Fetal hydrocephalus

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Fetal hydrocephalus

- Not uncommon (MMC/Chiari 2 excluded)
- Either mid- or late gestation, never acute
  - ultrasonography at 12w, 22w, 32w,
- Definition: hydrocephalus versus “ventriculomegaly”
- Ability to recover
- Aqueductal stenosis as the major etiology
Fetal hydrocephalus: material

- 41 cases in two groups, no overlap
  - 30 cases mid-gestation (19.4w-26.4w)
  - 11 cases late gestation (32.2w-38.4w)

- Follow-up, treatment: 8 cases
  - 5 cases mid-gestation (22.5w-26.2w)
  - 3 cases late gestation (38w-38.4w)
Fetal hydrocephalus vs fetal ventriculomegaly

1. Disproportionate ventriculomegaly
2. Effacement of pericerebral spaces
3. Cerebral mantle: thinning, dehiscence
4. An identified cause
5. Rupture of septum pellucidum
6. Macrocephaly
7. Follow-up and response to treatment
Fetal ventriculomegaly

- Measured at the atrium, on largest side
- Usually 5-8mm throughout gestation
- May be benign (reversible) or destructive
- By convention
  - normal <10mm
  - mild VM 10-15mm
  - moderate 15-20mm
  - severe > 20mm
Fetal hydrocephalus

- Measured at the atrium, on the largest side
  - symmetric in 9/41
- Active expansion of ventricles (obstructive)
- Cases of hydrocephalus
  - in 34/41: at, or larger than, 20mm
  - smallest 14.1mm (familial aqueductal stenosis)
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Wall defect: always early hydrocephalus with effaced pericerebral spaces
Fetal hydrocephalus: an identified cause

• Mid-gestation
  – aqueductal stenosis 28/30
    • hemorrhage in 1
  – others 2/30: AVF torcular (1), retro-cerebellar cyst (1)

• Late gestation
  – aqueductal stenosis 6/11
    • hemorrhage in 4
  – others 5/11:
    • vermian mass (1),
    • cysts (1 each): suprasellar, quadrigeminal, latero- and retro-cerebellar
Fetal hydrocephalus: head measurements

• Evaluation of macrocephaly
  – from BPD and HC
  – HC = ½ (BPD + FOD) x 3.14

• Quantified in weeks from average
  – but wide variations from average

• Results
  – BPD consistently above average
  – for HC, mostly increased but 6/40 are at, or slightly below average
   • poor cerebral growth due to hydrocephalus?

<table>
<thead>
<tr>
<th>Normal twin</th>
<th>Hydro twin</th>
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<tbody>
<tr>
<td>+ 0.2</td>
<td>+ 3</td>
</tr>
<tr>
<td>+ 2.4</td>
<td>+ 4.3</td>
</tr>
<tr>
<td>+ 4.3</td>
<td>+ 3.5</td>
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<tr>
<td>+ 2.2</td>
<td>+ 4</td>
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Fetal hydrocephalus: severity

- **Moderate:**
  - patent cerebral mantle
  - patent pericerebral spaces

- **Severe:**
  - effaced pericerebral spaces
  - dehiscent cerebral mantle: postero-medial mantle thinning and disruption (early only?)

- **Mid- versus late gestation**

normal (24w)

moderate (23w) aqueductal stenosis

severe (21.5w) aqueductal stenosis

Mid-gestation
Late gestation

normal (35w)

moderate (32.4w) aqueductal stenosis

severe (35.4w) hemorrhage aqueductal stenosis

Late gestation
Fetal hydrocephalus: morphological severity

- **Moderate:**
  - patent cerebral mantle,
  - patent pericerebral spaces

- **Severe:**
  - defect cerebral mantle
  - effaced pericerebral spaces

- **Mid- versus late gestation**

<table>
<thead>
<tr>
<th></th>
<th>moderate</th>
<th>severe</th>
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<tbody>
<tr>
<td>Mid-gestation</td>
<td>13/30</td>
<td>17/30</td>
</tr>
<tr>
<td>Late gestation</td>
<td>5/11</td>
<td>6/11</td>
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• What is the fetal pericerebral space due to?
• Wide in fetuses, not in preterms
  – post-natal CBF change: pulmonary, atrial foramen, ductus arteriosus
    • → drop of venous pressure
  – different absorption mechanisms? (absorption routes, AQP)
  – elastic skull, amniotic pressure
Fetal hydrocephalus: morphology summary

