancy in the normal cornual region of the uterus and is a differential diagnosis of interstitial or true cornual pregnancy. Anatomically, angular pregnancy implants medial to the round ligament, at the lateral angle of the endometrial/uterine cavity, and just medial to the uterotubal junction [17]. Angular pregnancy can progress to term because it is technically inside the uterine/endometrial cavity [5,23,24]. Some authors discourage the association of ectopic term with angular pregnancy due to the intrauterine or eccentric endometrial location of the developing fetus [25]. The myometrial mantle thickness in angular pregnancy is > 5 mm without an interstitial line sign [25]. Angular pregnancy has been associated with uterine rupture in up to 23%-29% of cases [8,26,27]. Angular pregnancy has been classified as a type of ectopic pregnancy owing to its proximity to the cornual region [28]. Another reason that angular pregnancy is regarded as a type of ectopic pregnancy is that it is difficult to differentiate interstitial from angular pregnancy, especially during the first trimester, and it also presents similar symptomatology to a typical ectopic pregnancy [9,17,29,30,31].

The diagnosis of these 3 types of pregnancies in the second trimester brings numerous challenges as far as management is concerned. For instance, angular pregnancy can mimic the clinical presentations of typical ectopic pregnancy, such as persistent pelvic pain and bleeding, uterine rupture, spontaneous abortion, postpartum endometritis, and severe bleeding leading to hysterectomy [24,47]. On the other hand, a relatively late diagnosis of cornual pregnancy is a prominent exacerbating factor for impending grave hemorrhage [32,33]. Interstitial ectopic pregnancy continues to progress into the second trimester owing to greater distensibility and hypervascularity, as mentioned above, leading to an inevitably worse prognosis in most cases [5,9].

Etiology and pathogenesis

In general, there are numerous risk factors for ectopic pregnancies, such as tubal pregnancy, ectopic pregnancy, intrauterine devices, pelvic inflammatory diseases, salpingitis

and infertility. Furthermore‘ exposure to diethylstilbesterol, age > 40 years, smoking, previous pelvic surgeries and assisted reproduction techniques have been implicated as potential risk factors for ectopic pregnancy [11,17,34]. Ipsilateral salpingectomy is the only known etiological factor specific to interstitial ectopic pregnancy [35].

Case report

A 25-year-old female G2P1, visited our emergency department (ED) with complaints of sharp, constant lower abdominal pain and no vaginal spotting/bleeding. The patient also had a history of polycystic ovarian syndrome (PCOS) and a cesarean section 2 years ago. Based on her health records, the patient was presumed to be in the second trimester.

The patient was admitted to the ED observation ward with stable vital signs. Late evening the patient developed vaginal spotting that quickly progressed to vaginal bleeding, superimposed with blood clots and severe cramping that radiated to the back. The ED physician ordered an urgent obstetric ultrasound on the same day to assess for threatened abortion. An urgent obstetric scan in our ultrasound department revealed a single live intrauterine pregnancy at 16 weeks. The technologist noted that the internal orifice of the cervix uteri (internal os) was not retraceable into the uterine cavity. Therefore, endovaginal or transvaginal scanning was performed to visualize the internal cervical os and to rule out vasa previa and placenta previa. (Fig. 1A-C)

The radiologist noted the sonographer’s impression (Fig. 1A–C) and suggested a repeat ultrasound at 20 weeks to better visualize the internal cervical os. The patient was sent back to the ED and subsequently discharged from our hospital, thus missing a potential ectopic pregnancy.

The patient returned to ED in less than 2 weeks, complaining of generalized abdominal pain, chest pain and lower back pain that was not positional or relieved with antianalgesics. In about a few hours, the patient reported that the pain had migrated to the right lower quadrant (RLQ) and flank area with episodes of nausea and vomiting. An emergent ultrasound was ordered to rule out appendicitis, right kidney and right ovarian pathology, and retroplacental abruption.

Upon scanning the patient, for the second time, age-appropriate gestation was documented without any signs of distress in the fetus (Fig. 2A andB). Furthermore, a mild to moderate amount of echogenic free fluid (FF) was noted in the pelvic region, especially the RLQ, denoting hemoperitoneum (Fig. 2C and D).

The area of extreme tenderness in the RLQ was scanned diligently. On the transabdominal scan, the sonographer suspected a uterus-like structure with a thin endometrial stripe. (Fig. 3A) The cine loop/video nicely reveals the separation of the uterus from the amniotic cavity upon a gradual transabdominal pressure with the transducer. (Supplementary Video 1) To further investigate this speculation, transvaginal scanning was performed.

