Cervical pregnancy: Diagnosis and management

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INTRODUCTION

Cervical pregnancy is a rare form of ectopic pregnancy in which the pregnancy implants in the lining of the endocervical canal. This entity accounts for less than 1 percent of ectopic pregnancies [1]. The incidence is approximately 1 in 9000 pregnancies. In a 10-year, population-based study of 1800 cases, no cervical pregnancies were encountered [2]. Cervical pregnancy may be more common in pregnancies achieved through assisted reproductive technologies; it occurs in 2 percent of in vitro fertilization ectopic gestations [3]. Diagnosis and treatment early in pregnancy are important since there is a high risk of severe hemorrhage, and prevention of the need for hysterectomy is a high priority.

The cause of cervical pregnancy is unknown; local pathology related to previous cervical or uterine surgery may play a role given an apparent association with a prior history of curettage or cesarean birth [2]. Another theory is rapid transport of the fertilized ovum into the endocervical canal before it is capable of nidation or because of an unreceptive endometrium.

The diagnosis and management of cervical pregnancy will be reviewed here. Related topics regarding ectopic pregnancy are discussed in detail separately, including:

- Epidemiology and risk factors (see "Ectopic pregnancy: Epidemiology, risk factors, and anatomic sites")
- Clinical manifestations and diagnosis (see "Ectopic pregnancy: Clinical manifestations and diagnosis")

- Choosing a treatment approach (see "Ectopic pregnancy: Choosing a treatment")
- Diagnosis and management of uncommon sites of ectopic or abnormal intrauterine pregnancies (see "Abdominal pregnancy" and "Ectopic pregnancy: Clinical manifestations and diagnosis", section on 'Heterotopic pregnancy' and "Ectopic pregnancy: Choosing a treatment", section on 'Heterotopic pregnancy' and "Cesarean scar pregnancy")

CLINICAL FEATURES

The most common symptom of cervical pregnancy is vaginal bleeding, which is often profuse and painless [2]. Lower abdominal pain or cramps occur in fewer than one-third of patients [2]; pain without bleeding is rare. This presentation in early pregnancy should raise concern for cervical pregnancy. Early diagnosis is critical to avoid severe blood loss and ensure successful treatment. Early cervical pregnancy may also be asymptomatic and be found incidentally on ultrasound.

Risk factors for cervical pregnancy are the same as for other ectopic pregnancy. A history of uterine curettage in a patient with first-trimester bleeding should increase suspicion of cervical pregnancy in particular. This is because uterine curettage may result in intrauterine adhesions and increase the risk of cervical implantation of a pregnancy. In patients treated with assisted reproductive technology, the risk factors in addition to curettage include a history of at least two pregnancies or miscarriages and smoking [3].

Unlike tubal ectopic pregnancy where the bleeding is inside the peritoneal cavity, the main risk of cervical pregnancy is uncontrolled vaginal bleeding given the inability of the cervix to contract.

EVALUATION

The general approach to evaluation of suspected ectopic pregnancy includes a medical history, physical examination, serum human chorionic gonadotropin (hCG), and transvaginal ultrasound (TVUS). This is discussed in detail separately. (See "Ectopic pregnancy: Clinical manifestations and diagnosis", section on 'Diagnostic evaluation'.)

Aspects of the evaluation that are particular to cervical pregnancy are reviewed here.

Physical examination — On presentation with bleeding during pregnancy, the patient should be immediately assessed with vital signs for hemodynamic stability and with an abdominal examination for an acute abdomen or other findings consistent with severe intraabdominal bleeding. Ectopic pregnancy may cause life-threatening hemorrhage.

Suspicion of cervical pregnancy may first arise with pelvic examination. Findings on examination help to differentiate a cervical pregnancy from an intrauterine pregnancy and, in particular, from an incomplete abortion.

A gentle speculum examination may be performed. On inspection, the cervix is hyperemic and bulging. The external cervical os is typically closed in early cervical pregnancy. By contrast, the cervix is dilated in an incomplete abortion. But in some cases, there are fetal membranes or pregnancy tissue at the external cervical os, which appear blue or purple, and the external os may be open. Infrequently, a cystic lesion on the cervical lip is observed and represents trophoblastic invasion into the cervical stroma.

