REVIEW

Review of Ectopic Pregnancies: Current Management Based on Ultrasound Findings

Herminia Al-Saffar, MD*

It has become imperative for radiologists and obstetricians to be familiar with the diagnosis and management of patients clinically at risk from ectopic pregnancy. The following is a brief review of ectopic pregnancies (EPs) and the currently accepted management of these patients.

Clinical Presentation

The incidence of implantation of the fertilised oocyte outside the uterine cavity is increasing. Studies in the United States showed a two fold increase in the 1970s and a three fold increase in the 1980s, accounting for about 5% of maternal deaths[1,2]. This was primarily due to the increased incidence of pelvic inflammatory disease, increased use of fertility drugs and surgical procedures, and better diagnostic imaging techniques which allowed for earlier diagnosis (10%–50% of EPs are thought to undergo spontaneous abortion or resorption in situ, if left alone)[3].

Whilst the incidence of EPs is increasing, the death rate has decreased from 3.5 deaths per 1,000 cases in 1970 to 0.8 in 1979 – 1980[1]; this is most likely the result of earlier diagnosis.

The clinical presentation of EPs is often non-specific. The "classic" clinical triad of pelvic pain, abnormal vaginal bleeding and a palpable adnexal mass is present in about 45% of patients with proven EPs[4]. Of 154 patients with proven EPs, 97% had pain, 86% had abnormal vaginal bleeding, 61% reported "missing" a menstrual period; only 41% had a palpable adnexal mass, 23% had a questionable adnexal mass and in 36% no mass was palpable[5].

Risk Factors

Any disease process or surgical procedure that causes pelvic adhesions, scarring or kinking of the fallopian tubes, will put the patient at increased risk by preventing or delaying the passage of the fertilised ovum into the uterine cavity. These risk factors include:

a) a prior history of pelvic inflammatory disease (30% to 50% of women with proven EPs have had a history of acute salpingitis)

b) a previous EP

c) prior tubal reconstructive surgery

* Chief Medical Resident
Radiology Department
Salmaniya Medical Centre
State of Bahrain

d) pregnancy following laparoscopic tubal coagulation for the induction of sterility (up to 50% of the women in whom the procedure fails to prevent pregnancy will have EPs)

e) endometriosis

f) developmental abnormalities of the tubes

Pregnancy with an IUCD in proper position also puts the patient into the high risk category. It should be stressed that the IUCD does not cause ectopic implantation of the fertilised ovum. The IUCD is effective only in preventing intrauterine implantation. Therefore, a patient who has a positive pregnancy test and an IUCD in proper position is at greater risk of harbouring an ectopic pregnancy[8].

The most important point, however, is that all women of childbearing age are at risk. The clinician must therefore have a high degree of clinical suspicion of any woman with a positive pregnancy test who presents with pelvic pain, with or without abnormal vaginal bleeding.

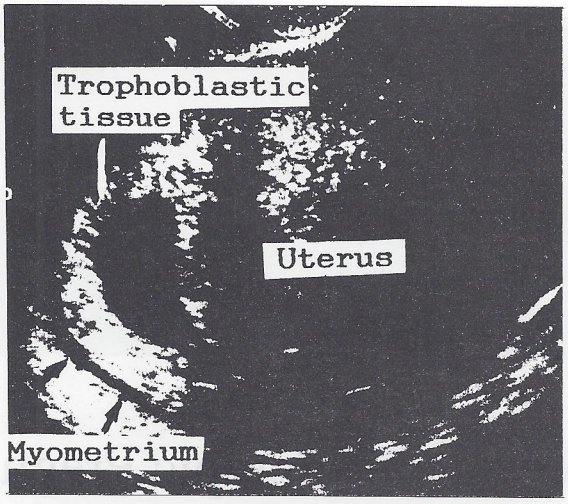

Figure 2: *Example of an interstital pregnancy. The gestational sac and surrounding echogenic trophoblastic tissue lie eccentrically within the uterus. The hypoechoic myometrium is very thin, measuring less than 5mm.*

Location of Ectopic Pregnancies

Almost all EPs are located in the Fallopian tubes. About 95% to 97% occur in the ampulla or isthmus (Fig 1). Only 2% to 5% occur in the cornual or interstitial portion of the Fallopian tube. On rare occasions an EP will occur in the ovary, the cervix, the fimbria of the Fallopian tube or outside the reproductive tract and within the abdominal cavity[9].