In our department, transvaginal scanning is not a routine examination in the second trimester and is required only in

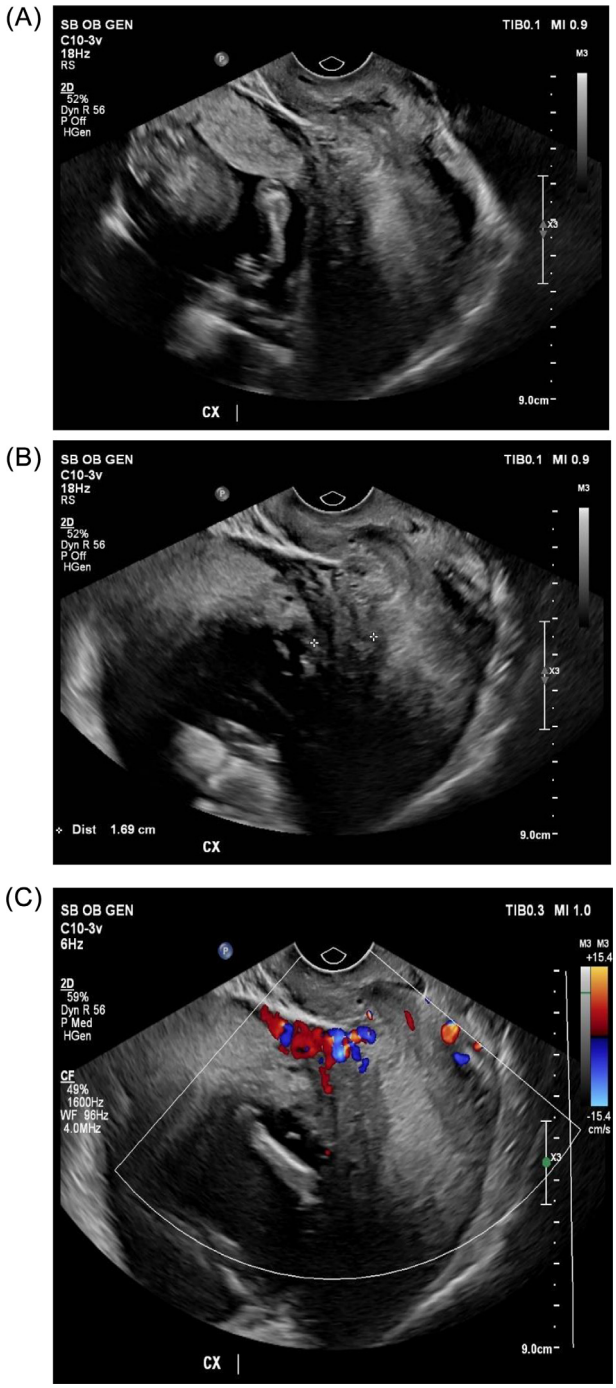

Fig. 1 – (A) Sagittal: Visualization of the cervical canal was difficult because the large size of the extrauterine pregnancy was displacing the cervix/uterus posteriorly and to the right. (B) Sagittal: A rough estimate for the potential distance from the lower edge of the placenta to the internal os was attempted. (C). Sagittal: Colour Doppler showing retroplacental flow extending to an area of myometrium near the suspected cervix.

