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Editorial

Catch me if you scan: ultrasound diagnosis of ectopic pregnancy

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In recent years, ultrasound has become an essential tool in the assessment of women with suspected early pregnancy complications[1]. A large number of studies has already been published, describing the value of ultrasound in the diagnosis of ectopic pregnancy[2,3]. So, why write yet another review on this topic? We run a busy Early Pregnancy Unit in the area with the highest prevalence of ectopic pregnancy in the UK, which also receives many referrals from other hospitals of women with an uncertain diagnosis of ectopic pregnancy. The most interesting fact that we have learned over the years is that the majority of women referred with suspected ectopic pregnancies in fact had intrauterine ones that were either missed on ultrasound examination or misinterpreted as ectopics. This may sound surprising to many, as ultrasound diagnosis of intrauterine pregnancy is considered to be relatively simple and accurate.

In many cases, ultrasound examination failed to identify a small amount of retained products of conception, due in part to inconsistencies in the sonographic diagnosis of incomplete miscarriage; this is often based on the use of arbitrary cut-off levels for endometrial thickness[4]. In other cases, however, sonographers were unable to decide whether a visible gestational sac represented an intrauterine or an ectopic pregnancy. In some cases with uncertain diagnosis, women had already received medical treatment with methotrexate prior to referral, leading to the loss of wanted normal intrauterine pregnancies. Another common problem is difficulty in differentiating between the various types of ectopic pregnancy. An accurate differential diagnosis is important in ectopics, as the management often differs depending on the type and exact location of the pregnancy.

The purpose of this review is to summarize the sonographic criteria for the diagnosis of both intrauterine and ectopic pregnancies and to describe the principles of differential diagnosis of various types of ectopic pregnancy. We will not cover management of pregnancies of unknown location, as this issue has been covered extensively in recent publications[5].

Intrauterine pregnancy

In women with normal uteri, the diagnosis of an intrauterine pregnancy is usually straightforward. A normal uterus is defined by the convex appearance of the uterine fundus, absence of any significant fundal indentation of the uterine cavity and the presence of two interstitial portions of the Fallopian tubes[6]. Finding interstitial portions of the tubes is very helpful to exclude the diagnosis of unicornuate uterus and is essential for making the diagnosis of interstitial pregnancy. By examining the fundal aspect of the uterus in a transverse section, the interstitial tubes can be identified as thin hyperechoic lines extending from the lateral aspect of the uterine cavity through the myometrium towards the uterine serosa[7]. They can be seen routinely in women with intrauterine pregnancies < 7 weeks' gestation. In women with extrauterine pregnancies, the uterine position and size are usually not affected by the growth of pregnancy and therefore it is possible to identify the interstitial segments of the tube as late as the second trimester of pregnancy.

In pregnancies < 6 weeks' gestation, before an embryo or yolk sac are visible, it is important not to confuse a small amount of fluid within the uterine cavity ('pseudosac') with an early gestational sac. An early intrauterine pregnancy is usually located eccentrically within the uterine cavity and is surrounded by an echogenic ring of trophoblast[8,9]. The endometrial midline echo is intact and the pregnancy can be seen implanted below the endometrial surface. A pseudosac is surrounded by a single layer of tissue and tends to follow the contour of the cavity. In longitudinal section, the midline endometrial echo cannot be seen, which helps to confirm the presence of fluid within the uterine cavity[10].

Once it has been established that a gestational sac is present, it is important to ensure that the pregnancy is intrauterine. In order to achieve this, the uterus should be examined in the longitudinal section to demonstrate continuity between the gestational sac and the cervical canal. We then advocate examination of the cervix in

an effort to exclude cervical and Cesarean section scar ectopic pregnancies. The internal cervical os is identified at the point of insertion of the uterine arteries[11]. The gestational sac should be located above the level of the internal os. If the gestational sac is found below this level, it is important to differentiate between the cervical phase of miscarriage, and cervical and Cesarean scar ectopic pregnancies. The ultrasound criteria that can be used to achieve this are discussed later.

