Ultrasound diagnosis of ectopic pregnancy

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Abstract Ectopic pregnancy (EP) remains the number one cause of first trimester maternal death. Traditionally, laparoscopy has been the gold standard for diagnosis of EP. The advent of high-resolution transvaginal scan (TVS) means more clinically stable women with EPs are diagnosed earlier, well before surgery becomes necessary in many cases. Early diagnosis by TVS is therefore potentially life saving and can reduce surgical morbidity by allowing elective surgery or even non-surgical conservative treatment options. Combining transabdominal and transvaginal scanning confers no benefit over transvaginal scanning alone. Reports that reads "…empty uterus, ectopic pregnancy cannot be excluded" should be a thing of the past. Diagnosis of EP should be based upon the positive identification of an adnexal mass using TVS rather than the absence of an intra-uterine gestational sac. A systematic approach to scanning the early pregnancy pelvis will diagnose the vast majority of EPs at the initial scan. Ultrasound, and in particular TVS, is fast becoming the new gold standard for diagnosis of all types of EP. In modern management, laparoscopy should be seen as the operative tool of choice while TVS the diagnostic tool of choice.

Introduction

The word ectopic comes from the Greek word "ektopos" which means "out of place". Ectopic pregnancy (EP) describes any pregnancy implantation outside of the uterine cavity. Classification of EPs can be broadly divided in to tubal main categories, tubal and non-tubal. The vast majority of EPs are tubal (95%). Although non-tubal EPs make up only 5% of all EPs, these disproportionately contribute to the morbidity and mortality associated with EPs. Non-tubal EPs occur in the uterine interstitium (cornual or angular), cervix, ovary and previous caesarian section scar. A heterotopic pregnancy describes the situation where there is concurrent intra-uterine and extra-uterine pregnancies.

Before the advent of sonography and sensitive rapid assay serum human chorionic gonadotrophin (hCG) quantification, EP was frequently a life-threatening diagnosis. EP remains an important cause of first trimester morbidity and mortality and based on US and UK figures accounts for 80% of all first trimester maternal deaths[1,2,3]. Two direct deaths were reported in Australia in the period 1997–2005[4].

Worldwide, the incidence of EP is increasing and reflects an increase in rates of Chlamydial infection[5]. Increasing utilisation of assisted reproductive technologies (ARTs) has seen an increase in heterotopic pregnancies. The first pregnancy ever conceived after in-vitro fertilisation/embryo transfer was an EP[6]. An increase in the caesarean section rate has also seen an increase in the number of caesarean section scar EPs[7,8,9]. Intra-uterine devices (IUDs) reduce the rate of EPs overall but a woman using an IUD who falls pregnant has an increased risk of the pregnancy being ectopic[10]. EP should be considered in users of IUDs who experience irregular bleeding. Currently, EP accounts for approximately 1:100 of all pregnancies.

Symptoms may present as early as five weeks in tubal EPs. The spectrum of presentations ranges from the asymptomatic woman picked up on transvaginal ultrasound (TVS) through to massive intra-abdominal haemorrhage and collapse presenting to the Emergency Department (ED). The classic clinical presentation for EP is described as a triad of amenorrhoea, followed by vaginal bleeding and pelvic pain. Complaint of shoulder tip pain (not always volunteered by the patient) should rouse suspicion for intrabdominal bleeding (blood irritating the diaphragm results in referred pain to the shoulder). Abdominal and cervical motion tenderness (blood in the pelvis) in a woman with a positive pregnancy test should alert the clinician to the possibility of an EP. However, the classic clinical findings are present in only 30% of presentations and the signs are non-specific.

Historically, before the introduction of routine ultrasound, the diagnosis of EP was made at time of surgery. Prior to 1970, more than 80% of EPs were recognised after rupture and almost 50% of cases presented with shock. As a result, almost all women were taken straight to theatre for surgery almost as soon as the diagnosis was made[11,12]. Fortunately, with the advent of high- resolution TVS and sensitive immunoassay of hCG, presentation to the ED with collapse and shock is now more the exception rather than the rule.

