AMSER Case of the Month
September 2023

36 year old female G2P0010 who was referred for evaluation of ventriculomegaly.

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HEALTH
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Patient Presentation

- **Pregnancy History**: One prior pregnancy at age 30 that ended in early spontaneous abortion.

- **Current Pregnancy**:
  - Dated by a 6w2d ultrasound not consistent with last menstrual period.
  - Complicated by maternal diabetes + advanced maternal age.
  - 23-week ultrasound demonstrated mild–moderate ventriculomegaly (right 12.2 mm, left 8.9 mm).
  - Cell-free DNA testing was low risk for aneuploidy.

What imaging should we order?

Applicable ACR Appropriateness Criteria

Variant 3: **Second and third trimester screening for abnormal finding on ultrasound: soft markers. Next imaging study.**

Procedure	Appropriateness Category	Relative Radiation Level
US pregnant uterus transabdominal detailed scan	Usually Appropriate	O
US pregnant uterus transabdominal follow-up	Usually Appropriate	O
US echocardiography fetal	May Be Appropriate	O
MRI fetal without IV contrast	Usually Not Appropriate	O
MRI fetal without and with IV contrast	Usually Not Appropriate	O

We ordered a transabdominal detailed ultrasound scan.

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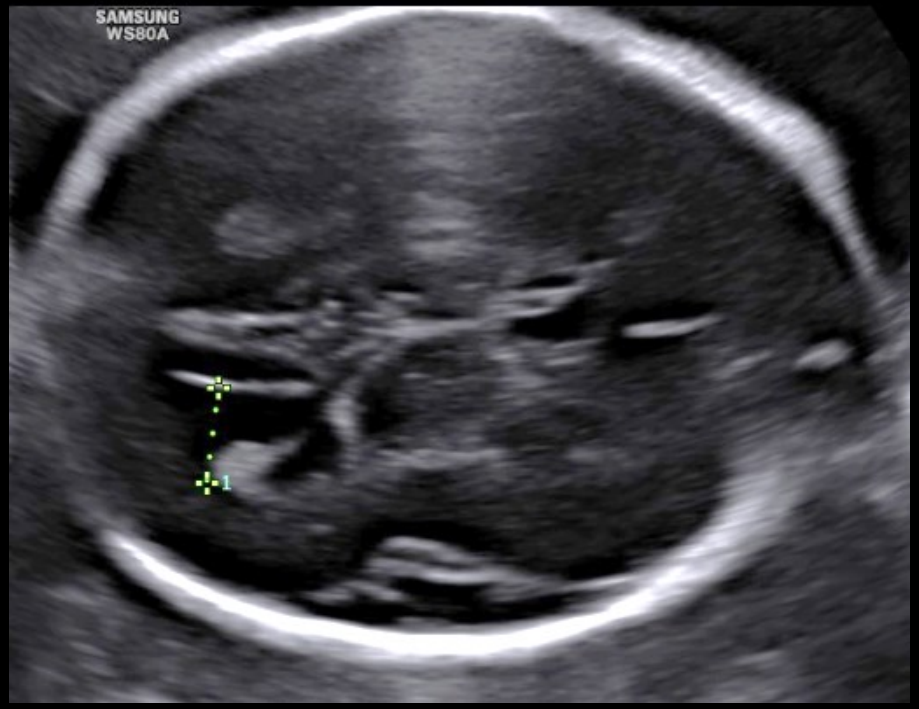
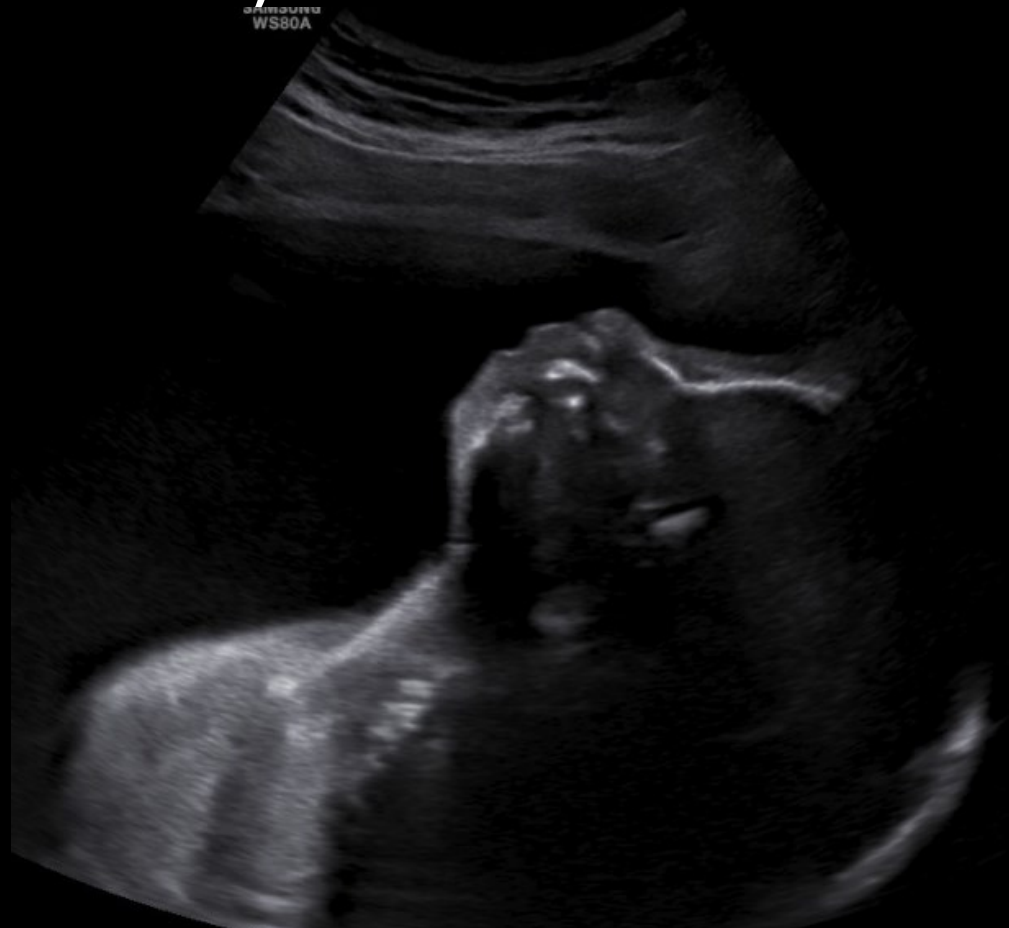
Detailed Fetal Ultrasound at 29 Weeks (unlabeled)