In women with normal uteri, problems can also occur when an early pregnancy is located in the upper lateral aspect of the uterine cavity, which may raise suspicion of an interstitial pregnancy. When the gestational sac is located medially to the interstitial part of the tubes, the pregnancy is intrauterine. If the interstitial portions of the Fallopian tubes cannot be seen, then it is important to examine the area medial to the sac. In intrauterine pregnancies it is possible to follow the endometrial–myometrial junction, which extends around the gestational sac. In addition, the communication between the sac and the uterine cavity is wide, which is not the case with interstitial pregnancies (Figure 1).

Some authors use the term 'angular pregnancy' to describe pregnancies located in the lateral aspect of the uterine cavity, close to the tubal ostium[12]. On laparoscopy, angular pregnancy is distinguished from an interstitial pregnancy by being located medial to the round ligament. It has even been suggested in the past that differential diagnosis between interstitial and angular pregnancy is difficult and that the term 'pregnancy in cornus' should be used to describe both of them[13]. However, with the use of modern ultrasound equipment it should always be possible to differentiate between an intrauterine and an ectopic pregnancy, and we therefore believe that the term 'angular pregnancy' is obsolete as it simply refers to a normal intrauterine pregnancy that happens to be located laterally within the uterine cavity.

The diagnosis of intrauterine pregnancy becomes more difficult if the uterus is enlarged by fibroids. Fibroids often distort the shape of the endometrial cavity and prevent the operator from visualizing in a single plane the continuity between the gestational sac and the cervical canal. In such cases, it is best to identify the cervix first and then follow the cervical canal into the endometrial cavity until the gestational sac is encountered, which would confirm an intrauterine pregnancy. Occasionally, the uterus becomes so enlarged that it is impossible to visualize the whole of the uterine cavity transvaginally. In these cases, a transabdominal scan is helpful to identify intrauterine pregnancies that could not be seen using the transvaginal route.

In cases of suspected congenital uterine anomalies, a careful examination of the fundal region may reveal a variety of abnormalities of the myometrial and endometrial cavities. A precise description of the uterine anomaly is often difficult and three-dimensional (3D) scanning is usually necessary to achieve this[6]. In anomalous uteri, the gestational sac is often found laterally in the uterus, which may resemble an interstitial pregnancy. The diagnosis of intrauterine pregnancy, however, should be based on the same criteria that are used in women with normal uteri, i.e. a gestational sac that is located medial to the interstitial tube and wide communication between the sac and the uterine cavity (Figures 1 and 2). It is useful to remember that bleeding often occurs in the empty half of the anomalous uterus, which may create the impression of a pseudosac adjacent to a normal pregnancy.

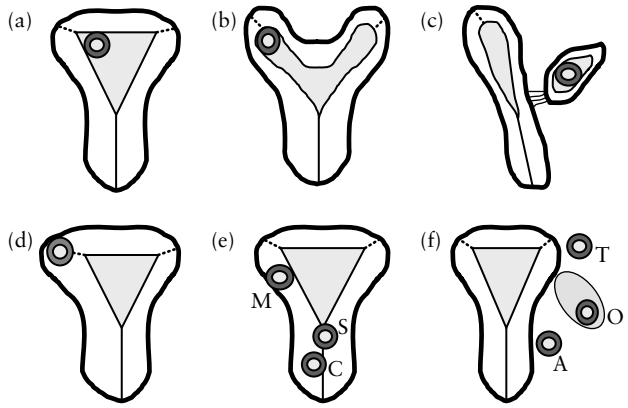

Figure 1 Schematic drawings illustrating the ultrasound criteria for the diagnosis of tubal and non-tubal ectopic pregnancies (····· interstitial tubes). (a) Intrauterine pregnancy located in the lateral aspect of a normal intrauterine cavity; (b) intrauterine pregnancy in the right cornu of a bicornuate uterus, demonstrating the wide communication between gestational sac and endometrial cavity; (c) pregnancy in the non-communicating rudimentary horn of a unicornuate uterus – note the presence of a single interstitial tube and the absence of communication between gestational sac and endometrial cavity; (d) interstitial pregnancy – note the narrow communication between gestational sac and endometrial cavity, representing the interstitial portion of the Fallopian tube, and the gestational sac is surrounded by a thin myometrial mantle; (e) intramural (M), Cesarean scar (S) and cervical (C) ectopic pregnancies showing the variable depth of myometrial involvement; (f) tubal (T), ovarian (O) and abdominal (A) ectopic pregnancies in their typical locations in relation to the uterus.

