Ectopic Pregnancy

Background
1. Definition
   o Ectopic pregnancy
     ▪ Any pregnancy that occurs outside the intrauterine cavity
   o Ruptured ectopic pregnancy
     ▪ Pregnancy outside the intrauterine cavity that outgrows the site of implantation and ruptures
   o Heterotopic pregnancy
     ▪ Coexistence of intrauterine and ectopic pregnancies
2. True medical emergency

Pathophysiology
1. Pathology
   o Fertilized ovum implants outside of the intrauterine cavity
   o Embryo implants with no decidua formed
   o Trophoblastic cells erode through mucosa & muscularis, destroying tissues, opening blood vessels and producing intratubal hemorrhage
     ▪ Hemorrhage increases size of tubal mass
     ▪ May cause rupture or more commonly slow leakage of blood out through fimbriated end of tube with accumulation in posterior cul-de-sac
   o Common sites of implantation
     ▪ Ampulla: 80%, ruptures at 8-10 wks
     ▪ Isthmus: 15%, ruptures at 6-8 wks
     ▪ Interstitial (corneal): 2.5%, ruptures at 8-16wks, can cause fatal hemorrhage due to involvement of ovarian and uterine vessels
2. Incidence, prevalence
   o Rate of ectopic pregnancy in North America climbed from <0.5% (4.5 per 1,000) of all pregnancies in 1970 to 1.97% (20 per 1,000) in 1992
   o Incidence of ectopic pregnancy rupture and fatality rate has declined from 35.5 deaths per 10,000 ectopics in 1970 to 3.8 per 10,000 in 1989
   o Incidence of heterotopic pregnancy 1:30,000 for naturally occurring pregnancies, approx 1:100 with the use of assisted reproductive technologies
3. Risk factors
   o PID most important risk factor but frequently absent
   o History of any process affecting fallopian tube
     ▪ Previous ectopic, tubal surgery, infertility
     ▪ In utero DES exposure
     ▪ Genital infections
   o Current smoking
   o Age >35
   o Pregnancy occurring in patient with an IUD in situ or s/p tubal sterilization
4. **Morbidity, mortality**
   - Leading cause of 1st trimester maternal death
   - Ruptured ectopic pregnancy accounts for 10-15% of all deaths during pregnancy

**Diagnostics**

1. **History**
   - High index of suspicion
     - Female of reproductive age with abdominal pain and vaginal bleeding after amenorrhea for approx 7 wks
     - PID history
     - IUD in situ
     - Previous ectopic or h/o infertility
     - Gynecologic procedures

2. **Physical exam**
   - Vital signs
     - Often normal
     - Hypotension suggestive of ruptured ectopic pregnancy
   - Cardiovascular
     - Hypotension or hemodynamic instability suspect ruptured ectopic pregnancy
   - Abdomen
     - Unremarkable if unruptured
       - Dull & aching
       - Poorly localized
     - If ruptured
       - Significant tenderness
       - Guarding with rebound tenderness
       - Generalized peritonitis
   - Pelvic
     - Unremarkable in 10% of patients
     - Normal or slightly enlarged uterus
     - Cervical motion tenderness
     - Adnexal tenderness/ palpable mass
     - Hemoperitoneum / bulging posterior cul-de-sac

3. **Diagnostic testing**
   - Laboratory evaluation
     - **Beta HCG**
       - Not to be used as the only test
       - Most helpful in conjunction with ultrasound
       - Urine qualitative
         - Use to diagnose pregnancy
         - Sensitive to 15-50 mIU/mL or 3-4 days post implantation
         - Obtain in women of reproductive age presenting with abdominal pain and/or vaginal bleeding
- Serum quantitative:
  - Should increase by at least 53-66% every 2 days, peaking at >100,000 IU/L
  - Beta-HCG >6500: transabdominal ultrasound should be accurate
  - Beta-HCG >1500: transvaginal ultrasound should be accurate

- Progesterone
  - Often not useful clinically
  - <11 ng/mL: suggests abnormal pregnancy, but not all abnormal pregnancies are ectopic
  - >20 ng/mL: viable IUPs, but 2.6% of patients with ectopic pregnancies have progesterone levels >20 ng/mL