The interstitial EP may appear as a normal intrauterine pregnancy to the untrained observer during ultrasound. The diagnosis depends upon visualisation of a gestational sac eccentrically positioned within the uterine cavity, covered by a thin rim of myometrium measuring 5mm or less (Fig 2)[10].

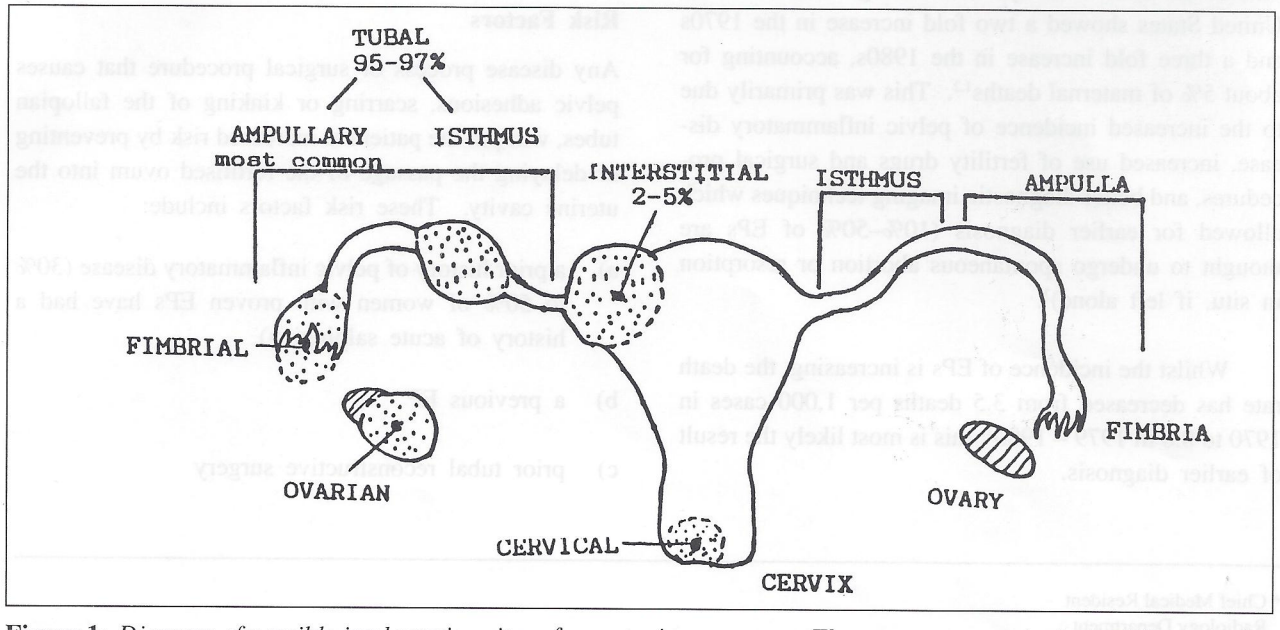

Figure 1: *Diagram of possible implantation sites of an ectopic pregnancy. The most common site is the fallopian tube, where about 95-97% of EPs occur. Rare sites include the ovary, cervix and fimbria.*

Pregnancy Tests

Measurement of human chorionic gonadotropin (hCH) in the urine or blood is the basis of a pregnancy test. This hormone is elaborated by the trophoblastic tissue. In a normal pregnancy, hCG doubles every two days for about the first six weeks.

The urine immunologic test for pregnancy may be falsely negative in 20% to 50% of EPs[4]. This is due to the lower levels of circulating chorionic gonadotropins produced by the EP and to the relative insensitivity of these tests.