Ideally, if cervical pregnancy is suspected, bimanual examination is avoided until imaging studies have excluded the diagnosis. If bimanual examination is performed, a digital examination of the endocervical canal should not be performed, as this may cause hemorrhage. On palpation, a prominent finding in patients with cervical pregnancy is a soft cervix that is disproportionately enlarged compared with the uterus; this has been called an "hourglass" shaped uterus. By comparison, in an intrauterine pregnancy, it is typical to have enlargement of the uterus without significant cervical enlargement, although the cervix does soften and become mildly congested.

Transvaginal ultrasound — TVUS may be performed safely in patients with cervical pregnancy, and the diagnosis depends mainly on ultrasound findings. A sonographic impression of cervical pregnancy is correct in 87.5 percent of cases. The sonographic criteria for diagnosis of a cervical pregnancy are [4]:

- Gestational sac or placenta within the cervix; this is the most important criterion (image 1). However, the presence of gestational sac or placenta within the cervix is usually an abortion in progress. To distinguish cervical pregnancy from an abortion in progress, either cardiac activity should be seen in the embryo or blood flow should be seen to the gestational sac. While either of these could be present for a very short period of time in an abortion in progress, they will be persistent in a live cervical pregnancy. The distinction between a cervical pregnancy that is no longer alive from an abortion in progress is less important since, like any other nonviable pregnancy, the sac should eventually pass.

- No evidence of intrauterine pregnancy.

- Visualization of an endometrial stripe.

- Hourglass (figure of eight) shaped uterus with ballooned cervical canal.

Other features that may be found in cervical pregnancy include:

- The gestational sac tends to have regular contours. An incomplete abortion sac often has irregular contours, is flattened, or may change shape during the scan.
- The gestational sac may have an echogenic rim; this rim may be absent or minimal in incomplete abortion.
- Cervical pregnancy rather than incomplete abortion is also suggested by a negative sliding sac sign, which is no movement of the intracervical sac when the vaginal transducer is used to apply gentle pressure to the cervix.
- The location of the gestational sac may be below the level of the internal cervical os or uterine arteries, although this may be seen in an incomplete abortion that has been expelled to that level.
- A closed internal cervical os.

If the diagnosis is uncertain and the patient is stable, the ultrasound may be repeated the next day to see if the sac has moved (suggestive of an incomplete abortion).

Infrequently, magnetic resonance imaging (MRI) is used if the location of the pregnancy is unclear and MRI is needed to guide management [5]. The typical MRI image of cervical pregnancy is a lobulated, solid mass with heterogeneous signal intensity of varying stages of hemorrhage and an enhancing, papillary, internal projection of products of conception in the cervix.

DIAGNOSIS

Cervical pregnancy is a clinical diagnosis based on transvaginal ultrasound findings in a patient with a positive pregnancy test and no intrauterine pregnancy. Heterotopic cervical pregnancy, in which there is both an intrauterine pregnancy and a cervical pregnancy, is exceedingly rare [6]. (See "Ectopic pregnancy: Epidemiology, risk factors, and anatomic sites", section on 'Heterotopic pregnancy'.)

Histologic confirmation of a cervical pregnancy is not required, and pathology evaluation is performed only if the patient undergoes hysterectomy. Rubin defined histologic criteria for cervical pregnancy: close attachment of the placenta to the cervix, cervical glands present opposite the implantation site, placental location below uterine vessel insertion or below anterior and posterior reflections of the visceral peritoneum of the uterus, and no fetal elements in the uterine corpus [7].

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of cervical pregnancy includes other etiologies of bleeding early in pregnancy [8]:

- Physiologic (ie, bleeding in early pregnancy without pathology, possibly related to normal implantation)
- Ectopic pregnancy in other locations
- Spontaneous abortion
- Gestational trophoblastic disease
- Cervical, vaginal, or uterine pathology
- Subchorionic hematoma

The differential diagnosis of ectopic pregnancy in general is discussed in detail separately. (See "Ectopic pregnancy: Clinical manifestations and diagnosis", section on 'Differential diagnosis'.)

In particular, cervical pregnancy and incomplete abortion present similarly and may have similar findings on physical examination. Heavy vaginal bleeding may be associated with either condition, but bleeding that is profuse and impacts hemodynamic stability is more likely to be cervical pregnancy. Bleeding in incomplete abortion tends to be self-limited. The differentiation is made on transvaginal ultrasound. (See 'Physical examination' above and 'Transvaginal ultrasound' above and "Pregnancy loss (miscarriage): Ultrasound diagnosis".)

Differential diagnosis also includes cesarean or hysterotomy scar pregnancy, which should be considered if ultrasound shows the gestational sac is in the anterior lower uterine segment and the uterine cavity and endocervical canal are empty [9,10]. (See "Cesarean scar pregnancy".)

