Review

Sonography in First Trimester Bleeding

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ABSTRACT: Vaginal bleeding is the most common cause of presentation to the emergency department in the first trimester. Approximately half of patients with first trimester vaginal bleeding will lose the pregnancy. Clinical assessment is difficult, and sonography is necessary to determine if a normal fetus is present and alive and to exclude other causes of bleeding (eg, ectopic or molar pregnancy). Diagnosis of a normal intrauterine pregnancy not only helps the physician in terms of management but also gives psychologic relief to the patient. Improved ultrasound technology and high-frequency endovaginal transducers have enabled early diagnosis of abnormal and ectopic pregnancies, decreasing maternal morbidity and mortality. The main differential considerations of first trimester bleeding are spontaneous abortion, ectopic pregnancy, or gestational trophoblastic disease. This article reviews the causes of first trimester bleeding and the sonographic findings, including normal features of first trimester pregnancy. © 2008 Wiley Periodicals, Inc. *J Clin Ultrasound* **36**:352–366, 2008; Published online in Wiley InterScience (www.interscience. wiley.com). DOI: 10.1002/jcu.20451

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Vaginal bleeding is a common presentation in the emergency department during the first trimester. Approximately half of patients who present with vaginal bleeding have a spontaneous abortion.[1] The primary causes of first trimester bleeding are spontaneous abortion, ectopic pregnancy, and gestational trophoblastic disease; however, the most common cause of bleeding is spotting caused by implantation of the conceptus into the endometrium. A complete assessment of the first trimester pregnancy requires correlation of serum β human chorionic gonadotropin (β-hCG) levels with the appearance of the gestational sac (GS) using sonography.

SPONTANEOUS ABORTION

Spontaneous abortion is defined as the termination of a pregnancy before the twentieth completed week of gestation. Sixty-five percent of spontaneous abortions occur in the first 16 weeks of pregnancy. The frequency decreases with increasing gestational age. Genetic abnormalities cause 50–70% of spontaneous abortions.[2] The causes of spontaneous abortion are listed in Table 1. Recurrent abortion is defined as 3 or more consecutive spontaneous abortions. Recurrent abortion occurs in 0.4–0.8% of all pregnancies and is commonly caused by maternal and environmental factors.[3]

Sonographic findings in abortion depend on the patient's symptoms at the developmental stage. The classification and corresponding sonographic features seen in first trimester spontaneous abortion are listed in Table 2. The sonographic features should correlate with serum β-hCG and gestational age. The findings in an abnormal GS are also classified into gestational sac, yolk sac, and embryonic criteria.

Gestational Sac Criteria

The size of the GS also correlates with the health of the developing fetus. If a GS is small for gestational age (Figure 1), it carries a poor prognosis

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TABLE 1
Etiology of Spontaneous Abortion

Genetic or fetal causes		
		Trisomy
		Polypoidy or aneuploidy
		Translocations
Environmental or maternal causes		
	Uterine	
		Congenital uterine anomalies
		Leiomyoma
		Intrauterine adhesions or synechiae (Asherman's syndrome)
	Endocrine	
		Progesterone deficiency (luteal phase defect)
		Hypothyroidism
		Diabetes mellitus (poorly controlled)
		Luteinizing hormone hypersecretion
	Immunologic	
		Autoimmunity: antiphospholipid syndrome, systemic lupus erythematosus
	Infections	
		Toxoplasma gondii, Listeria monocytogenes, *Chlamydia trachomatis*, *Ureaplasma urealyticum*, *Mycoplasma hominis*, herpes simplex, *Treponema pallidum*, *Borrelia burgdorferi*, *Neisseria gonorrhea*.

TABLE 2
Sonographic Findings in Spontaneous Abortion

Type	Clinical Definition	Sonographic Features
Threatened abortion	Bleeding without cervical dilatation	Empty uterus or intrauterine gestational sac with or without an embryo (depends on the stage of gestation)
Incomplete abortion	Cervical dilatation with partial expulsion of products	Retained products of conception, endometrial blood, and trophoblastic tissue
Missed abortion	Fetal demise without expulsion of products*	Absence of cardiac activity; Eembryo may be small for gestational age
Complete abortion	Complete expulsion of products	Empty uterus with normal appearance of endometrium

* Patient may or may not present with bleeding.

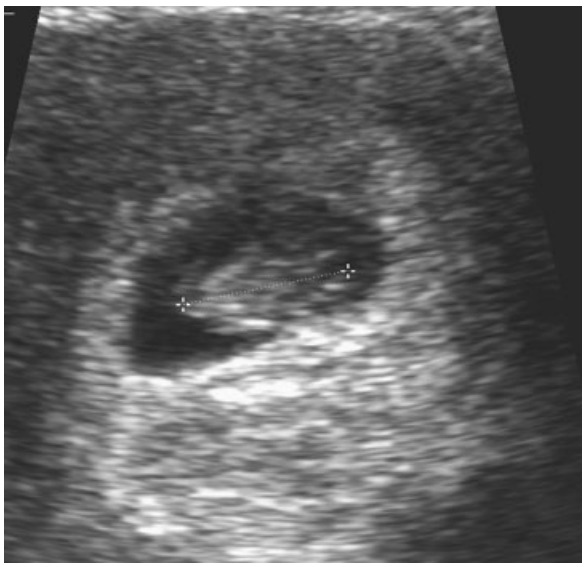

FIGURE 1. Sonogram shows a relatively small gestational sac compared with the embryo.

and a serial sonographic examination should be performed to assess the rate of growth.[4] A GS with a growth rate of <1 mm/day usually has a poor prognosis.[5] A small GS may be due to oligohydramnios, which is a predictor of poor outcome, even in the presence of normal embryonic cardiac activity.[5] As a rule of thumb, if the difference between the mean sac diameter (MSD) and crown–rump length (CRL) are <5 mm, there is an 80% risk of pregnancy loss.[5] Using transvaginal sonography, a GS with an MSD of ≥8 mm without a yolk sac and a GS with an MSD >16 mm without an embryo are important predictors of a nonviable gestation.[6] An empty sac without an embryo or yolk sac can be seen in an early intrauterine pregnancy, anembryonic pregnancy (blighted ovum), and a pseudogestational sac. A blighted ovum or anembryonic pregnancy is an early failure of the embryo to develop within the GS (Figure 2).[6] A pseudogestational sac is seen with an ectopic pregnancy and corresponds to intrauterine fluid collection rimmed by the endometrium. It is centrally located in the uterine cavity (a true sac is eccentric), has sharp angulations, and has an absent double decidual sign without a yolk sac.

The normal GS has a regular contour, whereas an abnormal sac has an irregular contour (Figure 3). Other findings that suggest an abnormal sac include a decidual reaction <2 mm, low position,

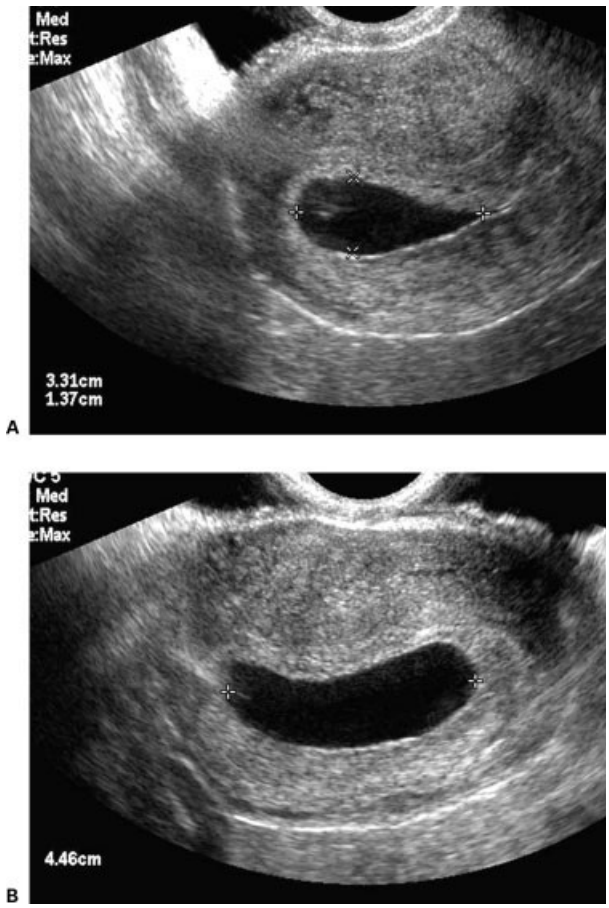

FIGURE 2. Anembryonic gestation. Sagittal **(A)** and transverse **(B)** sonogram of the uterus shows no embryonic pole. The absence of a yolk sac suggests an anembryonic gestation.

