Fetal obstructive hydrocephalus

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Diagnosis, treatment, and long-term outcomes of fetal hydrocephalus

Mami Yamasaki [a,b,*], Masahiro Nonaka [a], Yohei Bamba [b], Chika Teramoto [c], Chiaki Ban [d], Ritsuko K. Pooh [e]

Extensive definition
No mention of aqueductal stenosis

Table 2
Classification of fetal hydrocephalus and occurrence rate.

Classification of hydrocephalus	*n*	%
Primary hydrocephalus		
Isolated ventriculomegaly (IVM)		
True IVM	39	25
Syndromic hydrocephalus	18	12
Hydrocephalus associated with myelomeningocele	36	23
Dandy–Walker syndrome and Jobert syndrome	4	3
Holoprosencephaly	6	4
Cranial bifida (encephalocele)	9	6
Hydrocephalus associated with arachnoid cyst	12	8
Hydrocephalus associated with atresia of Monro	3	2
Corpus callosum agenesis	8	5
Fetal secondary hydrocephalus		13
Post-intracranial hemorrhage	9	
Hydrocephalus associated with brain tumor	8	
Post-infectious hydrocephalus	4	

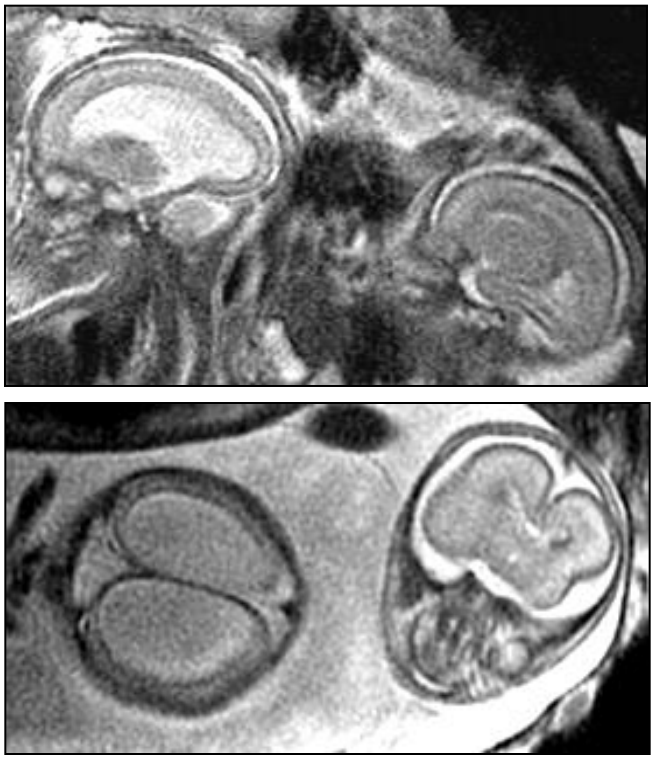
Purpose

- Working definition of hydrocephalus vs ventriculomegalies
- Features of fetal obstructive hydrocephalus
- Causal, and causally associated lesions
- Brain plasticity in fetal hydrocephalus

Working definition: hydrocephalus vs ventriculomegaly

1. Disproportionate ventriculomegaly
2. Increased cephalic measurements
3. An identified obstruction

Therefore, <u>obstructive hydrocephalus</u> only



Fetal obstructive hydrocephalus: ventricular size

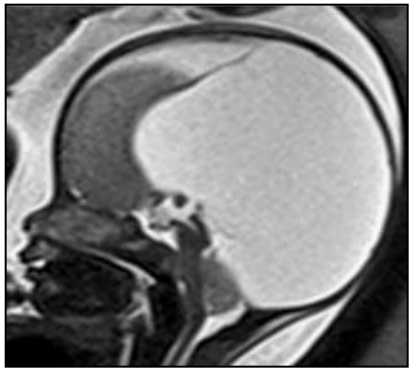
- Measured at the atrium, on largest side
  - normal 5-8mm throughout gestation
- Degree
  - severe >20mm: 40 cases
  - moderate 15-20mm: 11 cases
  - mild 10-15mm : 5 cases
    - 2 DW, 1 familial, 2 F/U confirmed
- Larger when late gestation, always larger on F/U studies
- Often asymmetric

14.1mm
familial

23.4w (28mm), 1d postnatal (58mm)