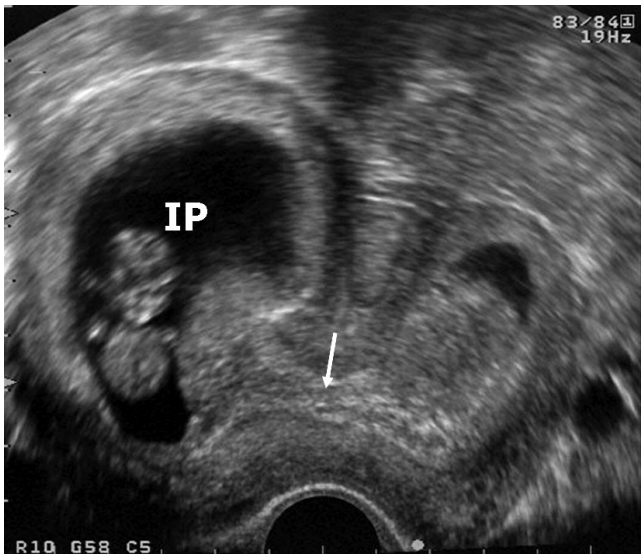

Figure 2 A case of intrauterine pregnancy (IP) in the right cornu of a bicornuate uterus at 11 + 2 weeks' gestation. Note the wide communication between gestational sac and the rest of the endometrial cavity (arrow).

Cornual pregnancy

Unicornuate uterus is a rare type of congenital uterine anomaly. The diagnosis is made when only a single interstitial tube is visible on ultrasound. In the majority of cases, a small non-communicating rudimentary horn can be seen adjacent to the medial aspect of the unicornuate uterus[14]. A pregnancy in the rudimentary cornu, despite being within the uterine cavity, is classified as cornual ectopic pregnancy because of its tendency to rupture during the second trimester. Failure to diagnose a cornual pregnancy can lead to serious complications, while an early diagnosis provides the option of safe and effective treatment[15,16]. The following criteria can be used to diagnose cornual pregnancy on ultrasound examination: 1) a single interstitial portion of Fallopian tube in the main uterine body; 2) a gestational sac, mobile and separate from the uterus, surrounded by myometrium; 3) a vascular pedicle adjoining the gestational sac to the unicornuate uterus (Figures 1 and 3). These criteria have been developed in our Unit and, by using them, we have managed to make a correct diagnosis of the eight cases of cornual pregnancy seen by us in the last 7 years[17]. The differential diagnosis between cornual and other forms of ectopic pregnancy is important because of the different clinical implications and management strategies. Surgical excision of cornual pregnancy is not technically difficult and complications are rare. This differs from surgery in cases of interstitial and abdominal pregnancies, which is often complex and hazardous[17,18].

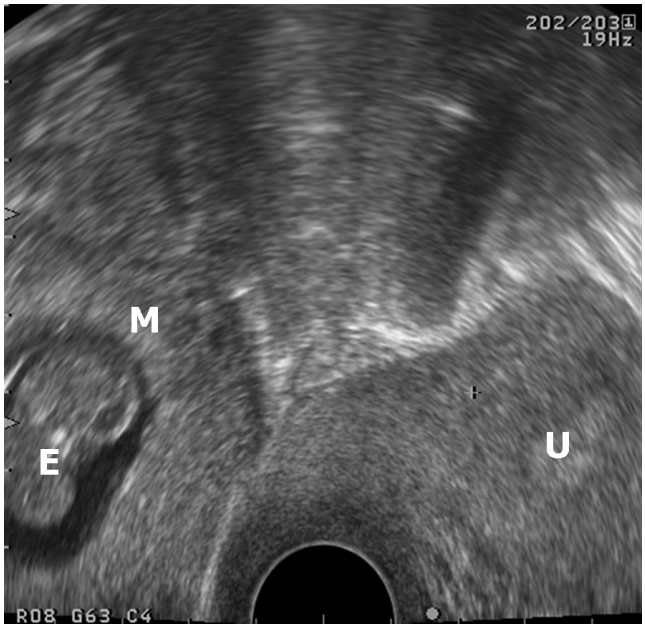

Figure 3 A case of first-trimester cornual pregnancy, showing a thick layer of myometrium (M) surrounding the ectopic gestational sac and embryo (E). Note the absence of communication between gestational sac and endometrial cavity of the unicornuate uterus (U).

