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A BIWEEKLY REVIEW OF CLINICAL RADIOLOGIC PRACTICE

Common and Uncommon Imaging Presentations of Ectopic Pregnancy

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This module meets the American Board of Radiology's (ABR's) criteria for self-assessment toward the purpose of fulfilling requirements in the ABR Maintenance of Certification (MOC) program.

Please note that, in addition to the SA-CME credits, subscribers completing the activity will receive the usual ACCME credits.

After participating in this educational activity, the diagnostic radiologist will be better able to identify common and uncommon imaging features of ectopic pregnancy, describe features that portend a poor prognosis, and offer management options.

Category: Women's Imaging
Subcategory: Genitourinary
Modality: Ultrasound

Key Words: Ectopic pregnancy, Imaging of ectopic pregnancy, Treatment of ectopic pregnancy

Ectopic pregnancy most commonly occurs in a fallopian tube (~95%¹) (Figure 1). Major risk factors for ectopic pregnancy include a history of pelvic inflammatory disease or previous tubal surgery. Additional risk factors include smoking, assisted reproductive technology, and the use of an intrauterine device.² Ectopic pregnancies located outside the fallopian tube have a poorer prognosis, as they have more blood supply, grow larger, and have an elevated risk of catastrophic hemorrhage if ruptured. The clinical presentation of pelvic pain, elevated β -human chorionic gonadotropin, and vaginal bleeding is similar, regardless of the location of an ectopic pregnancy; thus, imaging plays

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a crucial role in directing management. Early diagnosis by imaging has played a key role in reducing maternal mortality and allowing patients to pursue more conservative management options to reduce morbidity and preserve future fertility. However, ruptured ectopic pregnancy still remains the leading cause of maternal death in the first trimester.³ Uncommon locations of ectopic pregnancy often are missed or incorrectly diagnosed at initial imaging, resulting in poor outcomes.

Tubal Ectopic Pregnancy

The fallopian tube is the most common location for ectopic pregnancy, with the ampullary location (70%) far more common than the isthmic (12%) and fimbrial (11%) locations.¹ The embryo also may implant, less commonly, within the interstitial portion of the fallopian tube. Interstitial ectopic pregnancy will be discussed later in this article. Rupture of a tubal ectopic pregnancy has the best prognosis among the various locations of ectopic pregnancy. This is primarily due to the thin wall of the fallopian tube, which ruptures early in gestation. Early gestational rupture is associated with relatively less bleeding and thus a more favorable outcome.

Rupture of a tubal ectopic pregnancy has the best prognosis among the various locations of ectopic pregnancies.

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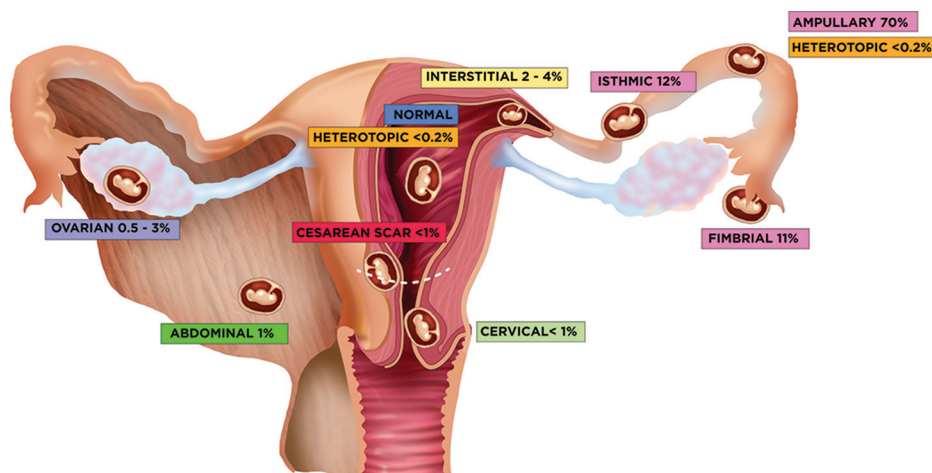


Figure 1. Locations of ectopic pregnancy and their occurrence rates. Approximately 95% of ectopic pregnancies occur within a fallopian tube. (Illustration by Philip J Cohen.)

The key findings of tubal ectopic pregnancy are an absent intrauterine pregnancy, elevated β -human chorionic gonadotropin levels, and an adnexal lesion. Free pelvic blood also may be present if the ectopic pregnancy has ruptured. An adnexal mass separate from the ovary distinguishes tubal ectopic pregnancy from a normal corpus luteum, which occurs exclusively within the ovary. In contrast to a corpus luteum, a dynamic ultrasound examination with pressure from the transducer can demonstrate the ovary moving separate from a tubal ectopic pregnancy. For a given adnexal lesion, the negative predictive value for ectopic pregnancy given the lack of separate movement is as high as 96.1%.⁴ A tubal ectopic pregnancy typically has a thick echogenic ring surrounding the ectopic gestational sac, brighter than that seen with a corpus

luteum.⁵ This so-called “tubal ring sign” (Figure 2) is another feature to differentiate an ectopic pregnancy from a corpus luteum. Another widely known feature of tubal ectopic pregnancy is the “ring of fire” sign