TREATMENT

Cervical pregnancy is rare, and there are no established criteria for candidates for medical versus surgical treatment as there are for tubal ectopic pregnancy. Treatment options include systemic methotrexate (MTX), local intragestational injection of MTX or potassium chloride (KCl), dilation and curettage (D&C), uterine artery embolization (UAE), and hysterectomy. A combination of methods is often required.

In our practice, hemodynamically stable patients are generally treated with MTX and hemodynamically unstable patients undergo immediate surgery. For patients with persistent bleeding after MTX treatment, we perform a D&C. If a patient continues to have bleeding, we perform UAE and then proceed with hysterectomy if all other measures fail. The latter is rarely needed.

Patients should be counseled about the high risk of hemorrhage and possibility of surgery. They should be asked about their future plans for pregnancy since this may guide the surgeon in terms of the measures taken to avoid hysterectomy. For patients who do not desire future pregnancy and desire definitive management, hysterectomy may be performed as the initial procedure.

Initial therapy

Preferred: Methotrexate alone — We use multidose MTX therapy as first-line therapy for all stable patients and add intraamniotic potassium chloride (KCl) injection if there is a fetal heartbeat present.

Experience with cervical pregnancy is too limited to allow any firm conclusions about optimal criteria for medical therapy, other than hemodynamic stability. As an example, the presence of fetal cardiac activity (present in 60 percent of cervical pregnancies in contrast to 10 percent of tubal pregnancies) is a poor prognostic factor for successful MTX therapy in tubal pregnancy, but whether this is also true for cervical pregnancy is not known. Another factor is that weighing risks and benefits of medical versus surgical therapy is different for cervical pregnancy than tubal pregnancy because surgical treatment of cervical pregnancy carries a significant risk of hemorrhage and possible hysterectomy.

Evidence of the use of MTX for treatment of cervical pregnancy is limited to case reports and small series [11-13]. Various medical therapies have been used (single- or multidose systemic MTX, local intrasac injection of MTX or KCl, or combinations of these therapies) and were efficacious in 80 to 90 percent of reported cases. There were no complications other than the usual side effects of MTX therapy. (See "Ectopic pregnancy: Methotrexate therapy", section on 'Adverse reactions'.)

In our institution, we use multidose MTX treatment since the multiple doses likely allow less risk of treatment failure and subsequent hemorrhage. Systemic intramuscular multidose MTX alone is often adequate for treatment of very early cervical pregnancies without fetal cardiac activity [14]. The multidose MTX drug protocol is the same as that used in patients with tubal ectopic pregnancy and is described separately. (See "Ectopic pregnancy: Methotrexate therapy", section on 'Patients with an interstitial pregnancy: Multiple-dose'.)

More advanced gestations with fetal cardiac activity are typically treated with combined treatment with both systemic multidose MTX and intraamniotic and/or intrafetal injection of KCl to cause prompt fetal death and thus facilitate pregnancy resorption, which can take a few months [15,16]. Intrasac injection is associated with a risk of hemorrhage when the sac collapses. In our practice, we have also successfully treated cervical pregnancy with fetal cardiac activity with systemic multidose MTX alone. This approach is a reasonable alternative and eliminates possible risks associated with intrasac KCl injection.

To perform KCl injection, a 20- to 22-gauge needle is advanced transvaginally into the gestational sac and fetal thorax under direct ultrasound visualization using a needle guide attachment. When the tip of the needle is in the embryo, KCl (1 to 5 mL of 20 percent KCl solution) is injected until there is cessation of cardiac activity.

Following MTX treatment, heavy vaginal bleeding when the pregnancy is involuting may require UAE to control hemorrhage.

Alternate: Methotrexate plus balloon catheter — Utilization of methotrexate plus a double balloon catheter has also been described with good results [16,17]. In a retrospective study including five patients with cervical pregnancy, management with a double balloon catheter plus a single dose of intramuscular methotrexate resulted in successful treatment of the cervical pregnancy in all cases; no cases of maternal hemorrhage requiring transfusion, hysterectomy, or intensive care unit admission were reported [17].

The procedure is similar to that used for management of cesarean scar pregnancy but with the lower (pressure) balloon inflated opposite the gestational sac in the endocervical canal (or below the external os) [16]. This is described in detail separately. (See "Cesarean scar pregnancy", section on 'Medical therapy'.)