Fetal obstructive hydrocephalus: cranial size

- Hydrocephalus
  - BPD ≥ 2 weeks-above-average 48/56
  - borderline in 8/56 but
    - 1 DW, 2 familial, 4 hemorrhages, 1 F/U
- Head circumference less increased than BPD
  - HC = ½ (BPD+ FOD) x 3.14
  - head becomes rounded, “turricephalic”

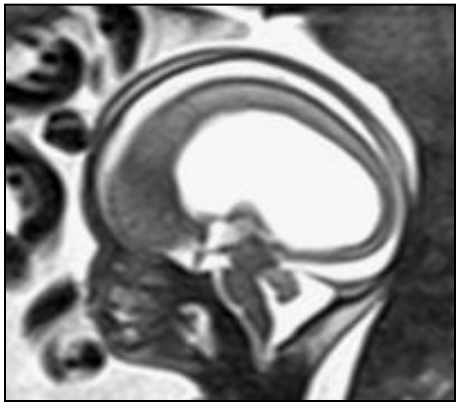


Fetal obstructive hydrocephalus: case series

- Fetal MR diagnosis: 56 cases
  - 44 “early” cases <32w (19.4w-29.5w)
  - 12 “late” cases >32w (32.4w-38.4w)
- Special context (early gestation only)
  - 1 family (2 siblings)
  - 9 twin gestations (20%) (general population 3.2%)
- Initial diagnosis confirmed by
  - fetopathology: 10 cases
  - pre- or post-natal MR F/Us: 10 cases

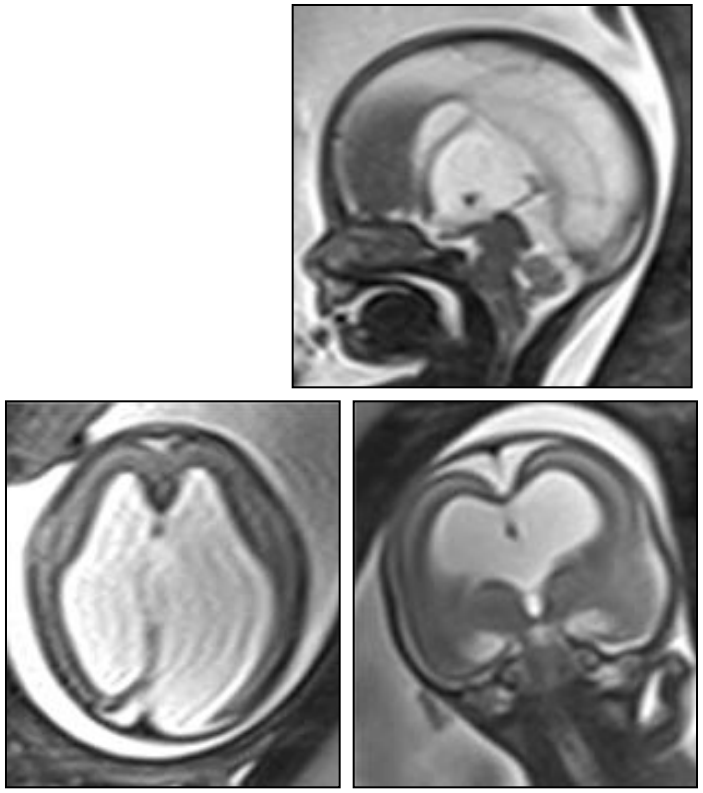
Early fetal obstructive hydrocephalus: subtypes

- Mild subtype
  - mantle thin but regular
  - pericerebral spaces maintained
  - septum pellucidum: rupture common
- Severe subtype
  - mantle thin and focally dehiscent
  - pericerebral spaces effaced
  - septum pellucidum: rupture common



Early fetal obstructive hydrocephalus: cerebral mantle

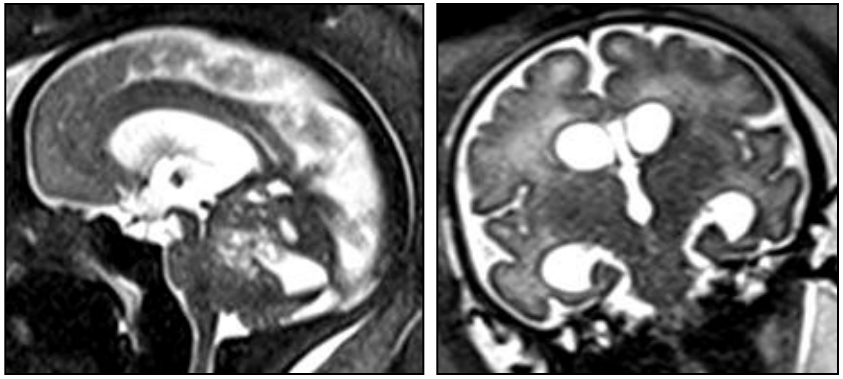
- Mild subtype
  - mantle thin but regular
  - pericerebral spaces maintained
  - septum pellucidum: rupture common
- Severe subtype
  - mantle thin and focally dehiscent
  - pericerebral spaces effaced
  - septum pellucidum: rupture common