Axial





Maximum Vertical Pocket of amniotic fluid = 10.7 cm

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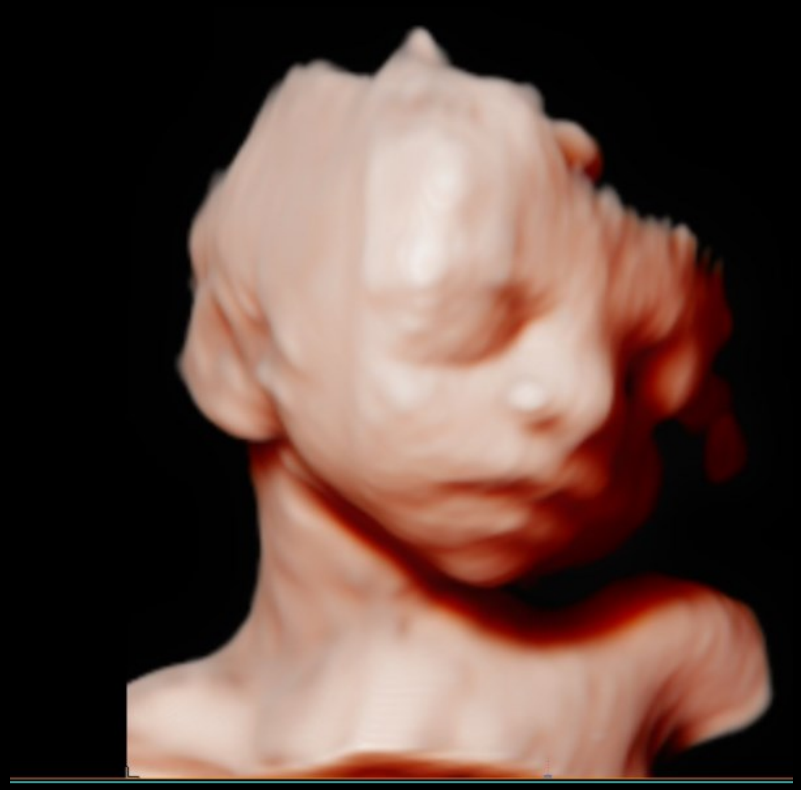