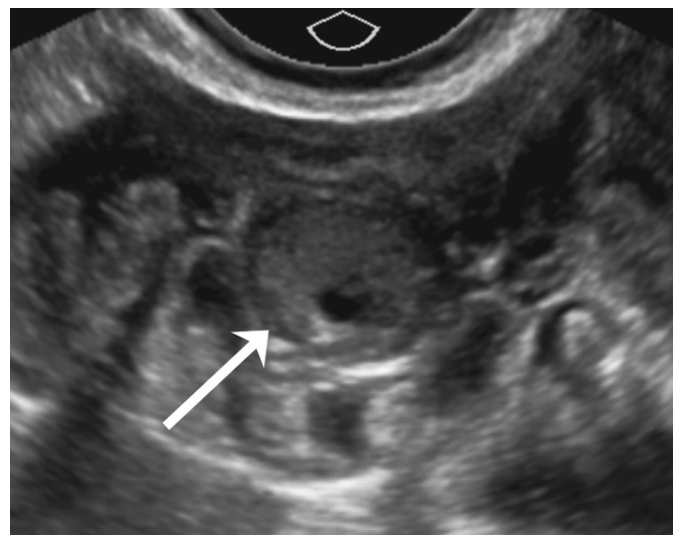


Figure 2. Tubal ectopic pregnancy with tubal ring sign (arrow), which represents a thick echogenic rim around a tubal ectopic pregnancy, brighter than that typically seen with a corpus luteum.

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(Figure 3). Duplex ultrasound will demonstrate a ring of intense color Doppler flow (often incomplete) corresponding to hypervascular trophoblastic tissue around an ectopic gestational sac. A corpus luteum also may have a similar ring of fire appearance, rendering the finding nonspecific (Figure 3). The ring of fire sign's highest utility is as a sensitive test to aid in the detection of suspicious lesions amid a complex adnexa, as seen with pelvic hemorrhage from ectopic pregnancy rupture.⁵

In the setting of ectopic pregnancy, a pseudogestational sac may be identified (Figure 4). A pseudogestational sac will appear as a teardrop-shaped, centrally located hypoechoic collection within the endometrial cavity surrounded by an echogenic lining. This imaging appearance is due to fluid or hemorrhage surrounded by endometrial decidual reaction. A pseudogestational sac should not be mistaken for a normal intrauterine pregnancy. A pseudogestational sac is distin-

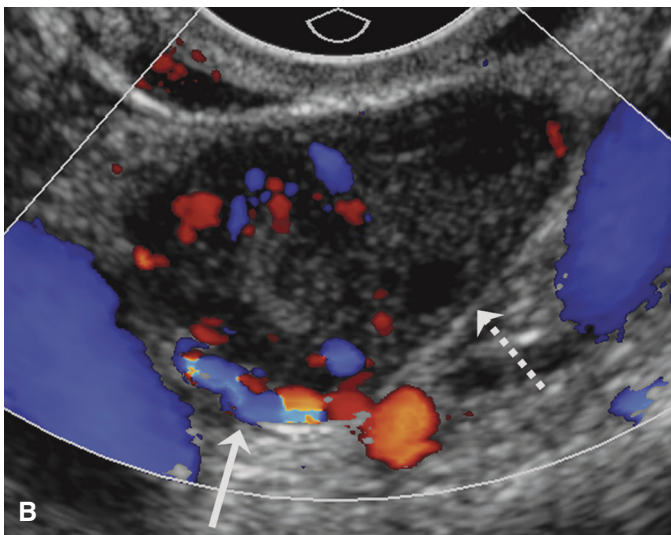
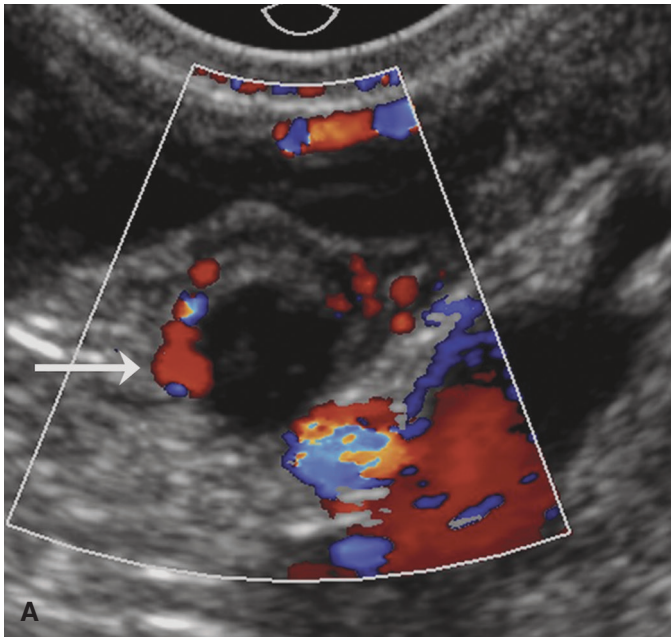


Figure 3. Tubal ectopic pregnancy. *A*: Ring of fire sign (*arrow*) representing hypervascular trophoblastic tissue surrounding an ectopic gestational sac within the left fallopian tube. *B*: Corpus luteum (*arrow*) within the same patient's left ovary (*dashed arrow*) also has a ring of fire sign, similar to that seen with tubal ectopic pregnancies, rendering the finding nonspecific.