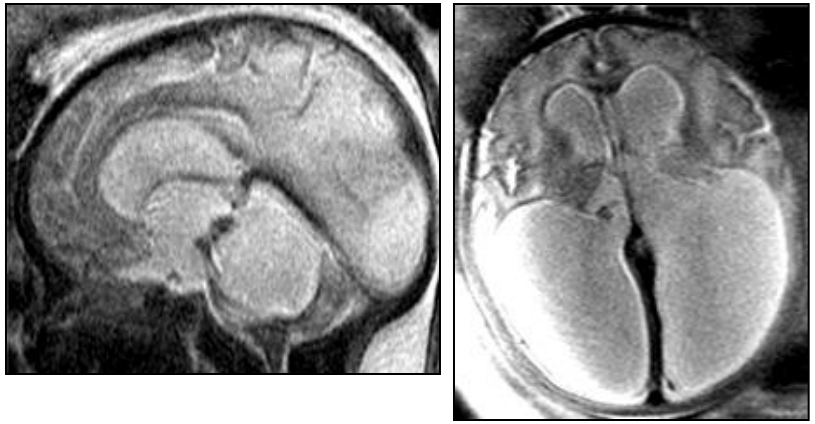


Late fetal obstructive hydrocephalus

Not really different from post-natal (“congenital”) hydrocephalus

- 1/12 mild hydrocephalus: superior vermian mass
- 11/12 severe hydrocephalus (partial mantle loss)





Fetal obstructive hydrocephalus: etiologies

	Early: N (%)	Late: N (%)
Isolated aqueductal stenosis	19 (43)	1
Rhombencephalosynapsis	11 (25)	
Ependymal nodules	6 (14)	1
Midline cysts	3 (7)	4 (33)
Hemorrhages	4 (9)	5 (42)
Others	1 (avf)	1 (mass)
	44 (100)	12 (100)

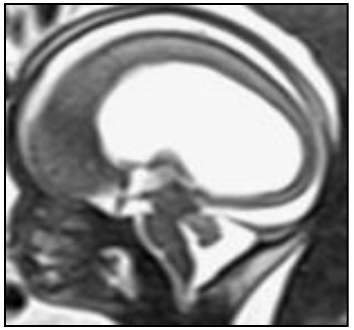
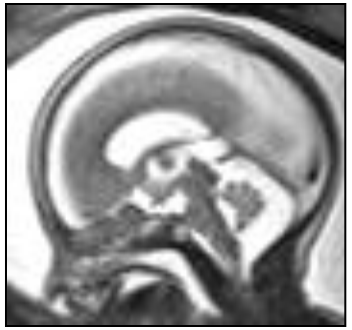
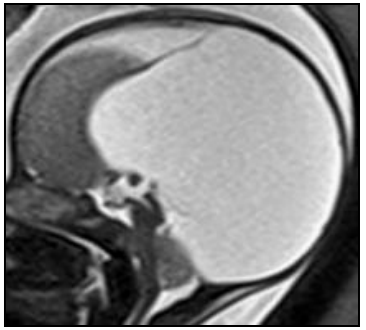
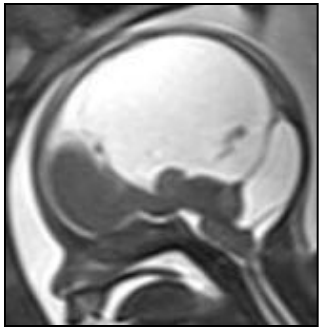
82%

75%

- Etiologies similar in mild and severe subtypes
- Etiologies of late hydrocephalus same as “congenital” hydrocephalus

Early fetal obstructive hydrocephalus: etiologies

- Aqueductal stenosis in 82%
  - isolated 43%
  - associated with other abnormalities
    - rhombencephalosynapsis (& midbrain, oosterior thalamus)
    - ependymal nodules
- Midline cyst, hemorrhage much less common