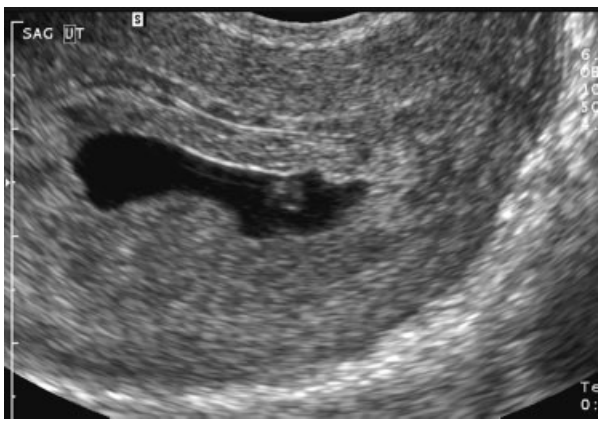

FIGURE 3. Sagittal transvaginal sonogram shows an abnormal gestational sac containing a yolk sac.

absent double decidual sac, decreased echogenecity of choriodecidual reaction, and a small sac.

Yolk Sac Criteria

The yolk sac increases in size during the first 6–10 weeks of gestation and then gradually decreases in size due to degeneration.[7] An abnormal sac is irregular in shape and can be smaller or larger than expected for gestational age (Figure 4). Failure to demonstrate a yolk sac in a GS with an MSD of $\geq$8 mm via transvaginal sonography is indicative of an abnormal gestation. Abnormal yolk sacs can also be calcified.[7]

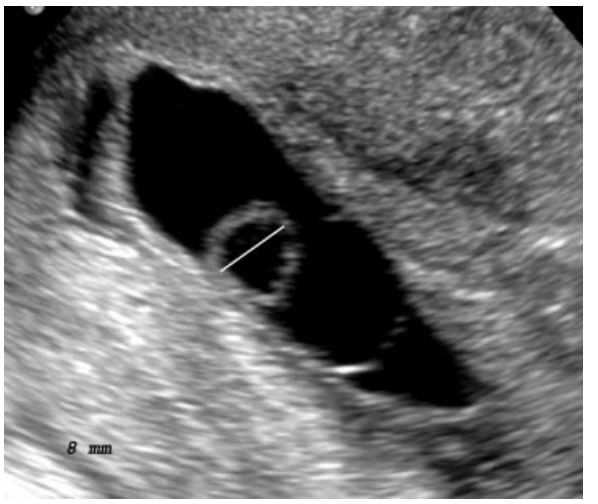

FIGURE 4. Transvaginal sonogram shows a large yolk sac measuring 8 mm.

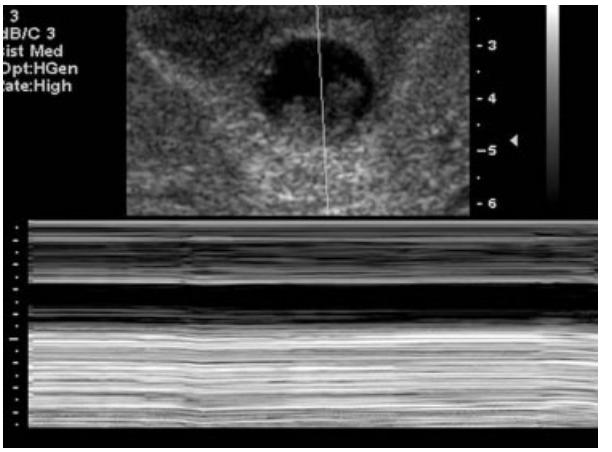

FIGURE 5. M-mode sonogram shows absence of a fetal heartbeat, confirming fetal demise.

Embryonic Criteria

Demonstration of embryonic cardiac activity in a patient with vaginal bleeding does not ensure future fetal viability, but its presence significantly decreases the risk of future pregnancy loss.[8] A definite diagnosis of embryonic demise can be made when there is no cardiac activity in an embryo with a CRL of $\geq$5 mm (Figure 5). Bradycardia is defined as a rate of $\leq$100 bpm at 6.2

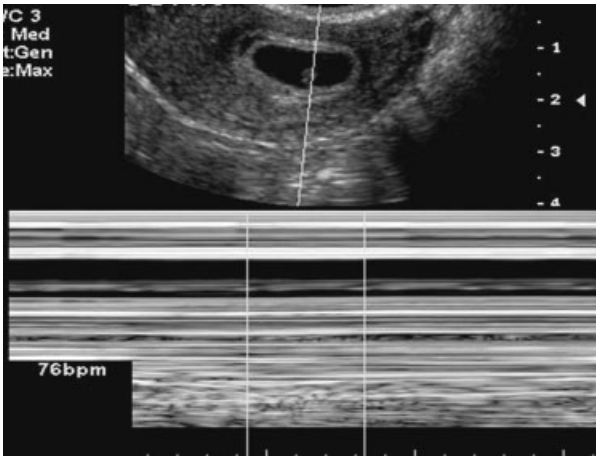

FIGURE 6. M-mode sonogram shows bradycardia with a fetal heart rate of 76 bpm.

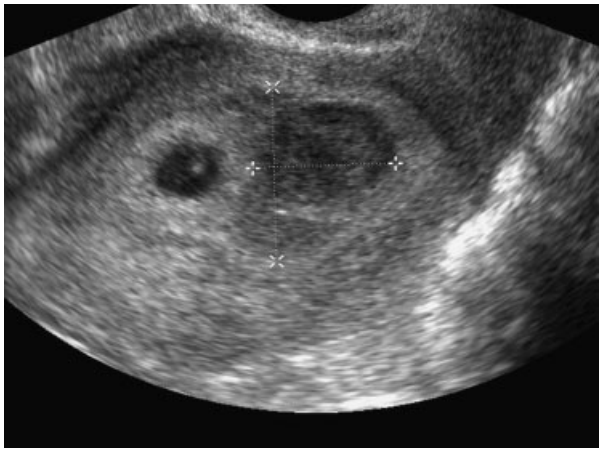

FIGURE 7. Sonogram shows a heterogenous cystic area (calipers) adjacent to the gestational sac consistent with a subchorionic hemorrhage.

weeks and ≤120 bpm at 6.3–7 weeks (Figure 6) and has a high association with spontaneous abortion.[9–11]

The following abnormal findings on transvaginal sonographic examination indicate embryonic demise: (1) no embryonic cardiac activity if the CRL is >5 mm; (2) no yolk sac is seen when the MSD is >8 mm; (3) no embryo is seen if MSD is >16 mm.