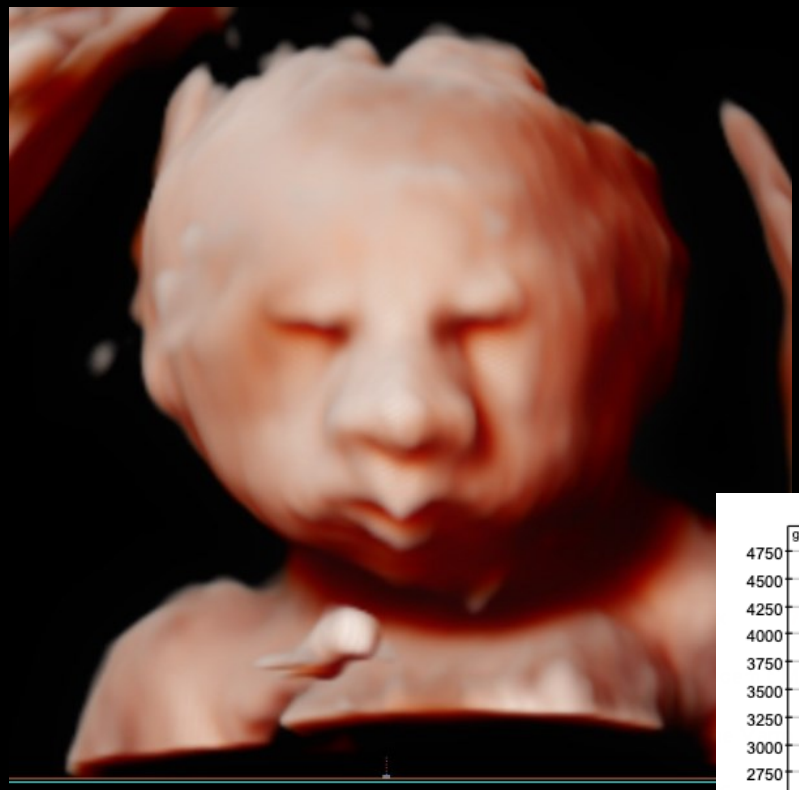
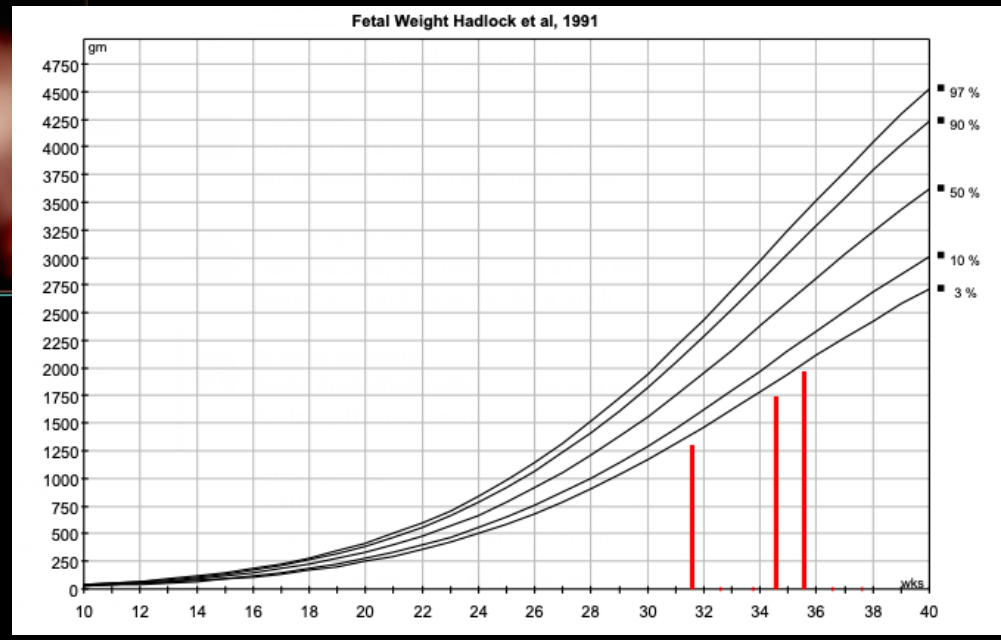
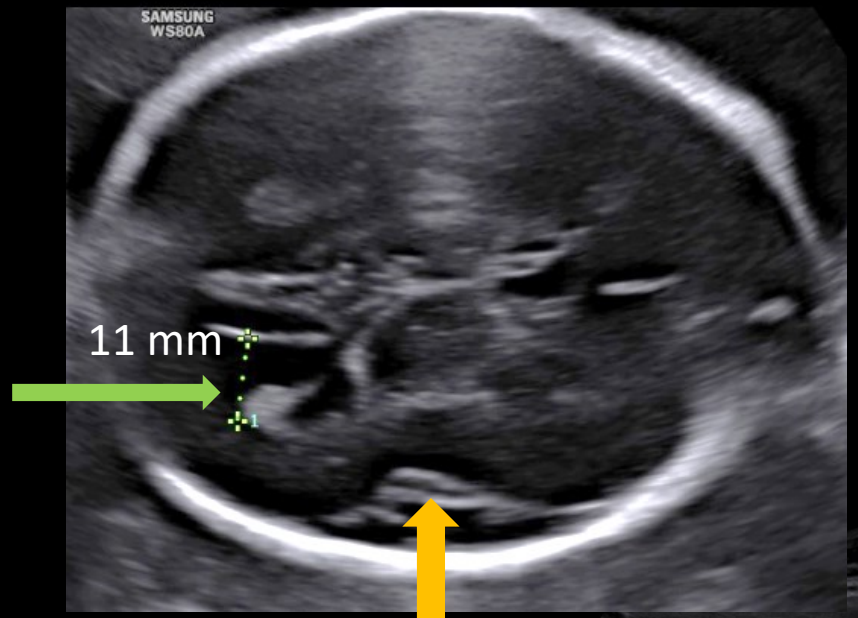
3D Ultrasound (unlabeled) & Fetal Growth Chart