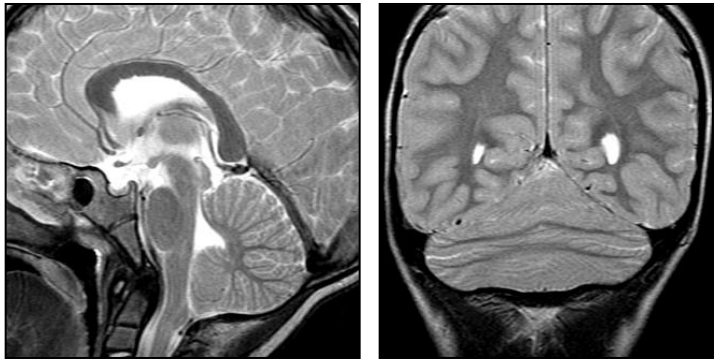
Early fetal obstructive hydrocephalus: etiologies

- Isolated aqueductal stenosis common = 43%
  - classic explanations
    - secondary to hydrocephalus
    - undocumented TORCH, hemorrhage, dormant mass
    - maldevelopment (D. Russel, DH Padget)
  - recent literature data: animal, human fetus
    - ependymal denudation +/- SCO changes
      - ependymal nodules (6 cases) (Ferland 2011, Rodriguez 2102)
      - factor of rupture of septum pellucidum?
      - cause or effect of hydrocephalus?

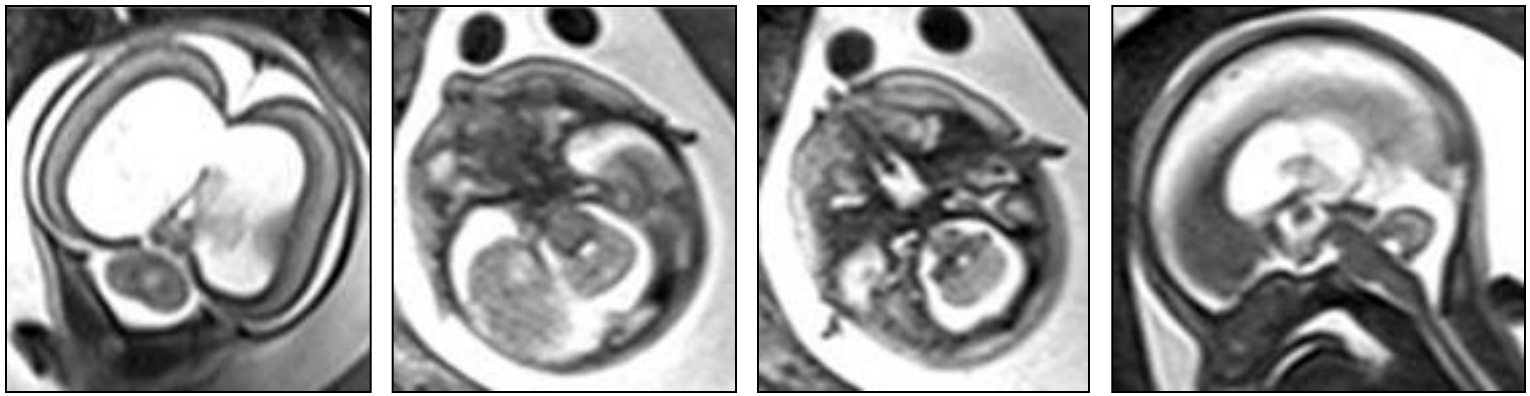
Ependymal denudation, SCO and nodules

- Del Bigio. *Neuropathological changes caused by hydrocephalus.* Acta Neuropathol 1993, 85:573-85
- Castañeyra-Perdomo et al. *Alterations of the subcommissural organ in the hydrocephalic human fetal brain*. Devel Brain Res 1994, 79:316-20
- Jimenez et al. *A programmed ependymal denudation precedes congenital hydrocephalus in the hyh mutant mouse*. J Neuropathol Exp Neurol 2001, 60(11):1105-19
- Galarza: *Evidence of the subcommissural organ in humans and its association with hydrocephalus*. Neurosurg Rev 2002, 25:205-15
- Dominguez-Pinos et al. *Ependymal denudation and alterations of the subventricular zone occur in human fetuses with a moderate communicating hydrocephalus*. J Neuropathol Exp Neurol 2005, 64(7):595-604
- Del Bigio MR. *Ependymal cells: biology and pathology*. Acta Neuropathol 2010, 119: 55-73
- Rodriguez et al. *A cell junction pathology of neural stem cells leads to abnormal neurogenesis and hydrocephalus*. Biol Res 2012, 45:231-41
- McAllister. *Pathophysiology of congenital and neonatal hydrocephalus*. Semin Fet Neonat Med 2012, 17:285-94