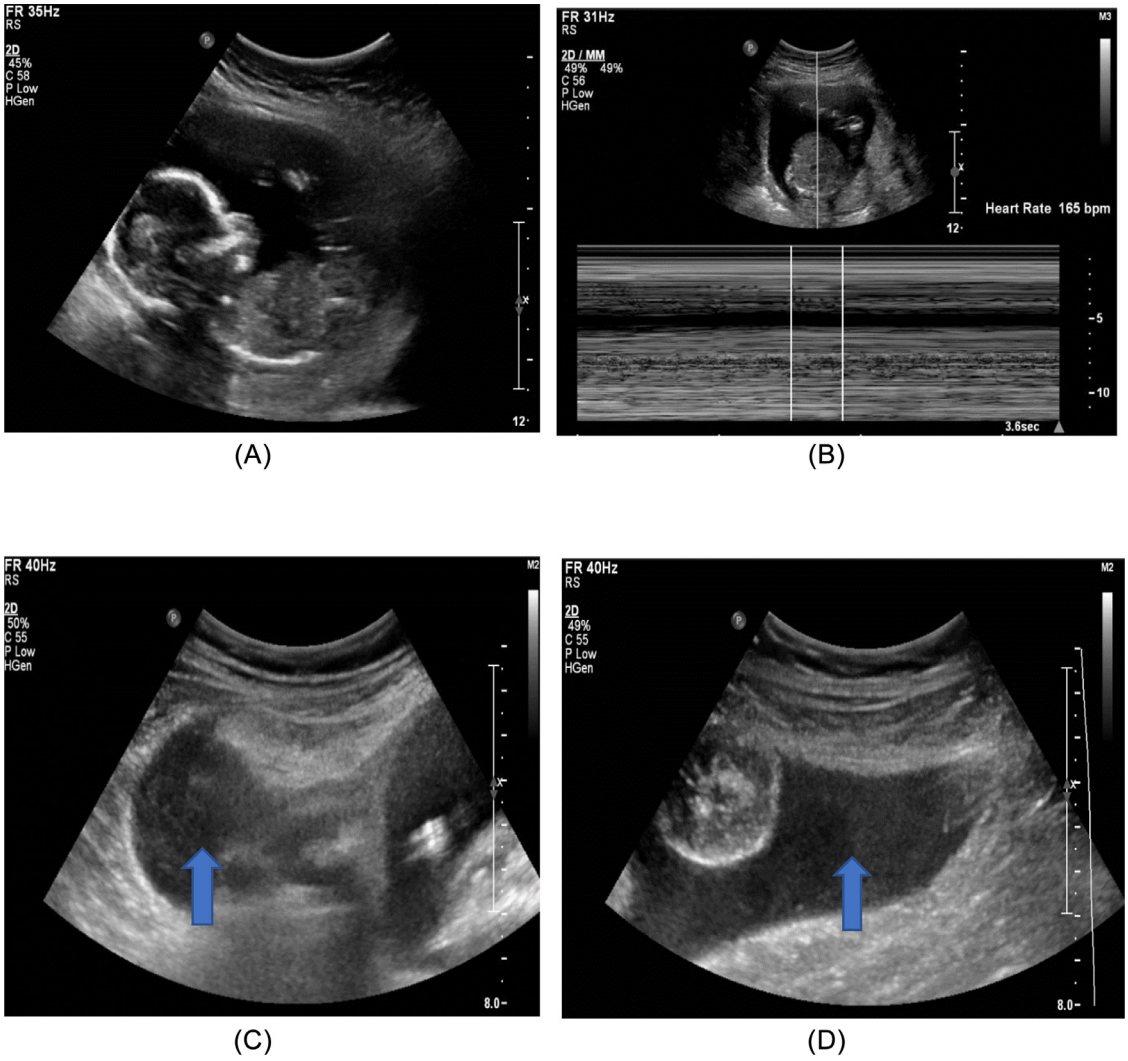

Fig. 2 – (A) Normal fetal development at 17 weeks. (B) Normal fetal heart rate. (C) Transverse: Echogenic FF in RLQ (arrow). (D) Sagittal: Echogenic FF in RLQ (arrow).

challenging cases to establish a diagnosis. The 8.6 cm structure in the right adnexal region was felt to be a retroverted uterus with an empty endometrial cavity and normal bilateral endometrial border at the fundus region of the uterus in the transverse scanning plane (Fig. 3C). The technologist attempted to convince the radiologist in his images by demonstrating the endocervical canal in communication with the uterine body, thereby lending more support to the fact that the endometrial cavity is empty in this nonpregnant uterus (Fig. 3D).

Upon scanning the right and left upper quadrants, free fluid was visualized in the hepatorenal (Morrison's pouch) and splenorenal recesses without any evidence of hydronephrosis in either kidney (Fig. 4A and B).

Despite the compelling sonographic images, the radiologist did not acknowledge the technologist's impression. Once again, the diagnosis of normal intrauterine pregnancy, along with numerous differential diagnoses, was provided in the report. Some of the differential diagnoses documented in the report were hemorrhagic neoplasm, heterotopic pregnancy, red degeneration of the fibroid, dermoid cyst, or decidualized endometrioma, and an ovarian origin mass with associated ovarian torsion. The patient was sent back to the ED for a second time. The patient was discharged after performing the necessary blood tests. Thus, the ED physician and the radiologist again missed the likelihood of a grave impending ectopic pregnancy in the cornual region (based on clinical symptomatology and pertinent imaging).

Surgical history

Four days after the last discharge, the patient developed hypotension and was immediately transferred to OR at a nearby tertiary hospital. For the first time, the obstetrical team diagnosed ectopic pregnancy in this patient and called it a "cornual ectopic pregnancy" to the left of the uterine cavity. The left cornual region of the uterus was ruptured, leading to hemoperitoneum and hypotension and the fetus was

