FETAL CENTRAL NERVOUS SYSTEM

Contents:
- Normal neural development and anatomy
  - Disease: hydrocephalus, neural tube defect, holoprosencephaly, agenesis of corpus callosum, destructive cerebral lesions, microcephaly, macrocephaly, choroid plexus cyst, vein of Galen aneurysm, arachnoid cyst, intracranial hemorrhage, periventricular leukomalacia
- Differential diagnosis
- Focus
- Pitfall

Study target:
- to understand normal neural development and anatomy
- to memorize basic sonographic features of CNS anomaly
- to know pseudo- abnormalities

I. NORMAL NEURAL ANATOMY

A. Development:
1. Neuralation (-3 weeks)
2. Diverticulation (4-8 weeks)
3. Mantle formation (9-term)

① Neuralation:
- neural plate - neural groove - neural tube (23 d- anterior neuropore, 25 d- posterior neuropore)
2 Diverticulation:
2 annular constriction (cephalic flexure, pontine flexure)
3 segmental dilatation
- forebrain (proencephalon); at 7th weeks/ telencephalon, diencephalon
- midbrain (mesencephalon)
- hindbrain (rhombencephalon); metencephalon/pons, cerebellum myelencephalon/medulla oblongata

4 Mantle formation:
Near internal limiting membrane-germinal cell-ependymal layer
Near outer limiting membrane-mantle layer (gray matter)

B. As gestational weeks

6th week:
- neural tube

7th Week:
- cephalic pole: sonolucent area (head discernible)
- fluid-filled rhombencephalic vesicle
- Rhombencephalon: 8 to 10 weeks
  cystic structure (posterior fossa, 4th ventricle)
  3-4 mm <CYR DR et al.>

8th Week:
- tortuous neural tube
- 4 sonolucencies
telencephalon----lateral V----cerebral hemisphere
diencephalon----3rd. V----thalami
mesencephalon----aqueduct----midbrain
metencephalon----4th. V----pons, cerebellum

9wks gestation
- two cerebral hemispheres
- falx
- choroid plexus

11wks gestation
- the brightly echogenic choroid plexuses filling the large lateral ventricles
- cerebellum, foramen magnum

C. Three screening planes

- transventricular plane: midline falx cerebri
  body of lateral ventricle with choroid plexus
- transthalamic plane: frontal horns of the lateral ventricle
  cavum septum pellucidum
  Sylvian cisterns
- transcerebellar plane: cerebellar hemisphere and vermis
  cisterna magna (2-10 mm)

D. Anatomy

1. Ventricle
   - Measurement: the width of atrium (inner to inner, perpendicular to the wall)
   - normal range: less than 10 mm (4 SD)
   - ratio not used anymore
   - choroid separation > 3 mm, ventricle < 10 mm: 80% normal, 20% abnormal
     <Hertzberg B.S et al>
   - pitfall: upside ventricle
     - change with time
     - pseudohydrocephalus
     - choroid plexus separation > 3 mm
     - left lateral V. slightly larger than right <Reliwen, 1997>

Ventriculomegally:
- hydrocephalus: obstructive
- maldevelopment: surrounding brain
- destruction brain: infection, infarction

2. Cerebellum
- join 14 weeks, fissure-18 weeks
- planes includes: cavum peduncles, cerebellar hemispheres
- cerebellar diameter: increases with gestational age
  1 mm/week (15-21 weeks)
  accurate than HC, FL, AC in asymmetric IUGR; <Lee, 1991>
- Hypoplasia in trisomy 18
- cerebellar vermis: closure by 17.5 weeks
- 4th ventricle and CM communicate at 14 weeks
- bright echo (numerous and deep gyri, sulci)

3. Cistern
- dilatation of subarachnoid space (space between the cortex and the bony skull)
- 4 cisterns of mid brain: dorsal - quadrigeminal C
  lateral - ambient C
  ventral - interpeduncular C
- Cisterna Magna: 5+3mm