Rhombencephalosynapsis



- Rhombencephalosynapsis (associated with aqueductal stenosis)
  - fused cerebellar hemispheres & dentates, no vermis
  - fused colliculi, posterior thalami
- Present in 11/44 early fetal hydrocephalus (25%)
  - otherwise very rare: 100 cases published (Passi 2015)



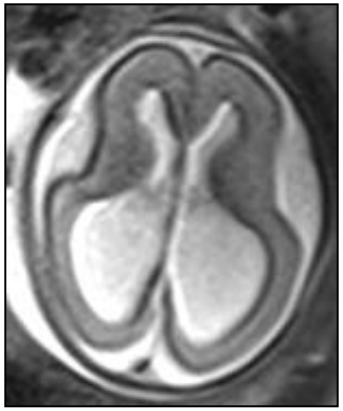
Rhombencephalosynapsis

- Pasquier et al. *Rhombencephalosynapsis and related anomalies: a neuropathological study of 40 fetal cases*. Acta Neuropatol 2009, 117:185-200
  - mesencephalo- / diencephalosynapsis, aqueductal abnormalities

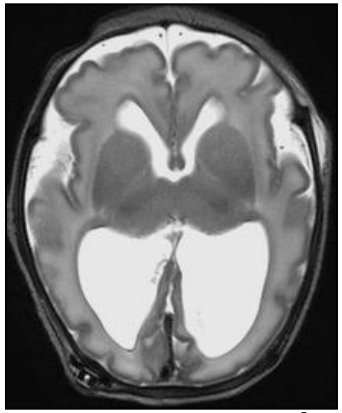
- Ishak et al. *Rhombencephalosynapsis: a hindbrain malformation associated with incomplete separation of midbrain and forebrain, hydrocephalus and a broad spectrum of severity*. Brain 2012, 135:1370-86
  - 42 postnatal cases
- Whitehead et al, *Rhombencephalosynapsis as a cause of aqueductal stenosis,* Pediatr Radiol 2014, 44;849-56
  - 20 postnatal cases

Early fetal hydrocephalus: evolution

- Ventriculomegaly increases (in weeks-above-average)
- Morphotype – mild or severe – does not change with advancing gestation
- Fetal hydrocephalus does not prevent gyration to develop
  - except for the dehiscent mantle segment
- When treated early, fetal hydrocephalus seems to recover a reasonable mantle thickness
  - except for the dehiscent mantle segment
  - cellular lineages?



25.4w

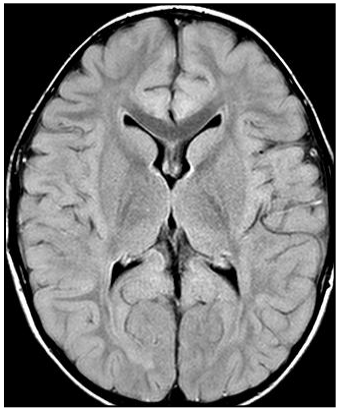


3d

8m/o

Early fetal aqueductal stenosis

38w



5y

Late fetal aqueductal stenosis
Hypomyelination

Plasticity: mantle restoration in early hydrocephalus

12d

4y

Neonatal (early fetal) aqueductal stenosis
Poor myelination

Early hydrocephalus and brain plasticity

- Persistent expression of signaling pathways for axonal growth andbranching
- Axonal progression and branching mostly subcortical
- Lack of myelination
  - myelin: most potent inhibitor of axonal development
  - myelin-associated inhibitors limit axon development

Bonfanti Prog Neurobiol 2006; Fancy et al Ann Rev Neurosc 2011; Akbik et al Exp Neurol 2012

Fetal hydrocephalus: summary

- Fetal hydrocephalus triad
  - ventriculomegaly, increased BPD, obstruction
    - ? communicating hydrocephalus
- Aqueductal stenosis, rhombencephalosynapsis & ependymal nodules surprisingly common
- Pathology: ependymal denudation common
  - cause vs effect of hydrocephalus
  - ependymal nodules & ruptured septum pellucidum
- Good morphologic recovery possible (role of lack of myelination?)