Early First trimester Ultrasound: Understanding our tools

Laura L. Tatpati, MD
Division of Reproductive Endocrinology
Department of Obstetrics and Gynecology
University of Kansas SOM - Wichita
Nothing to Disclose
Objectives

1. Review the basic components of early first trimester ultrasound
2. Discuss the how to successfully utilize both hCG levels and ultrasound in the first trimester for safe management of patients
Something tells me it's right under my nose...
Case 1
Pt: HT
HST

32 yo G1P0 with LMP 3/28 (EGA 5w2d), who spontaneously conceived. +hpt about 1 wk prior, spotting began about that time. She developed LLQ pain and bright red VB, presents to ER.

PMH: 1. Irritable bowels
   2. Primary infertility
      -Endometriosis
      -Partner: Asthenospermia
      -failed CC/IUI x 7

PSH: Operative laparoscopy w/ endometriosis cauterization and minor fimbrioplasty ("bridges lysed")
ER
- exam benign
- qhCG 2887 mIU/mL; A+
- US: Cyst vs Ectopic gestation
- pain persists, mild
- dismissed in stable condition for close f/u
HST at 5w3d

S: pain slightly better

O: hCG (different lab): 4747 mIU/mL (2887 yest)
US (different location): no clear finding of abnormality, small fluid collection near internal os
HST at 5w5d

Appt with OB provider
Pain improved, spotting only
Exam: Benign abdomen
Sent to REI clinic

Left-sided & suprapubic pain starts in car on way to REI clinic
HST at REI clinic

Exam: tender LLQ, no rebound, non-acute
Recommended surgical intervention due to increased pain

Sudden onset severe pain while preparing for surgery

Findings:
- Moderate amount of blood in pelvis
- Left ectopic gestation

qhCG negative 8wks post-op
Case #2
KD
28 yo G5P4004 at 5w by LMP  
S/P microsurgical tubal anastomosis 4 mo prior  
To ER for LLQ pain, concerned due to risk of ectopic

Call from ER

hCG 5,500

US: “complex cyst 1.8x2.3cm on the right ovary, nothing really in the uterus”
“I think she has an ectopic”

What questions should I ask?
Has she had other testing in this pregnancy?

qhCG #1: 190

#2 (+2d): 497 (6d before ER visit)

What do you think?
1. What does the complex cyst look like?  
   2.5cm, hemorrhagic cyst without hyperechoic “ring”  
   No adjacent mass

2. What do they mean “nothing really in the uterus”?  

“There may be a tiny pseudo-sac”
Clarify the report.
(complex cyst, possibly CL, no evidence of live ectopic, no definite evidence for viable fetus. Small fluid collection, 4x5x6.5mm. With hx of 5000 hCG, complex cyst could be a dead ectopic)

What is her risk of ectopic?

What should we see on US at 5w?

Do the numbers “add-up”?
(3884 at CFRM/5500 at ED = 42% higher)
Final Diagnosis: Normal IUP
TVUS: transvaginal ultrasound
Indications for early US
(not all-inclusive)

❖ Confirm IUP
❖ Evaluate for ectopic
❖ Evaluate vaginal bleeding or pain
❖ Estimate GA
❖ Dx/eval multiples
❖ Confirm FCA
❖ Imaging as adjunct to CVS, embryo transfer, localize / remove IUD
❖ Nuchal translucency
❖ Eval for molar pregnancy
Method

- Transabdominal or transvaginal
  - Lower freq transducer may be required for abdominal exam with high levels of obesity
  - Transvaginal should be completed for any limitations with transabdominal if possible

- Identify structures
  - GS - intrauterine or extrauterine
  - YS
  - Embryo/fetus w/ CRL
    - # of each, amnionicity/chorionicity as possible
  - FCA
    - note any irregularity of rhythm
  - Adnexal structures
  - Advancing GA - anatomical fetal and cervical evaluations as appropriate
Ultrasound Findings

- Locate Corpus Luteum and Gestational Sac
  - Mean Sac Diameter
  - Avg 3 dimensions of gestational sac
4-5.5 wks

- 4-5 wks
  - 2-5mm sac, eccentrically placed
  - MSD + 30 ~ EGA (d)

- 5-5.5 wks
  - Double decidual sign
  - 2 echogenic rings surround fluid collection (anechoic)
5.5 wks

- Yolk sac visible
- Confirms IUP (or ectopic)
- Visible w/ MSD 13mm
- 100% sensitivity/PPV
- Large Yolk Sac: assoc w/ pregnancy failure, not diagnostic of pregnancy failure, reassess 1-2 wks
6 wks

