Pitfalls in the diagnosis of miscarriage and ectopic pregnancy

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Introduction

Early pregnancy complications such as miscarriage and ectopic pregnancy (EP) are very common and associated with significant physical and emotional morbidity for the patient and her family. Transvaginal ultrasonography (TVS) is the diagnostic cornerstone of the management of women with early pregnancy complications, with high sensitivity of 87-99%, specificity of 94-99% and it is the investigative modality of choice.1 The challenge in the diagnosis of miscarriage is in making sure that it is correct, so as to not risk inadvertently terminating an ongoing pregnancy. Misdiagnosis of miscarriage should be a ‘never’ event. To quote the 1995 report on the misdiagnosis of miscarriage by Campbell and colleagues, “the death of an embryo should be regarded as of equal significance to that occurring at a later stage.”2

With EP, most sonographers are worried about missing the diagnosis. According to the most recent MBRRACE report, EPs were still the leading cause of maternal mortality in early pregnancy.3 Thankfully, the mortality rate has been declining steadily over the last 30 years with better diagnostic techniques, expertise and the establishment of early pregnancy assessment units (EPAU). In the UK and Ireland, nine women died of their EPs during 2009-2014, so given that approximately 60,000 EPs occurred over that time, the estimated mortality was 1:6,500 cases. Most women who die of their EP present to emergency departments with collapse, abdominal pain or diarrhoea, but there will be many more EPs that go under the diagnostic radar and resolve without intervention, so over-diagnosis can result in morbidity through over-treatment. It is important to be certain about the diagnosis of an EP, before offering treatments such as laparoscopy and methotrexate to avoid unnecessary surgery or inadvertent damage to an unrecognised very early intrauterine pregnancy (IUP). Errors with methotrexate use have become a significant issue in the USA and are associated with major congenital abnormalities if the embryo survives.4

This article reviews the errors that can occur during the clinical and ultrasound assessment of women during early pregnancy with the aim of minimising the risk of misdiagnosis.

Incomplete clinical assessment

During clinical assessment of women of reproductive age, patients should have a pregnancy test even when their symptoms are non-specific, because the symptoms and signs of EP can resemble those of other conditions (such as gastrointestinal conditions or urinary tract infections). Symptoms of EP include abdominal pain, vaginal bleeding (ranging from spotting to passing blood clots) or symptoms secondary to haemoperitoneum such as fainting, dizziness, shoulder tip pain and gastrointestinal symptoms such as vomiting or diarrhoea. Women in the reproductive age group with an acute presentation should not be referred for a pelvic ultrasound scan without having first had a pregnancy test, and the result should always be documented on the referral form. The risk of an EP is negligible in a woman with a negative pregnancy test and no recent history of a positive test; only a handful of cases have ever been reported.5

Suboptimal technique

Some EPAUs perform an abdominal ultrasound followed by a TVS if the diagnosis is unclear, but we recommend that the primary approach should be transvaginal. TVS usually gives the best view of the uterus and adnexa, and so yields the most diagnostic information regarding the location and viability of the pregnancy. The skill of the operator, and hence their diagnostic accuracy, improves with experience so if TVS is only used when a miscarriage or EP is suspected, the operator will not be as experienced in the technique when it is really needed. Inappropriate interventions due to incorrect scanning technique and approach can be potentially damaging and can have serious consequences. Errors such as the misdiagnosis of miscarriage have resulted in public inquiries in the UK and Ireland,6 and missed ectopic pregnancies are highlighted in the confidential inquiries into maternal deaths. In terms of keeping the patient informed, starting with TVS is the quickest route to inquiries into maternal deaths. In terms of keeping the patient informed, starting with TVS is the quickest route to a pelvic ultrasound scan by that brings, whether the news is good or bad. From a logistical point of view, it is also easier to run a clinical service when women need an empty bladder rather than a full one. Very few women object to TVS when they understand the reasons for using it.7 This is not to say that an abdominal approach will not be needed in these cases.