Development of the highly sensitive chorionic gonadotropin radioimmune assays (RIA) to detect serum levels of human chorionic gonadotropin (hCG) have changed the management of patients with suspected EPs. The antibodies used are specific to the beta subunit of the hormone. RIA can detect 1-2mIU/ml of hCG whereas the haemaglutination inhibition tests used in the past had a minimum threshold of 250-1,000 mIU/ml hCG[11].

There are two standards for the measurement of hCG activity. The Second International Standard (2nd IS) was first developed in the 1960s. A more purified form, the First International Reference Preparation (IRP), was later developed.

The knowledge of which standard the laboratory utilises is important. The level of hCG will be correlated to the ultrasound findings and may be pivotal in management of the patient.

The unit value of hCG in biological units varies by a factor of approximately two between the two standards. For example, 100mIU/ml (2nd IS) is equal to approximately 200mIU/ml (IRP).

Diagnosis of Early Intrauterine Pregnancy Versus Endometrial Changes in an Ectopic Pregnancy

Hormones produced by the EP can stimulate the endometrium, resulting in changes similar in appearance to those seen with an early intrauterine pregnancy during ultrasonographic examination. The endometrium may thicken and become hyperechoic, forming a decidual cast[12]. The appearance is similar to what one might see with an incomplete abortion. About 10% to 20% of EPs have a small intrauterine collection of fluid that may simulate a gestational sac and is therefore called a pseudogestational sac[12].

Visualisation of the yolk sac or embryo is a conclusive sign of a gestational sac. The yolk sac can be seen at six and a half weeks (menstrual age) and the embryo at seven weeks via transabdominal sonography[13]. The gestational sac itself will be seen as early as five weeks. It is between five and six and a half weeks when the gestational sac becomes visible but it is when definitive signs of an intrauterine pregnancy appear (ie. yolk sac or embryo) that one must be careful not to interpret the pseudogestational sac of an EP as a normal intrauterine pregnancy.

The double decidual sac sign (DDSS), described as specific for an early intrauterine pregnancy (IUP), consists of two concentric rings surrounding a portion of the gestational sac[14]. These concentric rings represent the decidua vera adjacent to the decidua capsularis (Figs 3 & 4). When neither the embryo nor yolk sac is visible, the DDSS should be sought to diagnose a normal intrauterine pregnancy. The pseudogestational sac of an EP will be surrounded by only a single echogenic ring.

Although the DDSS is accepted as specific for an IUP, follow-up examination is recommended to confirm normality of the IUP[14].

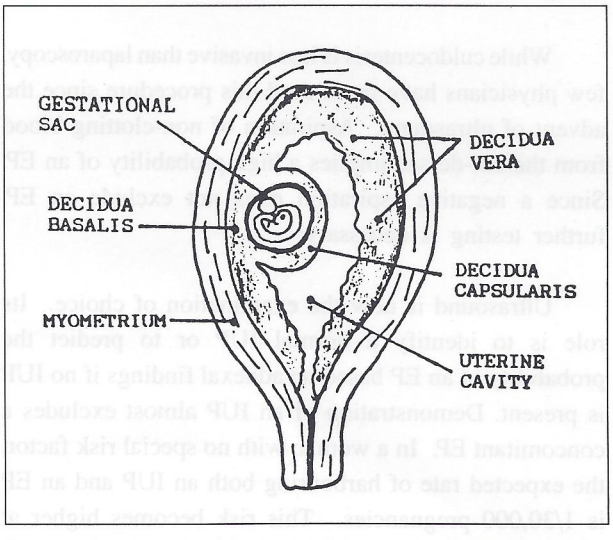

Figure 3: *The double decidual sac sign is composed of the decidual capsularis adjacent to the decidua basalis.*

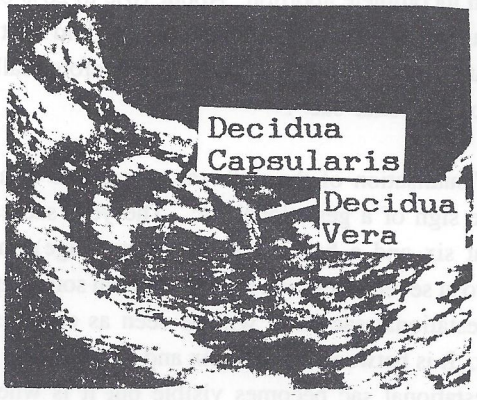

Figure 4: *Identification of the double decidual sac sign is considered to be specific for an early intrauterine pregnancy. Here the decidua vera and decidua capsularies are clearly seen due to the presence of a small amount of fluid within the uterine cavity.*