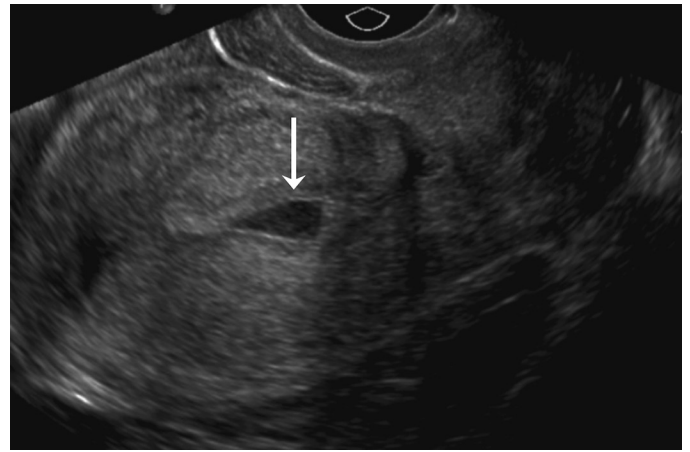


Figure 4. Pseudogestational sac (*white arrow*) in a patient with known tubal ectopic pregnancy. Pseudogestational sac is a teardrop-shaped, hypoechoic fluid collection located centrally within the endometrial cavity surrounded by an echogenic lining representing fluid or hemorrhage with surrounding endometrial decidual reaction.

guished by the aforementioned teardrop morphology, central location, movement of the fluid during the examination, and the lack of intradecidual and double decidual sac signs (characteristic signs of a normal intrauterine pregnancy).⁵ Finally, while rare, a live adnexal embryo is 100% specific for ectopic pregnancy.⁵

Interstitial Ectopic Pregnancy

Interstitial ectopic pregnancy (2%–4% of ectopic pregnancies) occurs when the embryo implants within the distal most portion (interstitial portion) of the fallopian tube, the 1- to 2-cm segment that traverses the myometrium.¹ This type of ectopic pregnancy often is referred to incorrectly as a cornual ectopic pregnancy. The term “cornual” ectopic pregnancy usually is reserved for an ectopic pregnancy within a rudimentary horn of a unicornuate uterus (this type of ectopic pregnancy will be discussed in detail later). Due to the thicker myometrial covering in this location, interstitial ectopic pregnancies have potential to grow large, sometimes into the second trimester, and thus portend a poor prognosis if ruptured.

An interstitial ectopic pregnancy occurs in the distal fallopian tube in the 1- to 2-cm segment that traverses the myometrium.

The initial clue to the diagnosis of an interstitial ectopic pregnancy is a gestational sac located in the upper uterine fundus with a lateralized, eccentric position. A thinned, overlying myometrium measuring less than 5 mm is a key secondary sign of an interstitial location.⁵ Although not seen commonly, the “interstitial line sign” is an echogenic line (representing the interstitial portion of the fallopian tube) connecting the suspected ectopic pregnancy to the endometrial complex. When present, the interstitial line sign is 98% specific for interstitial ectopic pregnancy¹ (Figure 5).

In combination with the above-mentioned imaging features, three-dimensional ultrasound (Figure 6) helps distinguish an interstitial ectopic pregnancy from an intrauterine angular pregnancy, the latter of which can progress to a live birth, although at high risk for complications, including

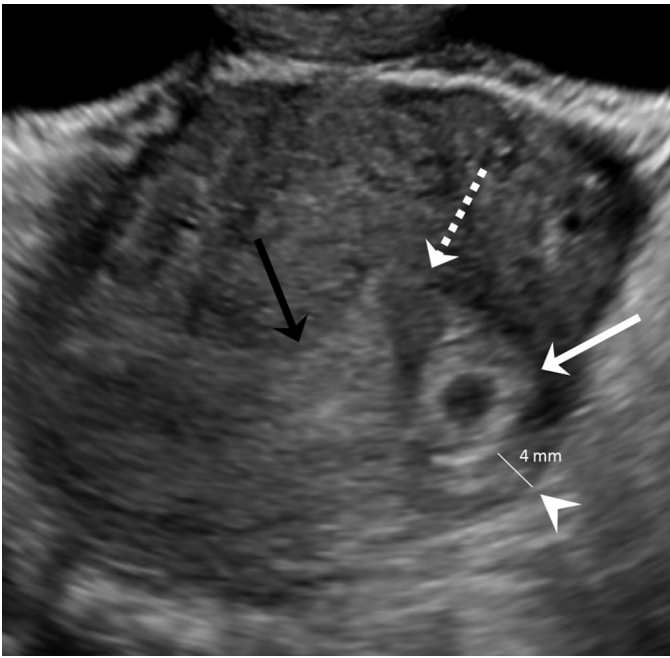


Figure 5. Transverse image of the uterus with interstitial ectopic pregnancy (*white arrow*) surrounded by a thin layer of overlying myometrium (*arrowhead*) (<5 mm), with presence of an interstitial line sign (*dashed arrow*) representing the interstitial portion of the fallopian tube extending from the ectopic pregnancy to the uterine endometrium (*black arrow*).