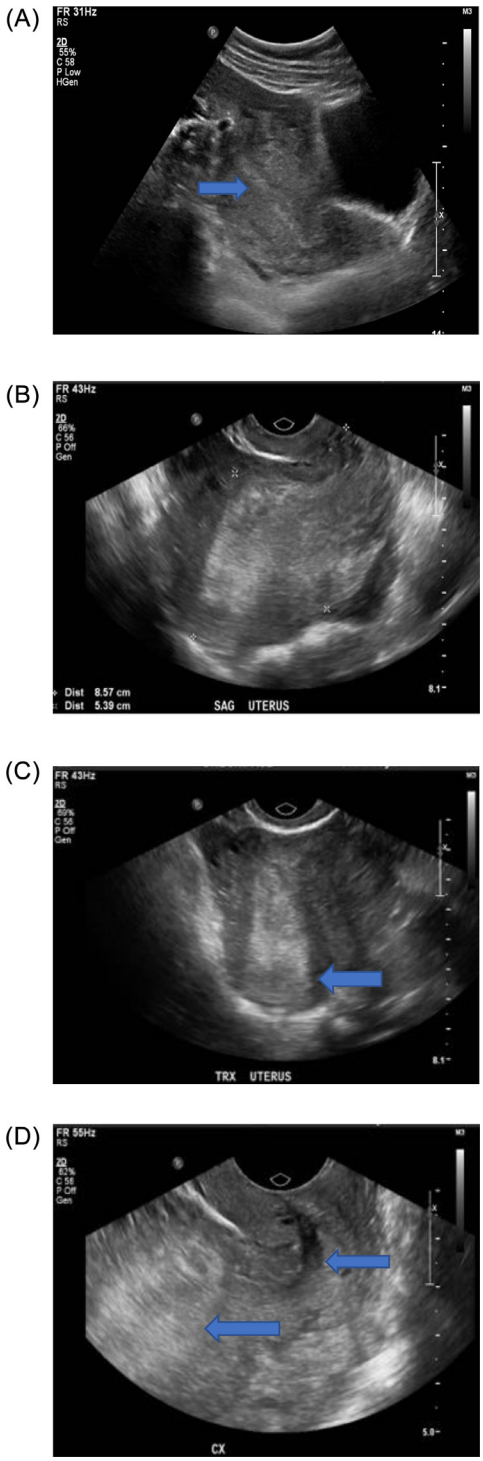

Fig. 3 – (A) Transabdominal sagittal plane: A presumed uterus is seen in the right adnexal region. Arrowhead denotes a potential endometrial stripe. (Supplementary Video 2 Fig. 3A). (B) Sagittal: Transvaginal ultrasound confirmed the uterus in the right adnexa. (C) Endovaginal transverse plane: The arrowhead depicts an empty left lateral endometrial region. (Supplementary Video 3 Fig. 3C). (D). Sagittal: Transvaginal image of the cervix & uterine body. The arrowheads show communication of the cervix with the uterine cavity. (Supplementary Video 4 Fig. 3D).

presumed to be in the abdomen without any signs of fetal heart activity. The obstetrician delivered the stillborn fetus and repaired the left uterine cornual area along with a left salpingo-oophorectomy (LSO). Ligation of the internal iliac artery was also performed to control the excessive bleeding associated with uterine rupture. Owing to the patient's life-threatening hemorrhage, a massive transfusion protocol was initiated in this case. Guidelines on massive transfusion protocols in adults vary worldwide, depending on the institution's preference or experience and patient's hemodynamic status. Obstetric bleeding presents additional challenges for clinicians. In this patient, the massive transfusion protocol consisted of 9 units of packed RBC, 1 Liter fresh frozen plasma (FFP), 4 g fibrinogen, 1 unit of platelets, and 6.5 Liter IV fluid. The products of conception (POC) were sent for pathological evaluation.

Pathological diagnosis

The pathologist also agreed with the obstetrician's impression of "cornual ectopic pregnancy" and reported the association of the decidua and myometrium with chorionic villi in the cornual region of the uterus. Additionally, the tissue around the left cornual region is reported necrotic, consistent with a left ruptured cornual ectopic pregnancy. The fetus, chorionic villi, tri-vascular umbilical cord, and fetal membranes were identified by microscopic examination of the gross pathological specimen. Products of conception were appropriately recognized on gross examination, but for technical reasons, gross pathological images of the POC cannot be obtained for publication purposes.

Our perspective

We followed up on the patient's earlier imaging 3 years ago at another tertiary hospital in the city. On this ultrasound scan, no evidence of uterine malformation was visualized sonographically. Based on this finding, the radiologist reported the normal shape of the uterus. If we were to apply the definition of true cornual ectopic to this case, it would not support the obstetrician or the pathologist's diagnosis based on the sonographic images (Fig. 3A–D, Fig. 5A and B) and the radiologist's impression documented 3 years earlier. We feel there is ambiguity in the correct diagnosis of this patient. Fig. 3B and C, and the supplementary videos 3 and 4 demonstrate the retroverted uterus with empty left lateral endometrium, thereby making the likelihood of angular pregnancy extremely unusual at this location. We believe that the most likely diagnosis in our patient was interstitial rather than cornual or angular due to the normal shape of the uterus and the empty left fundal endometrial cavity. We speculate that the obstetrician, in this case, might have based the clinical insight on cornual ectopic pregnancy due to the mass effect of the pregnancy in the cornual region of the uterus on laparotomy. Unfortunately, the patient did not have first-trimester scans for the current pregnancy, and thus, the diagnosis of angular

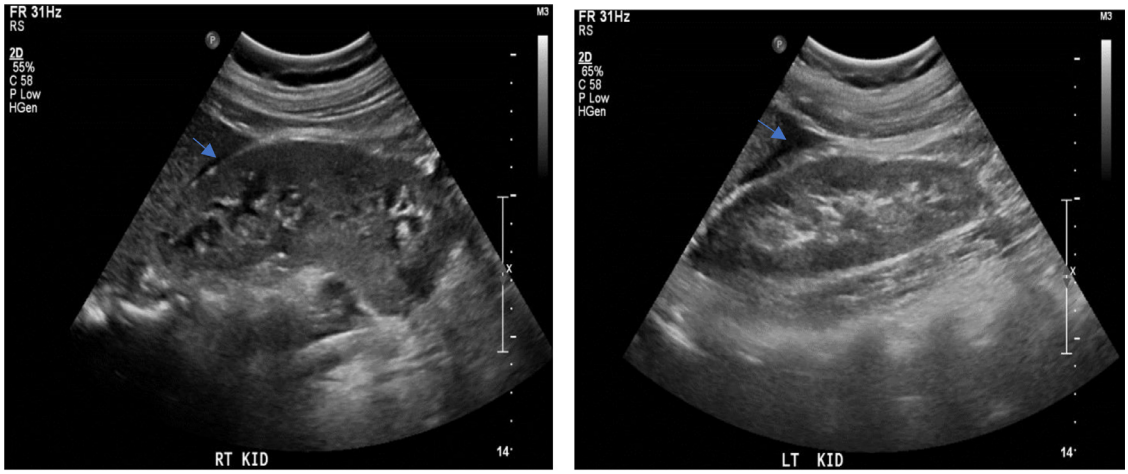

Fig. 4 – (A). Sagittal: Free fluid in the hepatorenal recess. (B) Sagittal: Free fluid in the splenorenal recess.

