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The Symptoms of Ectopic Pregnancy often Go Unnoticed

Keywords: Ectopic Pregnancy; Test; Diagnosis; Treatment

Abstract

Under normal circumstances, fertilization occurs in the fallopian tube. The fertilized egg divides at the same time by mitotic divisions and travels to the uterus. A few days after fertilization, the embryo is implanted in the uterus. In ectopic pregnancy, implantation occurs outside the uterus. In 95% of cases, an ectopic pregnancy is located in the fallopian tube. Very rare are the locations of ectopic pregnancy in the vagina, ovary, abdominal cavity, as well as in the cervix. The symptoms of an ectopic pregnancy depend on where it is located, but also on the duration of the pregnancy, ie the time that has elapsed since fertilization. The clinical picture can be varied and can mimic a number of early pregnancy disorders. The classic triad of symptoms includes absence of menstruation, abdominal pain, and vaginal bleeding. Abdominal pain is most often unilateral and located in the lower part, and dark-colored bleeding and irregular.

Introduction

A reproductive age female presenting with pelvic pain, a positive urine pregnancy test, and an inconclusive pelvic ultrasound provokes diagnostic uncertainty and anxiety for the practicing physician [1]. The spectrum of diagnostic possibilities ranges from a symptomatic but normally implanted pregnancy to an ectopic pregnancy implanted in the uterine tube or elsewhere outside of the uterus. While management of the patient with acute symptoms clearly calls for urgent surgical intervention, management of the asymptomatic patient whose implantation site is indeterminate requires patient follow-up with serial serum HCG levels, periodic ultrasound imaging, and repeat physical examinations. The clinician must cope with the risk of possible rupture of an ectopic pregnancy and its associated morbidities. Pregnancy of unknown location accounts for 1–2% of all gestations and 4–6% of pregnancy-related deaths worldwide.

Ectopic pregnancies account for approximately 2% of all pregnancies [2]. The fallopian tube is the location of the majority (93–98%) of ectopic pregnancies. The remainder of ectopic locations can be divided between the cervix, interstitium, ovary, Cesarean section scar, or the abdomen. Cervical pregnancies account for less than 1% of all ectopic pregnancies. The frequency has been reported from 1 in 10 000 to 1 in 50 000 pregnancies. The rate, however, is higher in patients undergoing in-vitro fertilization, where it accounts for up to 3.5% of ectopic pregnancies.

Due to their extremely low incidence, risk factors for cervical pregnancies have been difficult to determine. Two series found 50–70% of patients with cervical pregnancies have had a previous curettage. Another very small series showed that 75% of the patients have had a previous Cesarean delivery. Additional possible risk factors include Asherman syndrome and diethylstilbestrol (DES) exposure.

The incidence of ectopic pregnancy has been increasing since 1970, when the Centers for Disease Control and Prevention (CDC) first began collecting data, from 4.5 per 1000 reported pregnancies to 19.7 per 1000 pregnancies in 1992 [3]. The increased incidence is thought to be due to two factors: (1) the increased incidence of acute salpingitis, due to increased infection with *Chlamydia trachomatis*, and (2) improved diagnostic techniques, which enable diagnosis of unruptured ectopic pregnancy to be made earlier and with more precision. Other factors that appear to be associated with an increased risk of ectopic pregnancy include prior ectopic pregnancy, cigarette smoking, prior tubal surgery (especially for distal tubal disease), diethylstilbestrol exposure, increasing age, multiparity, and current use of an intrauterine device. The 10-year cumulative probability of ectopic pregnancy for all methods of tubal sterilization combined was shown to be 7.3 per 1000 procedures. An operative procedure on the oviducts themselves is a cause of ectopic pregnancy. The incidence of ectopic pregnancy after salpingoplasty or salpingostomy procedures to treat distal tubal disease ranges from 15% to 25%. The rate of ectopic pregnancy after reversal of sterilization procedures is about 4% because the tubes have not been damaged by infection. Women who have had a prior ectopic pregnancy, even if treated by unilateral salpingectomy, are at increased risk for a subsequent ectopic. Of women who conceive after having one ectopic pregnancy, about 25% of subsequent pregnancies are ectopic.

First Trimester

The most common symptoms of an ectopic pregnancy include pelvic pain, missed menses, and vaginal spotting [1]. Any reproductive age female who presents with abnormal vaginal bleeding must have a pregnancy test. A leaking or ruptured ectopic pregnancy may produce right upper quadrant or shoulder pain.

Vaginal bleeding is common during pregnancy and approximately one quarter of women experience bleeding during the first trimester [4]. Half of these women have uneventful prenatal courses. Cramping and abdominal pain increase the likelihood of spontaneous pregnancy loss (spontaneous abortion). If the cervix is dilated or products of conception are seen in the vagina, the prognosis is poor. If the cervical os is closed, transvaginal ultrasound and serial β -hCG levels help in the assessment of viability.

