Sonographic evaluation of first-trimester bleeding

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Vaginal bleeding in the first trimester of pregnancy is a common presentation in emergency care facilities. About 25% of all gestations present with vaginal spotting or frank bleeding in the first few weeks of pregnancy; half of these progress into miscarriage or abortion [1]. The acuity of these symptoms may vary from occasional spotting to severe hemorrhage, associated with cramping and abdominal pain. The bleeding often is self-limited and is most likely caused by implantation of the conceptus into the endometrium. The important causes of first-trimester bleeding are spontaneous abortion, ectopic pregnancy, and gestational trophoblastic disease. The clinical assessment of pregnancy outcome is unreliable and ultrasound (US) evaluation combined with quantitative beta human chorionic gonadotropin (β-hCG) is an established diagnostic tool in these patients. This article reviews the role of ultrasonography in the evaluation of patients presenting with first-trimester bleeding.

Sonographic anatomy

The uterus is a pear-shaped, muscular organ that varies greatly in size and shape depending on age and prior pregnancies. The normal postpuberty uterus in an adult measures approximately 7.5 to 8 cm in length, 4 to 5 cm in width, and about 2 cm in anteroposterior dimension. The normal cervix is 3.5 to 4 cm in length. The cervix is comprised of internal and external cervical os. The internal os is the junction of the uterine cavity and the cervical canal and the external os is the junction of the cervical canal and the vagina. Transvaginal US (TVUS) of the normal myometrium reveals three distinct layers. Arcuate vessels separate the thin outer layer from the thick middle layer, and both layers are homogeneous with the outer layer more hypoechoic relative to the middle layer [2]. The inner layer consists of a thin hypoechoic halo that surrounds the endometrium and corresponds to the junctional zone seen on MR imaging. The endometrial thickness measurements are optimally made on sagittal (long-axis) images of the uterus; this measurement should be performed on the thickest portion of the endometrium excluding the hypoechoic inner myometrium (Fig. 1). The endometrial thickness should be reported as the “double thickness” measurement [3]. If endometrial fluid is present, its diameter should be omitted; in such cases the endometrial thickness should be reported as the sum of the measurements obtained from the anterior and posterior endometrial walls. An endometrial thickness of 4 to 14 mm is normal in an adult premenopausal woman. Endometrial thickness and appearance vary with the phase of the menstrual cycle [4].

The position of the ovaries is variable but they are usually found in the posterior fold of the broad ligament, posterior and distal to the fallopian tubes. On sonography the ovaries can be localized anterior to the internal iliac vessels. The postpubertal ovary measures approximately 3 cm in length, 2 cm in width, and 1 cm in anteroposterior dimension. The upper limit for normal ovarian volume is highest in young adult women measuring approximately 9.8 to 14 mL and declines with increasing age [5]. Normal
Scanning technique

Ultrasound evaluation of the female pelvis is conducted with a real-time scanner, preferably using a sector or curvilinear transducer. The scanner is adjusted to operate at the highest clinically appropriate frequency, realizing that there is a trade-off between the resolution and beam penetration.

Transabdominal pelvic US is performed with a full bladder using transducer frequencies of 3.5 MHz and above. Adequate distention of the bladder displaces the bowel from the field of view. Transabdominal US gives an initial overview of the uterus, adnexa, and any intra-abdominal free fluid. TVUS is performed with the patient’s bladder being empty, using a transducer frequency of 5 to 7.5 MHz. TVUS gives detailed information about the uterus and the adnexa. Higher-frequency transvaginal probes can be positioned closer to the pelvic organs resulting in improved spatial resolution and diagnostic accuracy. Currently available transducers of 10 MHz and above can identify the finer details of intrauterine gestation and have greatly contributed to the early diagnosis of abnormal gestation and to the management of first-trimester bleeding. Color flow Doppler and pulsed Doppler may be added to the examination, as indicated by the gray-scale US findings. It is important to bear in mind that the energy output of Doppler US is substantially higher than that used for imaging and it may have potentially harmful effects on the conceptus [6]. Because of this risk, caution has been expressed over the routine use of Doppler US in early pregnancy evaluation. While performing Doppler US in early pregnancy, the concept of “as low as reasonably achievable” is important [7] and the advantages of the Doppler US should outweigh the potentially harmful effects on the conceptus.