If a patient declines a transvaginal scan, a transabdominal scan (TAS) should be performed after explaining its limitations. We would caution against relying on the use of focused assessment with sonography for trauma (FAST) scans in A&E to check for ruptured ectopic pregnancies by looking for free fluid in the pelvis, despite the recent MBRRACE recommendation. This is because a woman with ruptured or leaking EP typically collapses when she suddenly decompensates after bleeding into her peritoneal cavity over a period of time. This situation is different to rapid blood loss with trauma; with an ectopic pregnancy the blood is often clotted, and will not show as anechoic fluid on ultrasound examination, so may not be readily detected with a portable ultrasound in the hands of an emergency clinician. There is also a risk of false reassurance if a live ectopic
pregnancy is not recognised as such because FAST scans are not performed by staff familiar with identifying the uterus and endometrial cavity. A meticulous and systematic approach to early pregnancy ultrasound in every patient is key to avoiding misdiagnosis. This includes examination of the endometrial cavity from the internal os to the interstitial portion of each fallopian tube, documentation of uterine anomalies, visualisation of both ovaries and identification of the corpus luteum or corpora lutea. The relative anatomy of the embryo and extraembryonic structures should also be measured and documented. There should be regular performance reviews and supervision for the sonographers in EPAU, and a multidisciplinary review of difficult cases to optimise feedback and learning.

**Over-reliance on ‘cut-offs’ to diagnose miscarriage**

Up until 2011, RCOG/RCR guidance on the ultrasound diagnosis of miscarriage in the UK used cut-off values of mean gestational sac diameter (MSD) of 20mm or more with no visible embryo, or a crown-rump length (CRL) of 6mm or more without a heartbeat (Early Pregnancy Loss, Management Green-top Guideline No 25, 2006). In a systematic review of the evidence on which previous diagnostic criteria were based, Jeve et al concluded that guidelines were founded on a small number of old, poor quality studies. In the same issue, original papers were published that supported increasing the cut-off values to MSD ≥25mm, or an embryo with a CRL ≥7mm without a heartbeat to reduce the risk of diagnostic error. The potential pitfall of using cut-offs is the assumption that they can be absolutely relied upon to yield an accurate diagnosis. The 2011 paper had a relatively small number of cases at or around the critical decision boundaries used to define miscarriage and intervention if a miscarriage was diagnosed, so the assumption was made that the diagnoses were correct, rather than letting the diagnoses run their natural course to obtain true outcome data. Although uncommon, we sometimes encounter cases where the cut-off did not apply. Figure 1 illustrates a case where the MSD was 26mm and no embryo was seen. The sonographer erred on the side of caution and arranged a follow-up scan 14 days later. The follow-up scan showed an ongoing intrauterine pregnancy with an embryo measuring 21mm, so there must have been a seven-week size embryo at the time of the initial scan, but it was not seen. False positive diagnosis of a miscarriage could also occur in the case of a monochorionic twin pregnancy. We have not been able to find any data regarding the normal early development of the gestational sac and at what diameter the embryos are usually visible in these pregnancies. Failure to visualise an embryo that is actually present may also be due to patient factors such as adhesions, fibroids, adenomyosis or obesity. Failure to recognise the embryo may also be due to human error. This is why NICE recommended that the diagnosis of early embryonic demise should always be deferred for at least a week or checked by a second sonographer. The error may be due to poor technique or inexperience. We have encountered a few cases where chorionic bumps were misinterpreted as an embryo and the CRLs measured have led to an erroneous diagnosis of a failed pregnancy.

**Failure to leave sufficient time between scans**

In 2013, a prospective observational study of EPAU patients with pregancy <7mm or MSD >12mm had been seen at the initial scan, or after a minimum of 14 days if an empty gestational sac <12mm if sac size had not doubled in diameter. The same potential pitfalls apply to repeat scans, so great care must be taken to recognise suboptimal views with each ultrasound scan.

**Ectopic pregnancy pitfalls**

Delay in the diagnosis of ectopic pregnancy is the most common reason for an early pregnancy claim to the NHS Litigation Authority (personal communication). Approximately 70-85% of ectopic pregnancies are visualised at the first scan in a teaching hospital EPAU, with the remainder initially diagnosed as pregnancy of unknown location (PUL), probably due to the fact that they are too small and too early in the disease process. In our unit, only 1-2% of women with ectopic pregnancies present as emergencies and go straight for surgery, the remainder have a scan in EPAU. Of these, 15% require more than one scan before the diagnosis is made.