It is critical to rule out ectopic pregnancy in cases of first trimester bleeding. Risk factors for ectopic pregnancy include previous pelvic inflammatory disease, history of ectopic pregnancy, tubal surgery, assisted reproductive technology, and current use of an intrauterine device. Diagnosing ectopic pregnancy can be challenging. Patients may have first trimester bleeding or be asymptomatic. Pelvic pain begins insidiously or suddenly, is usually lateralized, and can be mild or severe. The uterine size may be smaller than expected and an adnexal mass may be present. Ultrasound may show a fetal pole or heartbeat visible outside the uterine cavity or a thick-walled adnexal mass without a yolk sac or fetal pole that is separate from the ovary.

Early diagnosis of an ectopic pregnancy is augmented using quantitative β -hCG (increase by at least 66% over 48 hours expected) and transvaginal ultrasound. Prompt identification and timely treatment are critical, as ectopic gestation occurs in 2% of total pregnancies and is the leading cause of maternal mortality during the first trimester.

Risk

Physical examination of the abdomen and pelvis in a patient with a suspected ectopic pregnancy may elicit variable degrees of pain [1]. Vague, nonspecific findings are notoriously common among women with ectopic pregnancies. Rebound abdominal tenderness or cervical motion tenderness suggests peritoneal irritation from the presence of blood in the peritoneal cavity. Shock-like vital signs and acutely worsening abdominal and pelvic pain symptoms suggest rupture.

Risk factors for ectopic pregnancy include prior ectopic pregnancy, history of infertility, history of sexually transmitted infection, smoking, increased age, previous miscarriage, previous pregnancy termination, prior pelvic or abdominal surgery, endometriosis, or conceiving while having an intrauterine device in place or being pregnant in spite of having a tubal ligation.

Pelvic Exam

The pelvic examination can be a very challenging examination to execute because of associated patient discomfort, anxiety, and embarrassment [5]. The American College of Physicians reported that 35 percent of surveyed women experience fear, anxiety, discomfort, and/or pain during their pelvic examination. Women who experienced pain with their pelvic examination were found to be less likely to return for their visit than those who did not have a negative experience. Another study sought to address suggestions to improve the examination process from patients that had negative experience. Explaining each step of the examination in advance, providing information about the reproductive organs, warming the instruments, increased gentleness, and maintaining eye contact have been suggested by the patients as ways to improve the overall experience of the basic GYN examination. All of these areas can be addressed with simulation training.

The pelvic examination is conducted to screen for pathology, with the examination made of three elements: inspection of the external genitalia; speculum examination of the vagina and cervix; and bimanual examination of the adnexa, uterus, ovaries, and bladder and sometimes a rectovaginal examination.

Teaching the pelvic examination portion of the basic GYN exam can start with an overview of the necessary materials. Reviewing the various swabs, Pap smear collection devices, bacterial wound culture, viral culture container, review of various specula (pediatric, nulliparous, multiparous speculum), and urine culture collection are some of the many various useful materials that a learner may not have seen before. Becoming familiar with these materials, recognizing what they look like, and indications and uses of collecting samples may be very helpful for the learner and lead to a more efficient and streamlined exam.

Having the opportunity to be instructed by a standardized patient on proper techniques for performing pelvic examinations is ideal as the anatomy is real and the feedback is immediate. Standardized patients are often utilized as both instructors and patients for these sessions. The standardized patient is able to talk the learner through proper bedside manner and work through a pelvic examination and bimanual examination usually with an instructor present to further provide brief lecture to the students prior to the examination. Often, the standardized patient provides the learner with feedback and helpful critiques to allow for improvement in clinical skills as both the content expert and patient.

Test

Women may present with acute onset unilateral abdominal/pelvic pain, associated with nausea and vomiting and a history of amenorrhoea with a positive pregnancy test [6]. They may or may not have had some vaginal spotting. Signs and symptoms of dizziness, shoulder-tip pain, tachycardia, hypotension and peritonism suggest a haemoperitoneum and therefore a ruptured ectopic. Classic features that may be elicited on bimanual examination include cervical excitation and marked adnexal tenderness. If a woman is stable and has an intact ectopic pregnancy, she may just present with a mild to moderate amount of pain with some possible vaginal bleeding.

A pregnancy test is the first investigation required in all women of reproductive age to determine whether the abdominal pain may be pregnancy or non-pregnancy related. Other essential baseline investigations include baseline blood tests (full blood count, electrolytes, serum β -hCG), urinalysis and a venous blood gas to measure levels of acidosis and lactate and for a quick measure of the patient's haemoglobin. A serum progesterone is not useful in predicting an ectopic pregnancy. Transvaginal ultrasound is the diagnostic investigation of choice in the case of a stable ectopic pregnancy, which has a reported sensitivity of 87%–99% and specificity of 94%–99%. In an unstable patient where rupture is suspected, patients should be taken straight to the operating theatre for a diagnostic laparoscopy.

