Intraamniotic Infection/Inflammation or Chorioamnionitis

Sarah Belensky, MD
High Risk OB Fellow at Swedish First Hill Medical Center
My passions

- Rural and international communities
- Outdoors and exercising
- Healthy living and wholeness
Objectives

- Define and characterize IAI
- Discuss options in treatment
- Discuss care for newborns of mothers with IAI
Your patient

- 23 year old G1 originally from Mexico at 40 weeks and 5 days with PROM ->
- Pitocin ->
- Complete + 45 minutes of pushing ->
- Fever of 102.2 + FHR of 170bpm ->
- Unasyn and Tylenol ->
- Two more hours of pushing -> SVD of well-appearing male infant.
- ROM to delivery = 30hrs
Name Controversy

- Triple I
- IAI = Intraamniotic Infection/Inflammation
- Chorioamnionitis
Maternal fever

- Per ACOG’s March 2016 workshop summary - *Evaluation and management of women and newborns with a maternal diagnosis of chorioamnionitis*

- Isolated maternal fever
  - $>39^\circ C = 102.2^\circ F$ once
  - $>38^\circ C = 100.4^\circ F$ twice
Maternal fever

- Consider alternative causes:
  - epidural
  - dehydration
  - hyperthyroidism
  - elevated ambient temperature
  - use of prostaglandins for induction
Suspected IAI

- Fever without a source +
  - Wbc >15,000 (w/o steroids)
  - Fetal tachycardia >160bpm
  - Purulent fluid from os
Confirmed IAI

- Suspected triple I +
  - Amniotic fluid Gram stain + for bacteria or high wbc (>30 cells/mm³)
  - Pathology confirmation in placenta, fetal membranes or cord
Mechanism

- Migration of bacteria in vagina and cervix through ruptured membranes
Diagnosis

- Gold standard = amniotic fluid culture (takes 24-48hrs)
- Markers of infection
  - IL-6 specificity 83%
  - MMP-8 60%
  - MMP-9 100%
  - MMP-9 + IL-6 100%
Organisms involved

- Genital mycoplasmas
  - ureaplasma, mycoplasma hominis
- GBS
- E coli
- Anaerobes
Prevalence

- Clinical vs histologic (2014 Cochrane)
  - Clinical: 1-2% term 5-10% preterm
  - Histologic: 20% term 50% preterm
Maternal morbidity

- C/S 2-3x
- Infection
  - endomyometritis
  - pelvic abscess
  - wound infection
  - bacteremia 3-4x
    - (18% of maternal sepsis associated with IAI)
- PPH 3-4x
Risk Factors

- <18 years
- non-Caucasian
- primiparous
- singleton
- induction
- prolonged or premature ROM
Risk Factors

- 1995 retrospective case-control study of 3109 patients published in ACOG
  - epidural
  - prolonged ROM (>24hrs)
  - long duration of labor (latent phase >8hrs)
- Are cervical exams introducing vaginal flora into upper genital tract?
Cervical Exams?

- 7.2% developed intrapartum fever
  - Number of exams not associated
    - Even subanalyzing for rupture of membranes and labor type
  - Previous studies with high risk PROM pts
  - **Increased duration of labor** is likely underlying the association found in previous studies
Epidural Use

- 8% of patients with epidural developed IAI, 1% without
- Epidural use was statistically associated with increased risk of IAI
- **Increased labor duration** was highly associated with epidural use (OR 23)
Amnioinfusion for chorio?

- Insufficient evidence based on August 2016 Cochrane Database Systematic Review
- One small trial with 34 participants compared women already receiving antibiotics.
- No decreased neonatal infection or postpartum endometritis
Chorio an indication for C/S?

- C/S does not routinely improve clinical outcomes in IAI
Antibiotic treatment

- Goal = cover for anaerobes and beta-lactamase-producing aerobes
  - Ampicillin + gentamicin
  - Ampicillin + gentamicin + clindamycin
  - Ampicillin/sulfabactam
  - Cefotetan or cefoxitin (2\textsuperscript{nd} gen)
  - Add clinda for C/S to cover anerobes
Duration of therapy

- 24hrs afebrile?
- One postpartum dose?
- No postpartum doses?
- Continue on oral antibiotics?
Quench the fire?