SUBCHORIONIC HEMORRHAGE

Subchorionic hemorrhage is defined as bleeding resulting in marginal abruption with separation of the chorion from the endometrial lining. The separation can extend to the margin of the placenta. On sonography, subchorionic hemorrhage is either hypoechoic or hyperechoic depending on the age of the blood products at the time of the scan (Figure 7). The majority of subchorionic hemorrhages occur in the late first trimester, and prognosis is generally good if the fetal heartbeat is seen and if the hemorrhage is not large. The size of the hemorrhage is determined based on the extent of chorionic membrane elevation or by calculating the volume of the hemorrhage.[12] Definite correlation between the size of the hemorrhage and pregnancy loss has not been confirmed, and there are conflicting views about this.[13,14] Hemorrhage in the fundus of the uterus is reported to have poor prognosis compared with that in the lower uterine segment.[15]

RETAINED PRODUCTS OF CONCEPTION

Retained products of conception (RPOC) can be seen in 1% of all pregnancies after an abortion or post partum. The incidence of retained products is increased in patients with a history of pregnancy termination and placenta accreta. Persistent vaginal bleeding after an abortion may be due to retained trophoblastic tissue,[16] but these women may also present with symptoms of infection, including pain and fever. Normal to mildly elevated β-hCG is common. Sonography is the preferred modality to diagnose retained products.

The absence of uterine contents or the presence of clear fluid has a strong negative predictive value for RPOC.[17–19] The presence of a GS makes the diagnosis of RPOC obvious. Findings on gray-scale transvaginal sonography are nonspecific with a thickened endometrial lining >8 mm and with or without hypoechoic material in the endometrial cavity (Figure 8). The endometrial blood clots may give a false positive diagnosis, because they appear similar. Therefore, the demonstration of vasculature within the uterine cavity contents with color or power Doppler is very useful to confirm the diagnosis and differentiate retained products from blood clots. The caveat is that color or power Doppler examination is not 100% sensitive for RPOC, so follow-up may be required in cases of intrauterine content without demonstrated vessels, because hypovascular or avascular (necrotic) RPOC may still be present.

In the presence of some uterine content and absence of vasculature with Doppler examination, the use of certain endometrial thickness measurements could be useful to differentiate clots from RPOC. The use of an 8-mm cutoff has been reported as 100% sensitive but 80% specific.[20] Some authors recommend the use of a 10-mm cutoff for clinically significant RPOC.[20] Differential diagnosis includes a normal postpartum uterus with blood clots, arteriovenous malformation, and gestational trophoblastic disease. Clinical assessment with serum β-hCG is important to differentiate these disorders.

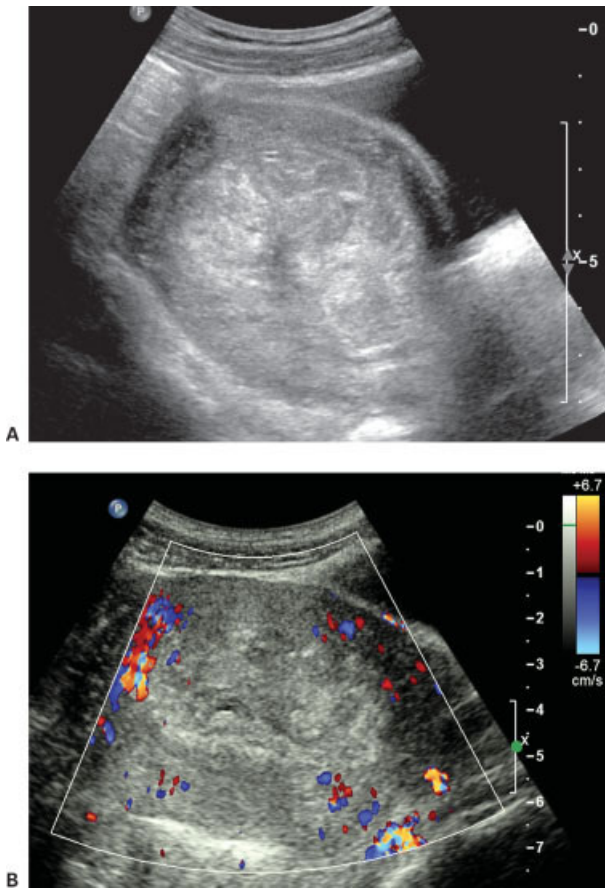

FIGURE 8. (A) Sagittal sonogram of a patient with postpartum bleeding and a positive β-hCG shows retained products of conception in the form of thickened endometrium containing a heterogenous mass. **(B)** Color Doppler sonogram shows mild vascularity within the mass.

TABLE 3
Location and Incidence of Ectopic Pregnancies

Location	Incidence
Fallopian tube	97%
Ampulla	55%
Isthmus	25%
Fimbria	15%
Ovary	3%
Cervix	3%
Interstitial	3%
Intra-abdominal	3%

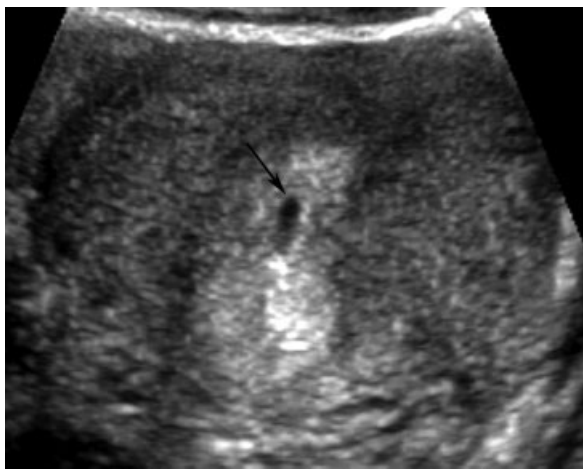

FIGURE 9. Coronal sonogram of the uterus shows a pseudo-gestational sac (arrow) in a patient with known ectopic pregnancy. Note the central location, lack of decidual reaction, and irregular shape.

ECTOPIC PREGNANCY

Ectopic pregnancy is still the leading cause of maternal deaths in first trimester pregnancies in the United States, accounting for 2% of all reported pregnancies and 9% of all pregnancy-related deaths from 1990 to 1992.[21] The prevalence of ectopic pregnancy varies with the patient population and their inherent risk factors, ranging from 10% to 40%.

Ectopic pregnancy is defined as a pregnancy that occurs outside the uterine cavity. The ectopic pregnancies can be classified by location (Table 3).[22] Predisposing factors for ectopic pregnancy include previous pelvic inflammatory disease, tubal surgery, previous ectopic pregnancy, intrauterine contraceptive device use, and endometriosis. The classical clinical triad seen is pain, abnormal vaginal bleeding, and a palpable adnexal mass; however, this is seen in only 45% of patients with ectopic pregnancy.[23]

The most definitive sonographic finding is the visualization of an extrauterine GS with a yolk sac or an embryo. Nonvisualization of an intrauterine or extrauterine GS in a patient with a positive pregnancy test may be due to an early intrauterine gestation or an early ectopic gestation. Correlation with serum quantitative β-hCG is important.[24] As described in the normal GS, the intradecidual sign and the double decidual sign can be used to identify an intrauterine pregnancy before visualization of the yolk sac or the embryo; however, it is to be distinguished from the decidual cast or pseudogestational sac of ectopic pregnancy[25] (Figure 9). Nyberg et al[26] demonstrated psuedogestational sacs in 10–20% of ectopic pregnancies. A psuedogestational sac can be differentiated from an early intrauterine GS by its central location, oval shape, thin echogenic rim, and absence of a double decidual sac sign.[27] A decidual cast is an intrauterine fluid collection surrounded by a single decidual layer, as opposed to the 2 concentric rings of the double decidual sign.[28] The presence of an extra ovarian adnexal mass is the most common sonographic finding in ectopic pregnancy, because the fallopian tube is

the most common location for an ectopic pregnancy (Figure 10). This adnexal mass may represent a dilated fallopian tube with a GS and may or may not be associated with hematosalphinx.

