FETAL ULTRASOUND FINDINGS: Normal or abnormal?

June 15, 2017
41st Annual Antepartum and Intrapartum Management

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WHY THIS TOPIC?

LEARNING OBJECTIVES

• Obstetrical ultrasound
  – History
  – Guidelines for its use
• Ultrasound findings of unclear significance
  – “Soft markers”
  – Patient counseling
  – Clinical management

DISCLOSURES

• No financial disclosures
THE ORIGIN OF ULTRASOUND

• 1842 Christian Doppler: the Doppler effect
  “observed frequency of a wave depends on the relative speed of the source and the observer”
• 1915 Paul Langevin: ultrasonic submarine detection
• 1943 Sir Robert Alexander Watson-Watt: radar
• 1952 Dr. Douglass Howry: water delay scanning
• 1953 Inge Edler & Carl Herz: M-mode ➔ heart

OBSTETRICAL ULTRASOUND HISTORY

• 1958 Diasonograph: Dr. Ian Donald & Thomas Brown
• 1960s Placenta previa, molar pregnancy
• 1970s Biometry, anomalies
• 1980s Acuson, TVUS, color Doppler
• 1990s Harmonics, Voluson 3D/4D
• 2000 Modern real time scanning on the market

OBSTETRICAL ULTRASOUND

• Guidelines for its use
  – ACOG & NICHD endorse use of OB ultrasound
• GA estimation, singleton v multiple gestation, fetal cardiac activity, placental location, congenital structural anomalies, fetal growth

IS OB ULTRASOUND EVIDENCE-BASED?

• RADIUS trial
  – 1st U.S. RCT of routine OB ultrasound screening
  – >15,000 women
  – Increased fetal anomaly detection (34.8 v 11%)
  – NO IMPROVEMENT OF PERINATAL OUTCOMES
    • Rate of adverse perinatal 5.0% v. 4.9%
IS OB ULTRASOUND EVIDENCE-BASED?

• Eurofetus study
  – Prospective study of 61 OB centers
  – Anomaly detection rate 56% (2593/4615)
    • Major anomaly detection rate 74% (46% for minor)
    • CNS 88% v major cardiac 39%
  – Higher rates of pregnancy termination

ULTRASOUND “SOFT MARKER”

• What IS it? What does it look like?
• How do I counsel the patient?
• What is the indicated follow-up?

AUDIENCE RESPONSE QUESTION #1
When you read “Echogenic intracardiac focus” (EIF) in your patient’s 2nd trimester ultrasound report, are you worried about T21?
A. Yes
B. No
C. It depends on other factors...
D. I don’t know

AUDIENCE RESPONSE QUESTION #2
When you read “pyelectasis” in your patient’s 2nd trimester ultrasound report but maternal serum cell free fetal DNA was negative, you are:
A. Worried about T21 primarily
B. Not worried about T21 but worried about GU anomalies (reflux, obstruction)
C. Not worried about anything
D. I don’t know
SOFT MARKERS OF ANEUPLOIDY

- Ultrasound findings of uncertain significance
  - Increased nuchal translucency (NT)
  - Absent or hypoplastic nasal bone
  - Echogenic intracardiac focus (EIF)
  - Choroid plexus cysts (CPCs)
  - Echogenic bowel
  - Pyelectasis (pelviectasis)
  - Thick nuchal fold (NF)
  - Ventriculomegaly
  - Shortened long bones


TRISOMY 21 ULTRASOUND FINDINGS

- Thick nuchal translucency (CRL 45-84mm, 11² – 14²)
  - >99th %ile for GA or ≥3.0 mm
  - Sequential screening 95% detection, 5% false+

<table>
<thead>
<tr>
<th>NT</th>
<th>ANEUPLOIDY (%)</th>
<th>FETAL DEATH (%)</th>
<th>MAJOR FETAL ANOMALY (%)</th>
<th>ALIVE &amp; WELL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;95th centile</td>
<td>0.2</td>
<td>1.3</td>
<td>1.6</td>
<td>97</td>
</tr>
<tr>
<td>95 – 99th centiles</td>
<td>3.7</td>
<td>1.3</td>
<td>2.5</td>
<td>93</td>
</tr>
<tr>
<td>3.5 – 4.4 mm</td>
<td>21.1</td>
<td>2.7</td>
<td>10.0</td>
<td>70</td>
</tr>
<tr>
<td>4.5 – 5.4 mm</td>
<td>33.3</td>
<td>3.4</td>
<td>18.5</td>
<td>50</td>
</tr>
<tr>
<td>5.5 – 6.4 mm</td>
<td>50.5</td>
<td>10.1</td>
<td>24.2</td>
<td>30</td>
</tr>
<tr>
<td>&gt;6.5 mm</td>
<td>64.5</td>
<td>19.0</td>
<td>46.2</td>
<td>15</td>
</tr>
</tbody>
</table>