Normal first-trimester sonography

Scanning in the first trimester may be performed either transabdominally or transvaginally. TVUS is preferred and is the community standard. The first-trimester milestones are given in Tables 1 and 2.

A gestational sac can be identified with TVUS at 5 weeks of gestational age, when it measures 5 mm. The yolk sac should always be seen by TVUS when a gestational sac measures greater than 10 mm and by transabdominal US when the mean sac diameter is greater than 20 mm [8,9]. An embryo with cardiac activity should be seen transvaginally when the gestational sac measures greater than 18 mm, and transabdominally when the gestational sac measures 2.5 cm. These discriminatory criteria should be used as guidelines. If the findings of the US examination are equivocal and the examination is technically difficult, a follow-up examination should be obtained.

Gestational sac

The blastocyst implants into the endometrium by approximately 23 days of menstrual age [10]. It measures 0.1 mm and is too small to be visualized on TVUS. Demonstration of peritrophoblastic flow by transvaginal color flow Doppler at this focal decidual thickening has improved the diagnostic sensitivity of intrauterine pregnancy (IUP) from 90% with TVUS alone to 99% using transvaginal color flow Doppler [11,12]. The peritrophoblastic flow has a characteristic high-velocity and low-impedance flow caused by shunting of blood from the spiral arteries into the intervillous spaces. According to Emerson et al [11], the peak systolic velocity of peritrophoblastic flow in a normal IUP ranges from 8 to 30 cm/second, before the visualization of the gestational sac. Yeh et al

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Table 1
First-trimester scanning milestones

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Transabdominal US</th>
<th>Transvaginal US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational sac</td>
<td>—</td>
<td>Present at 5 wk</td>
</tr>
<tr>
<td>Yolk sac</td>
<td>Always present</td>
<td>Always present</td>
</tr>
<tr>
<td></td>
<td>if GS &gt; 20 mm</td>
<td>when GS &gt; 10 mm</td>
</tr>
<tr>
<td>Cardiac activity</td>
<td>GS &gt; 2.5 cm</td>
<td>GS &gt; 18 mm</td>
</tr>
</tbody>
</table>

Abbreviations: GS, gestational sac; US, ultrasound.
[13] described a focal, eccentric, anechoic area in the endometrium caused by the embedded blastocyst as the “intradecidual sign.” They described this sign as early as 3.5 weeks of menstrual age on transabdominal US and reported a sensitivity rate of 92%, a specificity rate of 100%, and an accuracy rate of 93%. Laing et al[14] used TVUS to demonstrate this sign and found that the overall sensitivity, specificity, and accuracy for the intradecidual sign were only 48%, 66%, and 45%, respectively. With currently available high-frequency transvaginal probes, a gestational sac as small as 2 to 3 mm can be demonstrated at 4 weeks of gestational age [15–17]. On TVUS, the gestational sac is seen as a well-defined fluid-filled cavity with a surrounding hyperechoic rim, embedded eccentrically in the endometrial lining of the fundus or midbody of the uterus (Fig. 2). The sonographic term “gestational sac” represents the exocoelomic cavity of the blastocyst and the surrounding echogenic rim is caused by the developing chorionic villi and decidual tissue. The echogenic rim should have a minimum thickness of 2 mm and its echogenicity should exceed that of myometrium [1].

The double decidual sac sign of intrauterine gestation was first described in 1982 [18]. The double decidual sac sign consists of two concentric echogenic rings encasing a central anechoic focus that impress on the endometrial stripe. The inner echogenic rim represents the decidua capsularis and chorion laeve, whereas the outer echogenic rim represents the decidua parietalis; these echogenic rims are separated by a thin rim of fluid in the endometrial cavity (Fig. 3). This is a useful sign of IUP between 4 and 6 weeks of gestation. The crown-rump length (CRL) of the embryo is a more accurate indicator of gestational age than the mean gestational sac diameter. The mean gestational sac diameter should be recorded, however, when an embryo is not identified.