The sonographic appearance varies depending on the presence or absence of hematoma and the location (Table 4).

Fallopian Tube

The tubal ring in the adnexa is an important sonographic sign found in 68–78% of ectopic gestations.[29] Echogenic fluid in the cul-de-sac is an important feature of ectopic pregnancy[30–32] (Figure 11). Nyberg et al[30] demonstrated that echogenic fluid is the only abnormal finding in 15% of ectopic pregnancies. Echogenic fluid in the cul-de-sac is due to hemoperitoneum from tubal abortion or tubal rupture; however, echogenic fluid may also result from a ruptured corpus luteal cyst.

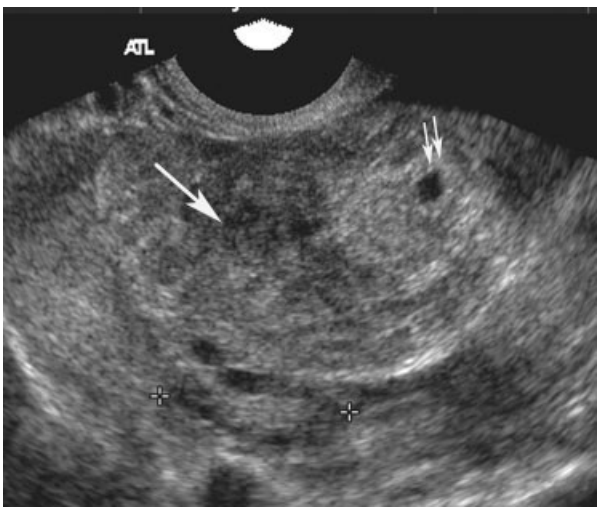

FIGURE 10. Transvaginal sonogram of a patient with a positive β-hCG and no intrauterine gestation consistent with an ectopic pregnancy shows a heterogenous mass (arrow) adjacent to the ovary (calipers) in the fallopian tube. Note the small gestational sac (double arrows) in the mass with surrounding decidual reaction.

Interstitial or Corneal Pregnancy

Interstitial pregnancy is caused by the implantation of the GS in the proximal portion of the fallopian tube that is within the muscular wall of the uterus. On sonography, an eccentric location of the GS with a thin or incomplete myometrial mantle around the sac is suggestive of an interstitial gestation. The thickness of the surrounding myometrial mantle is generally <5 mm[33–35] (Figure 12).

Cervical Pregnancy

Cervical pregnancy is a rare but potentially lethal ectopic pregnancy that must be differentiated from the cervical phase of an abortion in progress. The GS in cervical pregnancy is round or oval, but that in a cervical abortion is crenated[36] (Figure 13). Also, viewing peritrophoblastic flow on Doppler sonography may help distinguish a cervical implantation from a nonviable sac passing through the cervix.[37,38]

Ovarian Pregnancy

Spiegelberg's criteria of ovarian pregnancy includes location of the GS in the region of the ovary, attachment of the ectopic gestational gestation to the uterus by the ovarian ligament, intact ipsilateral fallopian tube, and the presence of ovarian tissue in the GS wall. Transvaginal sonography shows a well-defined echogenic ring that is indistinguishable from a corpus luteum cyst. Demonstration of a yolk sac or embryo will confirm the diagnosis.[39–41]

TABLE 4
Sonographic Features of Ectopic Pregnancy

Sonographic Feature	Action
Absence of an intrauterine gestational sac with serum β-hCG above the threshold level	Evaluate adnexa for ectopic pregnancy
Pseudogestational sac	Evaluate adnexa for ectopic pregnancy
Extraovarian complex ovarian mass	With elevated β-hCG suggestive of ectopic pregnancy with rupture
Gestational sac containing embryo	Unruptured ectopic gestation (live/demise)
Echogenic free fluid	Hemorrhage in the pelvis
Eccentric location of the gestational sac with a thin or incomplete myometrial mantle around the sac <5 mm	Interstital or corneal pregnancy
Low position of the gestational sac in the cervix	Cervical pregnancy (has to be distinguished from abortion in progress)
Gestational sac in the ovary	Ovarian ectopic pregnancy

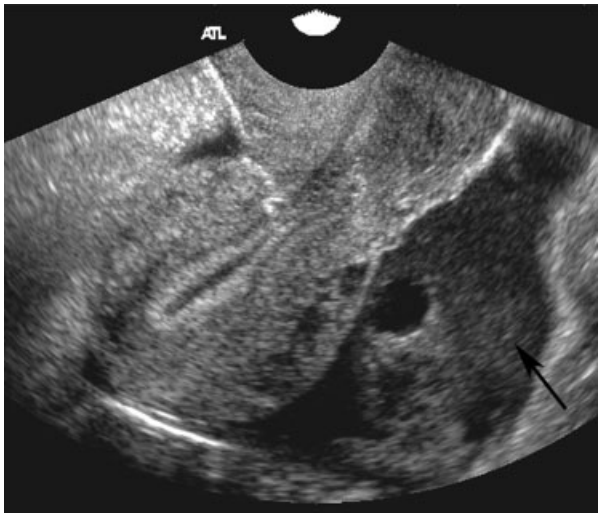

FIGURE 11. Transvaginal sonogram shows echogenic free fluid in the cul-de-sac (arrow).

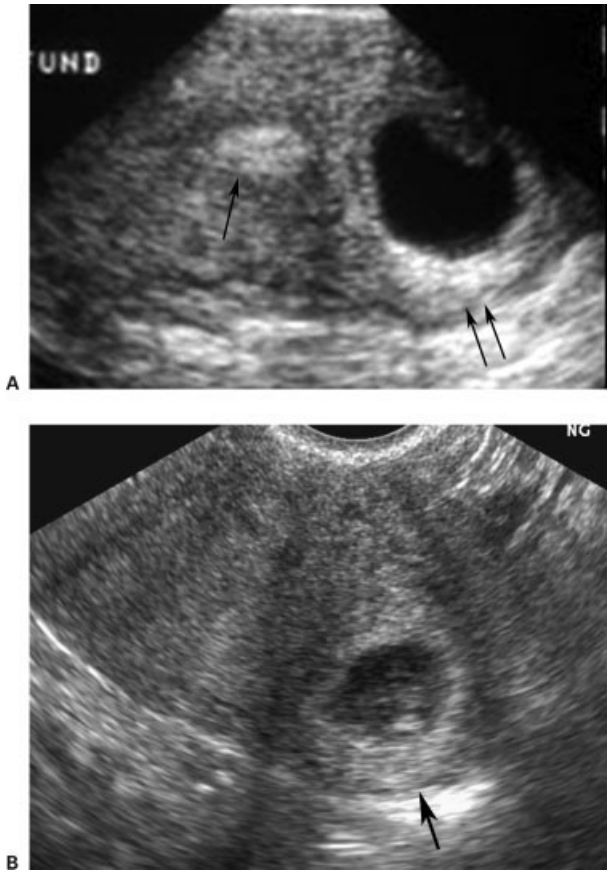

FIGURE 12. Cornual ectopic pregnancy on a coronal image of the uterus. **(A)** Transabdominal sonogram shows the abnormal location of the gestational sac in the lateral aspect of the uterus. The arrow indicates the endometrium. Note the thinning of the myometrium lateral to the gestational sac (double arrow). **(B)** Transvaginal coronal sonogram of the uterus clearly shows the thinning of the myometrium (arrow).

