Midline Abnormalities of the Fetal Brain

David M. Mirsky, MD
Assistant Professor of Radiology
University of Colorado School of Medicine
Director, Pediatric Neuroradiology Fellowship
Children's Hospital Colorado
Disclosures

• None
Outline

• Anomalies of **Dorsal Prosencephalon** Development
  – Corpus Callosum Anomalies
  – Absent Septum Pellucidum

• Anomalies of **Ventral Prosencephalon** Development
  – Holoprosencephalies
  – Septooptic Dysplasia

• Anomalies of **Midbrain-Hindbrain** Development
  – Dandy-Walker Continuum
Corpus Callosum

- “Front to Back”
- Complex set of events
- Formation begins as early as 8 wks
- Axons begin crossing midline at 13-14 wks
- Bidirectional growth → complete CC by 20 wks
Agenesis of the Corpus Callosum

• **Etiology**
  – Genetic: Multiple genes at play
  – Toxic: Alcohol, Valproate, Cocaine
  – Infection: Cytomegalovirus
  – Inborn errors of metabolism: NKH, PDD

• **Isolated callosal dysgenesis is not common**

• **Fetal MRI useful for associated CNS anomalies (50%)**
  – Heterotopia
  – Cortical dysplasia
  – Other midline anomalies
  – Abnormal hindbrain

• **Associated with >200 syndromes**: Aicardi, Dandy-Walker
Agenesis of the Corpus Callosum

Sagittal:
- Best delineates abnormality
- Absent cingulate sulcus
- Sulci radiate to 3rd ventricle

Coronal:
- Upturned anterior horns
  - Texas Longhorn, Trident
- Hippocampal malrotation

Axial:
- Parallel lateral ventricles
- Colpocephaly
- Probst bundles
Anomalies of the Corpus Callosum

• Confusing terminology: Hypogenesis vs Dysgenesis

• Associated meningeal dysplasia:
  – Interhemispheric Cyst: Types I or II
  – Lipoma: Derived from the meninx primitiva

28wks with heterotaxy, CHD, suspected holoprosencephaly

Courtesy D. Zarnow, CHOP
Septum Pellucidum

• Thin, vertically oriented, midline leaves
  – Undersurface of CC → Upper surface of fornices

• *Cavum septi pellucidi*: CSF cavity of the SP
  – Width increases 19-27wks, gradually closes 28wks-term
  – Present in 100% of premature infants; up to 15-20% adults
    • Increased incidence: intellectual disability, schizophrenia, trauma

• *Cavum Vergae*: Posterior extension between fornices
Septum Pellucidum

- Marker of **normal** fetal CNS development
- Isolated absence is **rare**
- Neurologic deficits present in the majority of cases
  - Brain should be **carefully scrutinized**
DDx Absent Septum Pellucidum

- Agenesis of the Corpus Callosum
- Holoprosencephaly
- Septo-optic Dysplasia
- Schizencephaly
- Chronic Severe Hydrocephalus
Holoprosencephaly (HPE)

- Failure of differentiation & midline cleavage of **prosencephalon**
  - Anterior frontal lobes, deep gray nuclei, olfactory regions

- Continuum **without clear distinction** between subtypes
  - Alobar $\rightarrow$ Semilobar $\rightarrow$ Lobar

- Clinical presentation depends upon the severity of malformation

- Etiology
  - Teratogens: EtOH, diabetes, retinoic acid
  - Genetic ($\leq$45%): Trisomy 13 (Patau), 18 (Edwards)
    Sonic hedgehog (SHH)

Alobar Holoprosencephaly

- Single "pancake" brain anteriorly
  - Fused thalami, hypothalami, basal ganglia
- Monoventricle \pm \text{communication with dorsal cyst}
- Absent callosum, falx, interhemispheric (IH) fissure
Semilobar Holoprosencephaly

- Partial cleavage of prosencephalon
  - Varying degrees of diencephalon separation
- IH fissure and falx are partially formed posteriorly
- Corpus callosum fails to develop anteriorly
Lobar Holoprosencephaly

- Frontal lobes are more fully developed
  - Rudimentary frontal horns present
- Thalami mostly cleaved
- IH fissure present; Falx hypoplastic anterior

![Image of brain scan](image.png)
Syntelencephaly (Middle Interhemispheric Variant)

- Variant of HPE
- Reduced induction of the **dorsal midline structures**
  - midline continuity post frontoparietal cortices & nl frontal pole
- Dysgenetic corpus callosum
HPE: *Face Predicts the Brain*

