AMSER Case of the Month January 2025

35 year old pregnant female presents for a first prenatal visit after a history of fetal loss due to cystic kidney disease

Orlando M. Martinez, MS4, Case Western Reserve University School of Medicine
Ruchi Yadav, MD, Thoracic Imaging, Cleveland Clinic Foundation

Cleveland Clinic
Imaging Institute

School of Medicine
Case Western Reserve University

AMSER

Patient Presentation

- HPI: Patient G3P0110 presented to the maternal fetal medicine clinic to establish care for a new pregnancy at 8 weeks gestational age.
- PMHx: Her first pregnancy ended with IUFD at 23 weeks, and her second required D&E at 21w for fetal bilateral multicystic dysplastic kidneys. Subsequent genetic testing found that both parents are carriers of the TMEM67 gene. Otherwise, she had no history of abnormal pap smears or STIs and denied any other pertinent medical history.
- Meds: Prenatal vitamin.
- Allergies: None.
- Physical Exam: Vitals within normal limits, not in acute distress, normal respiratory effort, and soft, non-distended abdomen.
- Labs: Within reference ranges.
- Plan: The patient was advised to return for fetal anomaly screening at 16 weeks gestational age.

What Imaging Should We Order?

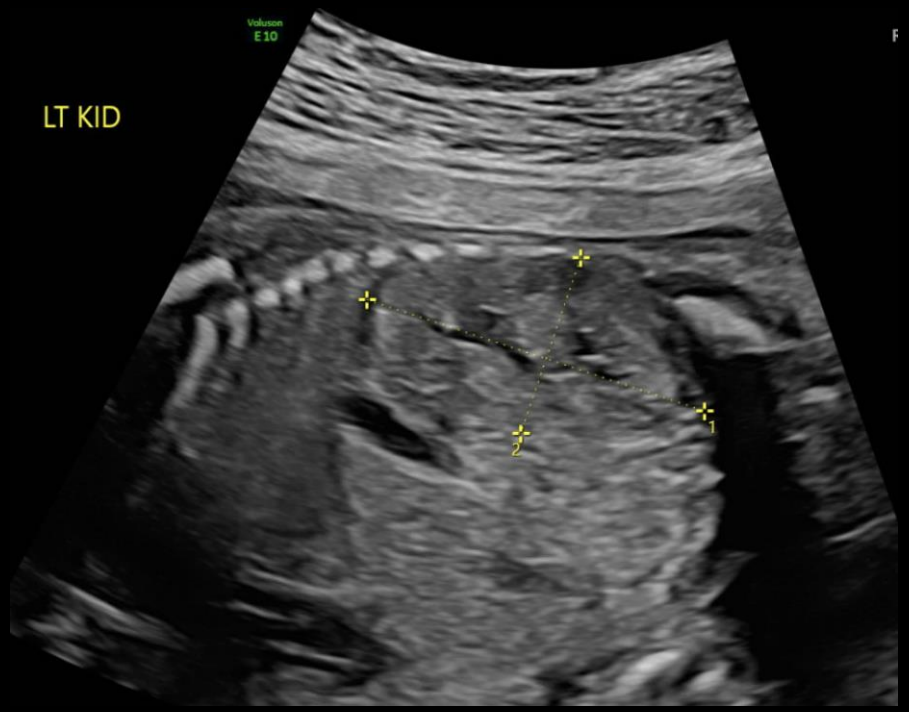
Select the applicable ACR Appropriateness Criteria

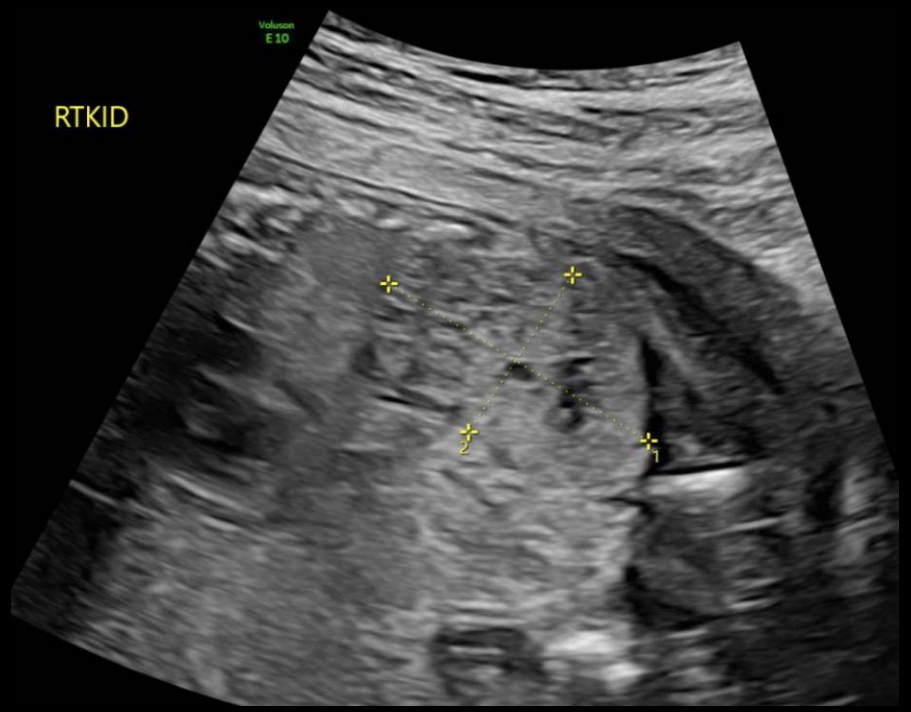
Scenario	Scenario ID	Procedure	Adult RRL	Peds RRL	Appropriateness Category
Fetal anomaly screening, gestation >= 14 weeks, high risk pregnancy, initial imaging	3194006	US pregnant uterus transabdominal detailed scan	0 mSv O	0 mSv [ped] O	Usually appropriate
		US echocardiography fetal	0 mSv O	0 mSv [ped] O	May be appropriate
		US pregnant uterus transabdominal anatomy scan	0 mSv O	0 mSv [ped] O	May be appropriate (Disagreement)
		MRI fetal without IV contrast	0 mSv O	0 mSv [ped] O	May be appropriate (Disagreement)
		MRI fetal without and with IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate

This was the modality chosen!

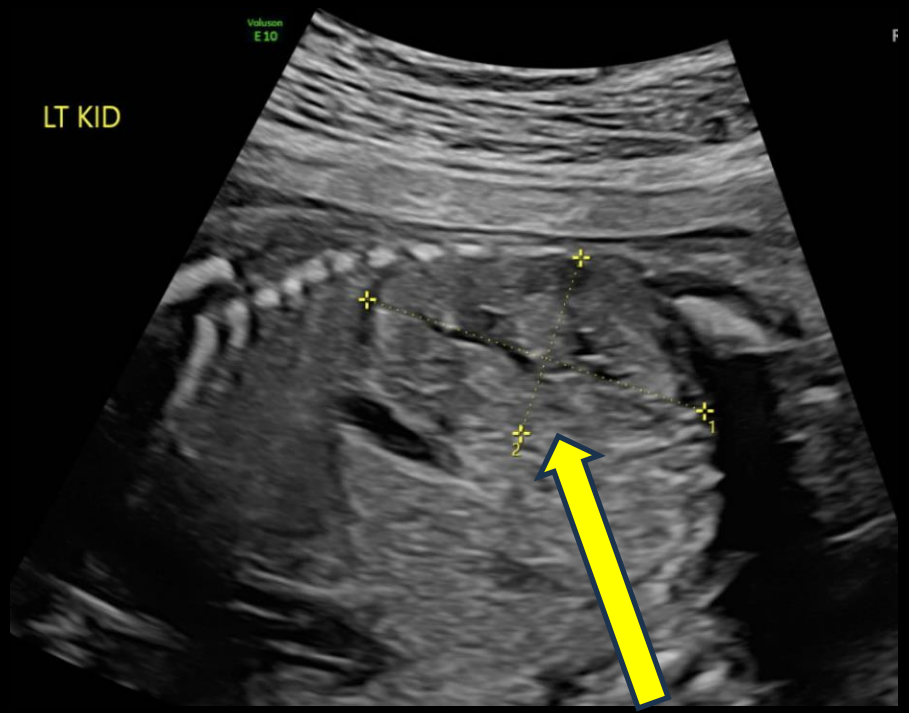
AMSER

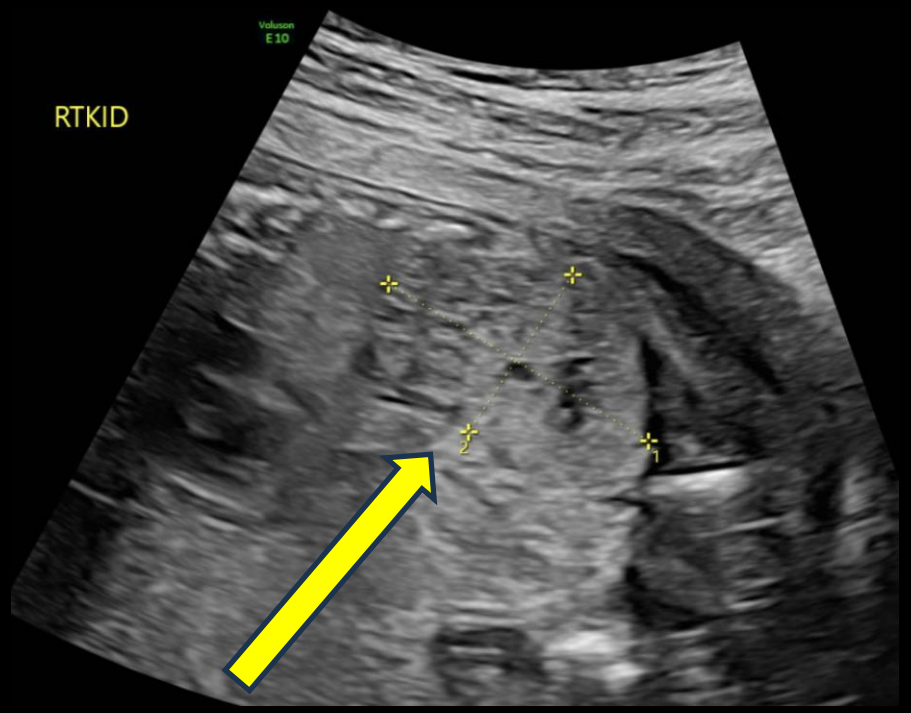
Findings (unlabeled)