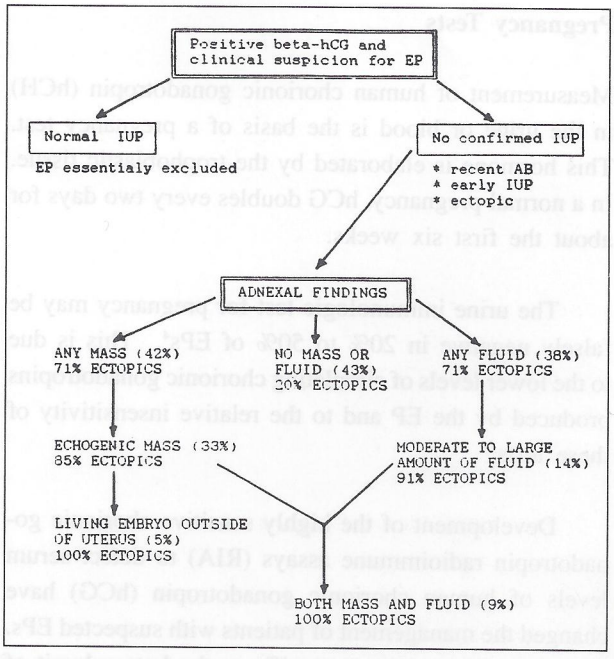

Figure 5: *Flow chart of a patient's risk of harbouring an ectopic pregnancy based on sonographic findings. This is based on a study of 219 patients who had positive beta-hcH levels and who were clinically at risk of an ectopic pregnancy.*

Evaluation of the Patient at Risk from an Ectopic Pregnancy

A positive pregnancy test confirms pregnancy but not whether there is a normal or abnormal IUP, recent spontaneous abortion, or an EP.

While laparoscopy is probably the most accurate procedure in confirming the presence of an EP before surgery, its routine use is impractical. It is invasive and only about 10% to 16% of the patients in the clinically suspect group will have ectopics[15]. It may also lead to iatrogenic compromise of a normal IUP.

While culdocentesis is less invasive than laparoscopy, few physicians have performed this procedure since the advent of ultrasound. Aspiration of non-clotting blood from the cul-de-sac implies a high probability of an EP. Since a negative aspiration does not exclude an EP, further testing is necessary.

Ultrasound is now the examination of choice. Its role is to identify a normal IUP or to predict the probability of an EP based on adnexal findings if no IUP is present. Demonstration of an IUP almost excludes a concomitant EP. In a woman with no special risk factor, the expected rate of harbouring both an IUP and an EP is 1/30,000 pregnancies. This risk becomes higher at 1/7,000 pregnancies for those women who are undergoing ovarian stimulation, as these will produce multiple ova per cycle[16].

In the absence of an IUP, the probability of an EP can be predicted, based on adnexal changes. The statistics come from a prospective study of 219 patients who had measurable levels of hCG and were clinically at risk from an EP[17] (Fig 5). The results revealed that the presence of any adnexal mass or free fluid puts the patient at a 71% risk of harbouring an EP. If the mass is echogenic the risk is slightly higher at 85%. If there is a moderate to large amount of free fluid the risk rises to 91%. Presence of both a mass and fluid or a living embryo outside the uterus, puts the patient at 100% risk of an EP. It is important to note that 20% of the patients with EPs had normal sonographic examinations.

Management of the patient depends upon the adnexal findings. As the presence of free fluid or an adnexal mass puts the patient at a 71% risk of harbouring an EP, further evaluation with laparoscopy is indicated. Direct laparotomy is indicated for those patients with either a living extrauterine embryo or an adnexal mass with free pelvic fluid.