Facial malformation correlates with **severity** of HPE

- Hypotelorism / Cyclopia
- Proboscis (ethmocephaly)
- Midline or bilat cleft lip/palate
- Single maxillary central incisor

Septooptic Dysplasia

- Described by de Morsier in 1956
  - Hypoplasia of the optic nerves
  - Hypoplasia or absence of the septum pellucidum

- Some consider SOD and lobar HPE to overlap

- Abnormal endocrine function (60%)

Septooptic Dysplasia

- Heterogeneous disorder:
  - Abnormal optic nerves/chiasm
  - Absent CSP
  - Pituitary hypoplasia
  - Schizencephaly
  - Perisylvian polymicrogyria
Septooptic Dysplasia
Vermian Development

- Vermis begins forming at 5 wks gestation
- 8-10wks: focal dilatation of neural tube in the dorsal aspect of the developing hindbrain
  - Rhombencephalic vesicle: predecessor to 4th ventricle
  - Roof of the RV is known as the membranous area

Vermian Development

• Roof $\rightarrow$ rostral anterior and caudal posterior MA
• Vermis: Rhombic lip at the superior margin of AMA
• Choroid Plexus develops in the crease
• Cavitation of the overlying meninx primitiva
  – Future subarachnoid space

Vermian Development

- As cerebellum grows inferiorly, PMA bulges
- Blake’s pouch fenestrates
  - Neck of pouch becomes the foramen of Magendie

Vermian Landmarks

17.5 weeks
- Fastigial point
- Primary fissure

21-27 weeks
- Post-pyramidal fissure
- Prepyramidal fissure
- Preculminate fissure
- 9 Lobules (27wk)
- Linear and symmetrical growth throughout gestation
- Cranio-caudal diameter
- Fastigium-decline line

Biometry

Tegmento-Vermian Angle

Method of measuring “closure” of the 4th ventricle

0 degrees = Normal

0-40 degrees = Unclear

>40 degrees = Pathologic
Tegmento-Vermian Angle

18-19wks: 4th ventricle “closed” (absolute 22-24wks)

False positives < 18 wks

- Morphology!
- Biometry!
  - Fundamental and Advanced Fetal Imaging

If vermian anatomy normal,
- Isolated Rotation
- Persistent Blake Pouch
True failure of “closure”

- Arrested development
- Inadequate fenestration of the 4th ventricular outflow foramina

Both likely contribute to Dandy Walker Continuum
Dandy Walker Continuum

• Heterogeneous group of PF malformations
  – Classic Dandy-Walker malformation
  – Vermian hypoplasia
  – Blake pouch cyst
  – Mega cisterna magna

• Terminology controversial

• Clinical severity ranges widely

Best to describe than provide titles!
Classic DW Malformation

- Vermian agenesis/hypogenesis
- Cystic dilatation of 4th ventricle with enlarged post fossa
- Elevation of torcular Herophili (torcular-lambdoid inversion)
- (Hydrocephalus)
Classic DW Malformation

- 2/3 associated CNS ± extracranial anomalies
  - Midline, craniofacial, cardiac
  - Trisomy 9, 13, 18
  - Meckel-Gruber, Walker-Warburg, PHACES

- Classic DWM: Poor prognosis
  - Developmental delay
  - Spastic paraplegia
  - Seizures
  - Variable intellectual disability
Vermian Hypoplasia

- Formerly Dandy Walker variant
- Defective ant/posterior membranous development
- Variable hypoplasia
- ± rotation/elevation of vermian tissue
- No PF enlargement or torcular-lambdoid inversion
Vermian Hypoplasia

Prognosis: Highly variable

- Cognitive abnormalities in 40%-50%
  - Normal neurodevelopment reported in isolated VH
Blake Pouch Cyst

- **Inadequate fenestration**: Blake’s pouch & Luschka
- Rotated but normal-appearing vermis
- Cyst wall often not seen

18 weeks
**Blake Pouch Cyst**

- Favorable outcome in *isolation*
  - Significant proportion associated with other anomalies
Cisterna Magna

- **Delayed** fenestration of the PMA
- Enlarged retrocerebellar CSF cistern (> 10 mm)
  - “Mega Blake’s pouch”
- Normal vermis and tegmento-vermian angle
- Incidental finding in isolation → normal outcomes
Summary

- Know your **midline profile**!

- **Embryology** is key

- **Biometric tables** are your friends

- Best to **describe** than provide titles
Gratitude

Ashley Robinson, MB, ChB, FRCR, FRCPC
Department of Radiology
Sidra Medical and Research Center
Thanks!