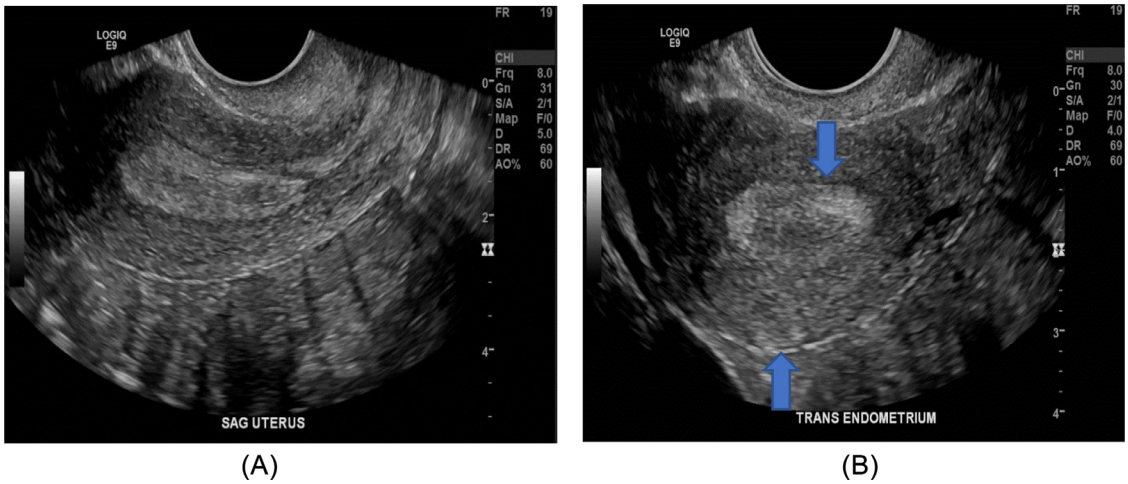

Fig. 5 – (A) Sagittal Normal contour of the uterine fundus and body. (B) Transverse Normal contour of endometrium & fundus (arrows).

or interstitial ectopic pregnancy is hard to elucidate with certainty. Regardless, as stated earlier, we postulate that the current ectopic pregnancy is probably interstitial rather than cornual or angular, owing to the recent ultrasound images in our department and prior sonographic imaging 3 years ago depicting the normal shape of the uterus (Fig. 3B and C, Fig.5A and B plus Supplementary videos 2, 3, and 4).

Literature review

Methodology

The authors (G.D., R.C., and L.Z.) searched for cornual, angular, and interstitial pregnancies in the second and third trimesters using the MedLine, Embase, and Web of Science databases. We adapted our search terms and techniques to all 3 databases. For instance, we used the following MeSH search terms for Medline: (pregnancy, cornual), (pregnancy, angular), (pregnancy, interstitial), (pregnancy trimester, second), and (pregnancy trimester, third). Likewise, instead of MeSH, Emtree was used in Embase by selecting "map terms to subject heading." Other keywords used were ectopic pregnancy, 13-to-40-week pregnancy, and rudimentary horn pregnancy. All gray literature was excluded, and only peer-reviewed case report articles were included in our final list. The search results were exported from all 3 databases to the Zotero 6.0.20 reference manager. Zotero was used to compile search results from all 3 databases into a single folder named "interstitial pregnancy," from which the process of deduplication or merging of the articles was performed.

We searched for cornual, interstitial and angular pregnancies only in the second and third trimesters to replicate our

Table 1 – Angular pregnancy case reports and sonographic features in the second or third trimester (2000-2023). Search performed on February 10, 2023.

Author	Year	Number of cases	Myometrial/endometrial thickness	Gestational age at presentation	Outcome
Mustafa et al. [43]	2021	1	Not reported	18 wk	Uterine rupture; fetal demise
Martinez et al. [44]	2008	1	thin myometrial wall	22	Hysterectomy at 22 wk
Yao et al. [45]	2021	1	Not reported	25 wk 6 d	5 cm of cornual region rupture; fetus status not reported distinctly
Hasanzadeh et al. [46]	2017	1	Not reported	20 wk 2 d	Left lateral endometrial angle rupture and repair of the uterus; a nonviable fetus.
Alanbay et al. [47]	2016	1	Endometrial thickness continuous with the central endometrial lining	32 wk	Viable female fetus
Marfori et al. [48]	2018	1	Myometrial mantle at 5 mm throughout the pregnancy	37 wk	Viable male fetus
Shekhar et al. [49]	2010	1	Thinned out with the potential of imminent Rupture	30 wk	Asphyxiated female fetus delivered.
Martadiansyah et al. [50]	2022	1	Thin myometrium	24 wk	A viable fetus was delivered but died soon after hysterotomy
Alves et al. [51]	2011	1	3 mm myometrial layer	36 wk	Viable female neonate
Kwon et al. [52]	2011	2	2 mm myometrium fetus 1 Not reported for fetus 2	16 wk fetus1; 25 wk fetus2	Both fetuses died after delivery.
Baldawa & Chaudhari et al. [53]	2008	1	Not reported	14 wk	Right lateral wall uterine rupture; subtotal hysterectomy with right salpingectomy; fetus in the peritoneal cavity.