Tait first described successful surgical treatment of EP in 1883. Shapiro described management by laparoscopy in 1973 and this is now the standard surgical approach[13]. For a long time, laparoscopy has been considered the gold standard in diagnosis of EP[14]. However, surgical diagnosis does not confer 100% sensitivity. Some EPs are self-limiting and therefore never seen at the time of laparoscopy whilst some EPs may be too small to be seen in the Fallopian tube during laparoscopy. There may also have been both false positive and false negative laparoscopic findings. Dilatation and curettage (D&C) was also used as a diagnostic tool before the introduction of high-resolution transvaginal probes to confirm or exclude an intra-uterine pregnancy (IUP). We believe that in modern management, there is no role for the use of D&C in the diagnosis of EP. In fact, the use of D&C may result in the inadvertent termination of early IUPs[15].

As a diagnostic tool, TVS now challenges laparoscopy

as the gold standard for the diagnosis of EP[16]. Due to the increased availability of high resolution TVS in early first trimester, more than 80% of EPs are now detected before rupture and more than 50% are diagnosed in asymptomatic women by US alone. Earlier diagnosis, in clinically stable women, allows for a greater range of conservative treatment options including medical (methotrexate (MTX)) management and a "wait and see" expectant approach. In fact the use of high resolution transvaginal ultrasound technology has created a revolution in non-surgical treatment management strategies[17]. It has been observed for a long time that a number of ectopic pregnancies will resolve spontaneously[18]. Careful selection of women for expectant management should decrease operative procedures such as laparoscopy and unnecessary D&C as well as reduce morbidity from surgery, transfusion and anaesthesia. Strict selection criteria for women for expectant management must be adhered too in order for maintaining safety without compromising care. The need for surgery with its attendant risks is thus reduced. However, it is beyond dispute that surgery should never be delayed in the haemodynamically unstable patient.

Role of ultrasound

While the diagnosis of EP is not traditionally based on TVS alone, we would argue that the vast majority (90.9%) of women who present with an EP can now be diagnosed reliably using TVS as a single stand-alone test. Ultrasound diagnosis of an EP should be based on the positive identification of an adnexal mass rather than the absence of a gestational sac in the uterine cavity[19]. The report that reads empty uterus, ectopic pregnancy cannot be excluded" should be a thing of the past. In fact, with experience, between 87–99% of tubal EPs can and should be visualised on TVS prior to treatment[20,21,22,23,24,25]. Importantly, almost 75% of all ectopics will be identified on the initial TVS, the remainder will be classified as a "Pregnancy of Unknown Location" (PUL).

When a woman has a positive pregnancy test, and no intra- or extra-uterine pregnancy or retained products of conception (RPOC) is visualised using TVS, the pregnancy should be categorised as a PUL. This is a descriptive term rather than a pathological entity and is not interchangeable with "possible" or "query" EP. Approximately 10% of women with a PUL will have an EP confirmed at follow up TVS. The remainder represent either failed PULs or IUPs (viable or non-viable)[26,27]. Failure to visualise an EP is not due to an EP being missed at the primary scan but rather due to the EP being in its early stages and therefore too small to be seen[28]. Women with an ultrasound classification of PUL represent an additional workload for Early Pregnancy Unit (EPU) staff, however outpatient follow up of these women avoids unnecessary surgery without compromising care[29].