4. Choroid plexus:
- from ependymal cells
- first evidenced at 9 weeks

5. Corpus Callosum
- connect the two cerebral hemispheres
- forming the floor of the interhemispheric fissure, the roof of the 3rd V
- relatively late developing structure
  begins developing 13 weeks
  not evident until 18-20 weeks
  full development 28 weeks

6. Sulci, Fissures and Gyri
- after 26-28 weeks primary sulcus
- Lateral sulcus (insula)
- Calosal sulcus, cingulate sulcus (cingulate gyrus)
- not perfectly symmetric

7 Tentorium
-an infolding of the dura that separates the contents of the post fossa from the rest of the cranial vault

8 Germinal matrix.
active mitotic activity (zone of neuronal, glial proliferation)
.near ventricle (ependyma)
.highly cellular, rich blood supply
.involutes by 34 weeks

II. CNS ABNORMALITY

* overall incidence of CNS abnormalities : > about 1 in 100

A Hydrocephalus

: Dilatation of the fetal lateral ventricles resulting from an increased quantity of cerebrospinal fluid and a subsequent increase in intraventricular pressure

Type; Non communicating; intraventricular obstruction of the normal CSF flow
Communicating; extraventricular cause

-Incidence; 0.3–0.5 per 1,000
33-43% aqueductal stenosis
13% : Dandy Walker malformation
38% : communicating H (Arnold-Chiari 2, absence of the arachnoid granulation)

-Progress: Occipital-temporal-frontal
-Ventriculonegally: hydrocephalus obstructive
.development surrounding brain
.destruction brain infection, infarction

-Associated anomalies (70 to 85%)
.tip of iceberg; extracranial abnormality, face, heart, kidney, abdominal
wall, thorax, limbs)
. chromosomal anomaly: trisomy 21

1. Communicating Hydrocephalus
   - form of enlargement of the ventricles and subarachnoid system caused by an obstruction to CSF flow outside the ventricular system

2. Non-communicating Hydrocephalus
   - Aqueductal Stenosis
     - NYC form of non-communicating H
     - caused by narrowing of the aqueduct of sylvius
     - Primary (X-linked) - 1.2% ventriculomegaly in male fetus
       - adducted thumb in mother
     - secondary to intrauterine infection, hemorrhage within the ventricle, pressure by cranial mass
     - Sonofindings: 1. bilateral ventriculomegaly
     - 2. 3rd ventricle dilatation
     - 3. normal 4th ventricle

3. Dandy - Walker Malformation
   - Common cause of non-communicating H
   - communicating with the 4th ventricle through a defect of the cerebellar vermis
   - Diagnosis
     * enlarged cisterna magna
     * 10 mm ventricle
     * 4th ventricle
     * agenesis or hypoplasia of the cerebellar vermis
   - Associated anomaly: encephalocele
     - ACC
     - aqueductal stenosis
     - VSD
     - infantile polycystic kidney
Surgical Treatment of hydrocephalus
- ventriculostomy with endoscopy (3rd V.)
  success rate 75%

B. Neural Tube Defect
Classification:
- Acrania (Exencephaly)
- Anencephaly
- Cephalocele
- Iniencephaly
- Spina bifida

Anencephaly
Incidence: 1 – 2 per 1000
- characterized by the absence of the cranial vault and telencephalon
- result from multifactorial influences (chromosomal, hyperthermia, folate deficiency)
- Diagnosis: midtrimester (not possible until 11 or 12wks)
  - acrani a (exencephaly): embryonic precursor of anencephaly

Cephalocele

* 1 per 5000 to 10,000
* protrusion of the intracranial contents through a bony defect of the skull
* arises from the midline in the occipital area
* brain tissue inside the lesion
* Cranial meningocele: only the meninges protrude
  associated with microcephaly
* Massive encephalocele: associated with microcephaly
* Neonatal mortality rate: about 40%
* sonofindings: 1. extracranial mass
  2. ventriculomegaly
  3. bony defect in the skull (occipital, parietal, frontal)
* prognosis: 1. meningocoele mortality 11% after surgical repair
2. Brain tissue herniated - mortality 71%