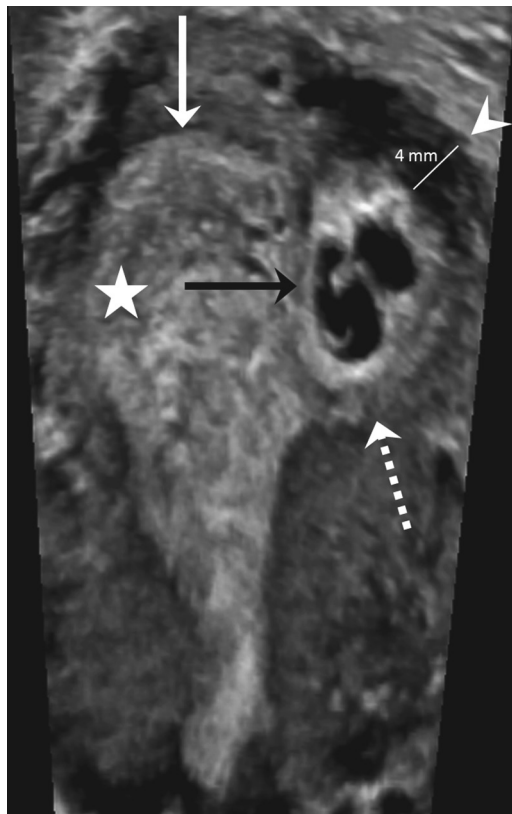


Figure 6. Three-dimensional ultrasound demonstrates a left-sided interstitial ectopic pregnancy (*black arrow*) with an eccentric gestational sac implanted within the interstitial portion of the fallopian tube (*dashed arrow*). The empty uterus (*white arrow*) and the thin myometrial layer overlying the interstitial pregnancy (*arrowhead*) are visualized. The *star* represents the hypothetical eccentric location of an uncommon mimic, an angular pregnancy, located in the far lateral uterine fundus near the tubal ostium completely surrounded by endometrium.

uterine rupture. An interstitial ectopic pregnancy is located within the fallopian tube, anatomically lateral to the round ligament, whereas an angular pregnancy is located within the most superior and lateral endometrium, just medial to the tubal ostium, and anatomically medial to the attachment of the round ligament.⁶ An angular pregnancy often is treated as an interstitial ectopic pregnancy, given its 40% miscarriage rate and its higher likelihood of associated uterine rupture, but it can be followed expectantly, as the gestational sac may migrate more medially in the endometrium.⁶ An interstitial ectopic pregnancy may be difficult to differentiate from an angular pregnancy by imaging; three-dimensional ultrasound or MRI may be needed to improve the accuracy of the diagnosis.^{1,6} In an interstitial ectopic pregnancy, there is a thin layer of myometrium between the endometrium and the gestational sac with the myometrium measuring less than 5 mm. In an angular pregnancy, the embryo is far lateral; however, it is still surrounded by the endometrium and has a thicker overlying myometrial layer.⁶ Both must be differentiated from the eccentricity of a normal pregnancy due to a transient uterine contraction. A contraction should be suspected when the gestational sac is near or within asymmetrically thickened myometrium. A contraction should resolve eventually during the examination or upon a close interval follow-up.⁶ A leiomyoma also may cause lateral deviation of a normally implanted gestational sac, mimicking the eccentric appearance of interstitial ectopic and angular pregnancies.⁶

Cornual Ectopic Pregnancy

Cornual pregnancy has been defined variably as a pregnancy in the upper lateral uterine cavity (the cornua) of an anatomically normal uterus or, more commonly, as a pregnancy in the horn of an anomalous uterus (implantation in the cornua of a septate or bicornuate uterus or within the rudimentary horn of a unicornuate uterus). The anomalous uteri have more prominent cornua; thus, an embryo is more likely to implant there.⁶

A cornual pregnancy is distinct from an interstitial pregnancy. A cornual pregnancy usually leads to a viable fetus, but complications are more common, mainly due to the nature of the uterine anomaly. Implantation within a certain form of unicornuate uterus—one with a noncommunicating rudimentary horn—is a relative medical emergency (Figure 7). Fertilization and subsequent implantation can occur in this scenario via intra-peritoneal passage of sperm to the contralateral fallopian tube. Although a low percentage of embryos in these cornual pregnancies can reach a viable age, the majority will rupture, and, therefore, they are surgically removed at the time of diagnosis.⁷

