Non-invasive Diagnosis of Fetal Anemia

Giancarlo Mari, M.D., M.B.A.
Professor and Chair
Department of Obstetrics and Gynecology
University of Tennessee Health Science Center
Memphis, TN
USA
Outline

- Definition of Fetal Anemia
- The Rh problem
- Ultrasonographic diagnosis of fetal anemia
At the end of this presentation the participants will be able:

• To understand how we arrived at the diagnosis of fetal anemia using ultrasound

• To understand when to use the MCA PSV to diagnose fetal anemia
Definition of Fetal Anemia

Hemoglobin value below the 5th percentile (2 SD; 95% CI) for gestational age
Causes of Fetal Anemia

- Red blood cell alloimmunization
- Infections
- Fetomaternal hemorrhage
- Twin-twin-transfusion syndrome
- Thalassemia
- Enzymopathies
- Fanconi anemia
- Diamond-Blackfan anemia
Rh Hemolytic Disease
United States

Rhogam (1968)

~ 4000 cases per year
## “Irregular” red blood cell antigens

### Blood group system Antigen

<table>
<thead>
<tr>
<th>Rh</th>
<th>C, c, e, E</th>
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<tbody>
<tr>
<td>Kell</td>
<td>K, k, Ko, Kp, Kp, Js, Js</td>
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<tr>
<td>Duffy</td>
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<td>Kidd</td>
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<td>MNSs</td>
<td>M, N, S, S, U, Mi, Mt, Vw, Mur, Hil, Hut</td>
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<tr>
<td>Lutheran</td>
<td>Lua, Lub</td>
</tr>
<tr>
<td>Diego</td>
<td>Dia, Dib</td>
</tr>
<tr>
<td>Xg</td>
<td>Xga</td>
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<tr>
<td>P</td>
<td>PP, p(Tj)</td>
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</table>

### Public antigens

- Yt, Yt, Lan, En, Ge, Jr, Co, Co

### Private antigens

- Batty, Becker, Berrens, Biles, Evans, Gonzales, Good, Heibel, Hunt, Jobbins, Radin, Rm, Ven, Wright, Wright, Zd

ACOG Educational Bulletin 227, 1996
Rh-Cell Alloimmunization: The Story

Discovery of the Rh antigen (Landsteiner, 1941)

Spectrophotometric analysis of amniotic fluid in the antepartum management of HDN (Bevis D, 1952)
1956: 1st amniocentesis
1961: Delta OD450 curve
1963: 1st intraperitoneal fetal transfusion
Rh Hemolytic Disease
United States

Rhogam (Sing-Sing Prisoners)
Fetoscopy

A) Diagnosis of open spina bifida
B) Fetal blood sampling

Valenti C. Am J Obstet Gynecol 1973;11:581
Cord Blood Sampling

Amniocentesis  Cordocentesis

Fetal Anemia
Risks of Cordocentesis

- Infection
- Fetal Bleeding
- Bradycardia
- PPROM
- Fetal demise

MCA - PSV = 56 cm/s
Blood Velocity in Anemia

- Viscosity ↓
- CO ↑
- Velocity ↑
A Few Concepts in Doppler Ultrasound
\[ \frac{2(fc \cdot \cos A \cdot V)}{c} \]
Fetal middle cerebral artery velocimetry

Normal Fetuses

MCA-PSV Diagnoses Fetal Anemia

What were we missing?
Prospective Study on an Intention to Treat

- Multicenter study in 5 tertiary referral centers
- 125 fetuses at risk for anemia
- MCA-PSV used for timing a cordocentesis

MCA-PSV predicts those fetuses that will become anemic

Severe and Moderate Anemia

Mild or Non Anemia

Which Patients are Candidates for the Assessment of the MCA-PSV?

- Patients at risk for having an anemic fetus
- Indiscriminate use of the MCA-PSV may cause more harm than good
Where to sample the MCA?
How do sonographers and sonologists achieve good training?

- Steps for the MCA-PSV assessment
- To contact centers for advice
Is the delta OD_{450} better than MCA-PSV or vice versa?

- Mari G, Am J Obstet Gynecol 1997 (SMFM);180:18
Doppler Ultrasonography versus Amniocentesis to Predict Fetal Anemia

Dick Oepkes, M.D., P. Gareth Seaward, M.B., B.Ch.,
Frank P.H.A. Vandenbussche, M.D., Rory Windrim, M.B., John Kingdom, M.D.,
Joseph Beyene, Ph.D., Humphrey H.H. Kanhai, M.D., Arne Ohlsson, M.D.,
and Greg Ryan, M.B., for the DIAMOND Study Group*
Is the MCA-PSV Standard of Care for the Diagnosis of Fetal Anemia?

*Do no harm*

- Training of sonographers and sonologists
- Referral to another center
- Amniocentesis

A COG
PRACTICE
BULLETIN

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OBSTETRICIAN–GYNECOLOGISTS
NUMBER 75, AUGUST 2006
(Replaces Educational Bulletin Number 227, August 1996)

Management of
Alloimmunization
During Pregnancy
Red Cell Alloimmunization Management Algorithm

Maternal Antibody Titer (Indirect Coombs) > Critical Value

Fetus’ Father Genotype

- Homozygous
- Does not have
- Heterozygous or not available

If

1. Patient declines amniocentesis
2. Amniocentesis not easy or high chance of placental crossing

Amniocentesis for fetal blood typing by PCR

- Fetus does not have the antigen
- Fetus has the antigen

MCA-PSV sequential studies
Is the MCA-PSV Reliable for the Diagnosis of Fetal Anemia due to other Causes?

- Parvovirus infection
- Fetomaternal hemorrhage
- Non-immune hydrops
- Monochorionic twins following the death of the co-twin
- TTTS following Laser therapy
28 y o G1P0 @ 36 weeks with decreased fetal movements

MCA peak systolic velocity: 110 cm/s
Conclusion
MCA-PSV and Fetal Anemia

- Diagnosis of fetal anemia is a mirror of what is happening in fetal medicine