If the ultrasound examination is normal, the next step is to quantitate the beta hCG levels. Via the transabdominal approach, sonography can detect all

normal singleton gestational sacs when the hCG level exceeds 3,600 mIU/ml (IRP) or 1,800 mIU/ml (2nd IS). Therefore, if the hCH level is greater than 3,600 mIU/ml (IRP) and there is no identifiable IUP, it is highly unlikely that the patient has a normal singleton intrauterine gestation.

It is uncommon for a patient who has recently spontaneously aborted to have a hCG level greater than 3,600 mIU/ml (IRP). A study of 39 such patients showed that only four had a hCG greater than 3,600 mIU/ml (IRP) and all four had a history of recent passage of tissue[18].

Therefore, the diagnosis of an EP should be strongly suspected in a patient with a hCG greater than 3,600 mIU/ml (IRP) or 1,800 mIU/ml (2nd IS) and no sonographic evidence of an IUP. Further evaluation with laparoscopy is indicated.

If the hCG level is below 3,600 mIU/ml (IRP), one should proceed either to a endovaginal sonography, or if this is not available, repeat the quantitative hCG in about two days time. If there has been a recent spontaneous abortion these levels will show a substantial decline within the same time- frame. EPs have subnormal increases in the hCG. Occasionally an EP will show a normal doubling time over 48 hours, simulating an IUP or a decline simulating a recent spontaneous abortion. If there is any doubt and clinically the patient is stable, serial hCG levels and repeat ultrasound may be necessary.

Use of Endovaginal Sonography in the Diagnosis of Ectopic Pregnancies

Evaluation of the uterus, via the transvaginal approach, allows for identification of a normal IUP at least one week earlier than is possible with the transabdominal technique. By decreasing the distance of the transducer to the uterus and by utilising a higher frequency transducer (usually 5 or 7.5 MHz), resolution is improved. A pregnancy can be identified as early as 32 days and with a hCG level as low as 1,000 mIU/ml (IRP) versus 3,600 mIU/ml (IRP) with the transabdominal approach[19].

An ectopic tubal ring has been described with the endovaginal approach in 49% of patients with EPs and 68% of unruptured tubal pregnancies. The tubal ring is a concentric echogenic ring created by the trophoblast of the ectopic pregnancy surrounding the chorionic sac. This sign is most useful in differentiating a corpus luteal cyst from an EP. The corpus luteal cyst will lie eccentrically within a rim of ovarian tissue and will not have an associated echogenic ring[10].

The transvaginal approach is also more sensitive to free echogenic pelvic fluid or blood clots in the cul-de-sac in patients without sonographic evidence of IUP. Small amounts of free anechogenic fluid are non-specific and may be present in normal patients.

Colour and pulse doppler are also useful in diagnosing an EP. Blood flow from the trophoblastic tissue has a high velocity, low resistance waveform. Although there is some overlap, the pattern is different from that of a corpus luteal cyst which has a low velocity, low resistance tracing. A normal ovary will have a high resistance tracing[20].

New Treatment

The goal in early diagnosis is to identify the EP before tubal rupture and to treat so as to minimise tubal scarring whilst maintaining tubal patency. Recently, a more conservative surgical approach has been utilised in small, unruptured EPs. At laparoscopy the tube is incised longitudinally over the implantation site and microdissection is used to remove the gestational sac. The incision is then left to heal by secondary intention. In one study, six out of 12 women had subsequent successful pregnancies and two had another tubal pregnancy[21,22].

Non-surgical management has also been successful in the treatment of early EPs. Cell growth inhibitors such as methotrexate are injected parenterally and the serum hCG levels are followed closely. Methotrexate kills the rapidly dividing trphoblastic cells, which are resorbed. Ideally, patency of the tubal lumen is preserved[23].

Endovaginal-guided salpingocentesis with injection of methotrexate or potassium chloride solution into the gestational sac has also had success[24].

CONCLUSION

The incidence of ectopic pregnancies is on the rise and therefore the radiologist and obstetrician must be familiar with the clinical presentation and

management, based on sonographic and laboratory findings. As we have seen, a woman who is in the clinically suspect group, with a positive hCG and normal sonogram, is still at a 20% risk from an EP. By utilising endovaginal sonography and/or serial quantitative hCG levels, the correct diagnosis can be achieved.