An initial diagnostic clue for an ectopic pregnancy within a noncommunicating rudimentary horn is an empty uterus with a single interstitial fallopian tube contralateral to an ectopic pregnancy, often at an advanced stage of development.⁷ A normal uterus, on the other hand, has two interstitial fallopian tubes. Therefore, the finding of a single interstitial fallopian tube in an empty uterus helps distinguish a unicornuate uterus with pregnancy in a rudimentary uterine horn from an abdominal or interstitial ectopic pregnancy, both of which also may present at an advanced stage of development. Early diagnosis is critical, as there is an extremely high risk of rupture with catastrophic hemorrhage.⁷ Three-dimensional ultrasound of the empty unicornuate uterus to identify the single

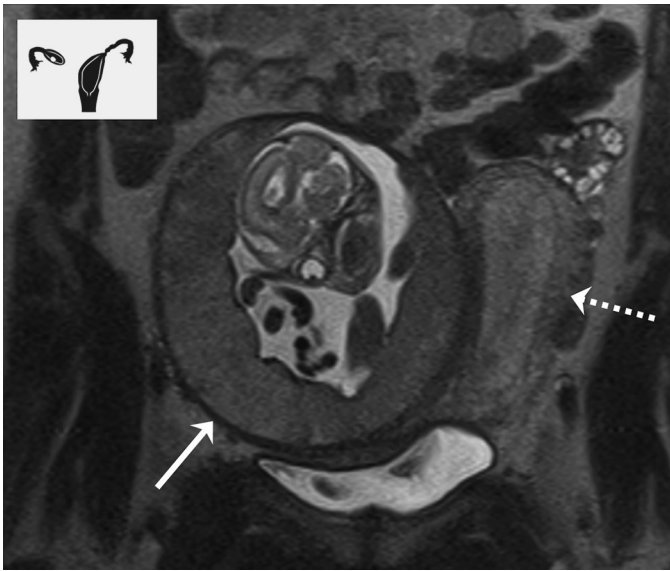


Figure 7. Cornual ectopic pregnancy with the large second-trimester fetus (*white arrow*) within the noncommunicating rudimentary horn of a unicornuate uterus (*dashed arrow*). Schematic image depicts the location of the implanted embryo.

interstitial fallopian tube may suggest the diagnosis, and myometrium encompassing the fetus confirms the diagnosis. MRI is occasionally needed for definitive diagnosis.⁷

Cervical Ectopic Pregnancy

Rarely (<1%), the embryo may implant within the cervix¹ (Figure 8). The imaging appearance is that of an eccentrically located gestational sac within the cervix in the setting of an empty uterine body. This can mimic the much more common abortion in progress; hence, care should be taken to distinguish between these two entities. Contrary to a cervical ectopic pregnancy, an abortion in progress will have a more

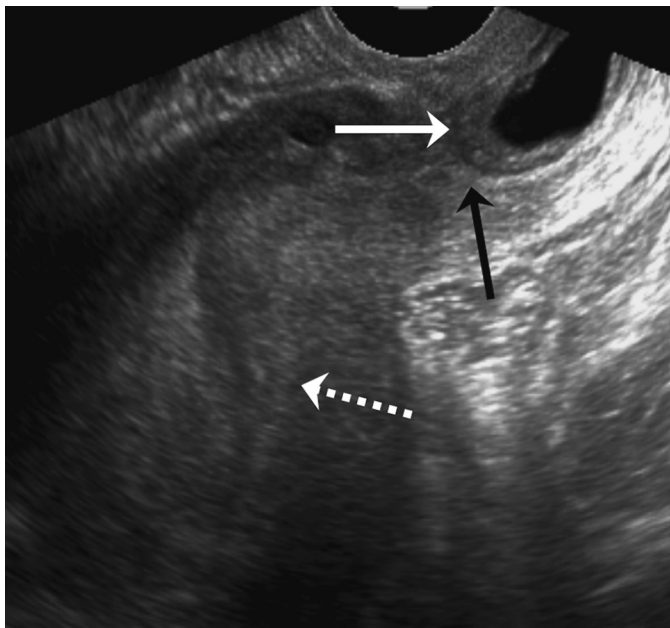


Figure 8. Cervical ectopic pregnancy visualized with a gestational sac (*white arrow*) implanted within the cervix and an empty uterus (*dashed arrow*). Eccentric position and closed internal os (*black arrow*) distinguish cervical ectopic from an abortion in progress, which is located more centrally and occurs with an open internal os.

central location within the cervical canal and there will be an open internal cervical os. Positive trophoblastic flow, seen on color Doppler, is present in cervical ectopic pregnancy, further distinguishing it from a separated, devascularized abortion in progress.¹

An abortion in progress can mimic a cervical ectopic pregnancy, but the former usually is centrally located within the cervix with an open internal cervical os, and the latter is eccentric with a closed internal os.

