Pregnancy of Unknown Location and Ectopic Pregnancy

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Disclosures: None

Learning Objectives

• Nomenclature regarding pregnancy of unknown location (PUL)
• Alternative approaches the diagnostic dilemma of evaluating a patient with a possible ectopic pregnancy.
• Understand the value of various diagnostic tests.
• Gain insight into the ultrasound findings in patients with an ectopic pregnancy

Consensus Nomenclature

1. Definite ectopic pregnancy (EP)
   – Extrauterine gestational sac with yolk sac and/or embryo (with or without cardiac activity)
2. Probable EP
   – Inhomogeneous adnexal mass or extrauterine sac-like structure
3. PUL
4. Probable intrauterine pregnancy
5. Definite IUP

Consensus Nomenclature

- PUL
  - no signs of either EP or IUP


Case Presentation

- 28 y.o. G1P0 presents with pelvic pain and scant vaginal spotting.
- LMP ~ 4-5 weeks ago
- + UPT at home
- Exam: VSS
  - Uterus AV, NT, TNS
  - Adnexa: NT, without masses
- hCG = 874 IU/L

Kadar et al. Obstet Gynecol 1981; 58: 162 (Yale)

Increase in hCG in early pregnancy

- Doubling time = 2.98 days
- 15% of normal pregnancies had abnormal β-hCG increases

Kadar et al. Obstet Gynecol 1981; 58: 162 (Yale)

Pregnancy of Unknown Location


Increase in hCG in early pregnancy

<table>
<thead>
<tr>
<th>Days</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.50</td>
</tr>
<tr>
<td>2</td>
<td>2.24</td>
</tr>
<tr>
<td>3</td>
<td>3.35</td>
</tr>
<tr>
<td>4</td>
<td>5.00</td>
</tr>
<tr>
<td>7</td>
<td>16.73</td>
</tr>
</tbody>
</table>

**Case Presentation**

Day 1  hCG = 874 IU/ml  
Day 3  hCG = 1,056 IU/ml  
Day 5  hCG = 1,110 IU/ml

**Threshold vs. Discriminatory Levels**

**Threshold level**  
- Lowest β-hCG level at which a normal intrauterine pregnancy can be detected

**Discriminatory level**  
- The level of β-hCG above which all normal intrauterine pregnancies should be seen

**Threshold vs. Discriminatory Levels**

Threshold level  
- β-hCG = 400-500 mIU/mL (1st IRP)

Discriminatory level  
- β-hCG = 1000-1500 mIU/mL (1st IRP)

**Dependencies**  
- Transducer frequency, uterine position, body habitus, operator experience/ability

**Evidence Against the hCG Discriminatory Level**

- January 1, 2000 - December 31, 2010  
- TVS and β-hCG on same day  
- No intrauterine fluid collection  
- Subsequent embryonic or fetal cardiac activity

**Evidence Against the hCG Discriminatory Level**

<table>
<thead>
<tr>
<th>hCG (3-4th IS)</th>
<th># (202)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1000</td>
<td>162</td>
<td>80.2</td>
</tr>
<tr>
<td>1000-1499</td>
<td>19</td>
<td>9.4</td>
</tr>
<tr>
<td>1500-1999</td>
<td>12</td>
<td>5.9</td>
</tr>
<tr>
<td>2000</td>
<td>9</td>
<td>4.5</td>
</tr>
</tbody>
</table>

**Reevaluation of Discriminatory and Threshold Levels**

- 651 patients  
- TVS and β-hCG within 6 hours of each other  
- Known intrauterine pregnancies  
- Findings visualized 99% of the time  
- 1st, 3rd, or 4th International Standard  
- 2nd I.S.~ ½ that of others

### Reevaluation of Discriminatory and Threshold Levels

<table>
<thead>
<tr>
<th></th>
<th>Gestational Sac</th>
<th>Yolk Sac</th>
<th>Embryo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threshold level</td>
<td>390</td>
<td>1094</td>
<td>1394</td>
</tr>
<tr>
<td>Discriminatory level</td>
<td>3510</td>
<td>17,716</td>
<td>47,685</td>
</tr>
</tbody>
</table>


### Case Presentation

- **Case Presentation**
  - 24 y.o. G2P0010 presents with scant vaginal spotting and pain
  - LMP ~ 5 weeks ago
  - Exam: VSS
    - Uterus NSSC, NT; Adnexa: NT
  - Initial: hCG = 710 IU/L
  - Repeat in 2 days: hCG = 980 IU/L

- **TVS**
  - Uterus
    - No evidence of IUP
  - Ovaries
    - Corpus luteum - left
  - Adnexa
    - No definite adnexal pathology

- **Current terminology** PUL
- **Treatment** MTX 50 mg/m²
### Endometrial Thickness in Ectopic Pregnancy when hCG < Discriminatory Zone