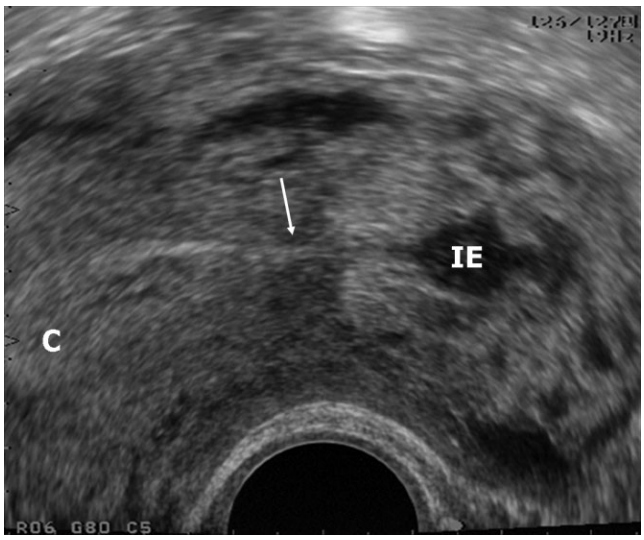

Figure 4 A case of left interstitial ectopic pregnancy (IE) diagnosed at 6 + 1 weeks' gestation. The interstitial portion of the tube is seen (arrow) as a narrow communication between the gestational sac and the endometrial cavity (C).

Interstitial pregnancy

The differential diagnosis between an interstitial pregnancy and a normal intrauterine pregnancy is often difficult to achieve. Interstitial pregnancies are surrounded by a layer of myometrium, which makes diagnosis difficult, particularly if transabdominal scanning is used[19,20]. Delayed diagnosis of interstitial pregnancy is the main factor contributing to the high maternal mortality rate in comparison to that for tubal ectopics; the mortality rate for tubal ectopic pregnancy was reported at 0.14%, whilst that for interstitial pregnancy was reported to be nearly 15 times higher, at 2–2.5%[21].

In 1993, Ackerman *et al.*[22] proposed a set of sonographic criteria for the diagnosis of interstitial pregnancy. Based on a retrospective study of 12 interstitial ectopic pregnancies, they reported that visualization of an echogenic line extending into the midportion of the gestational sac is a sensitive sign of an interstitial pregnancy, and postulated that this line represents the interstitial portion of the tube. Timor-Tritsch *et al.*[23] suggested that interstitial ectopics should be diagnosed in women with: 1) an empty uterine cavity; 2) a gestational sac > 1 cm from the most lateral point of the endometrial cavity; and 3) a gestational sac surrounded by a thin myometrial layer. These criteria were reviewed by Hafner *et al.* in 1999[24], who found that the interstitial segment of the tube often measured < 1 cm in length. Therefore, a strict application of a 1-cm cut-off may lead to an interstitial pregnancy being misdiagnosed as intrauterine pregnancy.

In our practice at King's, we have adopted a combination of two findings as being diagnostic of interstitial pregnancy: 1) visualization of the interstitial line adjoining the gestational sac and the lateral aspect of the uterine cavity; and 2) the continuation of myometrial mantle around the ectopic sac. 3D ultrasound facilitates

