VOLUMETRIC MRI BRAIN ASSESSMENT OF MACROCEPHALIC FETUSES

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The measurement of head circumference (HC) is an important factor in the evaluation of prenatal and postnatal development.

Deviations from normal head growth may be the first indication of an underlying congenital, genetic, or acquired problem.

The earlier the conditions associated with increased HC are detected, the earlier appropriate treatment, services, and genetic counseling can be provided.
DEFINITIONS

- **Macrocephaly** is defined as an HC greater than two standard deviations above the mean for a given age or gestation.

- **Megalencephaly** is the enlargement of the brain parenchyma.

- **OMIM** search of macrocephaly returned **395** entries (Nov, 2018).
TABLE I. Classification of Macrocephaly Conditions

1. Genetic types
   - Familial macrocephaly
     - Benign; symptomatic
   - Autism disorder
     - Multifactorial, non-syndromic type
2. Syndrome associations (many types)
   - With cutaneous findings
     - PTEN hamartoma syndromes
     - Neurofibromatosis, type 1
     - Hemimegalencephaly
   - With overgrowth
     - Sotos, Weaver
     - Macrocephaly cutis marmorata telangiectatica congenita
     - Simpson–Golabi–Behmel, Beckwith–Wiedemann syndrome
   - Neuro-cardio-facial-cutaneous syndromes
     - Noonan, Costello
     - Cardiofaciocutaneous (CFC)
     - LEOPARD
   - With mental retardation
     - Fragile X
3. Metabolic types
   - With leukodystrophy
     - Alexander, Canavan
   - Megalencephalic leukodystrophy
4. With organic acidurias
   - Glutaric aciduria, type 1
   - d-2-Hydroxyglutaric aciduria
   - With storage
5. Bone dysplasia/hyperplasia
6. Hydrocephalus
   - Aqueductal stenosis types
   - Multifactorial, non-obstructive types
7. Non-genetic types
   - Hydrocephalus
   - Hemorrhage
   - Infections; other causes
   - Subdural effusions
   - Post-traumatic and infectious
   - Arachnoid cysts

- Anatomic megalencephaly
- Metabolic megalencephaly

Williams CA, 2008, AJMG
US. PRENATAL DIAGNOSIS

- HC >2 SD? 3SD?
- **limitations in accuracy** of US HC measurements and inconsistency between prenatal and postnatal growth curves.
- Associated US anomalies may indicate syndromic macrocephaly.
- Evidence in US usually only at 3rd trimester.
- Most patients are non syndromic and have normal development.
Head circumference > 2 SD

Known gestational age

- Callosal dysgenesis – thick CC
- Malformations of cortical development
- Hypertelorism
- Nephromegaly
- Polydactyly

Search for associated anomalies

Unknown gestational age

Repeat exam in 2–3 weeks

History: consanguinity, familial macrocephaly
HC measurement of both parents and siblings

- No history
  - Family with normal HC
    - LGA
      - Overgrowth syndrome
    - AGA

- Positive history
  - Familial large HC
    - Syndromic macrocephaly
      - Poor prognosis
        - Detailed physical examination
          for stigmata of AD conditions
          
- Positive examination

Karyotype, fetal neurosonography, fetal brain MRI

Counseling according to specific diagnosis

Negative examination
HC < 2.5 SD

Usually good prognosis but occasionally mental retardation
Follow-up every 3–4 weeks

Maligner, 2011
Discrepancy in fetal head biometry between ultrasound and MRI in suspected microcephalic fetuses

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“There was no correlation between US-measured skull biometry and MRI-measured brain biometry.”
Volume of Structures in the Fetal Brain Measured with a New Semiautomated Method.

Ber R\textsuperscript{1}, Hoffman D\textsuperscript{2}, Hoffman C\textsuperscript{3,4}, Polat A\textsuperscript{2}, Derazne E\textsuperscript{4}, Mayer A\textsuperscript{3}, Katorza E\textsuperscript{2}.

Supratentorial brain

Left and right Lateral ventricles

Left and right hemispheres

Left and right eyeball

Cerebellum
Can fetal macrocephaly be diagnosed more accurately using volumetric MRI measurement? Sensitivity, specificity, PPV, NPV.

Is there a difference in proportional brain structures' volume comparing to normal fetuses?

Will the volumetric method better differentiate between the different etiologies.

What maternal parameters attribute to fetal macrocephalia?

Is there a neurodevelopmental significance to these findings?
INCLUSION & EXCLUSION CRITERIA

**Inclusion** criteria:
- HC > 1 SD
- Neurosonogram in Sheba
- Good quality brain MRI
- Labor in Sheba
- Full history and labor data in Chameleon

**Exclusion** criteria:
- Multifetal pregnancy
- Not enough data
- Absence of full US examination.
MATERIALS AND METHODS

- Data collection of 38 US suspected Macrocephalic fetuses, and 50 controls:
  - Maternal characteristics: age, diseases, medications, previous pregnancies, IVF.
  - Mode of delivery and antenatal and postnatal complications
  - US biometrics of the fetus.
  - Fetal Echocardiogram, Nuchal translucency, Karyotype and CMA
  - Birth weight, length, and other biometrics.
  - Apgar score
  - Developmental disorders

- Assessment of brain volumes using a semiautomated software.

- Neurodevelopmental assessment: preforming Vineland questionnaires
NEURODEVELOPMENTAL ASSESSMENT

VINELAND questionnaires.
- standardized measure of **adaptive behavior** - function in everyday lives.
- Adaptive behavioral skills:
  - Communication
  - Daily Living Skills
  - Socialization
- based on parental report of behavior
- Validated and compared to patients’ age group.
THANK YOU!

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Michal Gurevitch

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Mrs. Yafit Rot
Tomer Ziv– Baran