Because hCG production and gestational sac growth are related to trophoblastic function, there is excellent correlation of the serum hCG level, sac size, and the stage of pregnancy [19]. Kadar et al [20] first introduced the concept of a discriminatory level of the β subunit of hCG. The range of the serum β-hCG level at which an intrauterine gestational sac is visualized is the discriminatory zone. Although the discriminatory range of β-hCG varies from one laboratory to another, the widely accepted range is from

Table 2

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Embryologic change</th>
<th>Sonographic appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 d</td>
<td>Blastocyst implantation</td>
<td>Blastocyst measures 0.1 mm and is too small to visualize</td>
</tr>
<tr>
<td>3.5–4 wk</td>
<td>Decidual changes at implantation site</td>
<td>Focal echogenic decidual thickening at implantation site</td>
</tr>
<tr>
<td>4–4.5 wk</td>
<td>Trophoblastic tissue</td>
<td>High-velocity and low-impedance trophoblastic flow at the implantation site on TVCFD</td>
</tr>
<tr>
<td>4.5–5 wk</td>
<td>Exocoelomic cavity of the blastocyst</td>
<td>Gestational sac (a sonographic term) is always seen when it measures &gt; 5 mm and the serum β-hCG is between 1000 and 2000 mIU/mL (IRP)</td>
</tr>
<tr>
<td>5–5.5 wk</td>
<td>Secondary yolk sac</td>
<td>Yolk sac is seen as a thin-walled cystic structure within the gestational sac and should always be seen when the GS is &gt; 10 mm; it is the first sign of a true gestational sac before the visualization of embryo</td>
</tr>
<tr>
<td>5–6 wk</td>
<td>Embryo</td>
<td>Seen as a focal echogenic area adjacent to the yolk sac; should always be seen when the GS is &gt; 18 mm</td>
</tr>
<tr>
<td>5–6 wk</td>
<td>Embryonic cardiac activity</td>
<td>Embryonic cardiac activity should always be seen when the embryo is &gt; 5 mm; normal heart rate ranges from 100–115 beats/min between 5–6 wk of gestation</td>
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Abbreviations: CG, human chorionic gonadotropin; GS, gestational sac; IRP, international reference preparation; TVCFD, transvaginal color flow Doppler.
1000 to 2000 mIU/mL international reference preparation (IRP) for TVUS and 2400 to 3600 mIU/mL (IRP) for transabdominal US [10]. In normal pregnancy serum β-hCG should double or increase by at least 66% in 48 hours.

**Yolk sac**

The first structure to be seen within the gestational sac is the secondary yolk sac, which is a reliable indicator of a true IUP with a positive predictive value of 100%. The primary yolk sac is not seen by US because it shrinks at 4 weeks menstrual age and gradually disappears with the formation of the secondary yolk sac [21]. The secondary yolk sac is first seen on TVUS as a thin-walled cystic structure by the fifth gestational week and is virtually always seen by 5.5 weeks gestational age (Fig. 4) [22]. The yolk sac is round, measures less than 6 mm, and should be visualized by TVUS when a gestational sac measures more than 10 mm [10]. The yolk sac is involved in nutritive, metabolic, hemopoietic, and secretive functions during early embryonic development and organogenesis [23,24]. Abnormalities in its size and appearance are predictors of abnormal gestation [25].

**Embryo**

The embryo should always be visualized by TVUS when the gestational sac measures greater than 18 mm, and transabdominally when the gestational sac measures 2.5 cm (Fig. 5). With the currently available high-frequency transvaginal transducers, the embryonic disk is initially seen as a focal echogenic area of 1- to 2-mm thickness adjacent to the yolk sac between 5 and 6 weeks of gestational age [26–29]. Embryonic cardiac activity should always be seen when an embryo measures greater than 5 mm. Occasionally the heartbeat may be seen adjacent to the yolk sac even before the embryo is clearly visible.

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Fig. 3. Double decidual sac sign. (A) Coronal TVUS of the uterus reveals an intrauterine gestational sac (straight arrow), decidua capsularis (curved arrow), decidua parietalis (arrowhead), and effaced endometrial cavity (asterisks). (B) Corresponding line diagram.

Fig. 4. TVUS of the uterus demonstrates a yolk sac (thin arrow) outside the amniotic membrane (arrowhead), which has not yet fused with the chorion (curved arrow). Embryo (thick arrow) is seen within the amniotic sac.
Levi et al [3] suggested a 4-mm CRL cutoff because their study demonstrated cardiac activity in all embryos with a CRL of 4 mm [30]. Other studies demonstrated 5 mm as the discriminatory CRL for detecting cardiac activity [31,32]. Although visualization of a living embryo does not ensure a viable pregnancy, the abortion rate decreases for living embryos as the gestational age increases, with a 0.5% demise rate for living embryos between 6 and 10 mm [33]. If the length of the embryo is less than 5 mm, follow-up US should be performed until the expected CRL exceeds the discriminatory value. Most of the studies reported a heart rate of 100 to 115 beats per minute between 5 and 6 weeks [34–36] . By 9 weeks of gestational age, the mean heart rate increases to about 140 beats per minute. The cardiac activity should be documented by M-mode.