Associated with Meckel-Gruber syndrome (occipital cephalocele, bilateral polycystic kidneys, polydactyly)
Warburg syndrome (cerebellar hypoplasia, Dandy-Walker cyst, ocular abnormality)

3. Holoprosencephaly
- defect in the occiput involving the foramen magnum
- retroflexion of the entire spine (occiput directed towards the lumbar region)
- open spinal defects

4. Spina Bifida
* Lumbar, thoracolumbar or sacro-lumbar area: most affected (80%)  
* Diagnosis: from the midtrimester (12 weeks after)
* Transverse view: vertebral arch defect
* Sagittal view: assessing the severity and location of the lesion
* Two typical abnormal signs (95-100%)
  - banana sign (after 24 weeks - cerebellar absence)
  - lemon sign (90% more, 16-24 weeks)
* Hydrocephalus: all cases
Prognosis: associated with Anord-Chiari malformation
Delivery: Never vaginal delivery
Intra-uterine surgery
- 22 to 24 weeks gestation
- with omentum

C. Holoprosencephaly
; Failure of the prosencephal on of differentiate into the cerebral hemisphere and lateral ventricles (4-8 weeks)
* the abnormal midline separation of the cerebral hemispheres and the diencephalic structures
* May affect orbital and facial malformations (17%)
* Microcephaly in all three type
Alobar type: 1. Single common ventricle
   2. Fusion of thalamus. Absent third ventricle
   3. Absent interhemispheric fissure
   4. Orbital anomaly (cyclopia to hypotelorism)
   5. Nasal anomaly (absent nose to a single nostril)
   6. Median facial clefts
   7. Chromosomal abnormality (50% - trisomy 13, del 11q, del 13q, del 18p)

Semilobar type: 1. Partial separation of the ventricles
   2. Partial fusion of the thalamus

Lobar type: 1. Division of the ventricles and thalamus
   2. Septum pellucidum are missing
   3. Fused frontal horns

Facial anomalies - cyclopia to severe hypertelorism
   Median cleft lip and palate
   Absence or extremely flattened of nose

Incidence: - 1/250 voluntary terminations of pregnancy
   Unknown / birth

D. Agenesis of the Corpus Callosum
   An anomaly of uncertain prevalence and clinical significance
   - Genetic factors are probably predominant
   - Abnormal karyotype; trisomy 18, 8; 20%
   - Associated anomaly: 80%
   - Sonographic findings;
   - Increased atrial width
   - Failure to visualize the Cavum septum pellucidum
   - Lateral and superior displacement of the lateral ventricle
   Occipital horn dilation (tear drop sign)
- Distension of the inter-hemispheric fissure
- Dilatation and upward displacement of the 3rd ventricle
- Steer sign: angulated frontal and lateral ventricular horn
- Gyral pattern disarrayed (sunburst appearance)

E. Destructive Lesions

1. Congenital porencephaly
   - Presence of cystic cavities within the brain matter
   - Usually communicate with either the ventricular system, the subarachnoid space, or both.
   - Typically bilateral and symmetrical and is frequently associated with microcephaly
   - Pseudoporencephaly; unilateral lesion is usually found

2. Hydranencephaly
   - Caused by internal carotid artery occlusion
     - Extreme form of pseudoporencephaly
     - Most of the cerebral hemispheres are replaced by fluid brain stem and rhombencephalic structures; usually spared
   - Differential Diagnosis:
     - Severe HYDROCEPHALUS
     - HOLOPROSENCEPHALY
   - Sonographic findings:
     1. Brain tissue is replaced by fluid.
     2. Falx is usually present, but may be absent
     3. Choroid plexus may be observed
     4. Macrocephaly
     5. Hydroamnios

F. Microcephaly
   - 1 per 6,200 to 8,500
   - Clinical concern, mental retardation 85%
   - BPD, HC; Below -3SD
- HC/AC ratio (Campbell)

