Ventriculomegaly: The Tip of the Iceberg

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Introduction

• Ventriculomegaly (VM) is the most common prenatal CNS finding
• Ventriculomegaly itself is not a disease, but rather a sign representing a common endpoint of various pathologic processes
• It has different outcomes and prognoses**

** D’Antonio T, Papageorghiou AT. Expert Consult Series Obstetric Imaging. Chapter 43 Ventriculomegaly

Definition

• VM is further classified as:
  – Mild: 10 and 15 mm
  – Severe: > 15 mm

Introduction

• The clinical significance of VM is that it alerts to the possibility of associated anomalies of the brain or other organs.
• The final prognosis depends more on such anomalies than on the degree of ventricular dilatation.

Definition

- Although, some further sub-classify it into:
  - Mild, moderate and severe:
    - 10 to 12 mm
    - 13 to 15 mm
    - > 15 mm

Introduction

- Incidence of mild VM is ~ 1%*.
  - Male predominance (~75% of the cases)**.
  - In most cases mild VM is a variant of normal.
- Severe VM is rare.
  - No exact figures available***
  - Some will develop hydrocephaly
    - Incidence of neonatal hydrocephaly is 0.3-1.5 in 1000 births

**Melchiorre K et al. Counseling in isolated mild fetal ventriculomegaly. UOG: 2009;34:212

Ultrasound: Making the Diagnosis

- In the past, only the distal ventricle was measured due to sound attenuation of the near hemisphere.
- However, newer US machines allows visualization of both.
- Recent, data shows that mild VM may be unilateral in as much as 60% of the cases and bilateral in 40%**

*Melchiorre K et al. Counseling in isolated mild fetal ventriculomegaly. UOG: 2009;34:212

Transventricular plane: Landmarks

Anterior:
  - Frontal horns (FH)
  - Cavum septi pellucidi (CSP)
Posterior:
  - Posterior horn (PH)
  - Atrium with glomus of the choroid plexus (CP)

Warning!!!!

Do not confuse the CSP with the fornices!!

The fornices are seen several mm below the plane of the CSP and unlike the CSP have a linear echo in the center.
The cavum septi pellucidi on the axial planes

- Anechoic, rectangular fluid filled space
- Consistently seen after 18-20th week
- Its boundaries are the lateral walls of the cavum

Measuring the lateral ventricles: Caliper placement

Fetal Cerebral Ventricular Measurement: Time for Procedure Standardization
Correct Plane and Placement of Calipers*

Primary criteria:
1. Strict axial plane: symmetric & midline perpendicular to US beam
2. Anatomic level:
   - Anterior: CSP or fornix
   - Posterior: triangular V-shaped of ambiens cistern
3. Measurement opposite parieto-occipital sulcus

Secondary criteria
4. Caliper placement:
   - opposite internal parieto-occipital sulcus
   - On-to-on
5. Image size: whole screen

Examples of LV Measurements

At 20 weeks

At 28 weeks

Table 1 Image-scoring method

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary criteria</td>
<td></td>
</tr>
<tr>
<td>1. Strict axial plane</td>
<td>0-2</td>
</tr>
<tr>
<td>2. Adequate anatomical level</td>
<td>0-1</td>
</tr>
<tr>
<td>3. Location of the atrium</td>
<td>0-1</td>
</tr>
<tr>
<td>Secondary criteria</td>
<td></td>
</tr>
<tr>
<td>4. Caliper placement</td>
<td>0-2</td>
</tr>
<tr>
<td>5. Adequate image size</td>
<td>0-1</td>
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</tbody>
</table>

Maximum total score is 7.
Initial Approach Ventriculomegaly

1) Anatomical survey
2) Neurosonography
3) Fetal echo
4) Genetic counseling
5) Offer genetic testing
6) Test for fetal infections
7) Counseling
8) Offer MRI

ULTRASOUND: Targeted examination

- A detailed evaluation of the *entire fetal anatomy*, including echocardiography should be performed.

ULTRASOUND: Targeted examination

- A multiplanar (3D!) fetal neurosonography and a detailed evaluation of the spine.
  - Neurosonography, if possible performed with a high resolution vaginal probe.
- These examinations may be incomplete or limited during the 3rd trimester.

Isolated Mild Ventriculomegaly

- VM is termed *isolated*, if there is no other evidence of associated anomalies or markers of aneuploidy. *However, this is a provisional diagnosis of exclusion* *
- The prevalence of isolated mild VM is very variable and it has been reported at 0.15% to 0.7%*.

Associated Anomalies

- The incidence of associated anomalies ranges from 10 to 76%*.
- Mild VM may be a sign of brain anomalies only diagnosed later in the pregnancy or post-natally.

*Melchiorre K et al. Counseling in isolated mild fetal ventriculomegaly. UOG. 2009;34:212


Associated Anomalies

- Approximately 12.8% of associated anomalies are not diagnosed at the time of the diagnosis of mild VM.