- Fetal pole (CRL): 2-10 mm
- Hadlock - US dating
- Goldstein - Estimate GA up to 9 wks: 42 + CRL (mm)
- Cardiac activity (5w5d - 6w1d)
- Normal FP seen by GS of 20mm
- If no FP: 100% specificity of failed pregnancy dx
6.5 wks +

- 6.5 wks
  - FCA should be present
    - Mean 110 bpm at 6 wks
    - > 140 bpm by 7 wks
    - 8-9 wks often 170-180
  - CRL <=7mm w/o FCA, repeat in 1 week (usually seen by 5mm)
  - If present, typically the r/o miscarriage < 5% (higher w/ AMA/?infertility)
hCG
human chorionic gonadotropin
What is it?

- Recognized in the 1920s
- Dimeric glycoprotein with $\alpha$ and $\beta$ sub-units
  - $\alpha$ identical to that of LH, FSH, TSH
  - $\beta$ length and carbohydrate modifications differ
    - hCG $\beta$ is the longest and has 1/2 life $\sim$ 24 hours
    - Total ($\beta$) hCG is measured typically
- Maintains progesterone production by the corpus luteum
- Produced by syncytiotrophoblast
Detection

- Avg post-ovulation: 8d serum/11d urine
  - 95% by 11th day after surge (10d post-ovulation)
- By missed menses (14d post-ov) ~ 100mIU/mL
  - Peaks 100,000 mIU/mL 8-10 wks, then stabilizes at ~20,000 mIU/mL
The Tests: Urine

- Immunoenzymatic
- Sensitivity ~20mIU/mL
- Affected by proteinuria/hematuria
- Drugs may cause false + (methadone >100mg/d)
The tests: Serum

- Immunochemiluminometric assay (ICMA)
- Negative < 2-5 mIU/mL
- False positives: anti-animal antibodies
- Analytical sensitivity: 0.5 mIU/mL
- Referenced to WHO, 3rd International Standard
- Hook effect >1M
Why do we use hCG in early pregnancy?

Detect dangerous abnormal gestations (Ectopics) in a timely fashion while avoiding the unintentional interruption of normal gestations
What is “Normal” for hCG?

- The “Doubling time” concept
  - Kadar et al, 1981
    - Only 20 women
    - 66% in 2d (85% CI), (RIA)
- 287 subjects w/ viable IUPs (867 hCG levels) w/ pain or bleeding
  - Log linear curve
  - 53% minimal rise (Lower limit of 99% CI) for viable

Barnhart. Ob-Gyn 2004:104(1); 50-54
Establishing viability

- Normal rate of rise
  - (95% confidence interval) *dotted lines*
  - Median rise: 1d (50%) & 2d (124%)
  - Range 1d (24% to 81%)
  - Range 2d (53% to 228%)
  - Range 7d (338% to 6288%)

Barnhart. hCG Rise in Intrauterine Pregnancy. Ob Gyn 2004
US + hCG
What is the “Discriminatory Zone”? 
2 Answers:

The threshold of visualization of a gestational sac

1500-2000 mIU/mL
What if the qhCG is 800?

Should we see something on US?
Maybe

How many weeks is she?
screening hCG 1 (6/30): 226

qhCG 2 (7/7): 262
qhCG 3 (7/14): 281
qhCG 4 (7/15): 104 (diff lab)

qhCG 5 (7/16): 93 (rpt 2d)
qhCG 6 (7/17): 60 - hemorrhaging ectopic
US + hCG + Pregnancy Problems
Diagnoses of Pregnancy Loss in the First Trimester

- Anembryonic gestation (formerly blighted ovum)
- Incomplete abortion
  - Heterogeneous lining of variable thickness, typically no GS or one that has relocated
  - Cannot r/o ectopic on US alone
- Complete abortion
  - VB, tissue passage, closed cervix, undistorted endometrial echo
  - Cannot r/o ectopic on US alone
Declining hCG

- Non-viable: failed IUP vs ectopic
- Expectant mgmt vs intervention
  - Rate of fall
    - Cannot merely apply to MTX rule of 15%
  - 710 SABs/1543 pregnancies of unknown location
  - Quadratic curve for log hCG, steeper with higher initial level

Barnhart. Obstet Gynecol 2004;104:975-981
% decline serum hCG by initial level

Adapted from Barnhart et al; Fertil Steril 2006;85:508-510 & Obstet Gynecol 2004;104:975-981
Embryonic demise