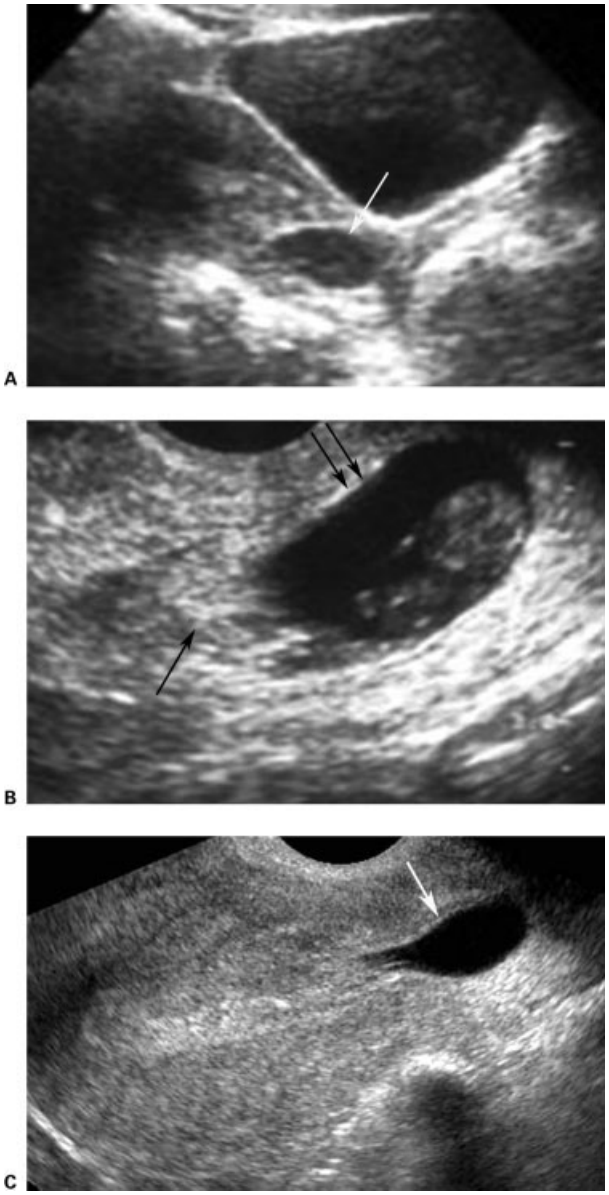

FIGURE 13. Cervical ectopic pregnancy. (A) Transabdominal sonogram shows the low location of the gestational sac in the lower uterine segment (white arrow). **(B)** Sagittal transvaginal sonogram shows the decidual reaction around the fetus (black arrow) with the uniform shape of the gestational sac (double black arrows). **(C)** Abortion in progress. Sagittal sonogram shows a low-lying gestational sac (white arrow) with no visible fetal pole or yolk sac. Note the absence of a hyperechoic decidual layer around the sac.

CHRONIC ECTOPIC PREGNANCY

A chronic ectopic pregnancy is a form of tubal pregnancy in which there is gradual disintegration of the tubal wall with slow and/or repeated episodes of hemorrhaging leading to the formation of a pelvic mass.[42] The presence of blood, trophoblastic tissue, and disrupted tubal tissue in the peritoneal cavity causes an inflammatory

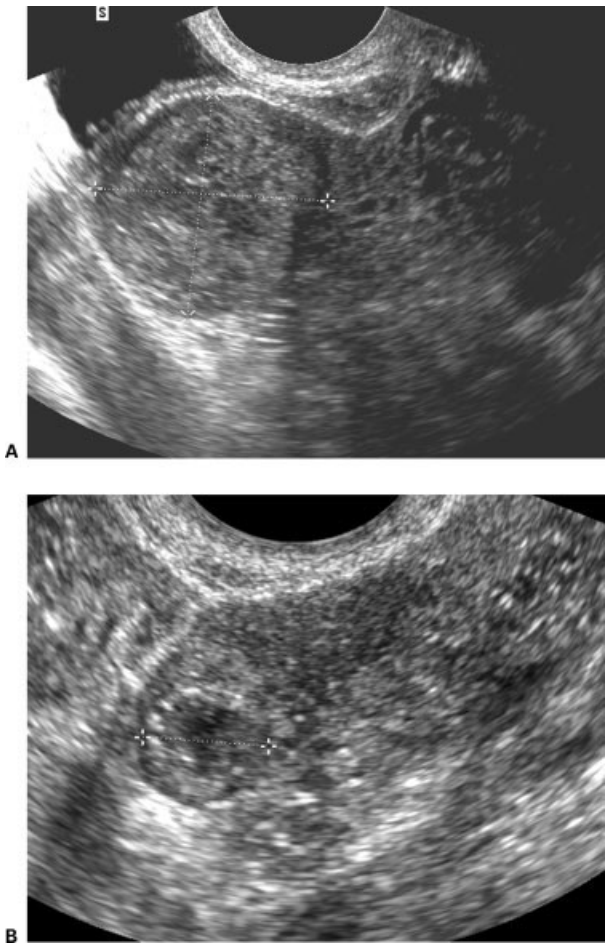

FIGURE 14. Chronic ectopic pregnancy. **(A)** Transverse transvaginal sonogram shows a complex mass in the right adnexa. The patient had a positive β-hCG and was started on methotrexate treatment. **(B)** Follow-up sonogram after 2 months shows decreased size of the mass. Further follow-up after 4 months revealed complete resolution of the mass.

response, resulting in adhesions and hematoma formation. The incidence of chronic ectopic pregnancy varies from 6.5% to 84% of all ectopic pregnancies.[43] The sonographic appearance of chronic ectopic varies due to the chronic inflammation and the adhesions from surrounding structures (Figure 14). A complex adnexal mass without an intrauterine pregnancy on transvaginal sonography accompanied by a positive serum β-hCG assay will help diagnosis a chronic ectopic pregnancy.[44]

ABDOMINAL ECTOPIC PREGNANCY

Abdominal ectopic pregnancy is an intrabdominal pregnancy secondary to expulsion of the GS following a tubal abortion or minor rupture of a tubal pregnancy. It can also be a primary event with implantation at the pouch of Douglas, posterior uterine wall, uterine fundus, liver, spleen, lesser sac of the peritoneal cavity, or diaphragm.[45] The ectopic gestation continues to develop in the abdominal cavity. It is a medical emergency because of high maternal and fetal morbidity and mortality. Several full-term abdominal pregnancies have been reported.[46–49] The imaging findings are nonspecific in early gestational age, but in later gestational age the uterus appears empty and the fetus is seen in the maternal abdominal cavity.[50]

HETEROTOPIC PREGNANCY

Heterotopic pregnancy is the simultaneous occurrence of 2 or more implantation sites. It is commonly manifested as concomitant intrauterine pregnancy and ectopic pregnancy.[51] Heterotopic pregnancy is rare in the general population, with an occurrence range estimated between 1:7,963 and 1:30,000.[52,53] The increased incidence of pelvic inflammatory disease, common use of ovarian stimulation, and advent of assisted reproductive techniques have contributed to the increasing incidence of both multiple gestations and heterotopic pregnancy in recent years. The diagnosis of this form of ectopic pregnancy is difficult and often is delayed. In patients with risk factors for ectopic pregnancy, rigorous sonographic examination of the adnexae and cul-de-sac must always be made even in presence of an intrauterine gestation.[54]