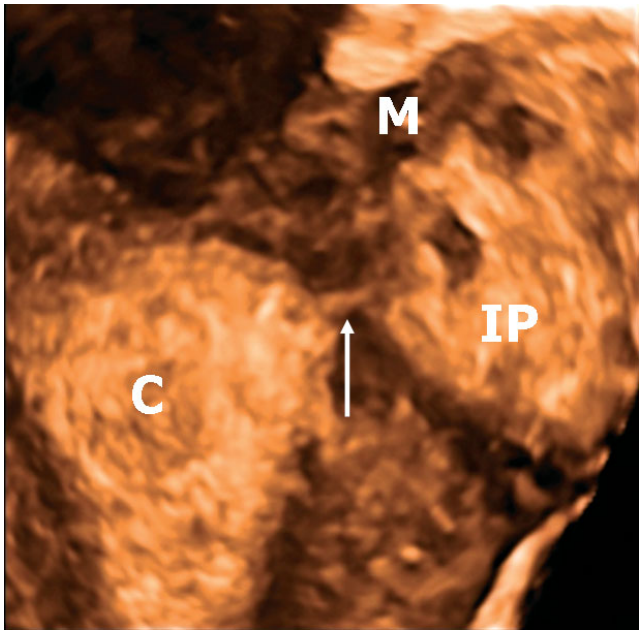

Figure 5 Demonstration by three-dimensional ultrasound of the interstitial portion of the Fallopian tube (arrow) connecting the gestational sac (IP) and the endometrial cavity (C) in a case of interstitial ectopic pregnancy diagnosed at 9 + 6 weeks' gestation. Myometrial mantle is seen surrounding the interstitial ectopic (M).

the visualization of the interstitial tube and it may be helpful to differentiate between intrauterine and interstitial pregnancies in difficult cases[25,26] (Figures 1, 4 and 5).

Intramural, Cesarean scar and cervical ectopic pregnancies

Another type of ectopic pregnancy that can be difficult to differentiate from intrauterine pregnancy is intramural pregnancy[27]. This is a rare form of ectopic pregnancy and some authors maintain that it cannot be diagnosed on ultrasound examination alone[28]. Others have shown, however, that the ultrasound diagnosis of intramural pregnancy can be made in cases with a gestational sac embedded into the myometrium of the uterine corpus with no visible communication between the sac and uterine cavity[29–31] (Figure 1). There are reports in the literature of intramural pregnancies being misdiagnosed as fibroids or intrauterine pregnancies[28,32]. They are probably caused by a previous myometrial injury, which usually occurs during an invasive intrauterine procedure, such as curettage; it is likely that the intramural pregnancy enters the myometrium through a false passage created during this previous surgical procedure[29]. Varying degrees of myometrial involvement is common in cases of cervical and Cesarean scar ectopic pregnancies, which are also caused by previous uterine trauma (Figure 1). We have seen a couple of cases of intramural Cesarean ectopics in which the pregnancy was completely embedded into the myometrium and it was impossible to remove using suction curettage.

Ultrasound criteria for the diagnosis of cervical pregnancy on transabdominal ultrasound were first described by Kobayashi *et al.* in 1969[33]. They were revised in 1987 and adapted for use in transvaginal scanning by Hofmann *et al.*[34], who suggested the following criteria to diagnose a cervical ectopic pregnancy: 1) no evidence of intrauterine pregnancy; 2) hourglass uterine shape with ballooned cervical canal; 3) presence of a gestational sac or placental tissue within the cervical canal; and 4) closed internal os (Figure 6).

Vial *et al.*[35] attempted to define ultrasound criteria for the diagnosis of Cesarean scar ectopic pregnancy. In their case report they distinguished between two types of Cesarean scar ectopic depending on the extent of myometrial involvement. In our Unit we tend to group cervical and Cesarean section scar ectopic pregnancies together as they follow a similar clinical course and are managed in a similar way. We use the following criteria for the diagnosis: 1) gestational sac located below the level of the internal os or within a visible myometrial defect at the site of the previous lower segment Cesarean section scar; 2) evidence of functional trophoblastic/placental circulation on color Doppler examination, characterized by high-velocity (peak velocity > 20 cm/s) and low-impedance (pulsatility index < 1) blood flow; 3) negative 'sliding organs sign', defined as the inability to displace the gestational sac from its position at the level of the internal os using gentle pressure applied by the transvaginal probe. These criteria enable operators to differentiate between the cervical phase of intrauterine miscarriage and true implantation of pregnancy below the level of the internal os. In cases of miscarriage, the gestational sac is mobile with no detectable peritrophoblastic blood flow, whilst the opposite is the case with ectopics implanted below the internal os.