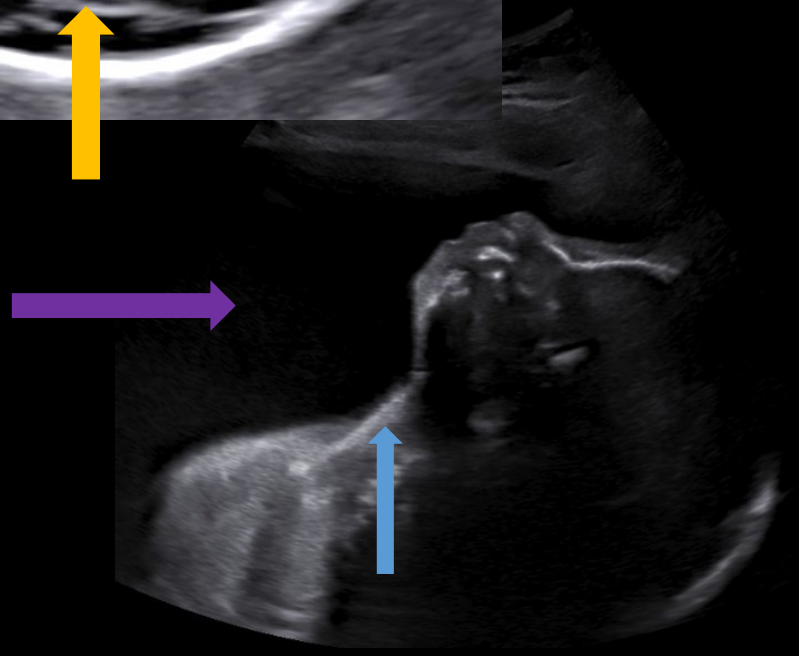




Detailed Ultrasound at 29 Weeks - Labeled



Axial



- Calipers measured the ventricles at 11 mm bilaterally.
- Smooth cortical mantle with a broad, shallow Sylvian fissure.
- The fetus had abnormal posturing with a highly extended neck; in real time, abnormal jerky movements were noted concerning for fetal seizure activity.
- The highly extended neck and abnormal posturing were well-seen due to polyhydramnios.