β-hCG Levels

When sonographic features are nonspecific, correlation with the serum β-hCG level improves the ability of sonography to distinguish between an intrauterine and an ectopic pregnancy. A negative β-hCG excludes the presence of a live pregnancy. The serum β-hCG test yields a positive result at approximately 23 days of gestation,[55] which is before a normal intrauterine GS is seen on transabdominal or transvaginal sonography. Nyberg and colleagues defined a β-hCG level of 1,800 mIU/ml (Second International Standard) as the threshold for visualization of a normal intrauterine GS transabdominally. A level of 1,000 mIU/ml has been proposed as the threshold for transvaginal sonography.[56,57] A general guideline for using β-hCG levels to assess pregnancy is shown in Table 5.[56]

If the β-hCG level is above the threshold level and an intrauterine GS is not seen, the patient is presumed to have an ectopic pregnancy. An early

TABLE 5
Discriminatory Levels of β-hCG for Early Pregnancy Findings

β-hCG (mIU/ml)	Gestational Sac	Yolk sac	Embryo + Heartbeat
<1,000	+/−	0	0
1,000–7,200	+	+/−	+/−
7,200–10,800	+	+	+/−
>10,800	+	+	+

complete or incomplete abortion may, however, yield a similar clinical and sonographic appearance. In indeterminate cases in which the patient is clinically stable, serial quantitative β-hCG levels may be helpful in distinguishing between ectopic pregnancy, abortion, and early intrauterine pregnancy. The β-hCG level in a normal pregnancy has a doubling time of approximately 2 days, whereas patients with an aborting gestation have falling β-hCG levels. Patients with ectopic pregnancy may have a slower increase in β-hCG levels.[57,58]

Serum Progesterone

Progesterone, a C-21 steroid hormone, is one of the primary products of the corpus luteum. In early pregnancy, it is essential for the maintenance of decidual function and structural integrity and also myometrial quiescence. Progesterone originates almost entirely from the corpus luteum before 6 weeks' gestation, and its production shifts more to the placenta after the seventh week. Beyond 12 weeks, the placenta is the dominant source of progesterone.[59] Progesterone concentrations are <2 nmol/L during the follicular phase of the normal menstrual cycle. In the luteal phase of conception cycles, progesterone concentrations rise approximately 2–4 nmol/l on the day of the luteinizing hormone surge to a plateau of approximately 20–70 nmol/l over the subsequent 7 days. Concentrations rise until 7 weeks' gestation and remain at a plateau until 10 weeks' gestation, from where concentrations gradually increase to term. At term, progesterone concentrations can range from 200 to 600 nmol/l.[60]

The ability of antiprogesterone agents to induce abortion confirms its crucial role in the maintenance of pregnancy. Progesterone production in early pregnancy reflects the dynamics of the corpus luteal-trophoblast axis and the status of the trophoblastic tissue. Because progesterone has a shorter half-life than β-hCG, the progesterone level will reflect any change in dynamics earlier in the pregnancy. In addition, progesterone is often used to establish the location of a pregnancy.

Several studies have demonstrated reduced progesterone levels in ectopic pregnancies.[61] This is thought to be due to abnormal implantation thus affecting the luteal-placental axis. A number of small studies have also shown low levels of progesterone in nonviable pregnancies. A progesterone level of <25 nmol/l in an anembryonic pregnancy has been shown to be diagnostic of nonviability.[62]

ARTERIOVENOUS MALFORMATIONS

Uterine vascular lesions are a rare but important cause of bleeding in women of reproductive age. This group of abnormalities includes arteriovenous malformations (AVMs), chorioangiomas, pseudo-aneurysms, and the more rare congenital uterine aneurysms. Although vaginal bleeding is the main presenting symptom, spontaneous abortion, amenorrhea, infertility, and congestive heart failure can be seen secondary to the presence of large arteriovenous (AV) shunts and anemia. This could be associated with a recent history of therapeutic abortion, cesarean section, dilatation and curettage, endometrial carcinoma, or gestational trophoblastic disease.

AVM is a rare but potentially life-threatening lesion. Its incidence is unknown and very difficult to estimate.[63] AVMs can be congenital or acquired. Congenital AVMs consist of a proliferation of vessels with AV fistula formation and thin walls due to abnormal development of blood vessels. The size of the vessels varies, as does the appearance of the lesion.

Posttraumatic acquired vascular abnormalities include a wide spectrum of abnormalities. On one end of the spectrum are complex structures similar to congenital AVMs. On the other end is the simple AV fistula, in which a single artery connects with a single vein. Pseudoaneurysms can also be seen in isolation or in combination with acquired AVMs.[64] Acquired AVMs tend to develop after uterine trauma, when there is the potential for formation of abnormal vascular communications between artery and vein during the healing process, as in the case of a pregnancy.

The modality of choice for screening and diagnosing AVMs is transabdominal and transvaginal Doppler sonography.[65,66] The AVM usually appears as a complex mass with tortuous tubular anechoic structures that shows presence of flow on color Doppler imaging (Figure 15). Spectral

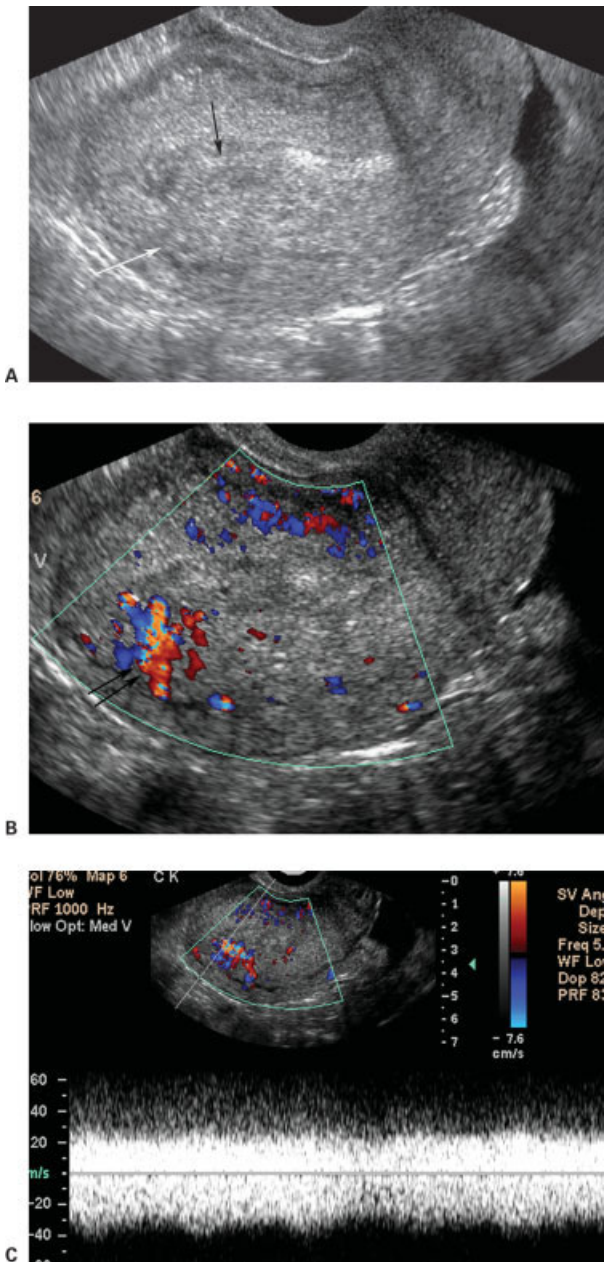

FIGURE 15. Arteriovenous malformation. **(A)** Sagittal sonogram of the uterus shows a complex mass (arrow) in the endometrium which is likely a group of blood clots with a heterogenous area in the myometrium (white arrow). **(B)** Color Doppler sonogram shows an area of increased vascularity in the myometrium (double arrow) with low resistance flow seen on spectral Doppler imaging **(C)**.