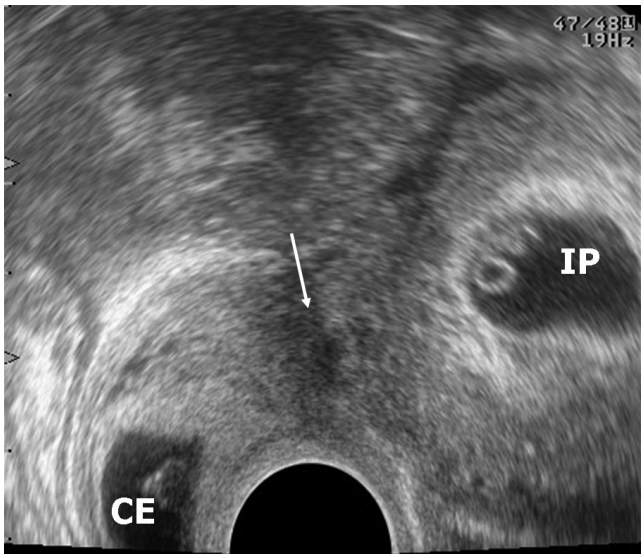

Figure 6 A case of heterotopic cervical pregnancy diagnosed at 6 + 6 weeks' gestation. An intrauterine pregnancy is seen to the right of the image (IP) whilst a cervical ectopic pregnancy (CE) is seen beneath the level of the internal os (arrow) on the left.

Tubal, abdominal, and ovarian ectopic pregnancies

Once the uterus has been examined in great detail and the possibility of intrauterine, interstitial, intramural, cervical or Cesarean scar pregnancy has been excluded, the differential diagnosis includes extrauterine ectopic pregnancies. The most common pregnancy of this type is tubal ectopic pregnancy, but rarer types such as abdominal or ovarian pregnancy should also be kept in mind.

The initial sonographic criteria for the diagnosis of a tubal ectopic were published by Kobayashi *et al.* in 1969[33]. Using transabdominal ultrasound, false-negative and false-positive findings were common, occurring in nearly 50% of cases. The accuracy of ultrasound diagnosis of tubal ectopic pregnancy improved significantly once transvaginal scanning became available[36–38]. In a study of 200 women, Cacciatore *et al.*[39] reported that the presence of an adnexal mass on ultrasound is a highly specific finding in cases of tubal ectopic pregnancy. In order to facilitate the distinction between corpus luteum and tubal ectopic pregnancy, some authors[2,40] have suggested that gentle pressure with the ultrasound probe combined with abdominal palpation may demonstrate free movement between the adnexal mass and the ovary (sliding organs sign). A meta-analysis[2] of findings in 2216 women showed that the presence of an adnexal mass other than a simple cyst separate from the ovary was a highly sensitive (84.4%) and specific (98.9%) test for the diagnosis of tubal pregnancy, even in the absence of a visible embryo. Another study by Shalev *et al.*[41], including 840 patients with 380 tubal ectopics, reported a sensitivity of 87% and a specificity of 94% in the ultrasound diagnosis of ectopic pregnancy based on the visualization of a ring-like structure or a non-homogeneous adnexal mass. More recent studies showed that advances in ultrasound technology have helped to further increase the accuracy of sonographic diagnosis of tubal ectopic pregnancy, with sensitivities and specificities well above 90%[3,42]. It is safe to say that with appropriate training and state-of-the art ultrasound equipment, a conclusive diagnosis of tubal ectopic pregnancy can be reached in most cases. The role of laparoscopy for the diagnosis of ectopic pregnancy is therefore rapidly diminishing and it should be used mainly for treatment.

The differential diagnosis of tubal pregnancy includes abdominal, ovarian, interstitial and cornual ectopic pregnancy (Figure 1). These less common types of ectopic pregnancy should always be considered when women present with viable ectopic pregnancies at advanced gestation, since tubal ectopics rarely progress beyond the first trimester[43]. In cases of tubal ectopics there is no visible communication between the gestational sac and the endometrial cavity, which helps to differentiate them from intrauterine and interstitial pregnancies. Furthermore, in contrast to abdominal and interstitial pregnancies, tubal ectopics tend to be mobile. The absence of a well-defined vascular pedicle helps to distinguish tubal from cornual ectopic pregnancies.