Persistent bleeding — Dilation and endocervical curettage is performed if there is persistent or recurrent bleeding after MTX treatment or if the patient is hemodynamically unstable at presentation due to hemorrhage. Other surgical measures that may be used in patients who continue to bleed include placement of hemostatic sutures locally in the cervix, bilateral internal iliac artery ligation, or bilateral uterine artery ligation. Hysteroscopic resection of the site of bleeding with a resectoscope has also been reported to be successful [18]. Hysterectomy is performed if there is uncontrolled hemorrhage despite all other measures. (See "Overview of postpartum hemorrhage".)

Endocervical curettage — Due to the high risk of severe bleeding and the impact of hysterectomy on a patient who desires future pregnancy, if surgery is performed, we employ several measures to reduce the risk of bleeding.

We employ all these measures concurrently prior to curettage:

- Intracervical vasopressin, given as multiple injections around the circumference of the exocervix to the depth of the dense cervical stroma. We use a total of 20 to 30 mL of vasopressin (0.5 units/mL) solution and a 1.5-inch 21-gauge needle.
- Transvaginal ligation of the cervicovaginal branches of the uterine artery. This is done by deviating the cervix to one side and placing a suture at 3 and 9 o'clock on the lateral side of the cervix. The suture is placed high just below the lateral vaginal fornix, similar to sutures placed for hemostasis during cold knife conization. We use 2-0 polyglactin

(Vicryl) [4]. Alternatively, for patients who do not desire future pregnancy, preoperative UAE is an option. There are data showing decreased ovarian reserve after UAE for uterine fibroids. (See 'Uterine artery embolization' below.)

Dilation is performed and then endocervical curettage until no more gestational tissue is obtained.

The main potential complication is a high risk of severe hemorrhage. In a study of nine patients treated with curettage without MTX, three patients underwent hysterectomy for uncontrollable bleeding in two cases and a ruptured cervix in another [19].

Role of balloon catheter — A balloon catheter (eg, Foley bladder catheter, double Cook catheter) may be used postoperatively if implantation site bleeding occurs. In our practice, we insert a size 26 Foley catheter with a 30 mL balloon into the dilated cervix, with the tip extending into the uterine cavity. Sterile water (as much as 95 mL) is then used to inflate the balloon and tamponade the bleeding vessels for 24 to 48 hours. A purse string suture can be placed around the external cervical os and tied after inflation of the balloon to prevent expulsion. After 24 to 48 hours, the balloon is gradually deflated over a period of hours to days and removed but may be reinflated at any time if bleeding picks up or recurs. The catheter also allows constant uterine drainage. Alternatively, one can use a double balloon catheter (picture 1), with the first balloon located in the uterine cavity and the second balloon in the endocervical canal. We have also used vaginal packing as an additional tamponade. In one retrospective study including 13 cases of cervical pregnancy, curettage plus balloon tamponade resulted in successful treatment in all cases [20].

Uterine artery embolization — If heavy bleeding persists after endocervical curettage despite all measures described above, we utilize UAE. UAE is reserved for use as a third-line measure because subsequent fertility and pregnancy outcomes are uncertain [21]. However, UAE may be more a more effective first-line treatment option compared with other types (eg, systemic MTX alone) of treatment [22]. (See "Postpartum hemorrhage: Medical and minimally invasive management", section on 'Consider uterine or hypogastric artery embolization' and "Uterine fibroids (leiomyomas): Treatment with uterine artery embolization", section on 'Reproductive outcomes'.)

Patients who do not desire future pregnancy may undergo UAE prior to endocervical curettage to minimize the risk of bleeding, as noted above [23]. In one small series, this approach was successful in avoiding hysterectomy or laparotomy in all 16 cases [24]. In another series, 19 cervical pregnancies were treated with UAE followed by curettage; no patients required blood transfusion or hysterectomy [25]. By comparison, a literature review reported 71 percent of 41 cases treated without such preoperative preparation resulted in massive hemorrhage; seven cases ended in hysterectomy, and five cases were treated with bilateral internal iliac or uterine artery ligation.

In such cases, embolization with absorbable gelatin powder provides temporary obstruction (two to six weeks) of the feeding blood vessels and allows for development of collateral blood flow. Because collateral flow begins to develop within hours of the procedure, surgical evacuation should be performed soon after embolization to achieve the full benefit of the procedure. The optimal interval between UAE and surgical evacuation has not been established; intervals of several hours to 24 hours have been described. (See "Postpartum hemorrhage: Medical and minimally invasive management", section on 'Consider uterine or hypogastric artery embolization'.)