- Diagnostic imaging
  - Ultrasound
    - Should be part of the initial evaluation (SOR:C)\(^3,7\)
    - Absence of intrauterine gestational sac with beta- hCG level
      - >2,000 IU/L transvaginal ultrasound
      - >6,500 IU/L transabdominal ultrasound
      - Presumptive ectopic pregnancy (SOR:C)\(^7\)
    - Limitations
      - Based on availability of ultrasound, gestational age and gestational number of pregnancy

- Other testing
  - Culdocentesis
    - Consider if ultrasound unavailable or indeterminant
    - 65% of ectopics will have positive test
    - Positive
      - Aspiration of >0.5 mL non-clotting blood
      - 65% nonruptured ectopics have (+) test
    - Negative
      - 0.5-5 mL serous fluid
      - Rules out ruptured ectopic only
    - Indeterminant
      - Dry tap or clotting blood
      - No conclusion can be drawn
  - Contraindicated with
    - Coagulopathy
    - Sharply retroverted uterus
    - Palpable posterior cul-de-sac mass

- Diagnostic criteria
  - Pregnancy not located on transvaginal ultrasound scan: obtain quantitative hCG
    - hCG <1,500 IU/L: repeat hCG level in 48 hr
    - hCG >2,000 IU/L: consider diagnostic uterine curettage or surgical
    - Exception: multiple gestations may not be seen until hCG >2,000 IU/L
• Pregnancy located on ultrasound scan
  • IUP on scan: is a threatened miscarriage if patient with pain and/or bleeding, needs re-evaluation in 2-3 days
  • Ectopic cardiac activity, ectopic gestational sac or ectopic mass: treatment of ectopic pregnancy

Differential Diagnoses
  1. Miscarriage/threatened spontaneous abortion
  2. PID
  3. Tubo-ovarian abscess
  4. Ruptured corpus luteum cyst
  5. Ovarian follicle
  6. Urinary calculi
  7. Acute appendicitis

Therapeutics
  1. Ruptured ectopic, Pt unstable
     o ABCs: ensure adequate or circulating volume
     o IV fluids, type and screen of type and cross-match, CBC
     o Emergent laparotomy (SOR:C)8
  2. Stable, unruptured ectopic
     o Methotrexate (SOR:B)3,8
       ▪ Criteria for use
         • No rupture
         • hCG <5,000 IU/L
         • No maternal liver, renal or pulmonary Dz
         • Ectopic mass <3.5 cm with no cardiac activity
         ▪ Methotrexate treated degenerating trophoblast is fragile
           • Careful physical exam only once
           • No ultrasound
           • Monitor with hCG levels
     o Laparoscopy with salpingostomy
       ▪ Preferred surgical method (SOR:A)8
     o Expectant management (SOR:C)3,8
       ▪ Criteria (88% resolution)
         • No rupture
         • Initial hCG <200 IU/L
         ▪ Ectopic mass <3 cm
         ▪ Absence of fetal heartbeat
         ▪ Must have close follow-up
     o Methotrexate vs tube-sparing laparoscopy
       ▪ No difference in overall outcomes (SOR:A)3

Follow-Up
  1. Medical management
     o hCG levels should begin declining day 4-7 after methotrexate
       ▪ Second dose may be required if hCG decline is <15% between day 4 and 7
Follow hCG weekly until none detected

- Treatment failure
  - Significantly worsening abdominal pain
  - Increasing hCG level after day 3 of Tx

2. Surgical management
   - hCG weekly until no longer detected
   - If hCG levels fail to decline, patient can be treated with methotrexate post-surgery

3. Expectant management
   - hCG weekly until no longer detected
   - Rising hCG level post-treatment
     - Surgical intervention necessary

**Prognosis**

1. Following treatment
   - Success rates with proper patient selection
     - 42-82% expectant mgmt
     - 90% medical mgmt
     - 92% surgical mgmt

2. Future fertility
   - Post-treatment conception rate approx 77% regardless of treatment

3. Risk of recurrence
   - 5-20%
   - 32% if two consecutive ectopic pregnancies

**Screening**

1. All women of reproductive age with abdominal pain or vaginal bleeding should have the diagnosis of ectopic pregnancy considered and expeditiously ruled out (SOR:B)^3

**References**

developers: Royal College of Obstetricians and Gynaecologists. Date released: May
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