Abdominal ectopics typically occur following a rupture of a tubal ectopic, which then implants again within the peritoneal cavity. They are most commonly located in the broad ligament and in the pouch of Douglas[18]. Allibone *et al.*[44] described a series of four abdominal pregnancies which were diagnosed on ultrasound examination in the second trimester using the following criteria: 1) demonstration of a fetus in a gestational sac outside the uterus; 2) failure to visualize the uterine wall between the fetus and urinary bladder; 3) close proximity between the fetus and the anterior abdominal wall; and 4) localization of the placenta outside the confines of the uterine cavity. More recently, the use of transvaginal ultrasound has enabled diagnosis in the first trimester[45,46]. Gerli *et al.*[46] reported a case of abdominal pregnancy at 8 weeks' gestation and proposed revised diagnostic criteria, including: 1) absence of an intrauterine gestational sac; 2) no evidence of tubal dilatation or a complex adnexal mass; 3) a gestational sac surrounded by loops of bowel and separated from the uterus; and 4) free mobility of the gestational sac. In our experience, however, abdominal ectopics are usually fixed deep within the pelvis. This feature helps to differentiate them from cornual pregnancies, which are typically mobile[17]. When an abdominal ectopic is suspected, a communication between the gestational sac and the endometrial cavity should be sought. If this is not found, intrauterine pregnancy in an anomalous uterus and interstitial ectopic pregnancy can be excluded. Unlike cornual pregnancies, abdominal pregnancies can be difficult to visualize because of the overlying bowel, and they are often complicated by intrauterine growth restriction and oligohydramnios because of poor placentation[18]. In addition, their blood supply is diffuse, in contrast to cornual pregnancies, which receive their blood supply through a well-defined vascular pedicle[17].

The last type of ectopic pregnancy to consider is ovarian pregnancy, which accounts for 0.15–3% of all ectopics[47,48]. Early unruptured ovarian pregnancies are surrounded by ovarian cortex, which helps to differentiate

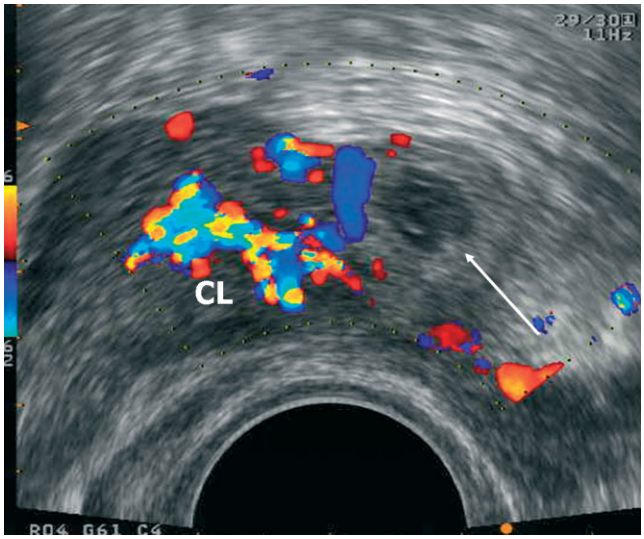

Figure 7 An image of a case of early ovarian pregnancy showing a gestational sac surrounded by ovarian stroma (arrow) and a solid corpus luteum (CL) with typical 'ring of fire' blood flow on Doppler examination.

them from tubal ectopics[49,50]. Typically, corpus luteum is seen adjacent to the ovarian pregnancy (Figure 7). On palpation, it is impossible to separate the gestational sac and the ipsilateral ovary (negative sliding organs sign). However, this finding is not entirely specific, as some tubal pregnancies are fixed to the ovary because of pelvic adhesions. Ruptured ovarian pregnancy cannot be differentiated from ruptured tubal ectopic pregnancy and it is also hard to distinguish them from ruptured hemorrhagic ovarian cyst. Ghi *et al.*[50] reported that the use of 3D ultrasound may provide useful additional information in difficult cases.

Conclusion

Some types of ectopic pregnancy described in this review are very rare and there are few sonographers who have seen more than a couple of such cases during their professional careers. The majority of studies quoted in this review include only a handful of patients and it is very unlikely that any of the proposed diagnostic criteria will ever be formally tested on a large scale. It is our belief, however, that, despite their rarity, a correct diagnosis of a particular type of ectopic pregnancy can be reached in most cases. This should be based on good understanding of pelvic anatomy and the pathophysiology of ectopic pregnancies, combined with a systematic examination of the key morphological features. We hope that the diagnostic approach described in this paper will help sonographers in their daily work, increase their confidence when faced with unusual cases and help them to avoid potentially harmful diagnostic errors.

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