**Amniotic sac**

The amniotic sac is formed in the fourth week of gestation between the ectoderm layer and the adjacent trophoblast. Before 6.5 weeks the amniotic membrane is so close to the embryo that the amniotic cavity around the embryo is not easily seen. The diameter of the amniotic cavity is nearly equal to the CRL. Between 5 and 7 weeks of gestational age the embryo is located between the amniotic and yolk sacs. On US, this amniotic sac–embryo–yolk sac complex appears as two small sacs and is called the double bleb sign [9]. The embryo and the inner amnion grow at a faster rate than the outer chorionic cavity with eventual fusion of the amniotic and chorionic membranes by 16 weeks of gestation [37]. Separation of the amniotic and chorionic membranes before 14 weeks of gestation is considered normal (see Figs. 4 and 5).

**Spontaneous abortion**

Spontaneous abortion is defined as pregnancy terminating before the 20th completed week of gestation. Approximately 80% of spontaneous abortions occur in the first trimester. The causes of spontaneous abortions fall into two categories: genetic and environmental (maternal) as listed next:

- **Genetic or fetal causes**
  - Trisomy
  - Polyploidy 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 gonorrhoeae*

Genetic abnormalities are the most common cause of spontaneous abortions accounting for almost 50% to 60% of cases. Autosomal trisomy is the most frequently identified chromosomal abnormality resulting in first-trimester abortions. The incidence of abortions secondary to chromosomal abnormalities markedly increases after the maternal age of 35 years.

The environmental or maternal causes account for a small percentage of spontaneous abortions. These include infection; anatomic defects (maternal Mullerian defects); endocrine factors (failure of corpus luteum); immunologic factors (antiphospholipid antibody syndrome); and maternal systemic disease (diabetes mellitus, hypothyroidism). The algorithmic approach to first-trimester bleeding is summarized in Fig. 6.

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**Fig. 5.** TVUS of the uterus shows a normal embryo and separate amniotic membrane (arrow) in close relation to the embryo. This should not be mistaken for nuchal translucency.
The most common morphologic finding in early spontaneous abortions is an abnormality of development of the zygote, embryo, early fetus, or the placenta. Spontaneous abortion is clinically classified into threatened, inevitable, missed, incomplete, and complete abortions (Table 3).

Ultrasound findings in abortion

The US findings depend on the developmental stage of the pregnancy at which the patient presents with symptoms. Familiarity with normal sonographic landmarks of first-trimester pregnancy is essential.
to diagnose a failing pregnancy. TVUS features of failing pregnancy are summarized in Table 4. The sonographic findings are to be correlated with serum \( \beta \)-hCG and menstrual age. In the pre-embryonic stage, the pregnancy outcome depends on the presence of the gestational sac and yolk sac and their morphologic features.

**Absent intrauterine gestational sac**

Failure to demonstrate intrauterine gestational sac by TVUS may be secondary to early IUP (\( \beta \)-hCG < 1000 mIU/mL) or secondary to ectopic pregnancy. When the serum \( \beta \)-hCG is more than 1000 mIU/mL (IRP) and there is no IUP, an ectopic pregnancy [19,20] must be excluded by careful evaluation of the adnexa. If there is no identifiable ectopic gestational sac, adnexal mass, or a large amount of adnexal fluid in the cul-de-sac, follow-up with \( \beta \)-hCG and TVUS is necessary until a definite diagnosis is made. When the endometrial lining is thick with echoes in the endometrial cavity and no intrauterine gestational sacs, an incomplete abortion with retained products of conception must be distinguished from decidual reaction of the gestational sac. Transvaginal color flow Doppler of the endometrial contents is useful in differentiating trophoblastic tissue from blood clots and pseudogestational sac. Sparse flow on color Doppler with low peak systolic velocities (< 6 cm/second) and to absent end diastolic flow suggests decidual reaction of an ectopic pregnancy (Fig. 7) [38,39]. With early IUP (< 5 weeks) multiple flashes of color with a peak systolic velocity of greater than 8 cm/second and high diastolic component caused by trophoblastic arterial flow are noted [40].