Cesarean Scar Ectopic Pregnancy

An embryo may also implant within a patient's prior cesarean scar (<1%), along the anterior wall of the myometrium in the lower uterine segment.¹ The imaging features of a cesarean scar ectopic pregnancy include eccentric location, closed internal cervical os, and positive trophoblastic flow, similar to those of a cervical ectopic pregnancy, with the additional feature of a very thin layer of myometrium overlying a bulging uterine contour at the scar.¹

Heterotopic Ectopic Pregnancy

Heterotopic ectopic pregnancy, defined as a concurrent normal intrauterine pregnancy with an ectopic pregnancy in any location (Figure 9), is rare, seen in fewer than one in 30,000 pregnancies. The incidence is increasing (~10-fold) due to the proliferation of assisted reproductive technology.¹ Risk factors for ectopic pregnancy should be taken into account when considering this diagnosis. Once a normal intrauterine pregnancy is identified, it is important to evaluate the adnexa closely for heterotopic ectopic pregnancy, especially in the setting of pelvic pain. Upon visualization of an indeterminate adnexal mass, dynamic compression examination to determine whether the ovary moves separately from the lesion is important, given the heightened clinical implications of this diagnosis. A patient with heterotopic ectopic pregnancy faces the same risks of laparoscopic surgery as in the setting of a normal viable intrauterine pregnancy.

In a pregnant patient, especially with pelvic pain, it is important to search for an additional heterotopic ectopic pregnancy once a normal intrauterine pregnancy is identified.

Ovarian Ectopic Pregnancy

Intraovarian implantation occurs in approximately 0.5% to 3% of ectopic pregnancies¹ (Figure 10). This diagnosis is often impossible to make definitively at initial imaging, as an ovarian ectopic pregnancy almost always appears identical to the ubiquitous corpus luteum, moving with the ovary on dynamic compression examination.⁸ A markedly echogenic, thick-walled ring surrounding a hypoechoic area within the ovary may suggest the diagnosis, a finding similar to the tubal ring sign seen in tubal ectopic pregnancy.⁸

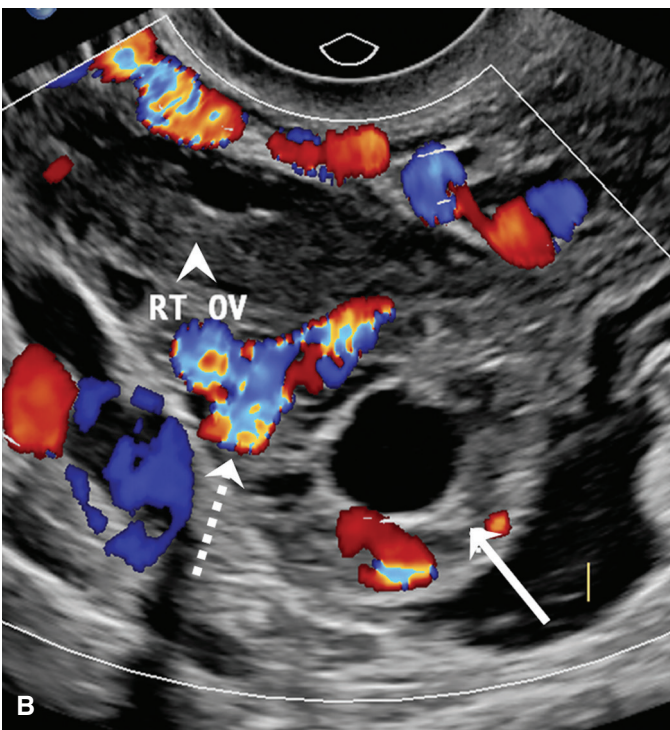
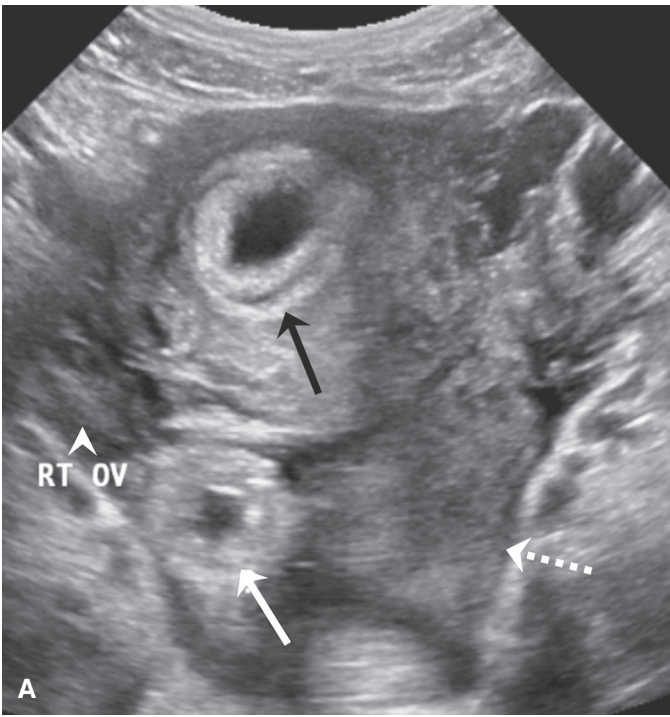


Figure 9. Ruptured heterotopic ectopic pregnancy. *A:* Live intrauterine pregnancy (*black arrow*), right adnexal lesion (*white arrow*) separate from the right ovary (*arrowhead*) consistent with tubal heterotopic ectopic pregnancy, and pelvic hemorrhage indicative of rupture (*dashed arrow*). *B:* Right adnexal lesion in the same patient (*white arrow*) with ring of fire sign (*dashed arrow*) and clear separation from the right ovary (*arrowhead*) consistent with tubal heterotopic ectopic pregnancy.