**Missing an intrauterine pregnancy**

Many units in the UK and USA will assume that there is an underlying ectopic pregnancy if a woman has a PUL and climbing serum human chorionic gonadotropin (hCG), and will treat as such with methotrexate or surgery. It is important to recognise that the ‘discriminatory’ level of hCG is the level at which a sonographer should expect to see the gestational sac of a normal, singleton pregnancy in a normal uterus. Most units assume this level to be approximately 1500IU/L, but the level will vary from unit to unit depending on the threshold used to diagnose an IUP. If the local protocol dictates that a yolk sac must be seen, then the level will be much higher. The most difficult IUPs to diagnose are those that are destined to fail. This is because the anatomy of the gestational sac is not normal and may be a small, condensed mass of trophoblast. In this situation, judicious use of colour (not pulsed) Doppler can help with confirming the presence of trophoblast within the endometrial cavity by identifying the feeding spiral artery, adhering to the ALARA principals and monitoring the safety indices at all times. A similar approach can be used to diagnose retained products of conception. It follows from the statement above that an IUP is more difficult to diagnose in a twin gestation due to the larger mass of trophoblast. In this situation, decidual cysts, usually deep in the endometrium, are found more commonly in women with ectopic pregnancies as are pseudosacs (figure 4). The majority of tubal ectopic pregnancies are solid masses, located in the ampulla, so are visualised above and medial to the ovary. Ectopic pregnancies and interstitial pregnancies are often superior to the uterus, so a thorough examination will include looking high in the pelvis so as not to miss these. It is only by recognising solid ectopic pregnancies with confidence that the bulk of ectopic pregnancies will be diagnosed. The majority of ectopic pregnancies are on the same side as the corpus luteum, and are separate to the ovary, so this is why it is important to be familiar with identifying the corpus luteum. If there is more than one corpus luteum, then the search should be made for an ectopic pregnancy, even if there is an obvious intrauterine pregnancy. The most dangerous ectopic pregnancies are those that are live and rupture late. Every year we see a two or three women who have been falsely diagnosed with an intrauterine pregnancy, often in a termination clinic or fetal medicine unit where the focus of the scan has been on determining the gestation or examining the fetus rather than accurately locating the pregnancy. These pregnancies are...
more likely to be non-tubal ectopic pregnancies. A previous ultrasound showing an intrauterine pregnancy should not be considered as excluding an ectopic pregnancy in a symptomatic woman.

**False positive diagnosis of ectopic pregnancy**

Tubal pregnancies tend to have characteristic morphologies on ultrasound, but not all tubal masses in women with positive pregnancy tests are ectopic pregnancies. We have mistaken tubal endosalpingiosis and schistosomiasis for ectopic pregnancies. Pulsed Doppler examination is useful to confirm an ectopic pregnancy when examining a tubal mass, as choriocic tissue will typically open up arteries, so the flow around an ectopic pregnancy will have a high velocity, low resistance pattern with continuous end diastolic flow. Trophoblast will typically be echogenic rather than hypoechoic, unless it has regressed, which case it appears solid and hypoechoic. In this situation, a distal tubal ectopic pregnancy that is adherent to the ovary may be very difficult to distinguish from a second corpus luteum.

Less common types of ectopic pregnancy may be difficult to diagnose as sonographers are less familiar with them. It can be very difficult to distinguish a pregnancy that is implanted high in the uterus, close to the tubal ostia from a pregnancy in the interstitial portion of the tube, particularly if the uterus is bicornuate or arcuate in shape, or the pregnancy is in the late first trimester. If the endometrium can be seen extending around the gestational sac, then it is an intrauterine pregnancy (figure 5). We have occasionally encountered an ovarian follicle misdiagnosed as an ovarian ectopic pregnancy – a ‘daughter cyst’ may be mistaken for a yolk sac, but in this case, there will not usually be an obvious ring of trophoblast or the typical blood flow pattern (figure 6).

**Conclusion**

An awareness of the potential pitfalls in diagnosis, along with a thorough and systematic approach to early pregnancy ultrasound and recourse to a second opinion when cases are difficult, should minimise the risks and consequences of misdiagnosis of miscarriage and ectopic pregnancy.

**References**