REFERENCES

1. Dorfman SF. Deaths from ectopic pregnancy, United States 1979 to 1980. Obstet Gynecol 1983;62:344.
2. Rubin GL, Peterson HB, Dorfman SF, et al. Ectopic pregnancy in the United States: 1970 through 1978. JAMA 1983;249:1725.
3. Pritchard JA, MacDonald PC, Gant FN. Williams Obstetrics. 17th ed. Connecticut: Appleton-Century Crofts, 1985:424.
4. Schwartz RO, Di Pietro DL. Beta-hCG as a diagnostic aid for suspected ectopic pregnancy. Obstet Gynecol 1980;56:197-203.
5. Weinstein L, Morris MD, Dotters D, Christian CD. Ectopic pregnancy - A new surgical epidemic. Obstet Gynecol 1983;61:698.
6. Breen J. A 21 year survey of 654 ectopic pregnancies. Am J Obstet Gynecol 1970;106:1004.
7. McCausland A. High rate of ectopic pregnancy following laparoscopic tubal coagulation failures, incidence and etiology. Am J Obstet Gynecol 1980;136:97.
8. Lawless M, Vassey M. Risk of intrauterine contraceptive devices (Letter). Br Med J 1984;288:1919.
9. Filly RA. Ectopic Pregnancy. In: Callen PW. Ultrasonography in Obstetrics and Gynecology. Philadelphia: WB Saunders, 1988:448.
10. Fleischer AC, Pennell RG, McKee MS, et al. Ectopic pregnancy: features at transvaginal sonography. Radiology 1990;174:375-8.
11. Pritchard JA, MacDonald PC, Gant NF. Williams Obstetrics. 17th ed. Connecticut: Appleton Century-Crofts, 1985:215.
12. Marks Wm, Filly RA, Dallen PW, et al. The decidual cast of ectopic pregnancy: A confusing ultrasonographic appearance. Radiology 1979;133:451.
13. Nyberg DA, Filly RA, Mahony BS, et al. Early gestation: Correlation of hCG levels and sonographic identification. AJR 1985;144:195.
14. Nyberg DA, Laing FC, Filly RA, et al. Ultrasonographic differentiation of the gestational sac of early intrauterine pregnancy from the pseudogestational sac of ectopic pregnancy. Radiology 1983;146:755.
15. Pederson JF. Ultrasounic scanning in suspected ectopic pregnancy. Br J Radiol 1980;53:1.
16. Berger MJ, Taymor ML. Simultaneous intrauterine and tubal pregnancies following ovulation induction. Am J Obstet Gynecol 1983;146:323.
17. Mahony BS, Filly RA, Nyberg DA, et al. Sonographic evaluation of ectopic pregnancy. J Ultrasond Med 1985;4:221.
18. Nyberg DA, Filly RA, Filho DL, et al. Abnormal pregnancy: Early diagnosis by US and serum chorionic gonadotropin levels. Radiology 1986;158:393.
19. Bree RL, Edwards ML, Bohm-Velez, et al. Transvaginal sonography in the evaluation of normal early pregnancy: correlation with hCG level. AJR 1989;153:75-9.
20. Taylor KW, Ramos IM, Feycock AL, et al. Ectopic pregnancy: duples Doppler evaluation. Radiology 1989;173:93-7.
21. DeCherney AH, Maheaux R, Naftolin F. Salpingostomy for ectopic pregnancy in the sole patent oviduct. Reproductive outcome. Fertil Steril 1982;37:619.
22. Stagel JJ. Recent techniques for the conservative management of tubal pregnancy. J Reprod Med 1986;31:98-101.
23. Ory SJ, Villanueva AL, Sand PK, et al. Conservative treatment of ectopic pregnancy with methotrexate. Am J Obstet Gynecol 1986;154:1299-1306.
24. Timor-Tritsch I, Baxi L, Peisner DB. Transvaginal salpingocentesis: A new technique for ectopic pregnancy. Am J Obstet Gynecol 1989;160:459-61.