**Intrauterine gestational sac without an embryo**

A common and difficult problem arises when the gestational sac in the uterus lacks an embryo or yolk sac [41–43]. This can be caused by early normal IUP,
anembryonic gestation, or a pseudogestational sac of ectopic pregnancy. Anembryonic gestation is a form of failed pregnancy defined as a gestational sac in which the embryo failed to develop (Fig. 8A). A mean gestational sac diameter greater than 18 mm (TVUS) without a visualized embryo is unequivocal evidence of a failed, anembryonic pregnancy [44]. This also is referred to as an “empty amnion” sign (Fig. 8B) because of its sonographic appearance of a large well-defined amniotic sac without an embryo [45]. The growth rate of an anembryonic gestational sac is slower than that of a normal gestational sac, which increases by 1.13 mm/day. An abnormal gestational sac can be identified confidently when the rate of increase of the mean sac diameter is less than 0.6 mm/d on follow-up US [46]. Other minor criteria of an abnormal gestational sac include distorted sac shape and weakly echogenic or irregular choriod decidual reaction (Fig. 9). The presence of gestational sac in the lower uterine segment or cervix is usually seen in patients with abortion in progress (Fig. 10), but can also be seen secondary to low implantation. Demonstration of trophoblastic vascular flow on color Doppler is useful in differentiating low implantation from abortion.

Yolk sac criteria of an abnormal gestation

The absence of a yolk sac when the mean sac diameter of the gestational sac is more than 10 mm is...
indicative of an abnormal gestation and is associated with spontaneous abortion [47–49]. A failing or failed pregnancy is also suggested when the yolk sac is abnormal in size and shape. Large (> 6 mm) irregular and calcified yolk sacs have been found to correlate with early pregnancy failure [50–52]. A large yolk sac is considered to be caused by an alteration of the metabolic functions of the yolk sac membrane with accumulation of secretions following embryonic death [53]. The association of a large yolk sac with aneuploidy has also been reported [50]. Although abnormal large yolk sac size is reported to be associated with subsequent pregnancy failure, another study with yolk sac diameter greater than the 95th percentile for gestational age reported normal pregnancy outcomes [54]. Because of this controversial issue, any patient with a large yolk sac should have a follow-up US because there is increased risk of spontaneous abortion. Apart from size, irregular, echogenic, calcified, or double yolk sacs (vitelline duct cyst) also are associated with early pregnancy failure [55,56].

**Gestational sac with an embryo**

Although visualization of a living embryo does not ensure a viable pregnancy, the abortion rate decreases for living embryos as the gestational age increases, with a 0.5% demise rate for living embryos between 6 and 10 mm [29]. Because cardiac activity may not be demonstrated [57] in early normal embryos (CRL < 4 mm), follow-up US and correlation with the serum β-hCG level is useful in determining the viability of the gestation. The most convincing evidence that a pregnancy has failed is to document absence of cardiac activity when CRL length is greater than 5 mm. In a missed abortion, the embryo may be small for the gestational age with a discrepancy between the mean sac diameter and the CRL (Fig. 11). Embryonic bradycardia is a poor prognosticator of pregnancy viability and requires follow-up [58]. Embryonic bradycardia is defined as a heart rate of less than 100 beats per minute before 6.2 weeks gestational age and less than 120 beats per minute between 6.3 and 7 weeks [59].

**Intrauterine growth restriction**

First-trimester growth restriction is a sign of a failing pregnancy. Growth restriction is detected by comparing the mean sac diameter with the CRL or by serial follow-up of these growth parameters. The average gestational sac diameters should be at least 5 mm larger than the CRL. A difference in size between mean sac diameter and CRL of less than 5 mm carries a high risk of subsequent embryonic demise [60]. When there is sac size and CRL discrepancy, a follow-up US examination is recommended because these fetuses have higher incidence of low birth weight and premature delivery [61,62].