Souka et al. AJOG 2005;192(4):1005

SOFT MARKERS OF ANEUPLOIDY

- Isolated soft marker 11-17% of normal fetuses
  - Multiple markers ↑likelihood of aneuploidy
  - Prevalence different by race/ethnicity


NT DIFFERENTIAL DIAGNOSIS

- Aneuploidy
- Noonan’s syndrome
- ↑Risk TTTS if mo/di
- Normal variant
TRISOMY 21 ULTRASOUND FINDINGS

• Thick nuchal fold 2\textsuperscript{nd} tri
  – ≥6 mm
  – 20-33\% of T21, 0.5-2\% of euploid

TRISOMY 21 ULTRASOUND FINDINGS

• Absent nasal bone
  – 1\textsuperscript{st} tri: 65\% of T21, 0.8\% of euploid
  – 2\textsuperscript{nd} tri: 30-40\% of T21, 0.3-0.7\% of euploid

TRISOMY 21 ULTRASOUND FINDINGS

• Hypoplastic nasal bone
  – Length ≤2.5 mm
  • BPD/NB, GA %ile threshold, MoM
  – 50-60\% of T21, 6-7\% of euploid

TRISOMY 21 ULTRASOUND FINDINGS

• Echogenic bowel
  – Bright as or brighter than bone
  – 13-21\% of T21 v 1-2\% euploid

ECHOCGENIC BOWEL

• Technique counts
  – Compare to iliac wing
  – Use 5 MHz or lower
  – Turn down gain
  – Take off harmonics

• Etiology
  – Aneuploidy
  – Ingested blood
  – Cystic fibrosis
  – IUGR
  – Infection
    • CMV, toxoplasmosis
    • More rare parvovirus, varicella, HSV
TRISOMY 21 ULTRASOUND FINDINGS

- Pyelectasis
  - Renal pelvis ≥4 mm 2nd trimester
  - 10-25% of T21 v 1-3% of euploid
  - Isolated finding: 0.3-0.9% risk of aneuploidy

PYELECTASIS ETIOLOGIES

- Common causes
  - Vesicoureteral reflux
  - Ureteropelvic junction
    - Obstruction or narrowing
  - Ureterovesical junction
    - Obstruction or narrowing
- Rare causes
  - Duplicated collection
  - Ectopic ureter
  - Ureterocele
  - Megaureter
  - Urachal cyst
  - Posterior urethral valve (males)

VENTRICULOMEGALY DDX

- Other than aneuploidy...
- Other CNS abnormalities?
  - Fetal brain MRI
- CSF obstruction
  - oNTD
  - Aqueductal stenosis
  - Intraventricular hemorrhage
  - Mass
  - Congenital infection → scarring → obstruction
    - CMV, toxoplasmosis
- Idiopathic/normal variant
TRISOMY 21 ULTRASOUND FINDINGS

• Shortened long bones
  – BPD/FL > 1.5 SD
  – Short humerus positive LR 4.8
  – Short femur positive LR 3.7

Lockwood et al. AJOG 1987; 157(4Pt1):803

SHORT LONG BONES

• If low risk aneuploidy... what else?
  – Normal variant?
  – IUGR?
    • Other biometry %iles – especially AC
  – Skeletal dysplasia?
    • Femur <5th centile or <2 SD from the mean for GA
    • Measure the humerus, radius, ulna, tibia, & fibula
    • Femur-foot length ratio <0.9
    • Fractures? Bowed? Mineralization?
    • Small thorax?
    • Less than expected interval growth
    • Referral to an experienced center

ISOLATED EIF

• If low risk aneuploidy screening... NORMAL
  – Many providers not reporting isolated EIF
• Isolated EIF is NOT a congenital birth defect
• Does not warrant follow up ultrasound
• Does not warrant fetal ECHO
**TRISOMY 21 ULTRASOUND FINDINGS**

- Clinodactyly
- Sandal gap foot

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**TRISOMY 18: EDWARDS SYNDROME**

- Soft markers
  - CPCs
    - 30-50% of T18
    - 0.6-3% of euploid
  - Thick NT, cystic hygroma
  - Ventriculomegaly
- Other
  - Clenched hands
  - Rocker bottom feet
  - Strawberry-shaped head
  - Micrognathia

- Anomalies
  - Cardiac
  - Intracranial
  - Omphalocele
  - CDH
  - Urogenital
  - SUA, cord cysts
  - Neural tube defects
  - IUGR
  - Facial cleft, low set ears

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**TRISOMY 18: EDWARDS SYNDROME**

- Soft markers
  - Nuchal thickening
  - Ventriculomegaly
- Other
  - Clenched hands
  - Polydactyly

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**TRISOMY 13: PATAU SYNDROME**

