Fetal Neurological Consult

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Goals of Presentation

1. Greater understanding of fetal imaging
2. Greater understanding of fetal brain development
3. Greater understanding of the types of questions/answers posed to neurologist
4. Directions for research
Fetal Imaging

- Movement in children and adults movement is restricted to two planes

- In Fetus, summersaults
Fetal MRI Sequences

- **Single Shot Fast Spin Echo (T2)**
  - workhorse of the fetal MRI

- **EPI T2* - for blood products and bone**
  - done with two levels of sensitivity, to help with sensitivity/specificity of diagnosing blood products vs other junk/vessels

- **Diffusion**
  - only started doing that in last two years, and has generally been very unhelpful

- **Fast T1**
  - optional for select cases based on what is shown on other sequences; hematomas, cortical malformations

- **MR Spectroscopy in specialized centers**
  - Lactate, NAA/Cho
Fetal Brain Development

1st Trimester
0 – 13 weeks

Organogenesis

Proliferation
Migration

Neurogenesis

2nd Trimester
14 – 26 weeks

Oligodendrocyte
Maturation

3rd Trimester
27 – 40 weeks

Myelination

Birth

Human Brain Growth

% Full-term Brain Weight

Gestational Age (wks)

3rd trimester
Clouchoux
Brain Struct Funct (2012)
Elements of Fetal Consult

Referral to Fetal Diagnosis Clinic
- Ventriculomegaly
- Posterior Fossa cyst
- Congenital heart defect
- Abdominal wall or Diaphragm defect
- Myelomeningocele
- Concerning Family History

Work up
- MRI Brain
- MRI Body
- Fetal Ultrasound (body/brain)
- Fetal Echo
- Genetics
- Maternal Fetal Medicine
Elements of Fetal Consult

• Neurology last to see family
• MFM and Genetics assessment available
• Neurology consult
  – Image review with family
  – Differential diagnosis discussion with family
  – Outcome vs quality of life assessment with family
  – Plan for follow up; both antenatal and postnatal
  – Plan for location of delivery
    • High level care needed or not

• Neurologist, priest and fortune teller
Referral

VENTRICULOMEGALY
Isolated Ventriculomegaly
One of the most common Indications
Isolated Ventriculomegaly

<10mm = normal
10 – 15mm = moderate
>15mm = severe
Isolated Ventriculomegaly

- Isolated = not associated with other structural CNS anomalies or other organ abnormalities
- Natural History Reversible (29%), Stable (57%), or lead to Hydrocephalus (14%)
- Prognosis:
  - Good if truly isolated and no progression
  - Bad if male gender (worse), severe enlargement (>15mm), progression to HC, or appears early in gestation
- Plan:
  - If progression – high level care; child neurology, neurosurgery, MRI
  - No progression – local delivery w/ child neuro follow up
Ventriculomegaly

• Of 156 fetal cases,
  – (Yamasaki Seminars in Fetal & Neonatal Medicine 2012)

• 57 (37%) were classified as Isolated
  – 39 (25%) cases of true isolated
  – 18 (12%) later found not to be isolated.

• 78 (50%) not Isolated
  – myelomeningocele (MMC, 36 cases),
  – Dandy Walker cyst (3 cases), Joubert syndrome (1 case), HPE (6 cases), encephalocele (9 cases), arachnoid cyst (12 cases), atresia of Monro (3 cases), and ACC (8 cases).

• 21 cases (13%) other, virus infection (4), fetal intracranial hemorrhage (9), fetal brain tumor (8).
Ventriculomegaly
Aqueductal Stenosis
OTHER VENTRICULOMEGALY
Fetal Stroke
Later Porencephalic Cyst
Fetal Holoprosencephaly
Fetal Chiari II Malformation and Myelomeningocele
Fetal Agenesis of the Corpus Callosum
Fetal Brain Tumor
Choroid Plexus papilloma diagnosed in-utero
Fetal Schizencephaly
Fetal Schizencephaly

• Often associated with Septo-Optic Dysplasia
• Variable outcome
  – Mild to severe
  – Seizures are common
  – Hemiplegia is common
• If SOD
  – Blindness vs. vision impairment
  – Pituitary insufficiency vs pan hypo-pit
Mild Septo-Optic Dysplasia
Moderate Septo-Optic Dysplasia
Moderate Septo-Optic Dysplasia
Severe Septo-Optic Dysplasia
Septo-Optic Dysplasia