**Subchorionic hematoma**

Up to 20% of women with a threatened abortion have a subchorionic hematoma [44]. Perigestational
hemorrhage from chorionic frondosum is the most common source of vaginal bleeding in the first trimester of pregnancy. Subchorionic hemorrhage is secondary to abruption of the edge of the chorion frondosum–decidua basalis complex or may be caused by marginal sinus rupture [63,64]. Although the hemorrhage usually abuts or elevates the edge of the chorion frondosum–decidua basalis complex, the bulk of the hemorrhage is usually situated between the decidua capsularis, chorion laeve, and the decidua vera. Acute hemorrhage may be hyperechoic or isoechoic relative to the chorion, and it becomes isoechoic with the chorionic fluid in 1 to 2 weeks (Fig. 12). Several studies have correlated the pregnancy outcome in these patients with the size of the subchorionic hematoma, gestational age, and the maternal age. One of the largest studies [65] showed that the rate of pregnancy loss increases with hematoma size, advancing maternal age, and earlier gestational age. In this study, the size of the hematoma was graded according to the percentage of the chorionic sac circumference elevated by the hematoma. It was graded as small when it involved less than one third of the chorionic sac circumference, moderate when it involved one-third to one-half of the chorionic sac circumference, and large when two-thirds or greater of the chorionic sac circumference was involved. There was little difference in the rates of spontaneous abortion between pregnancies with small- and moderate-size hematomas (7.7% and 9.2%, respectively), but the rate doubled with large hematomas (18.8%). The spontaneous abortion rate was also twice as high in women 35 years of age or older compared with that in younger women (13.8% versus 7.3%, respectively), and was 2.3 times higher in women who presented with vaginal bleeding at 8 weeks gestational age or less compared with that in women who presented with bleeding at more than 8 weeks gestational age (13.7% versus 5.9%, respectively). Some investigators have calculated the volume of a subchorionic hematoma as a percentage of the gestational sac volume. When the volume of a hematoma is less than 40% of the gestational sac volume, the pregnancy outcome is favorable [64,66].

Retained products of conception

Retained products of conception typically consist of retained placental tissue. An echogenic mass in the uterine cavity is the most suggestive US finding. A heterogeneous mass or collection in the central cavity may represent a blood clot, or some combination of retained placenta, necrotic debris, and clot (Fig. 13). Color Doppler may help to differentiate vascularized trophoblastic tissue from nonvascularized blood clots. A normal-appearing endometrial stripe or punctate echogenic foci not associated with a discrete mass makes retained products of conception unlikely.

Gestational trophoblastic disease

Gestational trophoblastic disease is a spectrum of pregnancy-related trophoblastic proliferative abnormalities that can present with first-trimester bleeding.

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Classification of gestational trophoblastic disease is as follows:

Hydatidiform mole
Complete mole
Partial mole
Gestational trophoblastic tumors
Choriocarcinoma
Invasive mole
Placental site trophoblastic tumor

Hydatidiform mole (molar pregnancy)

Molar pregnancy is a noninvasive process characterized by varying degrees of trophoblastic proliferation and edema of villous stroma. Its incidence is 1 in every 1000 to 2000 pregnancies [67] and is estimated to be as high as 1 in 41 in patients with miscarriages [68]. Hydatidiform mole constitutes 80% of the cases of gestational trophoblastic disease with relatively high frequency of molar pregnancy at the beginning and end of the childbearing period. Mole recurrence is seen in about 1% to 2% of cases [69]. The absence or presence of fetus or embryonic elements is used to classify a molar pregnancy into complete or partial moles. Complete molar pregnancies are most often 46 XX, with the chromosomes completely of paternal origin and are referred to as “androgenesis.” The karyotype in partial mole is usually triploid (69 XXY) or even tetraploid (92 XXXY) with one maternal and two paternal haploid compo-
ments. The fetus in partial mole is usually nonviable and exhibits features of triploidy, which include multiple congenital anomalies and growth restriction [70]. Histologically, the molar tissue has prominent villi with central acellular space corresponding to the macroscopic appearance of vesicles. In partial mole these changes are focal and less advanced.

The clinical presentation of molar pregnancy, listed below, has changed appreciably over the last decades because of early diagnosis with TVUS and quantitative $\beta$-hCG estimation.