- **Mid-gestation:** 30 cases
  - overwhelmingly idiopathic aqueductal stenosis (27/30)
    - 1 each: AVF, midline cyst, hemorrhage
  - more often severe (17 vs 13)
- **Late gestation:** 11 cases
  - idiopathic aqueductal stenosis 2/11 only
    - other 9: hemorrhagic 4, tumor 1, midline cysts 4
  - slightly more often severe
- **Mantle dehiscence:** specific for early occurrence?
Fetal hydrocephalus: evolution, outcome

- Only 8/40 cases F/U and treatment
  - 5 cases mid-gestation
  - 3 cases late gestation
- Mid-gestation 5
  - 2 moderate hydrocephalus → fair/good morphologic outcome 2
  - 3 severe hydrocephalus → poor morphologic outcome 2, deceased 1
- Late gestation 3
  - 3 moderate hydrocephalus → good morphologic outcome 3
Mid-gestation histogenesis

- Weeks 20-27
- Neuronal migration essentially completed
  - period of thalamo-cortical connectivity (weeks 22-27)
  - initiates cortical organization with later association-commissural connectivity
- Early cortical vascularization
  - week 22 onward
- Germinal matrices
  - mantle matrix → 28w
Late gestation histogenesis

- Weeks 31-47
- Intense connectivity-synaptogenesis
  - cortical organization with long association-commissural (27-32w) and short association (32-47w)
  - associated developing sulcation
- Intensely developing oligodendroglia
- Developing cortical vascularization
- Germinal matrices
  - ganglionic eminence matrix regresses <36w
Early hydrocephalus does not prevent, or only in part, the development of connectivity and sulcation.

Moderate, 23w (aqueductal stenosis)

Same 30w, delayed but developing sulcation.
moderate, 25.4w aqueductal stenosis

same, 3 d sulcation post shunt

same, 8m/o

Early moderate Follow-up
severe, 23.4w
aqueductal stenosis

Early severe
Follow-up

same, 1d
change in posterior fossa
partial sulcation

same, 4m
post VP shunt
Late gestation
Follow-up

late moderate aqueductal stenosis

congenital, but possibly early severe
Potential factors of recovery

- Persistent expression of signaling pathways for axon growth/branching
- Axonal progression and branching mostly subcortical
- Myelin: most potent inhibitor of axonal development
  - induced by neuronal activity
  - myelin associated inhibitors MAIs limit potential for axon development
    • essentially no hemispheric myelination before term

Fetal hydrocephalus: causes

- Mid-gestation: 30 cases
  - overwhelmingly idiopathic aqueductal stenosis (27/30)
    - 1 each: AVF, midline cyst, hemorrhage
- Late gestation 11 cases
  - idiopathic aqueductal stenosis only 2/11
    - others: hemorrhagic 4/11, tumor 1, midline cysts 4
    - quite similar to post-natal
Aqueductal stenosis: etiologies

- **Possible mechanisms**
  - primary stenosis, or secondary to hydrocephalus
  - TORCH: toxoplasmosis, mumps
  - undocumented hemorrhage, inflammation
  - low grade glioma/hamartoma
  - malformative (Dorothy Russell, 1955)

- **Context**
  - twin pregnancies (10%), siblings (1 family)

- **Feto-pathology & animal models**
  - subcommissural organ SCO
  - ependymal denudation


• Sival et al. *Neuroependymal denudation is in progress in full-term human foetal spina bifida aperta*. Brain Pathol 2011, 21:163-79

• Rodriguez et al. *A cell junction pathology of neural stem cells leads to abnormal neurogenesis and hydrocephalus*. Biol Res 2012, 45:231-41

Aqueductal stenosis: causes

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- Feto-pathology
  - subcommissural organ SCO
  - ependymal denudation
holoprosencephaly
33.5w

septo-optic dysplasia 30w

What is not hydrocephalus

L1CAM/CRASH
(X-linked hydrocephalus)

Walker Warburg 31w

hydranencephaly
35w
To try to summarize

- Patterns of early (mid-gestation) fetal hydrocephalus seem to be characteristic
  - overwhelmingly due to “idiopathic” aqueductal stenosis
    - ependymal denudation, SCO
  - well defined severity patterns
    - related morphological recovery potential
- Late fetal hydrocephalus more similar to post-natal
- Pathogenesis still more difficult than in post-natal
- Fairly reliable diagnostic features