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean (mm)</th>
<th>Range (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrauterine pregnancy</td>
<td>13.42</td>
<td>± 0.68</td>
</tr>
<tr>
<td>Spontaneous abortion</td>
<td>9.28</td>
<td>± 0.88</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>5.95</td>
<td>± 0.35</td>
</tr>
<tr>
<td>Abnormal pregnancy (97%)</td>
<td>&lt; 8</td>
<td></td>
</tr>
</tbody>
</table>

Case Presentation - #3

- 28 y.o. G1P0 presents with pelvic pain and scant vaginal spotting.
- LMP ~ 7 weeks ago
- Exam: VSS
  - Uterus TNS;
  - Mild adnexal discomfort
- hCG = 4,634 IU/L
Intrauterine Fluid with Ectopic Pregnancy

229 patients with ectopic

- No intrauterine fluid 191 (83.4)
- Intrauterine fluid 38 (16.6)
  - Adnexal mass 33 (86.8)


Intrauterine Fluid with Ectopic Pregnancy

38 patients

- Type A 31 (81.6)
  - Pointy edged 30 (78.9)
  - Echoes 28 (73.7)
  - Located with the cavity 21 (55.3)
- Type B 7 (18.4)
  - Smooth walled
  - Located in decidua or uncertain


Conclusions

- Findings
  - A smooth-walled anechoic intrauterine cystic structure
  - No adnexal mass
- Probability
  - Intrauterine pregnancy 99.8%
  - Ectopic pregnancy 0.02%

TVS for Diagnosing Ectopics

Inclusion criteria
- Clinical suspicion of ectopic pregnancy
- All patients underwent TVS
- All cases of EP were surgically confirmed
- No adnexal masses were excluded, except simple cysts

Reviewed 10 studies
- 2216 patients
  - Ectopic = 565 25.5%
  - No ectopic = 1651 74.5%


Criteria for ectopic pregnancy
A: Adnexal embryo with heartbeat
B: Adnexal mass containing yolk sac or embryo
C: Adnexal mass with central anechoic area and hyperechoic rim ("tubal ring")
D: Any adnexal mass other than a simple cyst or an intraovarian lesion

<table>
<thead>
<tr>
<th>TVS Finding</th>
<th>Likelihood of Ectopic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extrauterine embryo + heartbeat</td>
<td>100%</td>
</tr>
<tr>
<td>Adnexal mass with yolk sac or embryo without heartbeat</td>
<td>100%</td>
</tr>
<tr>
<td>Tubal ring</td>
<td>95%</td>
</tr>
<tr>
<td>Complex or solid adnexal mass</td>
<td>92%</td>
</tr>
<tr>
<td>No tubal ring, yolk sac, embryo</td>
<td></td>
</tr>
</tbody>
</table>


- Embryo without cardiac activity: 100%
- Adnexal mass with yolk sac: 100%
- Tubal ring (95%)
- Complex mass (92%)
Diagnosing Ectopic Pregnancy
Six Strategies

- Ultrasound followed by quantitative hCG
- Quantitative hCG followed by ultrasound
- Progesterone followed by ultrasound and quantitative hCG
- Progesterone followed by quantitative hCG and ultrasound
- Ultrasound followed by repeat ultrasound
- Clinical examination

Garcia and Barnhart. Obstet Gynecol 2001; 97: 464-70
(U. of Penn)

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Diagnosing Ectopic Pregnancy
Six Strategies-Recommendations

- Ultrasound followed by hCG
- hCG followed by ultrasound
- Either progesterone protocol
  - More missed ectopic pregnancies
- Ultrasound followed by repeat ultrasound
  - May be applicable in poorly compliant patient
- Clinical exam only – NOT recommended

Garcia and Barnhart. Obstet Gynecol 2001; 97: 464-70

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Diagnosing Ectopic Pregnancy
Six Strategies-Outcomes

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Missed EPI/10,000</th>
<th>Interrupted IUP/10,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>US → hCG</td>
<td>0</td>
<td>70</td>
</tr>
<tr>
<td>hCG → US</td>
<td>0</td>
<td>122</td>
</tr>
<tr>
<td>P → US → hCG</td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td>P → hCG → US</td>
<td>24</td>
<td>39</td>
</tr>
<tr>
<td>US → US</td>
<td>0</td>
<td>121</td>
</tr>
<tr>
<td>Clinical Exam</td>
<td>940</td>
<td>0</td>
</tr>
</tbody>
</table>

Garcia and Barnhart. Obstet Gynecol 2001; 97: 464-70
Case Presentation

- 41 G2P0010 with LMP 3 weeks ago
- c/o vaginal bleeding and abdominal pain
- Unprotected intercourse x 10 years
- + UCG

Quantitative hCG = 78

Ectopic Pregnancy

hCG Dynamics with Spontaneous Resolution of Ectopic

Helsinki, Finland
118 patients
Entry criteria
- Decreasing or stable hCG
- No signs of rupture/intrapertitoneal hemorrhage
- Adnexal mass < 4 cm
- No cardiac activity

(Finland)