Many old edition textbooks recommend a transabdominal followed by a transvaginal ultrasound scan; this is still standard practice in many centres. The experience in our EPU is that transabdominal scanning is not required and should not be used routinely in the diagnosis of EP. TVS alone is well tolerated by women, avoids the need for a full bladder and allows palpation of pelvic organs under direct vision. This non-invasive modality results in superior image quality as well as allows for small EPs to be visualised clearly. The term "pseudo sac", which was coined with the introduction of transabdominal ultrasound, should be shelved with ancient ultrasound textbooks. In modern ultrasound practice, when using TVS intra-cavitary fluid or blood within the endometrial cavity should be easily distinguished from a true gestational sac which is eccentrically located within the endometrium and surrounded by an echogenic ring of trophoblast. We believe that "pseudo sac" is an outdated term and therefore should be consigned to the dustbin of history. Combined transabdominal ultrasound and TVS provides no more information than TVS alone[30].

A systematic approach is essential to diagnose tubal ectopic pregnancy using transvaginal ultrasound

The finding of an IUP almost always excludes the diagnosis of EP. However, it is important to maintain a high index of suspicion in the symptomatic woman or where the woman has conceived using ARTs. Spontaneously arising heterotopic pregnancies (combined intra- and extra-uterine pregnancies) are rare (1: 20,000–1: 50,000) but the rate after ART pregnancies may be as high as 1:100[31]. When the uterus is empty, the adnexae should be thoroughly and systematically inspected.

Thoroughly inspect the adnexae using TVS

The normal Fallopian tubes are not routinely visualised by ultrasound but pathological changes that distend the tubes can be clearly visualised[32]. Many, 95%, of EPs are tubal. The corpus luteum seen as a "ring of fire" on colour Doppler will be on the ipsilateral side in 70–85% of cases of tubal EP and when present is a useful marker. Approximately 60% are seen as an inhomogeneous mass or "blob sign" adjacent to the ovary and moving separately to it (Fig. 1); 20% appear as a hyper-echoic ring or bagel sign (Fig. 2); and 13% have an obvious gestational sac with a fetal pole, with or without fetal cardiac activity (Fig. 3).

The Pouch of Douglas (POD) should be inspected for the presence of fluid

Anechoic fluid is common and is most often physiological. If fluid in the POD has a "ground glass" appearance this suggests haemorrhage (Fig. 4). The presence of haemoperitoneum in association with a tubal EP does not necessarily indicate rupture of the tube but is currently an established contraindication to MTX or expectant management. Leakage of blood from the fimbrial end is common in tubal EPs. Even if tubal rupture has occurred, almost half will not have active bleeding at time of surgery[33].

Inspection of Morison's Pouch

If a women has blood in the POD, then a complimentary transabdominal scan should be done to inspect Morison's Pouch. This is the space between Glisson's capsule of the liver and Gerota's fascia of the kidney (Fig. 5a). We believe that this is the only time the abdominal probe is necessary. Presence of blood indicates significant intra-abdominal haemorrhage. In fact, if Morison's pouch is positive for blood, this equates to a minimum of 670 mL of blood in the intra-peritoneal cavity (when the transabdominal scan is performed in the supine position)[17,34] (Fig. 5b).

Non-tubal ectopic pregnancy

As previously mentioned, 5% of all EPs are non-tubal however they contribute disproportionately to the morbidity and mortality in women with an EP. We will now describe the different non-tubal EP locations and their ultrasound appearances.

Fig. 1: Inhomogeneous mass in the Fallopian tube or "Blob sign".

Fig. 2: Empty gestational sac in the Fallopian tube or "Bagel sign".

Fig. 3: Gestational sac with an embryonic pole and positive cardiac activity.

Fig. 4: Blood noted on TVS in the Pouch of Douglas.

Fig. 5a: Morison's pouch without blood present.

Fig. 5b: Morison's pouch with blood present.

Fig. 6: Interstitial pregnancy. The gestational sac is located 1 cm lateral to the endometrium in a woman with a sub-septate uterus.

Fig. 7: Cervical pregnancy. The gestational sac is located below the level of the cervical internal os. Absence of the "sliding sign" clinches the ultrasound diagnosis.

Fig. 8a: Ovarian ectopic pregnancy.

Fig. 8b: Ovarian ectopic pregnancy which is highly vascular on colour Doppler assessment.