• Likely Genetic
  – Search for gene ongoing
• Pathology of Schizencephaly = gliosis
• ? Early thrombotic events?
• Middle Cerebral artery infarcts
• Germinal Matrix Infarcts
• Why the Optic Nerve hypoplasia?
Septo-Optic Dysplasia

• High-level peri-natal needs
  – MRI brain and orbits
  – EEG
  – Pediatric endocrinology
    • r/o hypoglycemia,
    • Cortisol
    • Thyroid
  – ophthalmology
Referral

POSTERIOR FOSSA CYST
Fetal Dandy-Walker Malformation

Dx confirmed by demonstrating elevation of the Torcula

Otherwise Dx is Vermian hypoplasia
Not Dandy Walker Cyst
Not Dandy Walker Cyst

• Please don’t call it a DWC-variant

• Confuses parents

• The dx is “Vermian Hypoplasia”
  – Associated with genetic disorders
    • Down’s most commonly
  – Isolated – associated with hypotonia
    • Clumsy kid, but otherwise normal
Unilateral Cerebellar and Vermian Hypoplasia

Note: no elevation of Torcula

Please do not call this DW ‘variant’
It leads to too much confusion
PHACES Syndrome

Posterior fossa, Hemangioma, Angiopathy, Cardiac, Eye, Sternal Pit
PHACES Syndrome

- Do not necessitate high-level post-natal care
- Do necessitate early referral to:
  - Dermatology
  - Neurology
  - Cardiology
- Will require prior to starting Inderal:
  - MRI Brain and Neck (with and without contrast)
  - MRA Brain and Neck (with contrast)
Unilateral Cerebellar and Vermian Hypoplasia

• Outcome dependent on Genetic syndrome (if present)
• Vermian hypoplasia common with Down’s
• Isolated Unilateral Cerebellar Hypoplasia is generally asymptomatic or mild symptomatic
• Associated with low tone and clumsiness
Referral

HEMORRHAGE
Fetal IVH

EPI T2*
Intra- and Extra-axial Hemorrhage
Intracranial Hemorrhage

- Prognosis based on visible parenchymal injury, hydrocephalus
- Intraventricular blood needs monthly Fetal HUS

Dx = CMV

Destruction of BG
Ventriculomegaly
Paucity of WM
Cerebellar injury
Hemorrhage Case

- 29yo healthy mom
- FUS at 36 week GA
- ‘partial agenesis of CC’ referral
Hemorrhage Case

- Birth at term –
- Vaginal because no further ventriculomegaly
Hemorrhage Case

- 1 month
- Social smile, normal sleep/feed
- Awoken suddenly + vomit/+ irritability
- To ER

It’s not over until the fat lady sings!!!
Referral

GENETICS
Fetal Agenesis of the Corpus Callosum

- Prognosis: Isolated vs Not Isolated
- Isolated = normal >80% (male gender favorable)
- Not Isolated, prognosis depends on associated findings
- Caveat – 15% of ‘isolated’ found to be ‘not isolated’ on post-natal imaging/exam
Fetal Agenesis of the Corpus Callosum

• Search for associated brain (head) anomalies
  – Interhemispheric cysts
  – Coloboma of eyes
  – Cortical dysgenesis
  – Cerebellar abnormalities vs chiari

• Search for associated somatic abnormalities
  – Congenital heart defects
  – Diaphragm herniation
  – Other evidence of syndrome
Aicardi Syndrome

Agenesis of the Corpus Callosum

Interhemispheric Cyst

Retinal Coloboma
Fetal Holoprosencephaly

- Variable outcome
Fetal Hypoxia
Sinovenous Thrombosis
Summary

• Role of Neurologist:
  – Aid in differential
  – Aid in decision making
  – Prognostication
  – Plan for antenatal, perinatal and postnatal care

• Remember
  – MRI is a picture! No function, no crystal ball
  – Every family is different – QOL is not yours to measure!
  – Never be more than cautiously optimistic or cautiously pessimistic.