- Maternal fever + cord acidosis -> increased risk of encephalopathy
- Tylenol
Preterm neonates

- IAI associated with 50% of preterm deliveries
- Accounts for 70% of perinatal deaths, 50% neurologic morbidity
- Higher neonatal mortality - 1.4/1000 of infants with chorio vs 0.8/1000
- Inflammation-induced white matter injury
Neonatal infection

- Early onset sepsis = a leading cause of death
- EOS incidence = ~1 in 1000 (0.061% vs 0.077% vs 0.098%)
- A 2010 RCS showed EOS risk in IAI of 4 in 1000
- IAI = 8.7 fold higher risk
- IAI is associated with 40% of EOS
- E coli and GBS
Neonatal mortality

- 2008 analysis of 2.28 million births at 37-42 weeks in US from birth and death certificate files revealed...
- IAI prevalence was 0.97%.
- In other studies rates up to 5%
- Neonatal mortality rate for exposed infants was 0.14%
  - (vs 0.081% w/o chorio)
Mechanism

- Mechanisms: altered BBB, endothelial damage, etc.
- Infection exposure in utero stimulates fetal inflammatory response
  - Bronchopulmonary dysplasia
  - Periventricular leukomalasia
  - IVH
CDC+AAP+NIH Guidelines

- Empiric broad spectrum antibiotics +
- Labs
  - blood cx
  - cbc with differential
  - +/- crp
Impact of maternal antibiotics

- Start upon diagnosis!
- 2011 study including 400,000 infants: Intrapartum abx to women with chorio reduced risk of EOS by 82%.
- In 1980s, EOS rate in IAI was 80-200/1000
  - Now 1-5/1000
- Widespread GBS screening
### Maternal and infant characteristics based on clinical chorioamnionitis status

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No CAM 29,869</th>
<th>CAM[a] 1,243</th>
<th><em>p</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age in wks, mean (SD)</td>
<td>38.9 (1.35)</td>
<td>39.3 (1.27)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Highest temperature, °F, median (range)</td>
<td>98.8 (95.5, 105.0)</td>
<td>101.2 (96.8, 105.1)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**Maternal vaginal GBS**

<table>
<thead>
<tr>
<th></th>
<th>No CAM</th>
<th>CAM</th>
<th><em>p</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBS test not done</td>
<td>3,468 (11.6)</td>
<td>52 (4.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>GBS test done</td>
<td>26,401 (88.4)</td>
<td>1,191 (95.8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Test positive</td>
<td>4,879 (16.3)</td>
<td>167 (13.4)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

**Intrapartum antibiotics**

<table>
<thead>
<tr>
<th></th>
<th>No CAM</th>
<th>CAM</th>
<th><em>p</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>13,768 (46.1)</td>
<td>1,229 (98.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>GBS-positive mothers</td>
<td>4,306 (88.3)</td>
<td>165 (98.8)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**Neonatal infection and antibiotic treatment**

<table>
<thead>
<tr>
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<th>No CAM</th>
<th>CAM</th>
<th><em>p</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Culture positive</strong></td>
<td>14 (0.05)</td>
<td>5 (0.4)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mother received intrapartum</td>
<td>6 (42.9)</td>
<td>5 (100)</td>
<td></td>
</tr>
<tr>
<td>antibiotics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture negative, antibiotics</td>
<td>211 (0.7)</td>
<td>42 (3.4)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 5 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother received intrapartum</td>
<td>133 (63.0)</td>
<td>42 (100)</td>
<td></td>
</tr>
<tr>
<td>antibiotics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture negative, antibiotics</td>
<td>1,043 (3.5)</td>
<td>318 (25.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>&lt; 5 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother received intrapartum</td>
<td>723 (69.3)</td>
<td>316 (99.4)</td>
<td></td>
</tr>
<tr>
<td>antibiotics</td>
<td></td>
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</table>
Serial Physical Exams

- World Journal of Pediatrics: Multicenter retrospective cohort study over 4 months evaluated 2092 asymptomatic neonates >35 wks with 216 initially managed with SPEs
- 32 of the neonates were intrapartum fever/chorio-exposed
  - 21.8% had signs of illness
  - 62.5% had sepsis w/u
  - 21.9% were given empirical antibiotics
Serial Physical Exams in IAI

