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APPROACH TO PRENATALLY DIAGNOSED MALFORMATIONS OF CORTICAL DEVELOPMENT

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NORMAL DEVELOPMENT OF THE FETAL CORTEX

Maturation of the normal fetal cortex MRI T2-weighted slices













Maturation of the normal fetal cortex-Coronal MRI T2-weighted slices



23W





27W



Maturation of the normal fetal cortex Coronal Ultrasound **33wk**

Can we diagnose MCD in utero?

Imaging Signs of Abnormal Sulcation MRI and Neurosonography

- Delayed cortical development
- Thick/thin cortex
- Abnormal appearance of sulci and gyri
- Irregular ventricular borders
- Irregular, abnormal, asymmetric hemisphere
- Simplified cortex
- Abnormal development of the operculum
- Non continuous cortex

DELAYED CORTICAL DEVELOPMENT

Delayed Cortical Development





23W



Delayed Cortical Development

- Lissencephaly
 - LIS1
 - DCX
 - Tubulinopathy
- Cobblestone Cortex
 - DAG1
 - POMT1

Lissencephaly signs

- Smooth cortex
- Abnormal lamination
- Delayed sulcation
- Abnormal operculization
- Ventriculomegaly
- Thick cortex
- Gradient in sulcation
- Associated cerebellar and\or corpus callosum anomalies

Lissencephaly



Smooth cortex

Normal cortex

Lissencephaly-abnormal operculization



Normal sulcation

Lissencephaly

Lissencephaly: Miller Dieker Syndrome Ch 17p13.3 deletion

24W



Abnormal Lamination

Top Magn Reson Imaging 2010;21; 387-394.

Lissencephaly



31W

Chen CP, Chang TY, Guo WY, Wu PC, Wang LK, Chern SR, Wu PS, Su JW, Chen YT, Chen LF, Wang W. Chromosome 17p13.3 deletion syndrome: aCGH characterization, prenatal findings and diagnosis, and literature review. Gene. 2013 Dec 10;532(1):152-9.

Anterior to Posterior Gradient







DCX mutation

Lissencephaly with cerebellar hypoplasia

Cerebellar hypoplasia

Tubulinopathy, reelin mutation?

Cobblestone malformation Signs

- Ventriculomegaly
- Thick —> thin cortex
- Irregular cortical surface
- Abnormal lamination
- Delayed sulcation
- Abnormal operculization
- Z shaped brainstem
- Cerebellar hypoplasia
- Cerebellar cysts

Cobblestone Malformation





29 GW

29 GW

Cobblestone Malformation



Cobblestone Malformation POMT1 mutation



34 weeks

Cobblestone Malformation



24 weeks

Small CC

Cobblestone Malformation



Cobblestone malformation



Neuroblasts in leptomeninges



24 weeks



Muscular dystrophy



Retinal dysplasia

Cobblestone Malformation DAG1 mutation



Retinal Detachment Microphthalmia







Ventriculomegaly



Irregular Ventricular Wall



Delaved Sulcation

Ultrasound

car

week

Neonatal MRI (age 2 days)



IRREGULAR, ABNORMAL, ASYMMETRIC HEMISPHERE

Hemimegalencephaly

- Asymmetric ventriculomegaly
- Abnormal ventricular shape
- Enlargement of one hemisphere
- Abnormal sulcation of the enlarged hemisphere

Hemimegalencephaly - MRI



Courtesy Daniela Prayer

GW 21+3 Asymmetry

Hemimegalencephalv



24 weeks



Irregular LV wall



Echodense white matter

25 weeks





29 weeks

Hemimegalencephaly



MRI at 29 weeks

Courtesy Mauricio Herrera

IRREGULAR VENTRICULAR BORDERS

Irregular Ventricular Borders

- Periventricular heterotopia
- Clastic lesions
 - CMV
 - Ischemia
 - Hemorrhage
- Underlying polymicrogyric cortex

Signs of Periventricular Heterotopia

- Irregular ventricular wall
- Nodular bulging into ventricle
- Ventriculomegaly
- **FLMNA** mutations
- "String of beads"
- Enlarged posterior fossa

Periventricular Heterotopia



31w5d

Filamin A mutation

Periventricular Heterotopia

11101 23.03.13/3





KIL3-9-0/UD

MI 1.2



16w5d

Periventricular Heterotopia



29GW

34GW

Courtesy Daniela Prayer

ABNORMAL APPEARANCE OF SULCI AND GYRI

Abnormal Appearance of Sulci and Gyri

- Polymicrogyria
- Dysgyria
- Pachygyria

Polymicrogyria

- Early sulcation
- Aberrant sulcation
- Abnormal sylvian fissure
- Irregular cortical surface
- Irregular ventricular wall
- Abnormal cortical thickness
- Cleft connecting ventricle and subarachnoid space

Polymicrogyria



Abnormal early gyri/sulci

Bilateral Frontal Polymicrogyria



Fetal MRI 28 weeks

Postnatal MRI

Bilateral Frontal Polymicrogyria













Postnatal

Tubulinopathy Associated Dysgyria

- Patchy and asymmetric abnormalities in gyral size and orientation
- Normal thickness
- Varying sulcal depths-the majority being shallow, with less frequent areas of sulci extending too deeply into the white matter
- Obliquely oriented sulci directed radially towards the center of the cerebrum
- Narrow gyri separated by abnormally deep or shallow sulci

Dysgyria

- Without imaging evidence of lissencephaly, pachygyria, cobblestone cortex, polymicrogyria or other cortical abnormalities
- Frequently associated with multiple cortical and subcortical abnormalities:
 - Microcephaly
 - Ventriculomegaly
 - Dysgenetic corpus callosum
 - Small pons
 - Pachygyria
 - Polymicrogyria
 - Abnormal basal ganglia

33 W





Autopsy 36 weeks



Areas with unusual sulci and gyri Areas of slightly thickened cortex





The Fetal Neurology Clinic

- US-Prenatal Diagnosis (Gustavo Malinger),
 Zvi Leibovitz, (Nina Haratz), Liat Gindes
 Modi Tamarkin
- MRI Liat Ben-Sira
- Pediatric Neurology Tally Lerman-Sagie
- Genetics Dorit Lev
- Social Worker
- Fetal Pathology Deborah Kidron



Thank you for your attention