- Causes: A. Inheritance
  - Chromosomal aberrations
  - Prenatal radiation
  - Maternal viral infection (CMV, rubella, toxoplasmosis)
  - Alcohol, heroin, mercury
  - Maternal PKU
  - Angelman syndrome, Brome syndrome
  - Chromosomal deletion (3p, 4p, 5p, 11q, 13q, 18p, 18q)

- Sonofindings:
  1. Small BPD, HC
  2. Head to abdomen disproportion
  3. disorganized brain tissue
  4. Intracerebral califications (parovirus, CMV)
  5. Ventriculomegaly
  6. VSD
  7. Polycystic kidney in Meckel-Gruber syndrome
  8. Limb disorder
  9. not diagnosed before 24 weeks.

* abnormal convolutional patterns (macro / micro / a-gyria)
* pathologic microcephaly-small frontal lobe
  (from the back of cavum to the inner calvarium)

<Goldstein, 1988>

- Prognosis: -3 to -2SD (MR--18%)
  - 3SD over (MR--72%)

G. Microcephaly
- An abnormally large brain
- Nonspecific familial (AD)
- A part of congenital abnormalities / syndrome
  - Beckwith-Wieden selection
  - achondroplasia
  - Osteopetrosis
  - Hunter syndrome
H. Choroid plexus cysts
- Mid trimester; 1-3%
- Composed of cerebrospinal fluid and cellular debris, which trapped within the Neuroepithelial folds
- Resolve by 24 weeks.
- Increased risk of chromosomal aberrations (4% Kupferminc, 2.5% Shield) of 7 aneuploidy: 5(18+), 21+, 47XXY
- No correlations between size, bilaterality
- Normal Triple test with isolated CPC risk of trisomy 18 (0.2%)
  in the absence of associated anomalies
  --> considered as normal anatomic variants
- DDx: subarachnoid cyst
corpus striatum (caudate N, internal capsule, lentiform N)
pseudocyst

I. Vein of Galen aneurysm
: midline vein located behind the third ventricle
  round, cigar shaped cyst behind the third ventricle
  color Doppler
  causes high output heart failure-hydrops fetalis, enlarged heart (95%)
  never diagnosed before 30 weeks

J. Arachnoid cyst
: round, fluid filled and surrounded by a thin wall
  do not connect with the Ventricle
e external to the brain matter
  unilocular
  Primary treatment-endoscopy
  favorable outcome

K. Porencephaly
: fluid filled area within the brain substance that communicates
with the Ventricles
result of destruction of the brain(infection, ischemia, hemorrhage)
internal to the brain matter
No mass effect
Frequent in monochorionic twin

**L. Lissencephaly**
: absence of cerebral gyri
Type 1-4 layer of cortex, ventriculomegaly
- ACC
- slight microcephaly
  - Miller-Diecker syndrome
Type 2-always Dandy-Walker malformation
- ocular anormaly, muscular dystrophy
  - Obstructive hydrocephalus

**M. Intracranial hemorrhage**
1. **Fetal ICH**
   1. germinal matrix of caudate N of frontal horn
   2. subdural
   Sonographic findings:
   hyperechogenicity
   focal echodense patch
   diffuse cerebral edema
   Secondary to maternal hemorrhage with hypertension
   Pancreatitis
   Seizure
   Isoimmune thrombocytopenia

2. **Neonatal ICH**
; results from sudden change in cerebral blood pressure
   perinatal asphyxia
   - most often in immature ( <1.5Kg, < 32 weeks)
   - 70% if assisted ventilation
   - first 3 days of life
N Periventricular Leukomalacia (PVL)

: Coagulation necrosis of white matter dorsal and lateral to the external angle to the lateral ventricles <Volpe, 1989>

Location: external area of frontal horn optic radiations at trigone results from rubella, CMV <Shackelford, 1983>

venous infarction <Volpe, 1989>

risky in IUGR, Pre-eclampsia, PROM

- Evolution

1. Initially-normal or increased periventricular echogenicity
2. Second, third weeks-multiple small cysts (necrosis, cavitation)