Doppler imaging demonstrates arterial waveforms with low resistance indices as well as pulsatile venous waveforms, both indicative of the presence of AV shunts.[67] CT and MRI can also demonstrate the presence of AVMs, particularly when angiographic multiphase protocols are performed. Conventional angiographic studies have traditionally been very useful for diagnosis, and embolization has become the therapy of choice for these lesions. Angiography demonstrates the presence of a complex tangle of vessels characteristic for AVMs, but also shows the blood supply and the presence of collateral vessels. Transcatheter arterial embolization is effective, with multiple advantages for the patient and health care system, including low complication rates, avoidance of surgical risks, fertility preservation, and shorter hospitalizations compared with surgical treatment.[68]

The differential diagnosis includes RPOC, hemangiomas, varicosities, uterine sarcoma, and trophoblastic disease. In patients with RPOC, the vascular abnormalities (mass) are usually within the uterine lumen, not in the myometrium, as in the case of AVM; they also are hyperechoic rather than anechoic, as in the case of AVM. Invasive trophoblastic disease and uterine sarcoma appear as an echogenic heterogeneous hypervascular mass infiltrating the myometrium. Occasionally it can be challenging to differentiate these lesions; some reports suggest that AVMs are overdiagnosed.[68] A combination of clinical history, gray-scale sonographic findings, and serologic tests (β-hCG) is necessary to differentiate these hypervascular lesions from an AVM. If the diagnosis is not clear, then CT angiography, magnetic resonance angiography, and/or angiography may play an important diagnostic role, as mentioned above.

GESTATIONAL TROPHOBLASTIC DISEASE

The concept of gestational trophoblastic disease is a spectrum of medical conditions, including hydatidiform mole, invasive mole, and choriocarcinoma. First trimester bleeding is one of the most common clinical presentations for this group of disorders. Other clinical signs and symptoms include rapid uterine enlargement, excessive uterine size for gestational date, and hyperemesis gravidarum or pre-eclampsia that occurs before 24 weeks. The common feature for this group of disorders is the abnormal proliferation of trophoblastic tissue with excessive production of β-hCG.

Hydatidiform Mole

Hydatidiform mole is a complication with malignant potential occurring in 1 of every 1,000–2,000 pregnancies. There are 2 types: complete and partial molar pregnancy. The complete hydatidiform mole (CHM) is the most common gestational trophoblastic disease. It results from the fecundation of a single egg with no active nu-

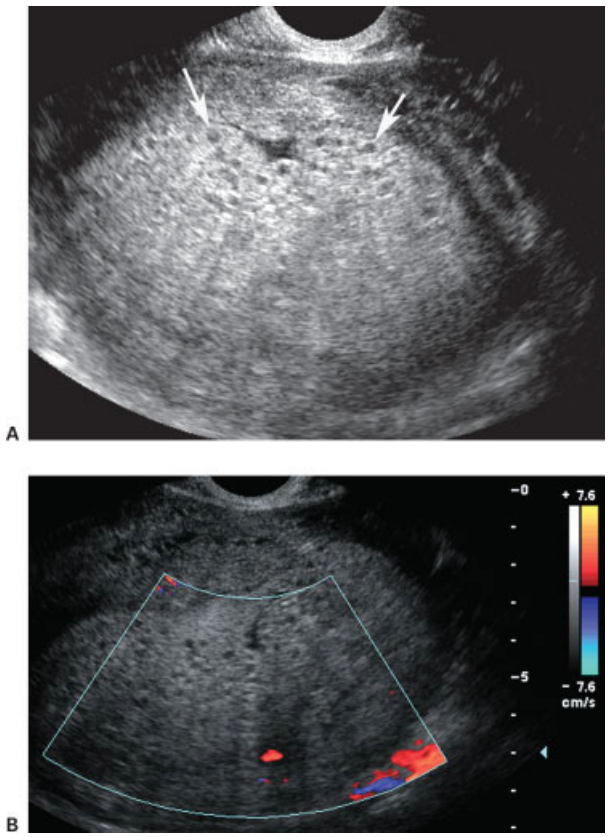

FIGURE 16. Hydatidiform mole. **(A)** Coronal transvaginal sonogram of the uterus shows a complex mass in the endometrium with multiple tiny cystic spaces within it (white arrows). **(B)** Color Doppler sonogram shows a lack of increased vascularity in the mass.

cleus, which means all the chromosomes present in the CHM are paternal. CHM is also known as uniparental disomy. Ninety percent of CHMs have a 46,XX karyotype; the remaing 10% have a 46,XY karyotype. This chromosomal anomaly causes early loss of the embryo and proliferation of the trophoblastic tissue with gross pathologic appearance of a complex multicystic mass, classically described as a "cluster of grapes."

The sonographic appearance of a CHM is usually described as a heterogeneous echogenic endometrial mass with multiple variable-sized cysts ("Swiss cheese" or "snowstorm" endometrium) and no visible embryo (Figure 16). Only slightly more than half of first trimester molar pregnancies have a classical appearance; the rest may present as an anembryonic GS, incomplete abortion, or heterogeneously thick endometrium without the characteristic vesicular appearance.[69] Doppler examination of a CHM reveals increased uterine vascularity. High velocities with a low resistance index in the main and arcuate uterine arteries are characteristic of a molar pregnancy compared with the low velocities of a normal pregnancy.[70]

Theca lutein cysts are present in 50% of CHM cases and are caused by hyperstimulation of the ovaries due to excessive production of β-hCG by abnormal trophoblastic tissue. They are rare in the first trimester, when the production of the hormone is not yet abnormal. Theca lutein cysts typically appear as multiple, large bilateral multiseptated ovarian cysts, some of which can be hemorrhagic.

The differential diagnosis includes placental hydropic degeneration and placental psuedomole. The former occurs after fetal demise and can appear identical to CHM on sonography. Doppler sonography demonstrates diminished vascularity compared with CHM. Placental pseudomole can be associated with preeclampsia and Beckwith-Wiedemann syndrome. There is presence of a fetus with normal growth in the first trimester.

Partial mole is caused by triploidy (69,XXY karyotype) or more rarely tetraploidy (92,XXXY karyotype) with 1 entire extra haploid set from paternal origin, which is known as diandry. This occurs when a normal ovum is fecundated by 2 spermatozoids or a diploid sperm. When triploidy is maternally derived, it results in other disorders such as intrauterine growth restriction or spontaneous abortion. A GS with a fetus is present, the placenta is enlarged, and some areas of the placenta have hydropic villi with multicystic appearance, though less in comparison with CHM (Figure 17). Sonographic appearance demonstrates an enlarged placenta with focal areas of multiple cysts. The fetus has multiple congenital anomalies and growth retardation. The differential diagnosis for partial mole includes the following:

1. Twin pregnancy with one normal fetus and placenta with an accompanying complete hydatidiform molar pregnancy. Diagnosis is made on the basis of normal anatomy and growth of the fetus.[71]
2. Fetal demise with hydropic degeneration of the placenta. Presentation is identical to partial molar pregnancy, and pathologic diagnosis is required.
3. Placental pseudomole. This condition can be seen in pre-eclampsia with mesenchymal dysplasia of the placenta. It is rare in the first trimester and is characterized by the presence of villus hydrops.
4. Infection.

