First, Do No Harm . . . to Early Pregnancies

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When a woman of childbearing age presents to a physician or other caregiver complaining of vaginal bleeding and/or pelvic pain, a pelvic ultrasound examination is often performed to assess the etiology of her symptoms.[1,2] If she has a positive pregnancy test, the major role of ultrasound is to assess whether she has a normal intrauterine pregnancy (IUP), an abnormal IUP, or an ectopic pregnancy. The information provided by ultrasound can be of great value in guiding management decisions and improving outcome.

Errors in ultrasound interpretation, however, can lead to mismanagement and, thereby, to bad pregnancy outcome. Potential interpretation errors include: (1) failure to conclude that there is a definite or probable IUP despite ultrasound images depicting such a finding; and (2) failure to conclude that there is a definite or probable ectopic pregnancy despite ultrasound images depicting such a finding. This editorial focuses on the former error.

Definition and Scope of the Problem

The issue addressed here involves the situation in which a woman with a positive pregnancy test and symptoms of bleeding and/or pain undergoes a pelvic ultrasound examination, and the scan demonstrates a nonspecific intrauterine fluid collection (Figure 1). By "nonspecific," we mean a fluid collection with curved edges in the central echogenic portion of the uterus (ie, in the decidua) with no visible embryo or yolk sac, that does not demonstrate one of the published signs of early IUP (double sac sign[3] or intradecidual sign[4]).

As we will show below, such a nonspecific intrauterine fluid collection is highly likely to be an IUP and should be reported as such. The failure to interpret and report sonograms in this way can lead to serious errors in patient management and to unfortunate outcomes, as illustrated in the following hypothetical case. A 25-year-old woman with a positive pregnancy test and pelvic pain is referred for an ultrasound examination. One of the sonographic images shows a small oval fluid collection in the decidua, with no visible embryo or yolk sac. The fluid collection does not demonstrate a double sac sign or intradecidual sign, and the physician interprets the study as showing no IUP. The patient is treated with intramuscular injection of methotrexate for presumed ectopic pregnancy. A follow-up scan 1 week later shows an IUP with an embryo but no heartbeat.

Ultrasound interpretation errors involving the failure to diagnose a definite or likely IUP, thus leading to an intervention that poses serious risk to the pregnancy (eg, uterine evacuation or administration of an embryotoxic medication), can contribute not only to embryonic demise—as in the above example—but also to fetal malformations.[5] There are no data on how often such errors occur, and it would be difficult or impossible to collect reliable data. But we have strong anecdotal evidence that it happens distressingly frequently. We have heard from numerous colleagues of cases at their institutions, and we are aware of several medical malpractice suits involving cases like that described in our hypothetical example: ultrasound showed a nonspecific intrauterine fluid collection in a woman with a positive pregnancy test complaining of pain and/or bleeding; the interpreting physician erroneously failed to report a likely IUP; methotrexate was administered for presumed ectopic pregnancy; and embryonic demise or birth of a malformed baby followed.

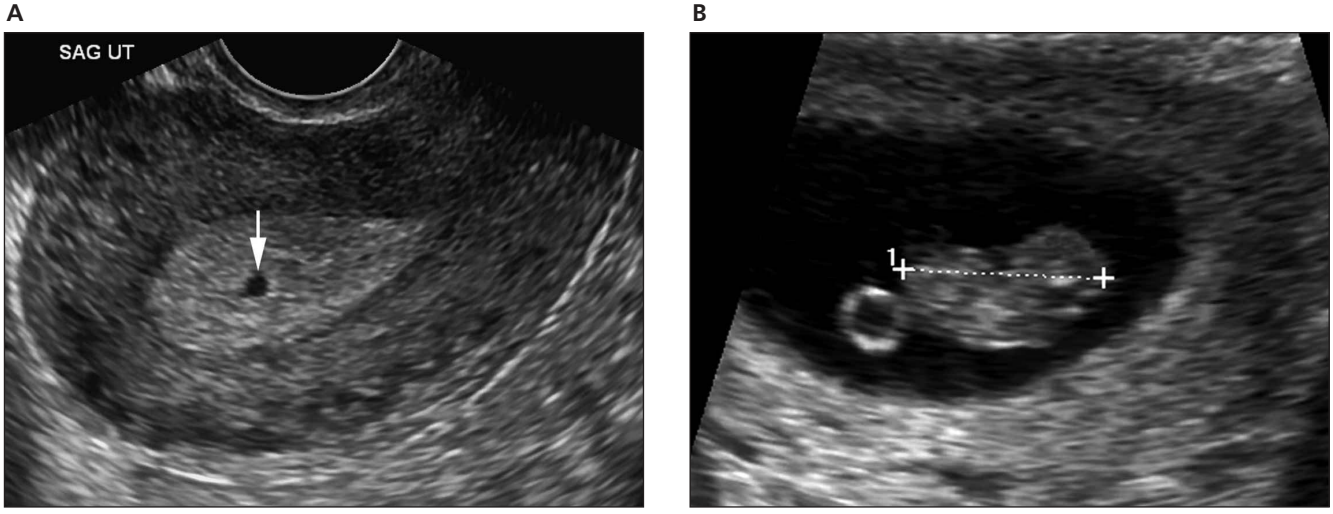
Why do such errors occur, and how can they be prevented? The errors result both from misinterpretation of the published signs of early pregnancy (especially the double sac sign) and from misapplication of the concept of the "pseudogestational sac."