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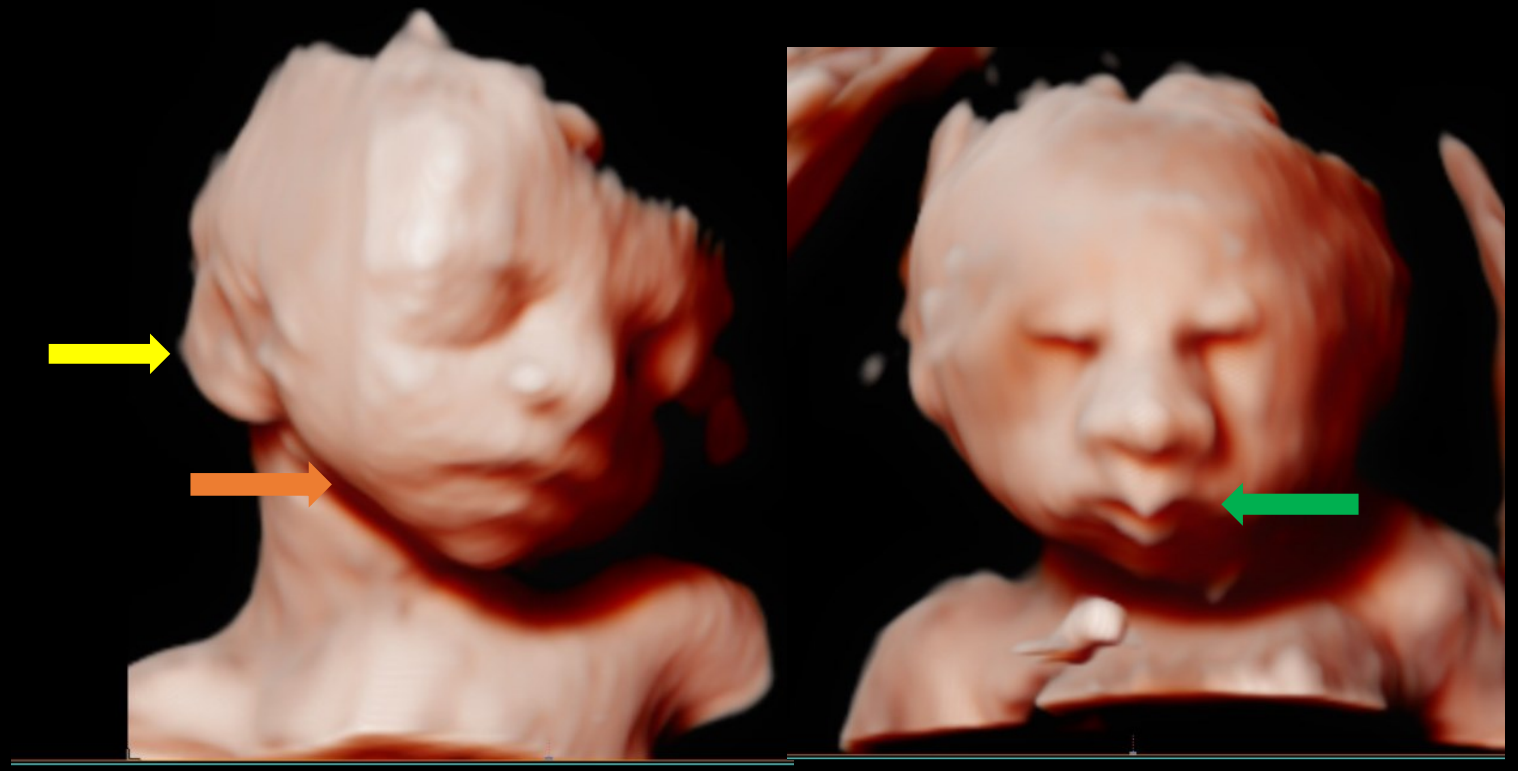
3D Ultrasound at 29 Weeks - Labeled