- Uterine bleeding, which may vary from spotting to profuse hemorrhage
- Uterine enlargement out of proportion to the duration of pregnancy in 50% of cases
- Absence of fetal parts or fetal heart sounds despite an enlarged uterus
- Pregnancy-induced hypertension before 24 weeks gestation
- Hyperemesis
- Thyrotoxicosis, which is usually subclinical
- History of passage of grape-like vesicles transvaginally

Uterine bleeding is the most common presentation and it may vary from spotting to profuse bleeding. Occasionally patients may pass grape-like vesicles transvaginally. Clinically the uterine fundal height is more than is expected for the gestational period. Diagnosis is made by markedly elevated serum $\beta$-hCG levels expected for the stage of gestation and by the characteristic sonographic appearance.

**Sonographic features of molar pregnancy**

Molar changes can be detected from 8 weeks of pregnancy by US. The uterine cavity is filled with multiple sonolucent areas of varying size and shape. This has been described as a “snow storm” appearance with low-frequency transabdominal scanning. With high-frequency transvaginal transducers, numerous discrete, anechoic (cystic) spaces are visualized corresponding to the hydropic villi (Fig. 14). These cystic spaces range from 1 to 30 mm in size and increase in size with gestational age. Large sonolucent areas or maternal lakes resulting from the stasis of maternal blood are seen between the vesicles. In partial mole, an intrauterine embryo is noted along with molar changes [71,72]. Because the trophoblastic changes develop at a slower rate in partial mole, it may present as enlarged placenta without macroscopic vesicular changes [73]. Women with a high $\beta$-hCG level for the gestational age without sonographic molar changes should have follow-up US to exclude partial mole. In missed abortion, impaired trophoblastic vascularity leads to hydropic degeneration of villi and can resemble a partial hydatidiform mole on US. The serum $\beta$-hCG is not elevated, however, and may be normal or at a lower level than for

![Fig. 14. Complete hydatidiform mole. (A) Transabdominal sonogram of the uterus shows a complex mass with multiple well-defined anechoic cystic areas (arrows) corresponding to the vesicles of hydatidiform mole. There was no associated embryo. (B) Corresponding T1-weighted postgadolinium image of the uterus demonstrates intrauterine complex mass (arrowheads) with multiple well-defined hypointense lesions that are not enhancing and represent vesicles of hydatidiform mole (arrow).](image)
the expected gestational age. Rarely, a viable fetus may be associated with complete molar pregnancy and is caused by the coexistence of a true mole and a normal fetus in dizygotic twin gestation. Demonstration of the typical trophoblastic flow is useful in differentiating the trophoblastic tissue of molar pregnancy from intrauterine blood clots in a patient with abortion. Theca-leutin ovarian cysts are seen in up to 25% to 60% of cases because of hyperstimulation of the ovaries by chorionic gonadotrophin secreted by the trophoblastic tissue. In this condition, the ovaries are enlarged with multiple cysts having a soap bubble or spoke-wheel appearance.

Treatment of hydatidiform mole consists of immediate evacuation of the mole and subsequent follow-up with serial measurement of serum \( \beta \)-hCG for detection of persistent trophoblastic proliferation or malignant change. TVUS is useful in monitoring patients following evacuation and chemotherapy. If the \( \beta \)-hCG levels plateau or continue to rise, persistent trophoblastic tissue is diagnosed. Following evacuation of a hydatidiform mole, 18% to 29% with complete hydatidiform mole and 1% to 11% with partial mole develop a persistent trophoblastic tumor. TVUS reveals nodules of residual echogenic trophoblastic tissue and central hypoechoic blood spaces. Doppler interrogation reveals typical low-resistance and high-peak systolic velocity vascular flow of trophoblastic tissue.

Gestational trophoblastic tumors

Gestational trophoblastic tumor refers to choriocarcinoma, invasive mole, and placental site trophoblastic tumor. It may follow a normal or a molar pregnancy, abortion, or ectopic pregnancy. Diagnosis is made primarily by persistent elevation of the serum \( \beta \)-hCG. Fifty percent of these tumors arise following hydatidiform mole, 25% following abortion, and 25% following normal or ectopic pregnancy.