Invasive Mole and Choriocarcinoma

Invasive moles present deep growth into the myometrium and beyond, sometimes with penetra-

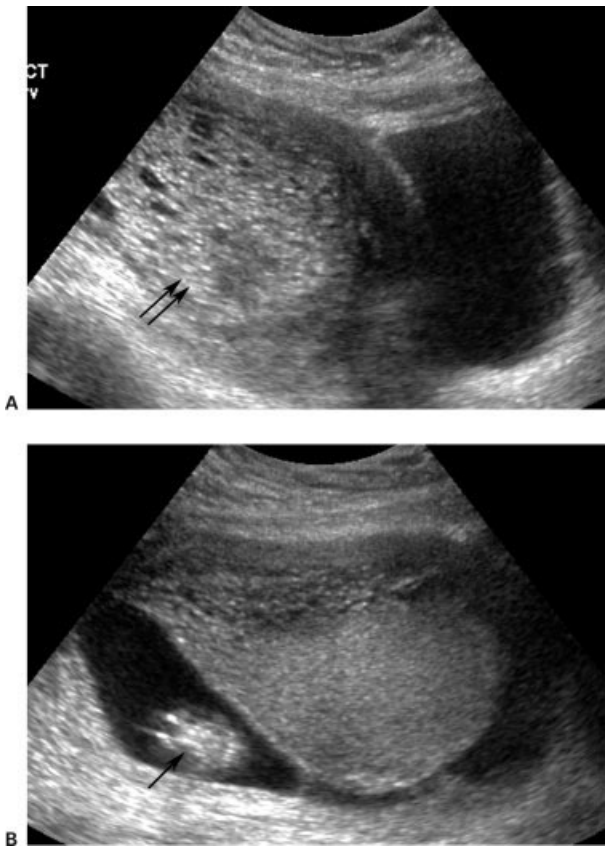

FIGURE 17. Partial molar pregnancy. **(A)** Transabdominal coronal sonogram of the upper half of the uterus shows the placenta and part of the fetus (arrow). **(B)** Transabdominal sonogram of the lower segment of the uterus shows the typical ''snowstorm'' appearance in a mole (double arrow). The presence of fetal parts indicates that this is a partial molar pregnancy.

tion into the peritoneum and parametria. These tumors are locally invasive but very rarely metastasize in contradistinction with choriocarcinoma that typically presents extensive metastasis to the lung and pelvic organs. Half of the tumors arise after a molar pregnancy, 25% after abortion, and 25% following an apparent normal pregnancy. Diagnosis is made when the gonadotropin levels remain elevated after the evacuation of pregnancy. Sonography can demonstrate the presence of a uterine mass identical to a CHM and sometimes the myometrial or adnexal invasion (Figure 18). CT is useful to detect distant metastasis to the lung (75%) and pelvis (50%). MRI can better demonstrate myometrial and vaginal invasion. Transcatheter arterial embolization can be used to treat excessive bleeding from vaginal metastasis.

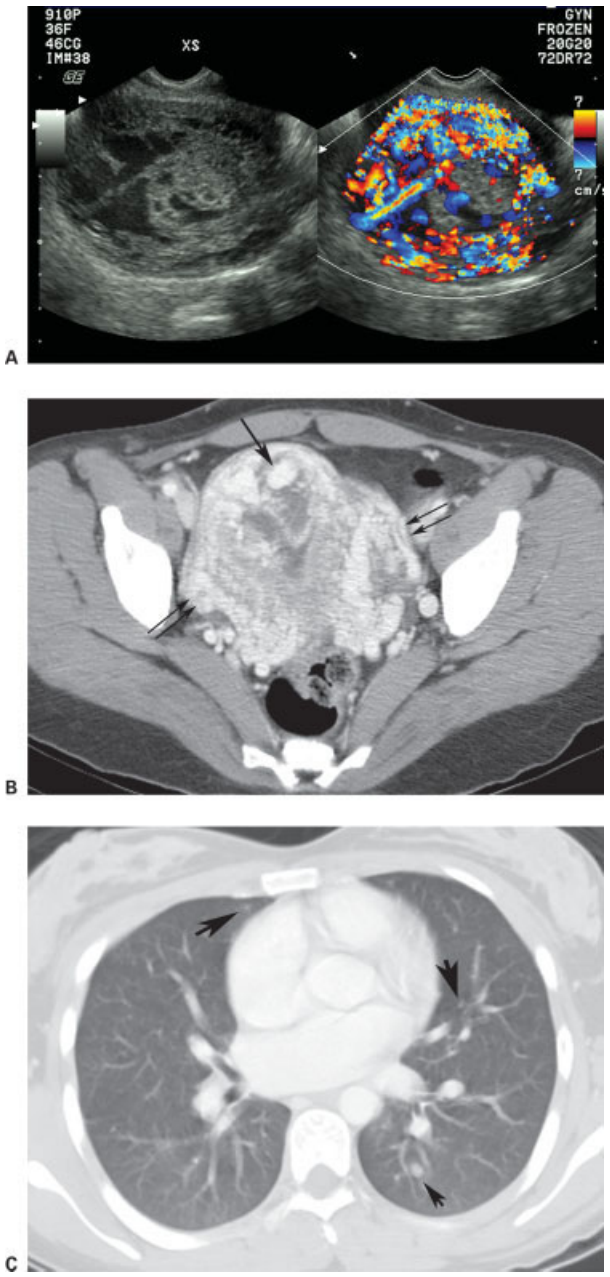

FIGURE 18. Choriocarcinoma. **(A)** Transverse sonograms of the uterus show a complex mass in the endometrium with increased vascularity on color Doppler imaging. Note the lack of normal myometrium, suggesting invasion. **(B)** Contrast CT scan shows the vascular mass in the endometrium (arrow) with dilated vessels in the adnexa (double arrow). **(C)** Chest CT scan shows multiple metastases in the lungs (arrows).

THREE-DIMENSIONAL SONOGRAPHY

Three-dimensional (3D) sonography has provided an opportunity to revisit previously abandoned or disregarded obstetric sonographic parameters, particularly in early pregnancy. 3D assessment of GS volume in the first trimester has been found to be a sensitive indicator of pregnancy outcome, with a smaller than expected GS volume being predictive of failing early pregnancy.[72,73] It has not, however, proved useful in determining the outcome of expectant management[74,75] or in predicting the success of medical treatment, and it

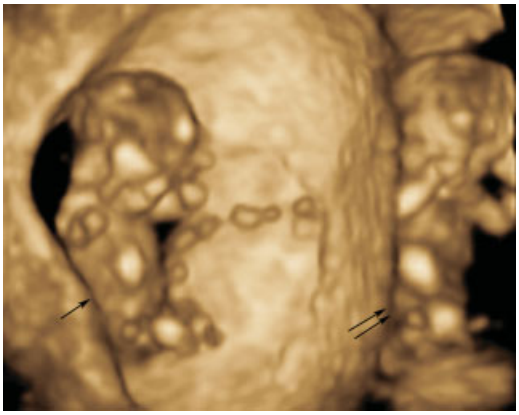

FIGURE 19. Three-dimensional image of a dichorionic diamniotic twin pregnancy. Twin A (black arrow) is on the left, twin B (double black arrow) is on the right.

appears to add little to the diagnostic or prognostic value of 2-dimensional (2D) imaging.[76] 3D sonography has been used to diagnose various anomalies in the first trimester, including skeletal dysplasia,[77] holoprosencephaly,[78] sacrococcygeal teratoma,[79] and conjoined twins.[80] Other abnormalities such as amniotic fluid volume can be calculated specially for pregnancies at increased risk of loss.[81] Shipp et al[82] reported an excellent correlation between the measurements of the nuchal translucency using standard 2D scanning and those obtained from 3D multiplanar reconstruction of the Z plane. This technique is potentially useful in fetuses that are not in an optimal position for standard 2D nuchal translucency measurement (Figure 19).

In conclusion, 3D sonography may help diagnose fetal anomalies earlier and with greater confidence. 3D sonography may also help in assessing nuchal translucency in difficult positions of the fetuses.

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