However, the only way to diagnose an ovarian ectopic pregnancy definitively at initial imaging is the presence of a yolk sac or fetal pole within an intraovarian gestational sac.⁸

Abdominal Ectopic Pregnancy

There are two types of abdominal ectopic pregnancy (1% of ectopic pregnancies¹): primary and secondary.⁹ Secondary

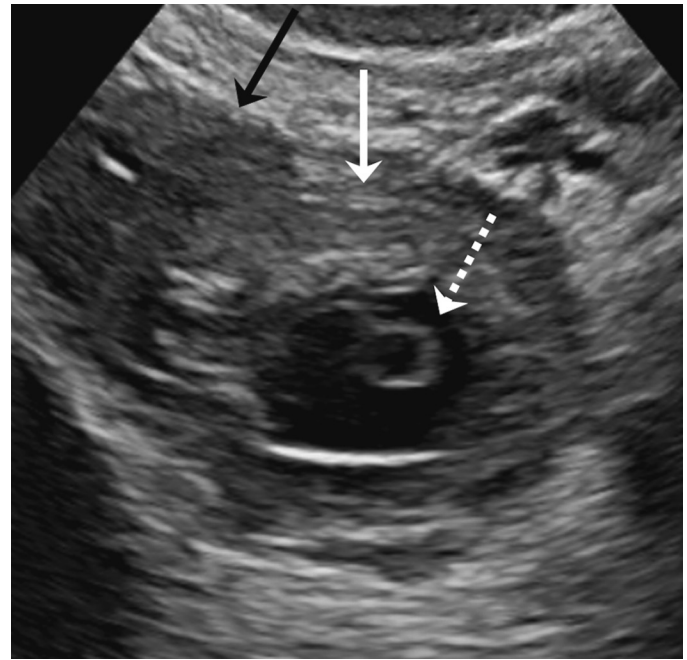


Figure 10. Ovarian ectopic pregnancy with fetal pole and yolk sac (*dashed arrow*) implanted within the right ovary (*black arrow*). Note the echogenic, thick-walled ring (*white arrow*) surrounding the intraovarian embryo, a finding similar to the tubal ring sign seen in tubal ectopic pregnancy. Intraovarian location was confirmed subsequently with dynamic examination and pressure from the transducer.

abdominal ectopic pregnancy, which is far more common than primary, occurs after rupture or extrusion of a tubal or other ectopic pregnancy followed by reimplantation anywhere within the abdominal cavity, most commonly within the rectouterine pouch of Douglas.⁹ Primary implantation of the embryo within the abdominal cavity (primary abdominal

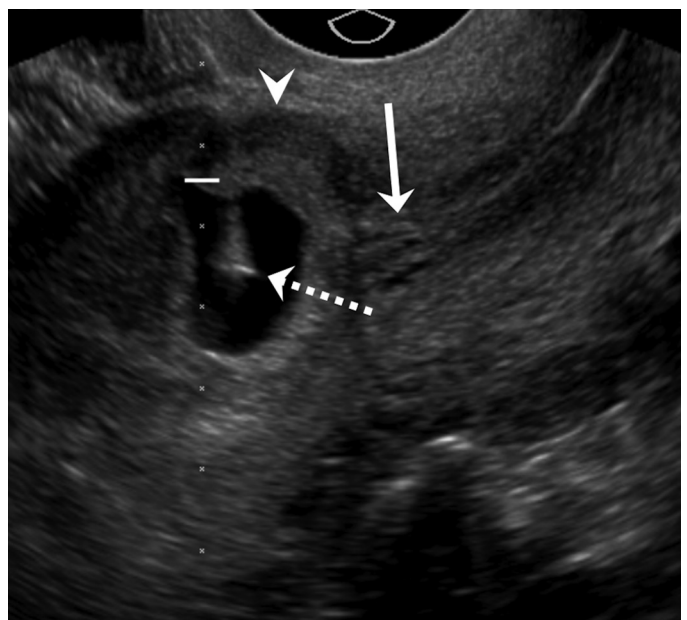


Figure 11. Transvaginal, ultrasound-guided injection of potassium chloride into an ectopic pregnancy at a cesarean delivery scar. The needle tip (*dashed arrow*) is centered within the gestational sac. Note the typical features of cesarean delivery scar ectopic pregnancy, including eccentric position of a lower uterine segment gestational sac with a thin overlying myometrial layer (*arrowhead*), and closed internal cervical os (*arrow*).

ectopic pregnancy) is extremely rare. As with any ectopic pregnancy located outside the fallopian tube, abdominal ectopic pregnancy carries a poor prognosis as the fetus may grow large and recruit a dense blood supply.⁹ On rare occasions, abdom-

inal ectopic pregnancy may grow and remain viable into the third trimester and, even more rarely, progress to live birth.