Table 2 – Interstitial pregnancy case reports and sonographic features in the second or third trimester. (2000-2023) Search performed on February 10, 2023.

Author	year	Number of cases	Myometrial thickness	Interstitial Line	Gestational age	Outcome
Hill et al.[54]	2013	1	Not reported	Not reported	32 wk	Viable fetus
Valbo et al.[55]	2008	1	Not reported	Not reported	22 wk	Fundal uterine rupture; subtotal hysterectomy; fetus status not reported
Najib et al. [56]	2021	1	Not reported	Not reported	38 wk	Viable fetus
Nagayama et al. [57]	2020	1	Not reported	Not reported	28 wk 1/7 d	Viable fetus
Pedroso et al. [58]	2014	1	Not reported	Not reported	15 wk	Fetal demise
Nkurunziza et al. [59]	2020	3	Not reported	Not reported	18 wk	Right interstitial pregnancy plus 2 intrauterine fetal demises; subtotal hysterectomy
Ahlschlager et al. [19]	2021	1	Not reported	Not reported	15 wk 3 d	Left interstitial pregnancy
Scarella et al. [60]	2012	1	Reduced myometrial thickness	Not reported	28 wk	Nonviable fetus
Dendas et al. [61]	2017	2	Not reported for interstitial pregnancy	Not reported	16 wk 2 d	Viable one intrauterine fetus is delivered at 33 wk; Ruptured right uterine cornua with subsequent delivery of a fetus in the abdomen.
Noor & Alias. [62]	2023	1	Not reported	Not reported	27 wk	Ruptured right interstitial; both mom and fetus died

case report in terms of symptomatology, prognosis, and outcome. Considering the rapid advances in the technological capabilities of imaging equipment, all case reports published before 2000 were excluded from our study. We excluded all systematic reviews and more extensive case series. We only included case reports in English to better understand the in-depth case history, diagnosis, treatment, and outcome in individual cases. The search results from Zotero were imported into Rayyan software to appropriately apply the above limitations/inclusion/exclusion criteria to the articles. Tables 1, 2 and 3 present the final lists of the selected case report articles.

Table 3 – Cornual/rudimentary horn/malformed uterus pregnancy case reports and sonographic features in the second or third trimester (2000-2023). Search performed on February 10, 2023.

Author	Year	Number of cases	Myometrial thickness	Pregnancy location/uterine anomaly	Gestational age	Outcome
Nash et al. [63]	2020	1	1 mm (pathology) 6mm (MRI)	Cornual region	19 wk	Abdominal hysterectomy
Corte et al.[64]	2019	1	Not reported	Unicornuate with communicating rudimentary horn	20 wk	Fetal demise; rudimentary horn excision; uterus anatomy restored.
Has et al.,[65]	2002	1	Not reported	Rudimentary horn	13 wk	Ruptured rudimentary horn resection; fetal demise
Fekih et al. [66]	2009	1	Not reported	Rudimentary horn	30 wks	Viable fetus
Brewer et al. [67]	2005	1	Not reported	Cornual	28 wk 5/7 d	Uterine rupture; viable fetus
Shin & Kim [68]	2005	1	Not reported	Rudimentary horn	34 wk	Viable fetus; rudimentary horn resection
Hassan et al. [69]	2011	1	Not reported	Rudimentary horn	19 wk	Nonviable fetus
Wang et al. [70]	2018	2	Not reported	Cornual region	33 wks, 3rd trimester (2nd case)	Fetal demise in both cases
Parveen, R [71]	2019	1	Not reported	Rudimentary horn; unicornuate association	17 wk	Missed abortion; rudimentary horn resection
Nathan and Sornum [72]	2013	1	Not reported	Rudimentary horn; unicornuate association	15 wk	Nonviable; right horn resection and salpingectomy
Kozar et al. [73]	2020	1	Not reported	Rudimentary horn	14 wk	Nonviable; uterine and rudimentary horn rupture.
Zhang et al. [74]	2020	1	Not reported	Rudimentary horn	38 wk	Viable fetus
Contreras et al. [75]	2008	1	Not reported	Rudimentary horn	19 wk	Nonviable
Shahid et al. [76]	2009	1	Not reported	Rudimentary horn	16 wk	Nonviable
Safiee & Ghazali [77]	2021	1	Not reported	Right cornual region	19 wk 3 d	Live fetus; Pregnancy terminated
Ozeren et al. [78]	2004	1	Not reported	Rudimentary horn	17 wk	Live fetus; Pregnancy terminated
Prenaud et al. [79]	2017	1	Not reported	Right Cornual region	Very early gestation	Right uterine rupture with salpingectomy; hemoperitoneal aspiration of the fetus.
Singh et al. [80]	2015	1	Not reported	Rudimentary horn	20 wk	No Fetal heart rate was reported at the time of diagnosis
Lennox et al. [81]	2013	1	Not reported	Rudimentary horn	16 wk	Pregnancy termination with rudimentary horn resection
Upadhyaya [82]	2011	1	Not reported	Rudimentary horn	14 wk	Fetal demise; emergent laparotomy
Feteh et al. [83]	2016	1	Not reported	Right rudimentary horn of a unicornuate uterus	42 wk 5 d	Fetal demise at 36 wk; excision of right with salpingectomy.
Kawthalkar et al.[84]	2011	1	Not reported	Left Unicornuate uterus with right noncommunicating rudimentary horn	37 wk	Viable fetus; total hysterectomy
Fitzmaurice et al.[85]	2010	1	Not reported	Unicornuate; Right rudimentary horn	24 wk 3 d	Fetal demise at delivery; hysterectomy 3 mo after c-section
Allouche et al. [86]	2010	1	Not reported	Noncommunicating rudimentary uterine horn	26 wk	Viable fetus; hemihysterectomy
Arslan et al. [87]	2009	1	Not reported	Noncommunicating rudimentary horn	37 wk	Viable fetus; rudimentary horn excision plus ipsilateral salpingectomy