- All had a normal outcome and none had culture-proven sepsis
- Standard intervals – 3/6/12/18/36/48 hrs
- Standard forms: clinical appearance
- However, 22% of term infants with EOS born to chorio mothers are asymptomatic at 72hrs of life
  - None of these infants died
According to an RCS of 400,000 infants with 81 cases of EOS in term infants, 22% had no clinical symptoms at 72 hours.
Neonatal clinical signs of illness

- Temp out side range 36.5-37.5 (rectal)
- Pallor
- Cyanosis
- Lethargy
- Irritability
- Respiratory distress
- Apnea
- Concerning rash
- Hypoglycemia
Physical exam + risk calculator

  - One had culture positive EOS.
  - 65% received lab tests+abx therapy
  - But EOS calculator and clinical appearance would lower lab tests+abx therapy to 12% without missing any cases.
Newborn Sepsis Calculator

- [http://newbornsepsiscalculator.org/](http://newbornsepsiscalculator.org/)
- Prevalence of culture-positive sepsis was 0.058%
Concerns

- Labs
  - 15% with abnormal I/T
  - 22% with abnormal crp
  - 0.7% with positive blood culture
  - 21.6% underwent lumbar puncture

= Large numbers of chorio-exposed infants were treated with prolonged abx therapy due to abnormal labs alone.
Concerns

- Most studies included in CDC guidelines were before widespread GBS screening
- Neonatal risks with antibiotics:
  - exposure to MDR bacteria
  - attachment and breastfeeding issues
  - altered gut flora
Concerns

- How many newborns would need labs and antibiotics to detect an infant with EOS?
  - NNT = 60-1400
- To prevent death -> NNT = 1785
- Treating all infants for 48hrs with abx in NICU = $$$
Babies with clinical signs of infection

Asymptomatic babies with risk factors

Premature baby < 37 weeks

No maternal clinical chorioamnionitis

Maternal chorioamnionitis or maternal systemic sepsis

Clinical chorioamnionitis defined by the combination of:
- Maternal fever
- Tachycardia
- Raised WCC / CRP
- Positive blood culture
- Urinary kindness
- Fetal monitoring digital changes
- Fetal tachycardia

Previous baby with early onset sepsis

ONE of the above risk factors

TWO of the above risk factors

Investigations:
- FBC/EU/FT/Blood culture
- LPP clinically stable and appropriate CRP 

Treatment:
- IV Fludrocortisone, 1mg/kg
- Broad spectrum antibiotics

OBS: 24 hours, on NEWS chart

15 – 24 hours post birth: Repeat CRP measurement

If any CRP > 10, blood culture positive or child remains clinically unwell, contact senior Paediatrician for advice.

The CRP should ideally be repeated 18-24 hours after the first CRP, but can be repeated up to 36hrs later. For all babies who are at risk of infection, neonatal sepsis advice ead be given to parents at time of discharge home.
Back to your patient...

- 23 year old G1 from Mexico at 40 weeks 5 days with PROM ->
- Pitocin ->
- Complete + 45 minutes of pushing ->
- Fever of 102.2 + FHR of 170bpm ->
- Unasyn and Tylenol ->
- Two more hours of pushing -> SVD
- ROM to delivery = 30hrs

What should we do with baby?
The bottom line for babies

- Early onset sepsis rate is 0.5 to 1 in 1000
  - IAI increases this risk by 4-8 times
- Neonatal morbidity is about 8 in 10,000
  - IAI doubles this risk
- Labs, 48hr NICU stay and antibiotics are standard of care
  - Clinicians worldwide are questioning if a kinder, gentler approach is reasonable
- Utilizing the sepsis calculator, serial physical exams and limited work up is one possible solution
Discussion with patient

- Use neonatal sepsis calculator
- Consider staff capabilities, ease of transfer
- Discuss risks vs benefits of standard Abx+labs+NICU stay
Take home points for IAI care

- Correctly establish diagnosis
- Start antibiotics once diagnosis established
- Provide optimum care for newborns of mothers diagnosed with IAI


Safe Prevention of the Primary Cesarean Delivery. ACOG Obstetric Care Consensus March 2014


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