Management of Ectopic Pregnancy

Multiple options are available for the management of ectopic pregnancy. Surgical management, most often laparoscopic, is a definitive treatment, although it is invasive and associated with a decrease in the patient's future fertility.³ Medical therapy, typically with methotrexate, is best suited for stable patients with smaller-sized ectopic pregnancies at an early gestation.³ Gestational sac injection may be employed, with ultrasound-guided injection of methotrexate or potassium chloride into the gestational sac (Figure 11). This treatment is best reserved for smaller ectopic pregnancies in unusual locations such as cesarean delivery scar, cervical, or heterotopic ectopic pregnancy.¹⁰ Uterine artery embolization by interventional radiology often is employed to control bleeding preemptively, before surgical resection of the ectopic pregnancy. This often is used in the setting of large, second-trimester ectopic pregnancies at a more advanced stage of development such as those in the rudimentary horn of a unicornuate uterus¹⁰ (Figure 12).

For treatment of small ectopic pregnancies, gestational sac injection of methotrexate or potassium chloride with ultrasound guidance may be employed.



Figure 12. Uterine artery embolization to control bleeding preemptively before surgical resection of a cornual ectopic pregnancy with a 20-week fetus (dashed arrow in B) within the noncommunicating rudimentary horn of a unicornuate uterus. A: Digital subtraction angiogram with microcatheter selection of the right uterine artery (white arrow) demonstrates dominant vascular supply to the rudimentary horn via the right uterine artery. B: Digital subtraction angiogram after injection of 500- to 700-µm particles demonstrates adequate devascularization of the rudimentary horn (black arrow in A and B). The patient's fertility was preserved, and she subsequently had two normal cesarean deliveries.

Conclusion

Imaging plays a pivotal role in diagnosing and guiding the management of ectopic pregnancy. This CME activity emphasizes that the ability to precisely localize an ectopic pregnancy is critical, as prognosis, risk of catastrophic hemorrhage from rupture, and management options are guided by the location of the ectopic pregnancy. Familiarization with the imaging features of tubal ectopic pregnancy and other, more atypical locations, can aid radiologists in providing optimal care to patients with this diagnosis.

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1. Which one of the following may be injected into the gestational sac with ultrasound guidance for treatment of a small ectopic pregnancy?
- Potassium chloride
 - Sodium chloride
 - Autologous whole blood
 - Thrombin
 - Platelets

See Reference No. 10 for further study

2. Which one of the following is *more* suggestive of a cervical ectopic pregnancy than an abortion in progress?
- Central location of the gestational sac
 - Open internal cervical os
 - Positive trophoblastic flow
 - Echogenic material within the gestational sac

See Reference No. 9 for further study

3. Which one of the following is the location of an interstitial ectopic pregnancy?
- Cervix
 - Most distal portion of the fallopian tube
 - Ovary
 - Cesarean delivery scar
 - Intra-abdominal

See Reference No. 1 for further study

4. Which one of the following ultrasound features of the uterus is *most* suggestive of the diagnosis of a unicornuate uterus with an ectopic pregnancy within a noncommunicating rudimentary horn?
- Interstitial line sign
 - Pseudogestational sac
 - Double decidua sign
 - Single interstitial fallopian tube
 - Angular pregnancy

See Reference No. 7 for further study

5. Which one of the following ultrasound features in a pregnant woman *best* aids in the localization of an adnexal mass as extraovarian, and thus suspicious for a tubal ectopic pregnancy, rather than an ovarian corpus luteum?
- Color Doppler
 - Increasing transducer gain
 - M-mode
 - Maximum pain directly overlying the adnexal lesion
 - Separation of the ovary from the adnexal mass on dynamic examination with pressure from the transducer

See Reference No. 4 for further study

6. Which one of the following statements concerning ovarian ectopic pregnancy is *false*?
- It represents an intraovarian implantation of a gestational sac.
 - It is more common than fimbrial ectopic pregnancy.
 - On ultrasound, it is difficult in the early stage to differentiate from a corpus luteum.
 - The presence of a yolk sac or fetal pole within an intraovarian gestational sac is diagnostic.

See Reference No. 8 for further study

7. All of the following are risk factors for ectopic pregnancy, *except*
- obesity.
 - history of pelvic inflammatory disease.
 - previous tubal surgery.
 - smoking.
 - assisted reproductive techniques.

See Reference No. 2 for further study

8. The location of an angular pregnancy is
- proximal fallopian tube.
 - distal fallopian tube.
 - intrauterine.
 - intraovarian.
 - cervical.

See Reference No. 6 for further study

9. Which one of the following ruptured ectopic pregnancies has the *best* prognosis?
- Cervical
 - Ovarian
 - Abdominal
 - Cesarean scar
 - Tubal

See Reference No. 3 for further study

10. The *most* common location for an ectopic pregnancy is the
- cervix.
 - isthmic portion of the fallopian tube.
 - ovary.
 - ampullary portion of the fallopian tube.
 - scar of a prior cesarean delivery.

See Reference No. 5 for further study