(*continued on next page*)

Table 3 (*continued*)

Author	Year	Number of cases	Myometrial thickness	Pregnancy location/uterine anomaly	Gestational age	Outcome
Rajbhandary et al. [88]	2020	1	Not reported	Right Rudimentary horn of the unicornuate uterus	15 wk	Nonviable fetus; ruptured rudimentary horn excision plus ipsilateral salpingectomy
Kuscu et al. [89]	2002	1	Not reported	Right rudimentary horn; unicornuate uterus	15 wk	Ruptured rudimentary horn; emergency laparotomy; POC resected
Jerbi et al. [90]	2005	1	Not reported	Rudimentary horn	18 wks	Excision of Ruptured rudimentary horn and ipsilateral salpingectomy; nonviable fetus.
Al Qarni et al. [91]	2005	1	Not reported	Left Rudimentary horn; bicornuate uterus.	32 wks	Excision of left ruptured rudimentary horn with salpingectomy; alive fetus
Mishra et al. [92]	2015	1	Not reported	Left rudimentary horn; unicornuate uterus	16 wks	Left rudimentary horn and ipsilateral salpingectomy excision; nonviable fetus
Stern el al. [93]	2018	1		Cornual pregnancy	15 wks	Hysterectomy; nonviable fetus
Jomaa et al. [94]	2021	1	Less than 2 mm	Left Rudimentary horn pregnancy; unicornuate association	16 wk	Rudimentary horn and salpingectomy excision; nonviable fetus
Demishev et al. [95]	2014	1	Not reported	Left cornual region	30 wk 4 d	Left cornual perforation; Viable fetus
Rana et al. [96]	2008	1	Not reported	Left rudimentary horn	27 wk 5 d	Ruptured rudimentary horn and extrusion of fetus into abdomen and survival for 1 mo; ex uterine nonviability; excision of the horn.
Gaber-patel & Smith [97]	2009	1	Not reported	Right cornua of the uterus	13 wk	Right cornual wedge resection; a nonviable fetus.
Thurber & Fleischer [98]	2018	1	Not reported	Right rudimentary horn	19 wk 4 d	Horn resection; nonviable fetus
Cuppett et al. [99]	2011	1	Not reported	Right horn	32 wk	Viable fetus
Goel et al. [100]	2007	1	Not reported	Unicornuate uterus; rudimentary horn	41 wk 3 d	Viable fetus
Patra et al. [101]	2007	1	Not reported	Rudimentary horn	37 wk	Viable fetus
Mitouarda et al. [102]	2016	1	Not reported	Left rudimentary horn	28 wk	Viable fetus

Discussion

A total of 61 case reports satisfied our inclusion criteria for ectopic pregnancy in the cornual region of the uterus. In the second and third trimesters, we assessed 11 and 10 case reports of angular and interstitial ectopic pregnancies, respectively. In contrast, cornual ectopic pregnancy included 40 case reports, constituting the majority of our search results. It is evident from the interstitial case reports that the sonographic "interstitial line" was not reported to be present in the second and third trimesters in all the studies and, thus is not helpful for the diagnosis. This further supports the argument that the interstitial line sign is only visible in the first trimester. In our search results, most articles described cornual ectopic pregnancies in the second and third trimesters. Most cornual ectopic pregnancy case reports describe gestation in the rudimentary horn of the uterus. In the case of angular pregnancy, 7 of the 11 case reports described the presence of the myometrium around the gestational sac, possibly due to its location within the endometrium. Hence, angular pregnancy carries the highest amount of myometrium around the gestational sac relative to interstitial and cornual ectopic pregnancy, achieving the most success for carrying the pregnancy to term.

Many authors feel uncomfortable with the notion that angular pregnancy is a type of ectopic pregnancy because it is eccentric and still in the endometrium [18]. Angular pregnancy, in essence, occurs within the endometrium; thus, technically, it does not fit the stringent definition of ectopic pregnancy. Therefore, it is expected that angular pregnancies are more successful in progressing to full-term pregnancies [9,25,30,35]. We believe that the distinction between interstitial and angular pregnancy becomes even more complicated when gestation enters the second trimester, as the interstitial line is lost [17]. Moawad et al. [9] suggested that interstitial pregnancy is

occasionally referred to as cornual pregnancy and incorrectly confused with angular pregnancy. Early diagnosis of cornual or interstitial pregnancy is recommended by many authors to appropriately manage these pregnancies [33,34]. Gestational age is critical for managing cornual, interstitial or angular pregnancies. Angular pregnancy has the added advantage of being in the endometrium and having relatively more myometrial support than the other 2 types of ectopic pregnancies [18].