In one review, 36 patients with cervical pregnancy were treated with combined UAE and MTX intraarterial infusion, and this was the sole management without need for secondary treatment in 15 of these cases [26]. Only one patient underwent a hysterectomy, and several subsequently had intrauterine pregnancies.

Hysterectomy — Hysterectomy is performed for uncontrolled bleeding from cervical pregnancy despite other measures. Patients who do not desire future pregnancy may be offered this as an option rather than an attempt at endocervical curettage. Hysterectomy is major surgery, and so MTX is typically first-line therapy even in patients who do not desire future pregnancy.

PREGNANCY OUTCOME IN SUBSEQUENT GESTATIONS

Data are limited, but it appears that patients with cervical pregnancy are at increased risk of repeat ectopic pregnancy, but that otherwise, obstetric outcomes are similar to the general population. A review of 37 pregnancies two months to several years after a cervical pregnancy reported the following: 21 patients delivered at term (including one set of twins at 38 weeks), four delivered prematurely (at 25, 28, 32, and 36 weeks of gestation), three miscarried at 8 to 9 weeks of gestation, two underwent pregnancy termination, two had tubal pregnancies, one had a repeat cervical pregnancy (pregnancy conceived by in vitro fertilization), and four had ongoing pregnancies at the time of the report. Three patients had a McDonald cerclage placed because of suspected cervical insufficiency.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Ectopic pregnancy".)

SUMMARY AND RECOMMENDATIONS

- Cervical pregnancy is a rare form of ectopic pregnancy in which the pregnancy implants in the lining of the endocervical canal. This entity accounts for less than 1 percent of ectopic pregnancies. The incidence is approximately 1 in 9000 pregnancies. (See 'Introduction' above.)

- The most common symptom of cervical pregnancy is vaginal bleeding, which is often profuse and painless. Lower abdominal pain or cramps occur in fewer than one-third of patients; pain without bleeding is rare. Early diagnosis is critical to avoid severe blood loss and ensure successful treatment. (See 'Clinical features' above.)

- The evaluation of cervical pregnancy includes a medical history, physical examination, serum human chorionic gonadotropin (hCG), and transvaginal ultrasound (TVUS). If cervical pregnancy is suspected, a bimanual pelvic examination and digital examination of the cervix should be avoided to prevent severe bleeding. (See 'Physical examination' above.)

- TVUS may be performed safely in patients with cervical pregnancy, and the diagnosis depends mainly on ultrasound findings. The sonographic criteria for diagnosis of a cervical pregnancy are a gestational sac or placenta within the cervix (typically with a fetal cardiac activity or blood flow), no evidence of intrauterine pregnancy, visualization of an endometrial stripe, and an hourglass (figure of eight) shaped uterus with ballooned cervical canal. (See 'Transvaginal ultrasound' above.)

- Methotrexate (MTX) is first-line therapy for hemodynamically stable patients, and immediate surgery is required if a patient is unstable. For persistent bleeding after MTX treatment, dilation and endocervical curettage is performed. Continued bleeding may be treated with uterine artery embolization, and then with hysterectomy if all other measures fail. Patients should be counseled about the high risk of hemorrhage and possibility of surgery. (See 'Treatment' above.)

- We suggest MTX treatment rather than surgery for cervical pregnancy (**Grade 2C**). We use multidose MTX therapy as first-line therapy for all stable patients and add intra-amniotic potassium chloride (KCl) injection if there is a fetal heartbeat present. (See 'Initial therapy' above.)