Fig. 9: Caesarean section scar ectopic pregnancy.

Interstitial pregnancy

Ultrasound diagnosis is based on the absence of an intra-uterine pregnancy with the presence of trophoblastic tissue located outside of the endometrial cavity (in that part of the Fallopian tube which traverses the myometrium). Interstitial pregnancies are surrounded by a thin myometrial mantle or continuous rim of myometrium. Traditionally, these tended to rupture at between 8–16 weeks because of the greater distensibility of the myometrium compared to the Fallopian tube. These pregnancies are highly vascular with blood supply from both the ovarian and uterine vessels and when rupture occurs, haemorrhage is profuse (Fig. 6).

Cervical pregnancy

Cervical pregnancy is rare with an incidence of one in 8600–12,400 pregnancies[9]. Ultrasound diagnosis is based upon an empty endometrial cavity, the cervix is barrel shaped and the gestational sac is implanted below the level of the uterine arteries, i.e. below the level of the internal cervical os. There is an absence of a "sliding sign" (when pressure is applied to cervix using the probe in a miscarriage, the gestational sac slides against the endocervical canal, but does not do so in a pregnancy implanted in the endocervix). Early detection and treatment of cervical pregnancy with MTX may prevent the need for hysterectomy. Previously, diagnosis was often made at D&C when massive haemorrhage ensued. Prior to 1979, 90% of cases underwent lifesaving hysterectomy (Fig. 7).

Interstitial and cervical pregnancies are most often treated with MTX in order to preserve the uterus and subsequent fertility. Surgery in inexperienced hands has a high risk of haemorrhage.

Ovarian ectopic pregnancy

Ultrasound diagnosis of an ovarian ectopic pregnancy may

Fig. 10: Heterotopic pregnancy.

be difficult to distinguish from ovarian germ cell tumours or other ovarian pathology. A high index of suspicion is based upon a combination of ultrasound findings (both grey scale and with colour Doppler), as well as high levels of serum hCG and sonographic experience. Nearly a third of women present with haemodynamic instability because of rupture. Diagnosis is based on the classic description of a cyst with a wide echogenic outer ring[35]. Ovarian ectopic pregnancies are most often treated surgically (Figs. 8a and 8b).

Caesarean section scar ectopic pregnancy

Caesarean section scar ectopic pregnancy (CSEP) seems to be diagnosed more than ever. This is primarily the result of increased awareness of the condition by EPUs. Although 19% of women will have a defect in the anterior myometrium at the level of the previous caesarean scar, only one in 1800–2200 pregnancies will have a CSEP[36]. The biggest risk in this rare form of EP is uterine rupture, haemorrhage and hysterectomy. Ultrasound diagnosis is based upon an empty endometrial cavity, and the gestational sac is located in the lower anterior myometrium at the level of the previous caesarean scar (Fig. 9). As with the cervical pregnancies, the "sliding sign" is absent.

Heterotopic pregnancy and bilateral tubal ectopic pregnancy

The spontaneous occurrence rate is between one in 10,000 to 1:50,000. However in ARTs, the rate may be as high as one in 100. Early detection not only prevents maternal morbidity and mortality but may also permit the salvage of the intrauterine pregnancy (Fig. 10). Bilateral tubal ectopic pregnancies are very rare with an estimated prevalence of 1:200,000[37].

Summary

Ultrasound diagnosis of EP using TVS is not only expected in the 21st century but should be the benchmark standard for all units involved with early pregnancy ultrasound. Early ultrasound diagnosis of EPs decreases mortality, surgical intervention and enables non–surgical conservative treatments to be offered. Laparoscopy is not necessary as a diagnostic tool in the modern management of women with EP. TVS is the new gold standard and diagnostic tool of choice for all forms of EP, both tubal and non-tubal. The vast majority of women who present with an EP can be diagnosed reliably using TVS as a single stand-alone test.

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