- Anomalies
  - Intracranial
  - Midline facial
  - Cardiac
  - Omphalocele
  - CDH
  - Neural tube defects
  - Polycystic kidneys
  - Other urogenital

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*Dagklis et al. Ultrasound Obstet Gynecol 2008;31(2):132*
#### PATIENT COUNSELING

<table>
<thead>
<tr>
<th>ULTRASOUND FINDING</th>
<th>SENSITIVITY RATE T21 DIAGNOSIS (%)</th>
<th>FALSE POSITIVE RATE</th>
<th>(+) LIKELIHOOD RATIO IF ISOLATED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent nasal bone</td>
<td>49 – 70</td>
<td>2 – 4</td>
<td>6.6</td>
</tr>
<tr>
<td>Ventriculomegaly</td>
<td>4 – 13</td>
<td>0.1 – 0.4</td>
<td>3.9</td>
</tr>
<tr>
<td>Thick nuchal fold</td>
<td>20 – 33</td>
<td>0.5 – 1.9</td>
<td>3.8</td>
</tr>
<tr>
<td>Echogenic bowel</td>
<td>13 – 21</td>
<td>0.8 – 1.5</td>
<td>1.7</td>
</tr>
<tr>
<td>Pyelectasis</td>
<td>11 – 17</td>
<td>1.4 – 2.0</td>
<td>1.1</td>
</tr>
<tr>
<td>EIF</td>
<td>21 – 28</td>
<td>3.4 – 4.5</td>
<td>0.95</td>
</tr>
<tr>
<td>Short humerus</td>
<td>17 – 48</td>
<td>2.8 – 7.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Short femur</td>
<td>19 – 38</td>
<td>4.7 – 8.8</td>
<td>0.6</td>
</tr>
<tr>
<td>NO SOFT MARKERS</td>
<td>MATERNAL SERUM RISK X 0.13 = ADJUSTED T21 RISK</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


#### PATIENT COUNSELING

<table>
<thead>
<tr>
<th>ULTRASOUND FINDING</th>
<th>(+) LIKELIHOOD RATIO IF ISOLATED</th>
<th>NUMBER NEEDED TO SCREEN: AVERAGE RISK</th>
<th>NUMBER NEEDED TO SCREEN: HIGH RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thick nuchal fold</td>
<td>17</td>
<td>15,893</td>
<td>6,818</td>
</tr>
<tr>
<td>Short humerus</td>
<td>7.5</td>
<td>8,038</td>
<td>3,448</td>
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<tr>
<td>Echogenic bowel</td>
<td>6.1</td>
<td>19,425</td>
<td>8,333</td>
</tr>
<tr>
<td>EIF</td>
<td>2.8</td>
<td>6,536</td>
<td>2,804</td>
</tr>
<tr>
<td>Short femur</td>
<td>2.7</td>
<td>4,454</td>
<td>1,911</td>
</tr>
<tr>
<td>Pyelectasis</td>
<td>1.9</td>
<td>30,404</td>
<td>13,043</td>
</tr>
<tr>
<td>Choroid plexus cyst</td>
<td>1.0</td>
<td>87,413</td>
<td>37,500</td>
</tr>
</tbody>
</table>

Smith- Bindman et al. JAMA 2001;285(8)

#### CLINICAL MANAGEMENT SUMMARY

- Patient counseling in context of aneuploidy risk
  - Detailed 2nd trimester fetal anatomy
  - Isolated soft marker?
  - IVF w/PGS?
  - Step-wise sequential screen result?
  - Cell free fetal DNA screen result (cffDNA)?
- Genetic counseling: testing options
  - cffDNA screening option if not yet done
  - Chorionic villous sampling (CVS) 10-14 wks
  - Amniocentesis ≥15-17 wks GA

ACOG Practice Bulletin No. 163, Obstet Gynecol. 2016;127

#### CLINICAL MANAGEMENT SUMMARY

- Additional lab tests
  - CF screening
    - Echogenic bowel
  - CMV & toxoplasmosis
    - Echogenic bowel, ventriculomegaly
- Fetal ECHO
  - Thick NT, NF
- 3rd trimester follow up ultrasound
  - Thick NT, thick NF, pyelectasis, echogenic bowel, ventriculomegaly, short long bones

ACOG Practice Bulletin No. 163, Obstet Gynecol. 2016;127
SMFM GUIDELINES

• If isolated soft marker & cffDNA negative:
  – Do NOT recommend diagnostic testing
  – Describe the soft marker as a normal variant
• If isolated soft marker & maternal serum screening negative:
  – Describe the soft marker as a normal variant

Norton et al. AJOG 2017;216(3):B2

AUDIENCE RESPONSE QUESTION #1
When you read “Echogenic intracardiac focus” (EIF) in your patient’s 2nd trimester ultrasound report, are you worried about T21?

A. Yes
B. No
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THANK YOU Dr. Bill Parer