Source of the Problem: 1. Misinterpretation of Published Sonographic Signs of Early Pregnancy

The double sac sign (sometimes called the "double decidual sac" sign) was first described and studied in 1982[3] as a means of excluding a diagnosis of ectopic pregnancy. The sign is present when two concentric echogenic bands are seen around an intrauterine fluid collection. These bands are thought to represent two layers of decidua—the decidua capsularis and the decidua vera—that surround most of an intrauterine gestational sac. The correct use of this sign, supported by the data in the initial and subsequent studies, is: *if a double sac sign is present, then there is an IUP (and hence ectopic pregnancy is virtually excluded)*. The data indicate that the converse—*if there is no double sac sign, then there is no IUP*—does not hold. In the original paper,[3] 34 of 44 patients (77.3%) with an IUP had a double sac sign, whereas none of the study patients with an ectopic pregnancy had a double sac sign. This clearly indicates that absence of the double sac sign does not exclude an IUP.

Another sonographic sign of early pregnancy, the intradecidual sign, was first described and studied in 1986.[4] This initial report found the intradecidual sign to be present in 33 of 36 IUPs

Figure 1. Intrauterine pregnancy. **A**, Ultrasound at 5 weeks' gestational age demonstrates a fluid collection (arrow) in the decidua, with curved edges and no characteristic features of a gestational sac: no double sac sign, intradecidual sign, yolk sac, or embryo. This is what we refer to as a "nonspecific intrauterine fluid collection." **B**, A follow-up scan 4 weeks later demonstrates a normal-appearing 9-week embryo (demarcated by calipers measuring the crown-rump length).



(91.7%). Like the double sac sign, the absence of the intradecidual sign did not unequivocally exclude an IUP.

Subsequent studies have found the double sac and intradecidual signs to be present in a smaller fraction of IUPs than in the original reports. A 1996 study[6] found that, among 94 IUPs without a visible embryo, yolk sac, or amnion, a double sac sign was present in 50 (53.2%). A study of the intradecidual sign in 1997[7] found it to be present in 31 of 91 IUPs (34.1%) and absent or indeterminate in the remaining 60 IUPs, and a subsequent study in 2004[8] found that obstetric imagers rated the sign as definitely or probably present in 92 of 153 IUPs (60.1%).

Our own experience corroborates these subsequent studies. We recently retrieved the records of all ultrasound examinations performed between January 2006 and December 2008 at our institution that met the following criteria: an initial ultrasound scan demonstrated an intrauterine fluid collection without a yolk sac or embryo, and a follow-up scan confirmed an IUP by demonstrating a yolk sac or embryo. There were 104 cases that met our criteria. We independently reviewed these cases, all of which included transvaginal images and most of which included video clips. One of us (P.M.D.) characterized the double sac sign as present in 37 (35.6%) of the initial sonograms, while the other (C.B.B.) noted a double sac sign in only 25 (24.0%). We also found that fewer than half the cases demonstrated an intradecidual sign. An important criterion for diagnosing an intradecidual sign is to demonstrate the gestational sac embedded in the decidua, not located in the uterine cavity, but the location of the uterine cavity could not be identified in 50 of our 104 cases (48.1%). Overall, we found that the appearance of our 104 early gestational sacs was highly variable.

We suspect that the lower frequency of the double sac and intradecidual signs with 21st century ultrasound scanners is directly related to the improved resolution of current equipment, as well as the routine use of transvaginal scanning, which was not widely available in the early-to-mid 1980s. Today's scanners can detect gestational sacs earlier in pregnancy than those of the 1980s, so it is to be expected that the sonographic findings of the earliest visible pregnancy will be different today than 25 years ago. Today's scanners also detect yolk sacs and embryos in smaller gestational sacs than was possible in the past, which also contributes to different occurrence rates of the double sac sign and intradecidual sign, since these signs are only applicable when there is no visible yolk sac or embryo. Finally, today's scanners are less likely to make hypoechoic areas of the decidua appear to be anechoic fluid.

Since the ultrasound literature does not support or advocate an *if there's no double sac sign, then there's no IUP* "rule," why is there an apparent misconception among many practitioners that this "rule" can be used? This probably occurs because the language in some of the scientific literature, review articles, and book chapters is somewhat ambiguous or misleading. Examples include: "the double sac is a reliable morphologic sign of early IUP"[3]; "the finding of a double decidual sac at ultrasonography is useful in making an early diagnosis of IUP"[9]; "the true intrauterine gestational sac actually has two echogenic rings, described as the double decidual sac sign"[10]; and "It is of utmost importance to always identify these two layers or rings."[11] It is easy to see how someone who reads these words could misinterpret them and erroneously conclude that a nonspecific intrauterine fluid collection is highly unlikely to be a gestational sac because it does not demonstrate the double sac sign.