- Low-set, posteriorly rotated ears
- Micrognathia
- Prominent upper lip



- The fetus presented with mild ventriculomegaly and low risk cell-free DNA in the setting of advanced maternal age.
- New observations include:
  - Abnormal brain sulcation
  - Abnormal facies
  - Abnormal fetal movements
  - Growth restriction
  - Polyhydramnios
- These findings are **highly** concerning for a major malformation or syndromic diagnosis.

What other imaging should we order?

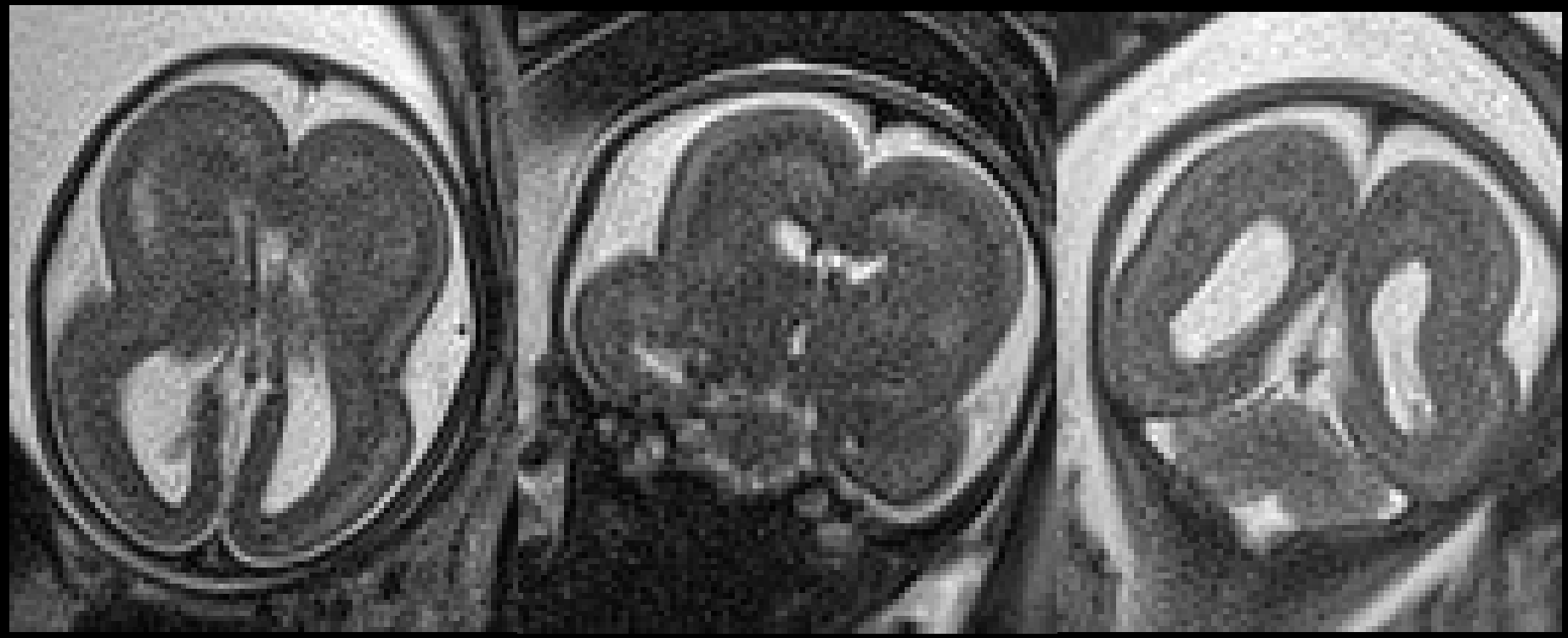
Applicable ACR Appropriateness Criteria

Variant 4: **Second and third trimester screening for abnormal finding on ultrasound: major anomalies. Next imaging study.**

Procedure	Appropriateness Category	Relative Radiation Level
US pregnant uterus transabdominal detailed scan	Usually Appropriate	O
MRI fetal without IV contrast	Usually Appropriate	O
US echocardiography fetal	Usually Appropriate	O
US pregnant uterus transabdominal follow-up	Usually Appropriate	O
MRI fetal without and with IV contrast	Usually Not Appropriate	O

We ordered a fetal MRI without contrast.