Laparoscopy

Laparoscopy has been used effectively as a valuable diagnostic tool for a wide variety of abdominal and pelvic pathologies [7]. It has been used for the assessment of acute or chronic pain, suspected ectopic pregnancy, endometriosis, adnexal torsion, or other extragenital pelvic pathologies. In most cases, the laparoscope is placed through an infraumbilical port, and a probe is placed through a second suprapubic port to manipulate the pelvic organs, if only a diagnostic

laparoscopy is performed. However, for operative laparoscopy other than the simplest procedures, the suprapubic port is not useful and is quite uncomfortable. If operative laparoscopy is performed, the accessory trocars should be placed in the right and left lower quadrants. For advanced laparoscopy, an accessory trocar at the level of the umbilicus lateral to the rectus muscle will allow the principal surgeon to operate comfortably and have access to the pelvis. If tubal patency is a concern, a dilute dye can be injected transcervically, a procedure termed chromopertubation.

Laparoscopy has become the surgical approach of choice for most ectopic pregnancies. The embryo and gestational sac are removed either through a longitudinal incision (linear salpingotomy) or by removing the tube (salpingectomy). Both were compared in a recent RCT. The cumulative ongoing pregnancy rate was similar after salpingotomy (60.7%) compared to 56.2% after salpingectomy. However, persistent trophoblast occurred more frequently following salpingotomy compared to salpingectomy. Recurrent ectopic pregnancy rate was 8% following salpingotomy and 5% following salpingectomy. Even a ruptured tubal pregnancy can be treated laparoscopically, as long as the patient is hemodynamically stable.

Diagnosis

Ultimately the diagnosis of ectopic pregnancy requires the combination of laboratory, clinical, and ultrasound findings [8]. For the emergency physician, the absence of hard signs of an IUP on ultrasound plus a quantitative hCG level above 1000 mIU/mL should trigger Ob/gyn consultation or formal ultrasound imaging to further investigate the possibility of an ectopic pregnancy. In stable patients with minimal symptoms, it may be reasonable to arrange repeat hCG testing in 48 hours; doubling of the level within 48 hours suggests early IUP.

The only ultrasound finding of ectopic pregnancy may be large amounts of free fluid in the pelvis. In some cases of ectopic pregnancy, fluid (blood) may be found in Morison's pouch.

Complications

Clinicians must be cognizant of the complications of a disease, so that they will understand how to follow and monitor the patient [9]. Sometimes, the student will have to make the diagnosis from clinical clues, and then apply his or her knowledge of the consequences of the pathologic process. For example, a woman who presents with lower abdominal pain, vaginal discharge, and dyspareunia is first diagnosed as having pelvic inflammatory disease or salpingitis (infection of the fallopian tubes). Long-term complications of this process would include ectopic pregnancy or infertility from tubal damage. Understanding the types of consequences also helps the clinician to be aware of the dangers to a patient. One life-threatening complication of a tubo-ovarian abscess (which is the end-stage of a tubal infection leading to a collection of pus in the region of the tubes and ovary) is rupture of the abscess. The clinical presentation is shock with hypotension, and the appropriate therapy is immediate surgery. In fact, not recognizing the rupture is commonly associated with patient mortality. The student applies this information when she or he sees a woman with a tubo-ovarian abscess on daily rounds, and monitors for hypotension, confusion, apprehension, and tachycardia. The clinician advises the team to be vigilant for any signs of abscess

rupture, and to be prepared to undertake immediate surgery should the need arise.

Treatment

If the β -hCG shows an abnormal rate of rise, including plateau, slow rise, or declining values, then ultrasound is warranted [10]. However, if the β -hCG value is below the discriminatory threshold, suction curettage is useful to distinguish between a nonviable intrauterine pregnancy and an ectopic gestation. The absence of chorionic villi in the curettage specimen in the presence of an elevated hCG is predictive of an ectopic pregnancy, though in early gestation the curettage may be falsely negative for villi.

Treatment of ectopic pregnancy is either surgical or medical depending on several variables. The surgical approach is definitive, but invasive and more costly than medical management. Medical management results in successful treatment for 90% of appropriately selected patients. Methotrexate is utilized for medical management. Appropriate indications for medical management require a hemodynamically stable patient who is compliant and has no medical contraindication to methotrexate. Relative contraindications include a gestational sac > 3.5 cm, presence of fetal cardiac motion, or a β -hCG value of > 15,000 mIU/mL. Administration of a single dose of methotrexate has reported efficacy of 84%. Use of multidose regimens increases the rate of success. Failure of the β -hCG value to fall by at least 15% within 4-7 days after treatment indicates that additional methotrexate or surgery is indicated. Patients who are Rh negative are given Rh₀(D) immune globulin whether treated medically or surgically. Other developments in medical management include the use of other agents such as potassium chloride, prostaglandins, and mifepristone, but these have not been studied as well as methotrexate.