- No interval growth
- Absent cardiac activity > 4mm or beyond 6.5 wks (in pregnancy with sure dating such as IVF)
- <80 bpm from 6-6.5 wks - 100% loss
- MSD - CRL <= 5mm assoc w/ 94% risk SAB


Radiology 1991;178:375-377
Subchorionic hematoma

- Crescent-shaped anechoic region between chorionic membrane and endometrium

- 9% loss rate, likely higher rate in AMA and when present at < 8wks
Ectopic Gestations

- 2% of all pregnancies
  
  - ER populations: 7-13% of VB in early pregnancy
  
  - Suspect with qhCG above 1500-2000 IU/L w/o IUP at any gestational age
  
  - Suspect with EGA > 5 wks w/o IUP
  
  - 1/2 of ectopics present w/ qhCG < 1500

Diagram showing the locations of ectopic gestations:
- Tube >90%
- Cervix 0.2%
- Cornu (2-3%)
- C/S Scar (<1%)
- Abdomen (1-2%)

hCG and the ectopic

- Silva et al. 200 women with confirmed ectopics:
  - No single way to characterize hCG pattern (60% rising/40% declining)

- Seeber OB GYN 2006;107:399-413: Hypothetical population

In 2 days:

- <53% rise in 2d
- or
- <21-35% decline
Normal decline does not eliminate risk of rupture of resolving ectopic
US and the Ectopic

- Heterogeneous adnexal mass, adjacent to ovary, often with lacunar flow
- Moves separately
- By 6 wks, may be a hyperechoic ring around the gestational sac (+/- YS, FP and FCA)
- Suspect with +hCG, pelvic pain and free fluid
Unclear Location

- Surgical evidence of location with D&C
  - 112 women w/ either hCG > 2000 w/o IUP or abnormally falling or rising <2000
  - 38.4% had nonviable IUPs rather than ectopics
  - 40% would have been “erroneously” treated w/ methotrexate

- Does presumptive MTX treatment reduce cost or complication rates?
  - Not necessarily

Obstet Gyncol 2002;100;505-510

Fertil Steril 2005;83:376-382
Finding the right algorithm

- 10,000 women
- 6 treatment algorithms studied
- Best =
  - TVUS of all women w/ pain and/or bleeding
  - If non-diagnostic, hCG indicated
  - Optimizes sensitivity, no ectopics missed and timely dx
  - “Few” potentially viable pregnancies were interrupted

Obstet Gynecol 2001;97:464-470
Take Home Points
❖ Remember the goal: Balance **nondisruption** of normal IUPs with efficient and accurate diagnosis of ectopic gestations

❖ The discriminatory zone refers to normal IUPs, not ectopic gestations

❖ Ectopic gestations can rupture “on the way down”

❖ 1/3 gestations with VB and abnormal quants w/o IUP have a failed IUP

❖ Persistent hCG should raise a flag prior to definitive surgeries which remove reproductive organs

❖ The patient’s reproductive goals play a role in the decision making tree

❖ Keep the clinical picture in the picture
Questions?
Persistent hCG
Some causes…

- False positive (phantom)
- Invasive gestational trophoblastic disease, choriocarcinoma
- Ovarian germ cell neoplasms
- Non-trophoblastic hCG producing malignancies
- Pituitary origin hCG
False-positive hCG (phantom)

- Nonspecific heterophile antibodies
  - cross-species antibodies (anti-animal antibody)
  - All commercial hCG test used today involve rabbit, mouse, goat, horse or sheep antibodies.
- USA hCG Reference Service
  - Avg 102 ± 152 mIU/ml [6.1-900 mIU/mL]
  - Plateau, do not respond to methotrexate

Gynecol Oncol 1998;71:325-329
Lancet 2000;355:712-715
Emerging strategies
Hyperglycosylated hCG (HhCG)

- Carbohydrate moiety is O-linked to the carboxyterminal of hCG
- Initially found in molar gestations
- Biologically independent to hCG
- Increases more rapidly in early gestation and declines sooner (6-8wks)
- Product of cytotrophoblasts (invasive cells)
hCG-H

- Sasake et al
  - Total HhCG and ratio of HhCG/hCG at implantation
  - Higher concentrations and ratios in those w/ term pregnancies than SABs
  - Ratio >50% in all term
  - 13/20 SABs ratios were <50%
  - Biochemical pregnancies
    - ¼ produce no hCG-H
    - ¾ produce borderline detection

Fertil Steril 2008;89:1781-1786
Ruling out heterophile antibodies

- Measure urine hCG
- Serially dilute serum (constant with 2- and 10-fold dilution)
- “Blocking” antibodies
- Run different manufacturer’s hCG tests
Bonus: What is this?