III. Differential Diagnosis

<table>
<thead>
<tr>
<th>Where</th>
<th>How</th>
<th>If</th>
<th>Then</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calvarium</td>
<td>Shape</td>
<td>bizzar</td>
<td>Anencephaly, Exencephaly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Amniotic band syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Craniosynostosis</td>
</tr>
<tr>
<td>Lemon</td>
<td>Density</td>
<td>decreased</td>
<td>OI, hypophosphatasa</td>
</tr>
<tr>
<td>Cloverleaf</td>
<td></td>
<td></td>
<td>Thanatophoric dysplasia</td>
</tr>
<tr>
<td>Sylvian fissure</td>
<td></td>
<td>delayed</td>
<td>Immature brain</td>
</tr>
<tr>
<td>Ventricle</td>
<td>Size</td>
<td>increased</td>
<td>Microcephaly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>decreased</td>
<td>Microcephaly</td>
</tr>
<tr>
<td></td>
<td>Gyrus</td>
<td>decreased</td>
<td>Lissencephaly</td>
</tr>
<tr>
<td></td>
<td>Sylvian fissure</td>
<td></td>
<td>Immature brain</td>
</tr>
<tr>
<td></td>
<td>Enlarged</td>
<td>Macrocephaly</td>
<td>Hydrocephalus</td>
</tr>
<tr>
<td></td>
<td>Ventricle</td>
<td>Microcephaly</td>
<td>Destructive</td>
</tr>
</tbody>
</table>
Anterior CSP (18-37 weeks) absent ACC, Holoprosencephaly

Posterior Cerebellum Banana shape Arnold-Chiari type 2 Dandy-Walker syndrome

No vermis Dandy-Walker syndrome

CM Communicated Dandy-Walker syndrome

Obstructed NTD

Cyst echogenic rim CPC

Between dura & pia Arachnoid cyst

Central color D Vein of Galen cyst

Communicating with V Porencephaly

Posterior, central Large CM

Midline, upward 3rd V in ACC

Bilateral cleft Schizencephaly

Center, Doppler Vein of Galen cyst

`C` : lateral hemisphere (lateral sulcus-insula)

ventricle
corpus callosum

IV. Focus

Mild ventriculomegaly (10-15 mm)

- Mahony (1988), 13 case, developmental delay 1/10 (10%)
- Drugan (1989), 5 0/5
- Bronhey (1991), 27 5/26 (19%)
- Patel (1994), 44 6/34 (18%)
- Alagappan (1994), 11 0/11
- Patriza (1998), 480000000 0/45

Total 148 12/131 (9.2%)

4 chromosomal anomalies (2.7%)

≥12mm : associated anomaly (56% vs 6%)
postnatal neurodevelopment (23% vs 3%) <Patrizia, 1998>

Next step: Targeted sono
  Visualization of Corpus Callosum
  Echocardiogram
  Serologic evaluation for congenital infection

V. Pitfalls in fetal CNS:

- early embryonic brain vesicle → brain anomaly
- white matter → hydrocephalus
- ventricle tilting → choroid plexus cyst
- posterior deep tilting → vermian agenesis
- fetal hair → posterior nuchal mass
- prominent CSP → third ventricle dilatation

References:

- Terry J. Dubose, RDMS, Fetal Sonography 1st Ed, Saunders company, 1996
- Reliwin Achiron, Cerebral lateral ventricular asymmetry:
  Is this a normal ultrasonographic finding in the fetal brain?
  Obstet and Gynecol 1997; 89: 233-7
- David C Merrill, The optimal route of delivery for fetal meningomyelocele
- R Achiron et al, Fetal intracranial haemorrhage: clinical significance of
  In utero ultrasonographic diagnosis: Obstet and Gynecol 1993; 995-999
- Volpe J.J current concepts of brain injury in the premature infant. AJR 1989
  153, 243-252
- WHpersutte et al, Correlation of fetal frontal lobe and cerebellar
  Diameter measurements: the utility of a new prenatal sonographic technique
  Ultrasound Obstet. Gynecol. 10(1997), 94-97