**D’Addario V. J. Perinat. Med. 2015; 43(1); 5-9
Associated Anomalies

- Open neural tube defects
  - Spina bifida
  - Encephalocele
- Posterior fossa & cerebral anomalies
- Prosencephalic anomalies
  - HPE, AGCC
- Cortical anomalies
  - Microcephaly
  - Megalencephaly
  - Lissencephaly
  - Schizencephaly
- Fetal infections
  - Toxoplasmosis, Cytomegalovirus, ZIKV
- Vascular insults
  - Porencephaly
  - Hydrancephaly
- Aneuploidies
  - Trisomy 21
- Choroid plexus anomalies
- Intracranial tumors, cysts & hemorrhage

Modified from Expert Consult Series Obstetric Imaging. Chapter 43 Ventriculomegaly.

First Exclude Prosencephalic Anomalies

- Holoprosencephaly (HPE)
- Agenesis of the corpus callosum (AGCC)

Second Exclude Open NTD

- Spina bifida
- Encephalocele

Third: look at the Spine

- Chiari 2 Malformation

Mild VM at 20 1/7 weeks

10.7 mm

Head shape - "Lemon" sign
Obliterated cisterna magna - no banana sign
Tectal beaking

Mild VM at 20 2/7 weeks

10.7 mm
First Exclude Prosencephalic Anomalies

• Holoprosencephaly (HPE)
• Agenesis of the corpus callosum (AGCC)

Agenesis of the corpus callosum

Widely separated left ventricles, interhemispheric fissure meets 3rd ventricle

Absent: CC, CSP

Colpocephaly

Absent: pericallosal artery

Posterior Fossa Abnormalities

• Rhombencephalosynapsis

Ventricles 18 & 19 mm

Small and abnormal appearing cerebellum

Intracranial Hemorrhage

LV: 1=16.6 and 2=14.2 mm

Cortical Abnormalities

• Gyration needs to be evaluated
• Main landmark is the Sylvian fissure operculization
• Abnormalities of operculization reflect underlying cortical dysplasia.

**Fetal Infections**

**Toxoplasmosis, Cytomegalovirus & ZIKV**

- All are associated with VM
- Toxoplasmosis & cytomegalovirus
  - Overall risk of infection
    - In VM (10-15mm) is ~1.5%*,
    - Mild VM (10.1 to 12 mm): 0.4%
- ZIKV
  - Overall risk of infection in VM is ??


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**Fetal Infection**

**Cytomegalovirus**
- Microcephaly
- Ventriculomegaly
- Calcifications
- Periventricular echogenicity & cysts
- Intraventricular synechia
- Striatal vasculopathy
- Cerebellar hypoplasia
- Malformations of cortical development

**Toxoplasmosis**
- Ventriculomegaly
- Calcifications
- Microcephaly
- Brain destruction
- Callosal dysgenesis
- Cerebellar involvement
- Eyes: chorioretinitis, cataracts and microphthalmia.

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**Cytomegalovirus infection**

VM is present in ~18% of proven fetal CMV infection

**Cytomegalovirus Infection**

- VM is not the ONLY US finding in cases of congenital infection; but one of the most common.

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**Toxoplasmosis**

- Classic triad:
  - Hydrocephalus, calcifications & chorioretinitis.

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**Aneuploidy Rates**

- Mostly trisomy 21
- Ventriculomegaly (10-15mm)
  - Overall risk is 5%
- Mild ventriculomegaly (10.1 to 12 mm)
  - Risk 3%

Aim: to report prevalence and findings of VM 11-14 wks

Methods: The ratio of the choroid plexus and lateral ventricle diameter (PDVDR) and choroid plexus and lateral ventricle length (PLVLR) and choroid plexus and lateral ventricle area (PAVAR) were calculated in 100 nl and 17 VM.

Results: The ratios were below the 5th centile in over 80% of cases with VM.

Conclusions: Found shrinkage of the CP rather than increased width of VM.

Role of MRI in the Evaluation of Ventriculomegaly

- The routine use of MRI in fetal VM remains controversial.
- Some studies have shown that it adds important information in 6-10% of the cases, specifically as it relates to cortical anomalies.
- Therefore, the appropriate time to perform an MRI is in the 3rd trimester.

Is fetal magnetic resonance imaging indicated when ultrasound isolated mild ventriculomegaly is present in pregnancies with no risk factors?

- AIM: Evaluate the role of MRI in mild isolated VM (10-12mm)
- METHODS: Retrospective study of 179 fetal MRI (mean GA 26 wks). NI karyotype and infection w/u
- Results: In 49/179 cases, MRI & US results differed, – Only in 2 of these cases did MRI studies provide clinically consistent additional information.
- In 130/179 cases, MRI confirmed US findings.

Is fetal magnetic resonance imaging indicated when ultrasound isolated mild ventriculomegaly is present in pregnancies with no risk factors?