Choriocarcinoma

Choriocarcinoma is a malignant form of trophoblastic tumor that invades uterine myometrium and blood vessels resulting in distant metastasis. The absence of villous pattern is characteristic of choriocarcinoma, in contrast to hydatidiform mole and invasive mole. The most common sites of metastases are the lungs (over 75%) and the vagina (50%). Other sites of metastases include the vulva, liver, kidneys, brain, ovaries, and bowel. The US appearance is indistinguishable from a complete mole, except in cases with myometrial and parametrial extension. TVUS reveals a heterogeneous intrauterine mass or without myometrial invasion. Doppler interrogation reveals typical trophoblastic flow and differentiates trophoblastic tissue from areas of hemorrhage and necrosis. Ovarian theca-leutin cysts are identified in more than a third of such cases. Cross-sectional imaging with CT and MR imaging is more accurate in demonstrating invasion of the myometrium and parametrium. Radiologic evaluation for distant metastases is mandatory in all cases of choriocarcinoma.

Invasive mole

This is defined as excessive trophoblastic overgrowth with invasion of the myometrium and occasional extension to the peritoneum or adjacent parametrium. Unlike choriocarcinoma there are no distant metastases. Invasive mole presents clinically as heavy vaginal bleeding after the evacuation of the molar pregnancy with persistent elevation of serum \( \beta \)-hCG. On TVUS it appears as focal areas of increased echogenicity within the myometrium. Doppler color flow mapping of this area can evaluate the extent of this lesion and its subsequent response to chemotherapy (Fig. 15).

Placental site trophoblastic tumor

This is a very rare trophoblastic tumor, which arises from the placental implantation site following either a normal term pregnancy or abortion. These patients present with either abnormal bleeding or amenorrhea and might be presumed to be pregnant. Moreover, the \( \beta \)-hCG levels are not as high as in other forms of gestational trophoblastic disease. They may invade the myometrium and in 15% to 20% cases behave in a malignant fashion with distant metastases. US features are indistinguishable from those of other gestational trophoblastic tumors.

Arteriovenous malformation of the uterus

It is important to consider arteriovenous malformations in the differential diagnosis of first-trimester bleeding because of their sonographic resemblance to retained products of conception and gestational trophoblastic disease. Vascular malformations of the uterus are rare and potentially life-threatening lesions. They can be congenital or acquired following uterine trauma (surgery or curettage); use of intrauterine contraceptive devices; endometrial or cervical carcinoma; and previous treatment of gestational trophoblastic tumors. Congenital arteriovenous malformations have multiple arteriovenous communications and may extend through the myometrium into the parametrium. Acquired lesions are arterio-
venous fistulas between a single artery and a vein. Vascular malformations persist following treatment in 10% to 15% of patients with gestational trophoblastic tumors. Gray-scale US shows multiple anechoic spaces with mosaic pattern of color signals within the cystic spaces on color Doppler US. Spectral analysis of the vessels shows high-velocity blood flow with a low resistive index [95,96], indistinguishable from a gestational trophoblastic disease (Fig. 16). These vessels can be distinguished from gestational trophoblastic disease because the serum β-hCG is normal.

Uterine arteriovenous malformations are one of the common causes of spontaneous abortions. Contrast-enhanced CT, MR imaging, and angiography are other imaging modalities used to diagnose uterine arteriovenous malformations. The diagnosis of uterine arteriovenous malformations as the cause of vaginal bleeding is crucial because treatment is entirely different from that for retained products of conception or gestational trophoblastic disease, which can mimic arteriovenous malformations. The treatment of arteriovenous malformations is by embolization if the

Fig. 15. Invasive mole. (A) TVUS showing molar tissue invading the myometrial wall (arrowheads) of the fundus and endometrial cavity (arrow). (B) Color flow Doppler evaluation shows vascularity of the invaded myometrium. Endometrial cavity is shown by arrow. (C) Corresponding T2-weighted, sagittal image of the uterus demonstrates hyperintense myometrium (arrow) representing invasive molar tissue. Uninvolved endometrial lining is shown (arrowheads).
Summary

Vaginal bleeding is a leading cause of presentation for emergency care during the first trimester of the pregnancy. Clinical assessment of the pregnancy outcome at this stage is less reliable. US examination is crucial in establishing IUP and early pregnancy failure and to exclude other causes of bleeding, such as ectopic pregnancy and molar pregnancy. Diagnosis of a normal IUP at this stage not only assists the physician in an expectant management, but also gives a psychologic boost to the patient. With recent advances in US technology and the availability of high-frequency transvaginal transducers, reliable diagnosis of early pregnancy failure can be made even before the embryo is visible.

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