Ectopic Pregnancy

Alberta
District VIII
Midnight Teaching Presentation

Case Presentation

- 27 yo ♀ presents with +++RLQ abdominal pain x 2 days. Progressively worse. 10/10 at times. No nausea, no vomiting, no appetite. Diarrhea x 5
- Vaginal spotting x days
- LMP 3 weeks ago
- Morning-after pill taken ~ 3 weeks ago

- Afebrile, VSS
- + McBurney’s point tenderness
- Pelvic exam:
  - no cervical motion tenderness
  - Rt adnexal tenderness
  - Uterus anteverted and small

Labs

- Hb 12.4, WBC 13.8 (N° 11.2), Plt 349
- Na 137, K 3.2
- β-hCG 12,060 IU/L
- +++ free fluid on abdominal U/S in ER
- Transvaginal U/S later by gyne staff – empty uterus, +++clots in abdomen

- To OR
- Rt tubal ectopic
- Laparoscopic Rt linear salpingostomy
- Evacuation of hemoperitoneum
- Normal-looking Lt tube, uterus, ovaries
- No immediate complications
- F/U HCG declines to zero (follow hcg since not a salpingectomy)

Approach

- Airway, Breathing, Circulation
- Hx, Physical Exam
- Quantitative Serum β-hCG
- Blood type and screen, crossmatch
- CBC
- Transvaginal ultrasound

Ectopic Pregnancy

- Classic triad of:
  1. Abdominal Pain 90-100%
  2. Amenorrhea 75-85%
  3. Vaginal Bleeding 50-85%
- Also:
  - Adnexal tenderness 80-90%
  - Adnexal mass 40%
- 50% are asymptomatic before rupture

Ectopic Pregnancy

- Developing blastocyst becomes implanted somewhere besides the endometrium
- Most common extra-uterine site is the fallopian tube (98%)
- Despite ++ change in detection and management, remains the leading cause of maternal death in 1st trimester (10% of all maternal deaths)

Risk Factors for Ectopic Pregnancy

Degree of Risk	Risk Factors
High	-Previous Ectopic Pregnancy -Previous Tubal Surgery -Tubal Pathology -In utero DES exposure
Moderate	-Previous genital infections -Infertility -Multiple sexual Partners
Low	-Previous Pelvic/Abdo Surgery -Smoking -Early age of intercourse (<18yrs)

Where do ectopics
occur?

Sites of ectopic

- Fallopian Tube (95%)
  - factors that delay the passage of fertilized oocyte OR inherent embryonic factors that force premature implantation
  - Distribution:
    - Ampullary (70%)
    - Isthmic (12%)
    - Fimbrial (11%)
- Ovarian (3.2%)
  - PID, IUDs, infertility DO NOT increase a woman's risk (overall rate of pregnancy lower)
  - A random event that does not increase risk for future ectopics
- Interstitial/Cornual (2.4%)
  - Swelling lateral to insertion of round ligament
  - Uterine rupture common (20% that progress to 12 weeks)
- Abdominal (1.3%)
  - Can be primary (blastocyst implants on viscera) or secondary (extrusion of embryo from tube)
  - Wide spectrum of symptoms, and rarely end up with a viable infant
  - Often need laparoscopy to differentiate abdominal from tubal implantation
- Cervical Pregnancy
    - 1:9,000 of all pregnancies-more common when using assisted reproduction
    - 0.1% of IVF pregnancies (3.7% of IVF ectopics)

What are some clinical signs of an ectopic pregnancy?

Clinical Manifestations

- Typically 6-8 weeks after missed period (later in interstitial)
- Classic symptoms
- Shoulder pain
- Urge to defecate
- May display other symptoms of pregnancy
- 50% are asymptomatic before rupture and have no risk factors

Physical Exam

- Orthostatic changes
- Fever
- Cervical motion tenderness
- Abdo/pelvic pain or adnexal tenderness
- Adnexal mass
- Uterine enlargement
- NOTHING

What is your
differential diagnosis?

Differential Diagnosis

- Miscarriage
- Ruptured/bleeding corpus luteum
- UTI/calculi, diverticulitis, appendicitis, adnexal torsion, ruptured ovarian cyst, torsion/degeneration of fibroid, PID, endometriosis, abnormal uterine bleeding
- May display other symptoms of pregnancy

Diagnosis

- Clinical Presentation
- Transvaginal ultrasound (TVS) and serial serum β-HCGs are hallmark of diagnosis
- Possible laparoscopy
- Possible culdocentesis
- High risk women should be monitored ASAP after missed period

Diagnosis of intrauterine pregnancy

- Best by seeing true gestational sac (double echogenic rings), or a yolk sac on ultrasound
- Fluid in the uterus produces pseudosac
- With TVS…
  - Gestational sac visible at 4.5 to 5 weeks
  - Yolk sac at 5-6 weeks (until 10 weeks)
  - Fetal pole with cardiac activity at 5.5-6
  - NB: leiomyomas can make sacs hard to see

Suggestive Transvaginal U/S findings of Ectopic Pregnancy

- (+) uterine size and decidual response
- No yolk sac by 5.5 weeks or with bHCG >1500-2000mIU/ml
- No free fluid in cul de sac
- Complex adnexal mass

Diagnosis of extrauterine pregnancy

- Sac containing yolk sac or embryo only seen in 16-32% of cases
- Negative pelvic U/S does not exclude dx of ectopic
- Complex adnexal mass and empty uterus is 99% specific and 85% sensitive for ectopic
- Can use colour-flow Doppler (20-45% ↑ blood flow in tube with ectopic)
- fluid in belly does not confirm (ruptured cyst)
- Postive HCG but negative villi on D&C sample

β-HCG

- Can be detected 8 days post LH surge
- In normal intrauterine pregnancy, doubles q1.4-2.1 days
- Plateaus at 100,000 IU/L at 41 days GA
- 15% of NORMAL pregnancies do not have normal doubling
- 15% of ectopics DO have normal doubling
- Same lab is important; 10-15% interassay variability

What are appropriate levels for B-hCG?