Surgical options for treatment of ectopic pregnancy are intended to remove the ectopic gestation and preserve functional Fallopian tube, if possible. If the patient is hemodynamically stable, the laparoscopic approach is usually preferred. If she is in shock or if the abdomen is distended with blood, emergent laparotomy is necessary. If the Fallopian tube is generally healthy, a salpingostomy is possible whereby the involved section of the Fallopian tube is removed through an incision in the antimesenteric portion of the tube, while leaving the remainder of the tube intact. If the tube is more extensively damaged, complete or partial salpingectomy is recommended. If conservative approaches to preserve the Fallopian tube are utilized, the β -hCG value should be monitored postoperatively until normalization occurs.

Clinical Presentation

The clinical presentation of ectopic pregnancy is very variable and reflects the biological potential of pregnancy to develop beyond a very early stage [11]. This in turn is largely determined by the location of pregnancy within the tube. In general, more proximal implantation to the uterine cavity shows more advanced development. Ampullary ectopics, which represent 70% of all tubal ectopics, rarely develop beyond a very early stage and clinical symptoms of tubal abortion may be present as early as 5 weeks' gestation. On the other hand, one-third of interstitial tubal ectopics develop in a similar way to healthy intrauterine pregnancies with evidence of a live embryo on ultrasound examination. These pregnancies tend to be clinically silent

until sudden rupture occurs.

Most ectopic pregnancies represent a form of early pregnancy failure and the first symptom is usually brown vaginal discharge, which starts soon after the missed menstrual period. However, the amount of bleeding varies and in some women it can be quite heavy. Passage of a decidual cast may sometimes lead to an erroneous diagnosis of miscarriage. Abdominal pain is usually a late feature in the clinical presentation of ectopic pregnancy. The localization of pain is not specific and it is not unusual for women to complain of pain on the side contralateral to the ectopic. Some women may complain of period - like pain or upper abdominal discomfort. The pain is usually caused by tubal miscarriage and bleeding through the fimbrial end of the tube into the peritoneal cavity. The pain varies in intensity and does not necessarily reflect the volume of blood lost inside the abdominal cavity. About 10 – 20% of ectopic pregnancies present without bleeding. In a significant proportion of these cases a viable embryo is detected on ultrasound scan, which increases the risk of rupture. Pain associated with rupture tends to be more intense, with signs of peritonism on abdominal palpation. Severe rupture sometimes presents with nausea, vomiting and diarrhoea, which may resemble a gastrointestinal disorder. This confusing picture may cause delay in the diagnosis of ectopic pregnancy.

Women with suspected early pregnancy complications have traditionally been subjected to vaginal examination including speculum and bimanual palpation. Speculum examination has very little value in the detection of ectopic pregnancy. It may help to diagnose miscarriage by visualization of the products of conception within the cervix or vagina. Although this reduces the chance of an ectopic, it does not eliminate the possibility of a heterotopic pregnancy.

Emotional Support

The woman with an ectopic pregnancy requires support throughout diagnosis, treatment, and aftercare [12]. A woman's psychological reaction to an ectopic pregnancy is unpredictable. However, it is important to recognize she has experienced a pregnancy loss in addition to undergoing treatment for a potentially life-threatening condition. The woman may find it difficult to comprehend what has happened to her because events occur so quickly. In the woman's mind, she had just started a pregnancy and now it has ended abruptly. Help her to make this experience "more real" by encouraging her and her family to express their feelings and concerns openly, and validating that this is a loss of pregnancy and it is okay to grieve over the loss.

Provide emotional support, spiritual care, client education, and information about community support groups available as the client grieves for the loss of her unborn child and comes to terms with the medical complications of the situation. Acknowledge the client's pregnancy and allow her to discuss her feelings about what the pregnancy means. Also, stress the need for follow-up blood testing for several weeks to monitor hCG titers until they return to zero,

indicating resolution of the ectopic pregnancy. Ask about her feelings and concerns about her future fertility, and provide teaching about the need to use contraceptives for at least three menstrual cycles to allow her reproductive tract to heal and the tissue to be repaired. Include the woman's partner in this discussion to make sure both parties understand what has happened, what intervention is needed, and what the future holds regarding childbearing.

Conclusion

Ectopic pregnancy is a life-threatening condition for a woman, and her symptoms often go unnoticed. It occurs in about 1.4% of all pregnancies, and up to three times more often in pregnancies achieved by assisted reproduction methods. It is extremely important for every woman to recognize the symptoms in order to contact the doctor in time and prevent unwanted complications.

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