• WHAT ELSE CAN WE OFFER?
Congenital Heart Defects

- Using Diffusion Tensors demonstrated abnormal white matter development
- Tools highly specialized – poor generalizability
Congenital Heart Defects

- 42 term CHD infants (TGA and HLHS)
- Smaller Head Circ
- Developed MRI based observational scale
- Demonstrated immaturity of WM, cortical folding
Brain Anatomic Maturation in CHD

- Total Maturation Score
  - Degree of cortical folding
  - Myelination
  - Presence/absence of Germinal Matrix
  - Migrating glial cells

Historical controls from original validation paper Licht et al JTCVS 2009;137:529-37
Congenital Heart Defects

Brain immaturity is associated with brain injury before and after neonatal cardiac surgery with high-flow bypass and cerebral oxygenation monitoring

JTCVS 2010

- Not only are brains immature
- Immaturity = leading cause for WM injury
- Pre- and post-op
Congenital Heart Defects

• Immaturity predicts Neurodevelopmental outcomes at 2 years (BSID III)
Congenital Heart Defects

Brain Volume and Metabolism in Fetuses With Congenital Heart Disease
Evaluation With Quantitative Magnetic Resonance Imaging and Spectroscopy

Catherine Limperopoulos, PhD; Wayne Tworetzky, MD; Doff B. McElhinney, MD; Jane W. Newburger, MD, MPH; David W. Brown, MD; Richard L. Robertson, Jr, MD; Nicolas Guizard, MEng; Ellen McGrath, BSc, RN; Judith Geva, MSW; David Annese, RT(R); Carolyn Dunbar-Masterson, BSc, RN; Bethany Trainor, BSc, RN; Peter C. Laussen, MD; Adrė J. du Plessis, MBChB, MPH

• Normal (n = 55) v CHD (n = 50)
• Similar GA range: 25 to 37 wk
Materials and Methods

- **Development of the Semiquantitative Brain Maturation Score**
  - Major modifications and additions to previously used *postnatal* brain maturation scores
    - Childs AM, AJNR 2001
    - Licht DJ, JTCVS 2009
  - Six morphologic criteria
  - Right and left scored separately
  - A cumulative total score was computed

<table>
<thead>
<tr>
<th>Morphologic Criteria</th>
<th>Score</th>
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<tbody>
<tr>
<td>Myelination</td>
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<tr>
<td>Frontal and Occipital Cortex</td>
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<tr>
<td>Insular Cortex</td>
<td></td>
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<tr>
<td>Germinal Matrix</td>
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<tr>
<td>Superior Temporal Sulcus</td>
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<tr>
<td>Inferior Temporal Sulcus</td>
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- Two independent readers,
- blinded with respect to gestational age and brain volume
Materials and Methods

Frontal and Occipital Cortex Scoring

1

4
Materials and Methods
Superior and Inferior Temporal Sulcus Scoring

No Superior or Inferior Sulcus

Deep right and shallow left superior sulcus – No inferior sulcus

Deep Superior and Inferior Sulci

[Graphs showing TS and TI scores against GA_MRI]
Results

Correlation between two independent readers

Pearson $r = 0.951$,

ICC single measure = 0.896, ICC average = 0.945
Results - Correlations

Segmented Brain Volume with Gestational Age
\( r = 0.955, \ p < 0.001 \)

Fetal maturational score with Brain Volume
\( r = 0.969, \ p < 0.001 \)
Fetal Maturational Score with Gestational Age

\[ r = 0.971, \ p < 0.001 \]

Development and Validation of a Semiquantitative Brain Maturation Score on Fetal MR Images: Initial Results.
Results

- The model was accurate in predicting gestational age with absolute error of 3.99 days.

- The leave-one-out cross-validation analysis demonstrated:
  - $R^2$ (prediction) = 0.91 for gestational age
  - $R^2$ (prediction) = 0.89 for brain volume.
Fetal TMS

- Test fTMS on CHD fetuses
- Compared to normals
Fetal Interventions

• Surgical interventions
  – MMC
  – Lung and neck masses

• Procedural interventions
  – AS/AA, HLHS intact intra-atrial septum

• Sequential fTMS followed by post-natal MRI

• Now Medical Interventions!!
Summary

• Fetal neurologists leading role in fetal medical interventions
  – CHD
  – IUGR
  – TORCH?
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