MRI at 31 Weeks (Unlabeled)



T2 Axial

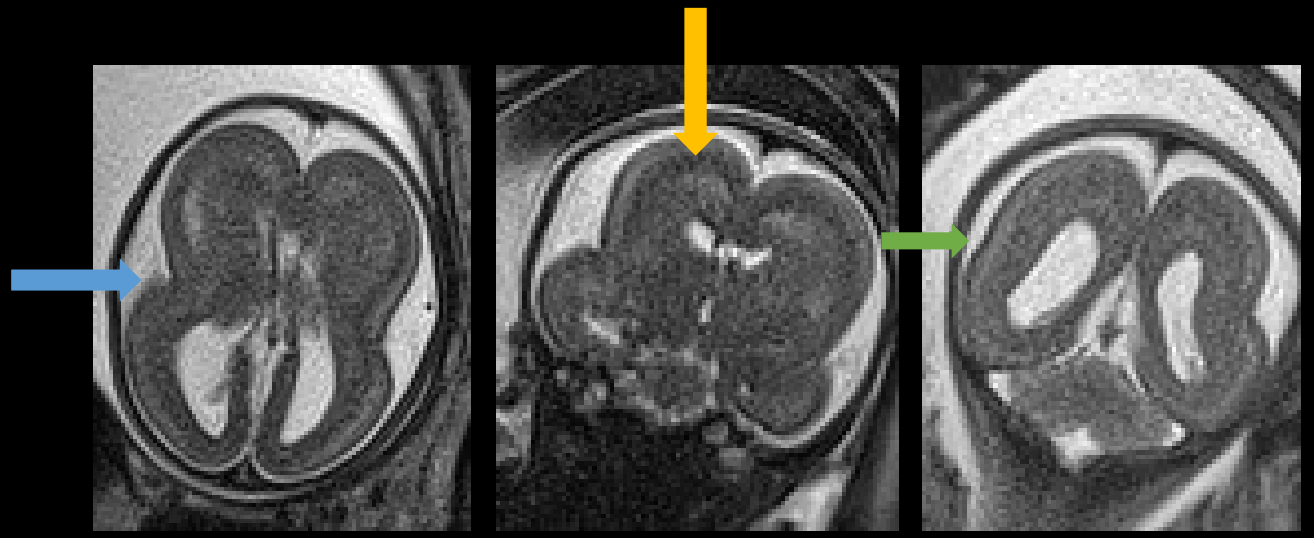
T2 Coronal - Anterior

T2 Coronal - Posterior

MRI at 31 Weeks - Labeled

The brain is markedly abnormal demonstrating **widespread agyria** with:

- Layered pattern to the parenchyma.
- Hourglass or figure-of-eight configuration.
- Shallow dip where the Sylvian fissure should lie.



Follow-up ultrasound demonstrated severe fetal growth restriction and polyhydramnios.