Source of the Problem: 2. Misuse of the Concept of "Pseudogestational Sac"

Misuse of the concept of pseudogestational sac (also termed "decidual cast" in the early obstetric ultrasound literature[12]) is another factor contributing to the type of error described here. "Pseudogestational sac" refers to fluid (blood or secretions) in the uterine cavity that is occasionally seen in a woman with ectopic pregnancy. The frequency of a pseudogestational sac in women with ectopic pregnancies was initially reported to be 20%,[12] but more recent studies have found a somewhat lower incidence of approximately 10%.[13–15] It is likely that many of the early descriptions of pseudogestational sacs were due to hypoechoic areas in the decidua

appearing anechoic, since we have rarely seen pseudogestational sacs in recent years, despite a high volume of ectopic pregnancies scanned at our institution.

Simple arithmetic shows that fluid in the uterus in a woman with a positive pregnancy test is far more likely to be a gestational sac than a pseudogestational sac, even if it is not surrounded by two echogenic rings. The relevant data are: ectopic pregnancies constitute about 2% of all pregnancies (based on the most recent data from the Centers for Disease Control and Prevention[16]); the double sac sign appears in about half of early IUPs; and a pseudogestational sac appears in at most 10% of ectopic pregnancies. From these data, it follows that when a nonspecific intrauterine fluid collection is seen, the odds favoring a gestational sac over a pseudogestational sac are approximately 245:1. To see this, consider a sample of 1000 early pregnancy sonograms in which there is an intrauterine fluid collection with no visible yolk sac or embryo. Of these pregnancies, 980 will be intrauterine, of which about 490 will lack a double sac sign. Of the 20 ectopic pregnancies, 2 will have a pseudogestational sac. Hence the odds favoring an IUP are 490:2, or 245:1. The odds may be even higher if, as we suspect, the frequency of pseudogestational sacs in ectopic pregnancies is even lower than 10%. Translating odds into probabilities: if a nonspecific intrauterine fluid collection is seen in a woman with a positive pregnancy test, the probability of it being a gestational sac is more than 99.5%, while that of a pseudogestational sac is less than 0.5%. The likelihood of a gestational sac is even higher—virtually 100%—if the fluid collection is not "nonspecific," but instead demonstrates a double sac or intradecidual sign or contains a yolk sac or embryo. (Note: a similar arithmetic exercise demonstrates that a nonspecific fluid collection in a woman with a positive pregnancy test is far more likely to be an IUP than a decidual cyst, which has been reported to be present in some cases of ectopic pregnancy.[17])

We have not commented on the quantitative β-human chorionic gonadotropin (β-hCG).[18–20] That is because, when attempting to differentiate between IUP and ectopic pregnancy, the quantitative β-hCG is helpful when no intrauterine fluid collection is seen on ultrasound. Specifically, if a patient's quantitative β-hCG is above a "discriminatory" level, the finding of no intrauterine fluid collection is worrisome for ectopic pregnancy.[2,11,21,22] This editorial, however, does not deal with cases in which there is no intrauterine fluid collection, instead addressing the situation in which a nonspecific fluid collection is seen on ultrasound.

This arithmetic exercise indicates that the notion of "pseudogestational sac" is of little or no value. If a scan shows a definite extrauterine pregnancy (such as an adnexal mass with an embryo and cardiac activity), then the presence or absence of a pseudogestational sac is clinically irrelevant. In virtually all other cases, it would be inappropriate (and potentially dangerous) to call a nonspecific intrauterine fluid collection a pseudogestational sac, because of the powerful odds in favor of it being a gestational sac. In accordance with *Occam's razor*[23] (also known as the *Law of Parsimony*) or its more familiar variant *when you hear hoofbeats, think horses, not zebras*: when you see fluid in the uterus, think gestational sac, not pseudogestational sac.

Besides probabilities, medical factors also favor considering a nonspecific intrauterine fluid collection to be a gestational sac until proven otherwise instead of a pseudogestational sac until proven otherwise. Administering an embryotoxic agent to, or evacuating the uterus of, a woman with an IUP—which could occur if a gestational sac is erroneously called a pseudogestational sac—is a serious error, whereas delaying treatment in a woman with ectopic pregnancy—which could occur if a pseudogestational sac is erroneously called a gestational sac—will often have little effect on outcome if the patient is medically stable.[24]

Conclusion

In summary, adherence to the following guidelines will prevent sonographic interpretation errors that result in harm to the developing embryo:

1. Do not misuse the double sac and intradecidual signs; absence of these signs does not mean that there is no IUP.
2. Avoid using the term "pseudogestational sac,"

since it is much more likely to lead to errors than to correct diagnoses.

3. Most importantly: In a woman with a positive pregnancy test, any fluid collection with curved edges in the central echogenic portion of the uterus should be interpreted as a probable gestational sac, and treatments that could damage the embryo should be avoided until IUP is definitely excluded.

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