- OBJECTIVE: Assess the accuracy of expert neurosonography at a tertiary referral center
- METHODS: Retrospective analysis of 773 fetuses with confirmed CNS abnormalities
- MRI was performed in 126 (16.3%) cases.
- RESULTS: NSG and MRI were concordant & correct in 109/126 (87.2%) cases.
- In cases with space-occupying lesions, MRI identifying clinically relevant findings in 42.9% (3/7) of these cases.
OBJECTIVE: Assess the accuracy of expert neurosonography at a tertiary referral center

METHODS: Retrospective analysis of 773 fetuses with confirmed CNS abnormalities. MRI was performed in 126 (16.3%) cases.

RESULTS: NSG and MRI were concordant & correct in 109/126 (87.2%) cases. In cases with space-occupying lesions, MRI identifying clinically relevant findings in 42.9% (3/7) of these cases.

CONCLUSIONS: In a tertiary referral center with good neurosonography expertise, MRI is likely to help in a limited proportion of cases (8%). More useful after 24 weeks. Lesions whose diagnosis are most likely to benefit are gross space-occupying lesions.

Monitoring During Pregnancy

Worsening and late appearance of associated anomalies has been reported.
- One study of 167 fetuses showed progression in 11% (defined as ventricular measurement of > 3mm).
  - In 7% of ongoing pregnancies, f/u scan showed major abnormalities missed at the initial scan.
  - A recent review found risk of progression 15.7% and rate of anomalies not visible at the initial scan 12.8%.

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AIM: To examine the incidence of major cerebral abnormalities on postnatal imaging in cases of isolated fetal mild VM and to evaluate the relationship between such defects and prenatal ultrasound factors.

METHODS: 130 fetuses with isolated MVM (10-15 mm).

RESULTS: Post-natal imaging identified 6.5% (9 fetuses) with major anomaly- in 66% (6 fetuses) anomaly was known or suspected by prenatal imaging.
  - Multivariate analysis: persistence or progression of VM (OR 21.1%) was the only significant predictor of major cerebral abnormalities.

AIM: To examine the incidence of major cerebral abnormalities on postnatal imaging in cases of isolated fetal mild VM and to evaluate the relationship between such defects and prenatal ultrasound factors.

CONCLUSION: Prenatal ultrasound follow-up identifies fetuses at higher risk for a major cerebral abnormality among cases with isolated mild VM. In cases with persistent or progressive enlargement, fetal MRI and postnatal imaging seem appropriate.
Neurological Outcomes

- **Overall risk** of neurological abnormality in mild-moderate VM (10-15mm): 14%
  - If infection is negative & chromosomes normal the rate falls to 12%.
  - If VM is progressive the risk of neurological sequelae increases.
- In isolated mild VM (10.1-12.0mm) overall neurological abnormality: 4%


**OBJECTIVES:** Assess the prevalence of neurodevelopmental delay in isolated mild fetal VM (10 - 15 mm).

- Neurodevelopmental delay defined as an abnormal quotient score.

**CONCLUSION:** The incidence of neurodevelopmental delay in truly isolated VM of ≤15mm is 7.9%.
This rate is similar to that noted in the general population

(Lipitz et al., 1998; Senat et al., 1999; Durfee et al., 2001; Kinzler et al., 2001; Sadan et al., 2007)

Are there differences in degree of VM in male or female fetuses?

- **Higher prevalence** of male fetuses with VM and better neurodevelopmental outcome reported in male than female fetuses*
- This finding would suggest that male fetuses have slightly larger atrial width compared to female**

*Pilu et al. 1999; Gaglioti et al. 2000 **Patel et al., 1995; Nadel; Benacerraf, 1995 ***Haddad et al., 2003; Kramer et al., 1997

**Does uni- or bilateral Mild VM affect outcome?**

- Bilateral or unilateral does **not** affect outcome

Are there differences in degree of VM in male or female fetuses?

- Others*** found no difference between sexes or found differences that were statistically, but not clinically, significant.
- **These data, therefore, should be** used with caution when counseling prospective parents in cases of VM.

*Pilu et al. 1999; Gaglioti et al. 2000 **Patel et al., 1995; Nadel; Benacerraf, 1995 ***Haddad et al., 2001; Kramer et al., 1997
Summary: Counseling

- **Very difficult undertaking**
- In the *presence* of associated anomalies, abnormal karyotype or infection:
  - since the cause of the VM is known counseling is easier
  - however, in the presence of conditions such as AGCC, with its variable outcomes, counseling is challenging and the couple will face difficulty in interpreting or deciding the best next step.

Conclusion

- The clinical significance of VM is that it *alerts* to the possibility of *associated anomalies* of the brain or other organs.
- The *final prognosis* depends more on the anomalies than on the degree of ventricular dilatation.
- *Persistent or progressive VM carries a worse neurodevelopmental prognosis.*
  - *Unilateral or bilateral VMs have similar outcomes*