Ectopic Pregnancy

hCG Dynamics with Spontaneous Resolution of Ectopic

Rate of Spontaneous Resolution

- hCG < 200 IU/L 88%
- hCG > 2000 IU/L 25%

Case Presentation

- 36 y.o. G3P0020 seen in ER with c/o slight spotting and mild abdominal discomfort
- Uterus: Mid-position, TNS
- Adnexa: No definite masses
- hCG = 357 IU/L
- Hct = 36.4
- D/C home with F/U 2 days in WCC

Case Presentation

- WCC
  - c/o increasing pain and weakness

Serum hCG and Tubal Rupture

<table>
<thead>
<tr>
<th>hCG (IU/L)</th>
<th>Unruptured</th>
<th>Ruptured</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100</td>
<td>9.2%</td>
<td>11.4%</td>
</tr>
<tr>
<td>100 – 999</td>
<td>47.3%</td>
<td>38.6%</td>
</tr>
<tr>
<td>1000 – 9,999</td>
<td>38.2%</td>
<td>38.6%</td>
</tr>
<tr>
<td>&gt; 10,000</td>
<td>5.3%</td>
<td>11.4%</td>
</tr>
</tbody>
</table>

Saxon et al. Obstet Gynecol 1997; 90: 46
(McGill, Cleveland Clinic)
Serum hCG and Tubal Rupture

<table>
<thead>
<tr>
<th>hCG, mIU/mL</th>
<th>Unruptured</th>
<th>Ruptured</th>
<th>Rupture Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1000</td>
<td>53</td>
<td>14 (41.2%)</td>
<td>20.9</td>
</tr>
<tr>
<td>1000-1999</td>
<td>14</td>
<td>6 (17.6%)</td>
<td>30.0</td>
</tr>
<tr>
<td>&gt; 2000</td>
<td>38</td>
<td>14 (41.2%)</td>
<td>26.9</td>
</tr>
</tbody>
</table>


Case Presentation

21 yo G1P0 at 6w3d by LMP
• c/o vaginal bleeding x 1 day
• LLQ pain x 1 day
• + home pregnancy test 3 days ago
• BC: progestin oral contraceptives
• Negative past gyn history
• Quantitative hCG = 25,340

Case Presentation

• Ultrasound
  • Uterus
    – IUP with + yolk sac, CRL c/w 5w6d
    – + cardiac activity
  • Left adnexa
    – Mass = 4 x 3 x 4 cm, with gestational sac
• Diagnosis: heterotopic pregnancy
Heterotopic Pregnancy

• More common with ART
• Incidence
  - Spontaneous 1:30,000
  - ART 1:110-1:667


Case presentation

• 28 y.o. G2P0010
• Presents with pelvic pain and vaginal spotting
• LMP = 7 weeks ago
• hCG: positive

 Courtesy of William W. Brown, III, M.D.
Ultrasound Diagnosis of Interstitial Pregnancy

- Empty uterine cavity
- Chorionic sac > 1 cm from the lateral edge of the uterine cavity (endometrium)
- Thin (<5 mm) layer of myometrium surrounding the chorionic sac

Terminology

- **Interstitial pregnancy**
  - Embryo implants in the interstitial or intramural portion of the Fallopian tube
- **Cornual pregnancy**
  - Pregnancies that occur in a rudimentary horn, unicorne uterus, cornual region of a septate uterus, a bicornuate uterus, or a uterus didelphys
- **Angular pregnancy**
  - Embryo implants in one of the lateral angles of the uterine cavity, medial to the utero-tubal junction
Case Presentation

- 23 y.o. G2P1001
- Enters c/o slight spotting and cramping
- LMP = Unknown
- UCG = positive
- hCG = 2,392

12/30/10
ET = 17.84 mm
hCG = 2392
Consensus Nomenclature

- Pregnancy of unknown location (PUL)
  - Possible IUP
  - Increased endometrial thickness

Quantitative hCG

12/30/10  2392
1/01/11  7721

Ectopic Pregnancy-Summary

- Ultrasound can be justified prior to obtaining a quantitative hCG
  - ~50% of ruptured ectopics had hCG levels below the discriminatory zone (<1000 IU)
- Endometrial thickness when hCG < discriminatory level
  - An endometrial thickness < 8 mm is associated with an abnormal pregnancy 97% of the time

Ectopic Pregnancy-Summary

- The discriminatory level has changed
  - It may be as high as 2500-3500 IU/L
  - A cystic structure within the endometrium, in the absence of an adnexal mass
    - Is associated with an IUP in >99% of patients

Ectopic Pregnancy-Summary

- Finding an IUP r/o ectopic pregnancy
  - Exception: heterotopic pregnancy
    - (1:667-1:30,000)
  - Finding of embryo + heart beat or yolk sac in adnexa
    - Diagnostic of ectopic pregnancy
  - No IUP. Complex/solid mass, sep from ovary
    - 92% likelihood of ectopic

Thank You