Utility of perinatal pathology for the obstetrician and neonatologist

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Disclosures

• I have the following disclosure:
  – Author for UpToDate
Utility of perinatal pathology

• Explains a “bad” outcome
• Determine cause of death
• Predicts recurrence
• Provides risk assessment for immediate and eventual outcome
• Nearly always helpful in defense of medical malpractice claims
Case

• 28 y/o G1P0 with obesity presents at term with LGA fetus and delivers with shoulder dystocia. APGARS 2,4,7.
Placenta

- 850g, >99th percentile
- Slightly immature villi
- Chorangiosis
- Multiple intervillous thrombi
Longstanding descriptions of placentas associated with DM

- Heavy placentas
- Villous immaturity
- Chorangiosis
- Villous fibrinoid necrosis
- Decreased intervillous space
- Syncytiotrophoblastic necrosis
- Cytotrophoblastic hyperplasia
- Thickening of the villous trophoblastic basement membrane

All might be modulated by the timing of the glucose intolerance, quality of the glucose control, and the complication of hypertension.
Hypothesis

• GDM results in increased trophoblastic apoptosis which results in placental pathology
Longstanding descriptions of GDM exposed placentas

- Heavy placentas
- Villous immaturity
- Chorangiosis
- **Villous fibrinoid necrosis**
- Decreased intervillous space
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Trophoblast from Human Placentas

![Bar chart showing TUNEL positive cells as a percentage of total cells. The chart compares Non-diabetic and GDM samples. The GDM sample shows a significantly higher percentage of TUNEL positive cells.](chart.png)

Unpublished data
Another example of trophoblastic necrosis/apoptosis

Intervillous Thrombi
Intervillous thrombi

- Relatively common findings (~5% of all placentas)
  - Laminated fibrin and red blood cells in intervillous space
  - Limited “collateral damage” of surrounding villi
- Thought to be due to fetal hemorrhage into the maternal space and maternal “clotting” of the hemorrhage (controversial)
  - Presence of HgbF
- Associated with male gender*

Study design

- Database of well characterized DM in pregnancy with placental pathology available.
- 206 cases of DM including:
  - T1DM: 39
  - T2DM: 37
  - GDM: 130
- Histology and pathology reports reviewed
- GA matched controls from cohort of placentas examined ONLY for indication of GBS carrier
  - Euglycemia confirmed by EMR review
- Collected cases of IVT

Work done with K. Basnet
IVT are significantly increased in GDM

<table>
<thead>
<tr>
<th></th>
<th>Any DM (n = 206) p = 0.04</th>
<th>GDM (n = 130) p = 0.03</th>
<th>Type I DM (n = 39) p = 0.73</th>
<th>Type II DM (n = 37) p = 0.19</th>
<th>Controls (n = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% IVT</td>
<td>15.5</td>
<td>16.9</td>
<td>10.3</td>
<td>16.2</td>
<td>7.1</td>
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</tbody>
</table>
Source of IVT

• Subset of IVTs from DM (9) and controls (5) were sent to Nationwide Children’s Hospital in Columbus, Ohio for HgbF IHC
• All controls and 6 of 9 cases showed at least focal +IHC for HgbF in the thrombi
Placentas in DM

• Pathological diagnosis should suggest findings consistent with maternal glucose intolerance, for example:
  – Heavy immature or slightly immature placenta
  – Chorangiosis
  – Intervillous thrombi
  – Increased villous fibrinoid necrosis
Example

• 41 y/o G4P0-1 with FVL homozygosity and h/o DVT/PE
• 39 week spontaneous labor with sudden fetal bradycardia
• STAT c/s APGARS 0,0,0
Dilatation of chorionic plate vessels
Vascular thrombosis
Fetal Vascular Malperfusion

• Etiology
  – Obstruction: cord knots, membranous vessels
  – Slow flow: heart failure, high red cell mass
  – Coagulopathy: sepsis, inherited*, malignancy
  – Vascular injury: inflammation, meconium, pressure necrosis

* Second “hit” usually required
Cord obstruction
Case

- 36 week infant to a 16 y/o primigravida
- NSVD
- APGARS 8,9
- Goes home but returns on DOL 4 with seizures
CMV PLACENTITIS
histopathologic findings

• Lymphoplasmacytic villitis
• Sclerosis of the villous capillaries
• Chorionic vessel thromboses
• Necrotizing villitis
• Hemosiderin deposition in the villous stroma
• Normoblastemia
• Viral inclusions observed in 10% of cases
CMV with IUFD

- Rare
- High viral load
- Consider evaluation for HIV
Case

- 38 week with NRFHT and maternal fever
- C/S delivery
- APGARS 2,3,5
- Cord pH 6.97 base deficit 13
- Hypoxic-ischemic encephalopathy
- NICU admission for cooling
Chorioamnionitis
Placental Pathology

• Acute chorioamnionitis:
  – Maternal and fetal stage (anatomic location) and grade (intensity)
  – Mycoplasma, E. Coli, GBS, GAS, Fusobacteria, Candida
  – Non-infectious

• Acute villitis: Listeria, GBS, E.coli
• Intervillositis: malaria
Chorioamnionitis

• Clinical chorioamnionitis defined by maternal fever
• Histologic chorioamnionitis not always correlated with maternal symptoms
  – Common in preterm deliveries
  – Preterm chorioamnionitis usually infectious.
  – Term chorioamnionitis can be non-infectious
  – Fetal response predictive of neurological outcome
Importance of fetal side inflammation in acute chorioamnionitis

• Higher association with neonatal morbidity
  – Sepsis
  – Pneumonia
  – RDS/BPD
  – Necrotizing enterocolitis
  – Intraventricular hemorrhage
  – ?Stroke and HIE
Hypoxic Ischemic Encephalopathy

- Fetal inflammatory response
- Fetal vascular malperfusion
- Acute insult findings:
  - Acute villous edema
  - Meconium
- Maternal vascular malperfusion
Preterm pre-eclampsia with severe features – maternal vascular malperfusion
Chronic Abruption
Why are the placental findings of maternal vascular malperfusion important?

- Confers a risk for the development of neurocompromise
  - Especially preterm PET
  - Especially with decidual arteriopathy and atherosis
Placenta critical

• Essential part of any perinatal autopsy
• Should be performed even if no autopsy consent granted.
• All placentas from NICU admissions should be examined
• Any unexpected (or expected) “bad” outcomes should have the placenta examined
• Any abnormal placenta at delivery should be examined
Placenta “recruitment”

• Different strategies for placenta submission for pathologic exam
  – Obstetric indications
  – Pediatric indications
  – Maternal indications
  – Litigious indications
  – “funny looking placenta”
Communication

• If something does not make sense
• Findings of immediate clinical utility
  – Specific infection
  – Malignancy
  – Storage disorders
• Findings worrisome for neurocompromise
In conclusion

• Placental pathology is an essential part of the perinatal autopsy and can be helpful when autopsy consent is declined
• Placental pathology can help in the treatment of the newborn and in predicting neurological outcome of the infant
• Pathologists are an important part of the OB/GYN and Pediatric team.
Case

- 35 week delivery
- C/S delivery for IUGR at <3\textsuperscript{rd} %ile
- Mild hydrops fetalis
- NICU admission for respiratory complications
Inborn errors of metabolism

- Most “storage” diseases could be diagnosed at birth by placental pathology
- Early diagnosis = early treatment
- Family counselling