Interstitial pregnancies can continue to grow past the first trimester until they manifest life-threatening symptomatology later in pregnancy, especially in the second trimester [31]. It is unfortunate that none of the healthcare professionals were thinking about ectopic pregnancy in the cornual region in our patient. Timely diagnosis of this abnormal pregnancy would have prevented the patient from experiencing life-threatening hemorrhage or a worse prognosis. This case illustrates the need for clinicians to understand this dubious diagnosis in any pregnant woman presenting with complex symptomatology in the pelvic region, particularly during the second and third trimesters.

Moreover, it is regrettable that in this case, no alternative modality was considered to diagnose this complex second-trimester gestation, especially when ultrasound was equivocal despite the apparent clinical symptomatology in the patient. We speculate that MRI would have been very beneficial in diagnosing this pregnancy in the cornual region, potentially saving the patient from life-threatening hemorrhage. Three-dimensional sonography and MRI can help distinguish interstitial ectopic pregnancy from normal intrauterine pregnancy, particularly in the first trimester [34,36]. Judicious use of 2-D, 3-D and transvaginal ultrasound is vital to correctly diagnose each of the 3 types of pregnancies. If ultrasound findings are ambiguous or inconclusive, many authors recommend using MRI or, very rarely, a CT scan for such cases [19,37,38]. 3-D MRI has brought innovation to the diagnosis and distinction between angular and interstitial ectopic pregnancies [39].

Currently, medical and conservative surgical approaches are utilized to achieve the best outcomes of the 3 ectopic pregnancies in the cornual region of the uterus [20,40]. Surgical treatment is preferred in cases of pregnancy rupture, anemia, impending low blood pressure, gestational sac diameter $>$ 4 cm on ultrasonography scan, or lower abdominal/pelvic pain that persists for more than 24 hours [41]. Laparotomy with cornual resection or hysterectomy is the most common surgical approach for ruptured interstitial pregnancies, especially after the first trimester [29,42]. In contrast to the past, because of advances in laparoscopic techniques, cornual resection, cornuostomy or hysteroscopic removal of ectopic interstitial tissue is performed laparoscopically [29]. Hysterectomy is generally considered acceptable in cases of life-threatening hemorrhage [22].

Strength and limitations

Based on a comprehensive literature search, we understand that our study is one of the few that concisely attempts to delineate some salient features separating cornual, interstitial and angular pregnancies in the second and third trimesters. Our case report reminds clinicians and technologists about the peculiarities and ambiguity involved in differentiating these 3 ectopic pregnancies in the cornual region of the uterus, especially after the first trimester. One of the shortcomings of our study is that we included only case reports and excluded all systematic reviews and larger case series. Moreover, we excluded all case reports published before 2000. The rationale behind choosing these inclusion and exclusion criteria is described in the Methodology section.

Conclusion

It is well known that there is ample confusion among radiologists and obstetricians regarding terminology surrounding ectopic pregnancy in the cornual region of the uterus. To remain consistent, we advocate using the term “cornual ectopic pregnancy” only for pregnancies involving uterine malformations. Regardless, any eccentric location of the gestational sac in the uterus should raise concerns among sonographers and radiologists for a potential angular, interstitial or cornual ectopic pregnancy. Hence, the first-trimester transvaginal scan is exceptionally critical for determining the exact type of ectopic pregnancy in the cornual region of the uterus. The first trimester is the only period in pregnancy when it is possible to establish subtle sonographic signs for the accurate diagnosis of ectopic pregnancy in the cornual region of the uterus. During the first trimester, it is vital to visualize the endometrium around the gestational sac in all the scanning planes. After the first trimester, the enlarging gestational sac inevitably obliterates the distinction between the 3 easily confused pregnancies in the cornual area, as mentioned above.

Furthermore, a transvaginal scan should be attempted if transabdominal scanning does not demonstrate communication between the internal cervical os and uterine cavity in the second trimester. The inability to extrapolate internal os to the uterine cavity should be perceived as a sonographic impression of a potential ectopic in the cornual region. Although ultrasound is the primary diagnostic radiological modality in pregnant patients, clinicians should not be afraid to explore other imaging modalities for the patient’s benefit, especially when sonographic images are equivocal or inconclusive. Robust collaboration between sonographers, radiologists, and obstetricians is vital for the management of angular, interstitial and cornual pregnancies. We conclude that extreme caution should be exercised when diagnosing and differentiating angular, interstitial, or cornual pregnancy whenever the gestational sac is visualized in the cornual region of the uterus, preferably in the first trimester.

Author contributions

GD: conception and design of the study, literature review including analysis and interpretation of data, drafting the article, and revising the manuscript critically. AG: revising the manuscript critically for intellectual content and final approval before submission. LZ and RC: literature review and final approval of the manuscript. MF: revision and final approval

of the manuscript. AB: obtained patient consent, revision, and final approval of the manuscript.

Patient consent

Written informed consent was obtained from the patient for this case study on January 17, 2023. The case study received formal approval from the Research Ethics and Compliance Committee (affiliated with the University of Manitoba) for publication, Dated: February 28, 2023, with the following REB number: REB Registry Number: H2023:043 (HS25876)

Supplementary materials

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2023.04.028.

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