Impression: **Grade 1 severe lissencephaly**

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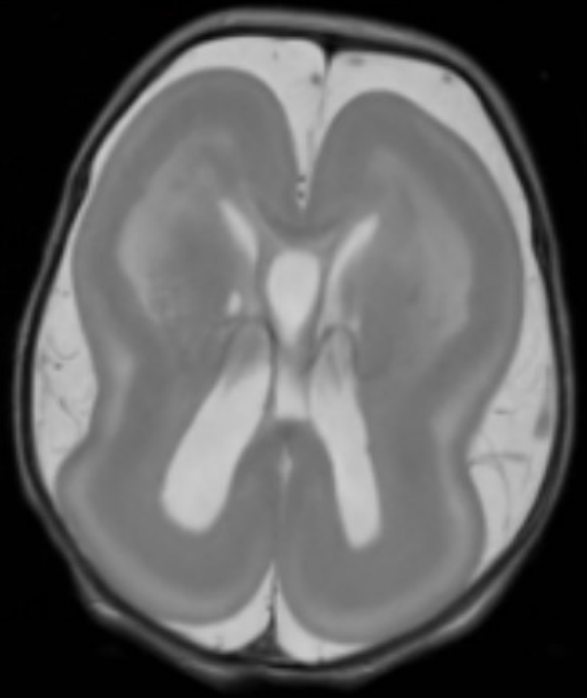
Final Diagnosis

The constellation of findings in this fetus, including widespread agyria, mild ventriculomegaly, micrognathia, low-set, posteriorly rotated ears, growth restriction, and polyhydramnios led to a preliminary diagnosis of **Miller-Dieker syndrome**, which occurs due to a deletion at chromosome 17 p13.3 involving the *LIS1* and *YWHAE* genes.[1]

This baby was born at 37-weeks gestation via induced labor due to intrauterine growth restriction. Genetic testing confirmed **Miller-Dieker syndrome**.



Axial T2 MRI w/o contrast at 6-days-old confirmed Grade 1 severe lissencephaly.

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Case Discussion – Diagnostic Approach to Mild Fetal Ventriculomegaly

Fetal ventriculomegaly is defined as:

1. >10 mm width of the atria of the posterior lateral ventricles at any point in gestation

OR

2. A separation of more than 3 mm of the choroid plexus from the medial wall of the lateral ventricle[2]

No established criteria for grading fetal ventriculomegaly; mild is generally 10-12 mm, moderate 13-15 mm, and severe > 15 mm.[3]

Differential for Mild Ventriculomegaly[4]

Obstructive:
- Chiari II malformation
- Dandy-Walker spectrum
- Aqueductal stenosis
- Obstructing masses

Destructive:
- Hydranencephaly
- Periventricular leukomalacia
- Intracranial hemorrhage

Dysgenesis:
- Agenesis of the corpus callosum
- Septo-optic dysplasia
- Holoprosencephaly
- Schizencephaly

- **Can also be isolated, for which the likelihood of survival with normal neurodevelopment is documented to be over 90%.[5]**

Mild ventriculomegaly is associated with a wide variety of diagnoses—a selection of the most common diagnoses is listed here.

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Case Discussion – Miller-Dieker Syndrome

Life expectancy: **Poor prognosis** with most children dying before age 2.[6]

Epidemiology: Rare disorder with unknown prevalence.[6]

Inheritance: Most cases are sporadic. Approximately **12%** of children with Miller-Dieker syndrome have a **parent with a balanced translocation on chromosome 17**; in these cases, Miller-Dieker syndrome is considered to have autosomal dominant inheritance.[7]

- Such translocations are also associated with early fetal loss.

Take Home Points

- Common, “mild” findings can lead to very specific and devastating diagnoses. Mild ventriculomegaly is particularly challenging—the outcome can vary from normal intellectual development to a syndromic diagnosis with a severe outcome and recurrence risk for future pregnancies.
- Ultrasound can suggest a diagnosis of lissencephaly, but MRI should be used for confirmation and for assessment of additional abnormal findings that may not be sonographically apparent.
- Although a relatively small percentage of Miller-Dieker syndrome cases occur due to an inheritable mutation, genetic testing may be indicated in prospective parents desiring future pregnancies; this is particularly true if there is a history of early fetal loss.

References

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2. Fox NS, Monteagudo A, Kuller JA, Craigo S, Norton ME. Mild fetal ventriculomegaly: diagnosis, evaluation, and management. Am J Obstet Gynecol 2018;219:B2–9. https://doi.org/10.1016/j.ajog.2018.04.039.
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6. Medline Plus [Internet].Bethesda (MD): National Library of Medicine (US); [updated 2009 Nov 1]. Miller-Dieker Syndrome; [cited 2023 Jan 11]; available from https://medlineplus.gov/genetics/condition/miller-dieker-syndrome/.
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