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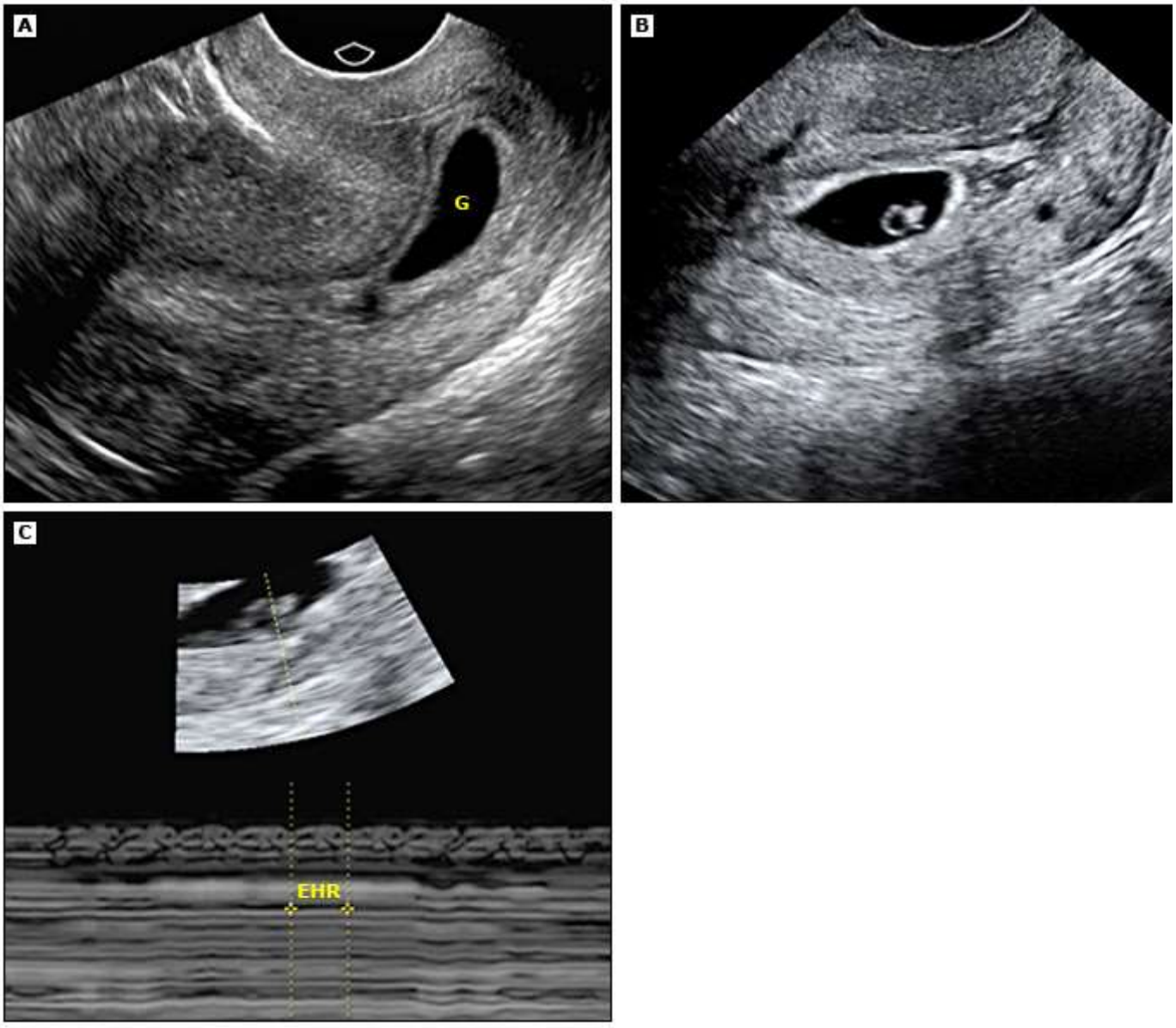
GRAPHICS

Cervical pregnancy



Three views of cervical ectopic pregnancy obtained at different fields of view. (Panel A) A gestational sac seen in the cervix (G). Closer inspection shows a yolk sac and tiny embryo (panel B) with cardiac activity (panel C).

EHR: embryonic heart rate.

Courtesy of Tejas S Mehta, MD, MPH.

Graphic 57961 Version 5.0

Transcervical balloon catheter

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Contributor Disclosures

Togas Tulandi, MD, MHCM, FRCSC, FACOG, FCAHS No relevant financial relationship(s) with ineligible companies to disclose. **Courtney A Schreiber, MD, MPH** Patent Holder: Penn, Saul [Medical management of nonviable pregnancy]. Grant/Research/Clinical Trial Support: Athenium Pharma [Early pregnancy loss]; Bayer [Contraception]; Medicines360 [Contraception]; VeraCept [Contraception]. Consultant/Advisory Boards: Danco Pharmaceuticals [Early pregnancy loss]. Other Financial Interest: American Board of Obstetrics and Gynecology [Member of Board of Directors, Chair of Division of Complex Family Planning]; Athenium Pharmaceuticals [Royalties]. All of the relevant financial relationships listed have been mitigated. **Deborah Levine, MD** No relevant financial relationship(s) with ineligible companies to disclose. **Alana Chakrabarti, MD** No relevant financial relationship(s) with ineligible companies to disclose.

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