- β-hCG is 10 at time of missed menses, 100,000 at 10 weeks and 10,000 at term
- ~1500 at 5 weeks
- ~6000 at 6 weeks
- Gestational sac can sometimes be seen at β-hCG of 800 IU/L, but usually 1,500-2,000 IU/L
- Absence of intrauterine gestational sac with β-hCG > 2,000 IU/L suggests ectopic

Laparoscopy

- Rare for diagnosis

MRI

- Not cost-effective

Culdocentesis

- Blood can be from hemorrhagic ovarian cyst or retrograde menstruation

Natural history of ectopic

- Tubal Rupture
  - Profound hemorrhage
  - Requires quick surgery
  - Remains major cause of pregnancy-related maternal mortality in 1st trimester
- Tubal Abortion
  - Expulsion of products through the fimbria
  - Can be followed by abdominal pregnancy, ovarian pregnancy after re-implantation of the trophoblasts
  - May be accompanied by +++ bleeding
  - Surgery not always necessary
- Spontaneous regression

Treatment for Ectopics

- Medical
  - Methotrexate
  - Has replaced surgical treatment in many cases
  - Success rate 86-94% (in appropriately selected women)
- Surgical
  - Laparotomoy/Laparoscopy
  - Salpingectomy/Salpingostomy
  - Segmental Resection
  - U/S guided injection of KCL or MTX
- Expectent (only in selected patients)

Methotrexate

- Folic acid antagonist
- Competitively binds to dihydrofolate reductase, thus preventing formation of active intracellular metabolite folinic acid
- Purine, pyrimidine (amino acid) metabolism is dependent on folinic acid
- Inhibits DNA metabolism in rapidly dividing cells (malignant, trophoblast, fetal cells)
- Patients should stop taking prenatal vitamins while being treated

What are the criteria for medical management of an ectopic?

Good candidates for medical Rx

- ACOG Criteria
  - Absolute Indications
    - Hemodynamic stability
    - Desiring future fertility
    - Significant risks for General Anesthesia
    - No MTX contraindications
    - Highly reliable patient
  - Relative Indications
    - Unruptured mass <3.5 cm
    - No fetal cardiac motion
    - BhCG not exceeding 6000-15000mIU/ml

Contraindications

Absolute

- Known sensitivity to MTX
- Breastfeeding
- Active pulmonary disease or peptic ulcer
- Hepatic, renal or hematologic dysfunction
- Pre-existing blood dyscrasias or anemia
- Alcoholism
- Evidence of immunodeficiency
- Noncompliance
- Hemodynamic instability

Relative

- Fetal cardiac motion
- Gestation sac >3.5 cm

What are the side effects of methotrexate?

Side Effects

- Mild and self-limiting
- Stomatitis, conjunctivitis
- Nausea/vomiting
- Abdominal pain
- Rarely,↑ liver enzymes, gastritis, enteritis, dermatitis, pleuritis, alopecia and bone marrow suppression
- Slightly higher in multi-dose therapy

Indications for surgical treatment

- Better for women with ↑ β-hCG (> 5000IU/L), large ectopic, fetal cardiac activity (probably)
- Ruptured ectopic
- Non-compliance
- Tubal rupture during medical treatment

Medical vs surgical methods

- Several studies suggest success rate is about the same
- Complications slightly higher with medical treatment
- β-hCG drop faster with surgery (less post treatment monitoring)
- Need RCT/more cohort studies to compare salpingostomy and salpingectomy

Expectant management

- Different trials have shown success rates of 57-70%
- Reasonable when ectopic is suspected, but TVUS is negative and β-hCG is equivocal
- Women with cardiac instability, bad pain, hemoperitoneum should be excluded
- Must have close monitoring (tubal rupture)

What about fertility after an ectopic pregnancy?

Fertility after treatment

- Incidence of recurrence is ~15% after one ectopic, and ~30% after two ectopics
- History of infertility is the most important factor for predicting subsequent fertility
- Ipsilateral periadenexal adhesions gives poor prognosis
- Maternal age >35 factor for decreased rate of subsequent intrauterine pregnancy
- Most conceive by 18 months post-ectopic

References

- UpToDate®
- Farquhar and Sowter. Ectopic Pregnancy: an update. *Curr Opin Obstet Gynecol* **16** (2004), pp. 289-93.
- Stovall *et al*. Methotrexate treatment of unruptured ectopic pregnancy: a report of 100 cases. *Obstet Gynecol* **77** (1991), pp. 741-53.
- Tulandi and Ahmed. Surgical Management of Ectopic Pregnancy. *Clin Obstet Gynecol* **42** (1999), pp. 31-8.
- Tulandi and Yoa. Current status of surgical and nonsurgical management of ectopic pregnancy. *Fertil Steril* **67** (1997), pp.421-33.