Ultrasound Findings at 16 weeks gestational age





- Bilaterally enlarged, mildly echogenic kidneys that measure >99% corrected for gestational age
- Left kidney measures 1.1 x 2.2 x 1.2 cm and the right kidney measures 2.2 x 1.5 x 1.1 cm

- Plan: given these findings, the patient was advised to return at 28 weeks gestational age for further imaging

AMSER

What Imaging Should We Order Next?

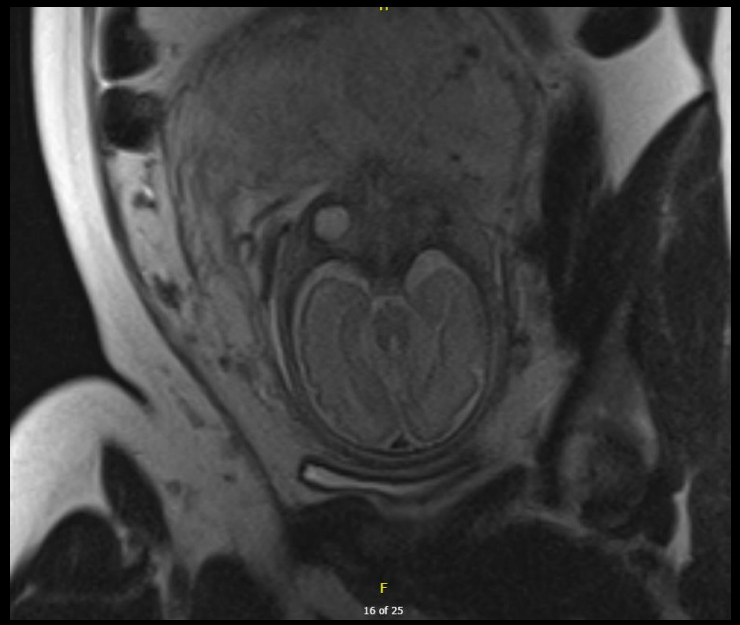
Select the applicable ACR Appropriateness Criteria

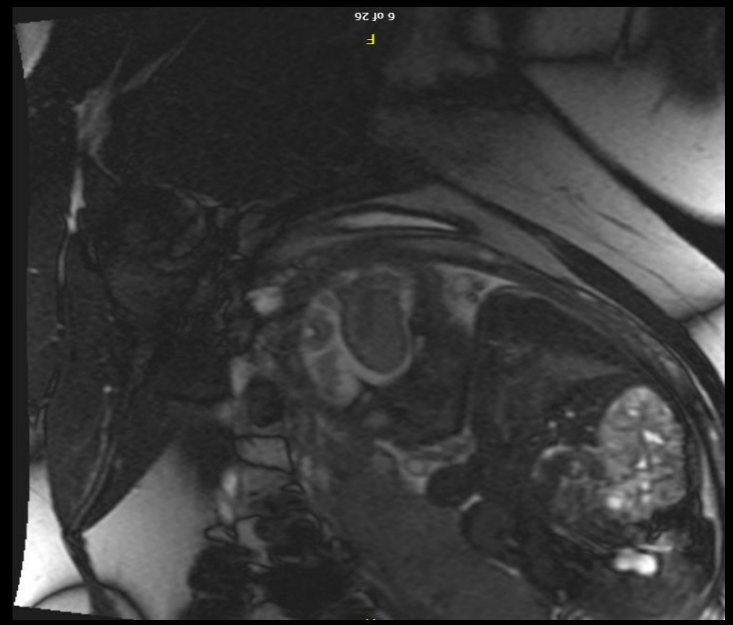
Scenario	Scenario ID	Procedure	Adult RRL	Peds RRL	Appropriateness Category
Fetal anomaly screening, gestation >= 14 weeks, major anomalies on US, next imaging study	3194008	US echocardiography fetal	0 mSv O	0 mSv [ped] O	Usually appropriate
		US pregnant uterus transabdominal detailed scan	0 mSv O	0 mSv [ped] O	Usually appropriate
		US pregnant uterus transabdominal follow-up	0 mSv O	0 mSv [ped] O	Usually appropriate
		MRI fetal without IV contrast	0 mSv O	0 mSv [ped] O	Usually appropriate
		MRI fetal without and with IV contrast	0 mSv O	0 mSv [ped] O	Usually not appropriate

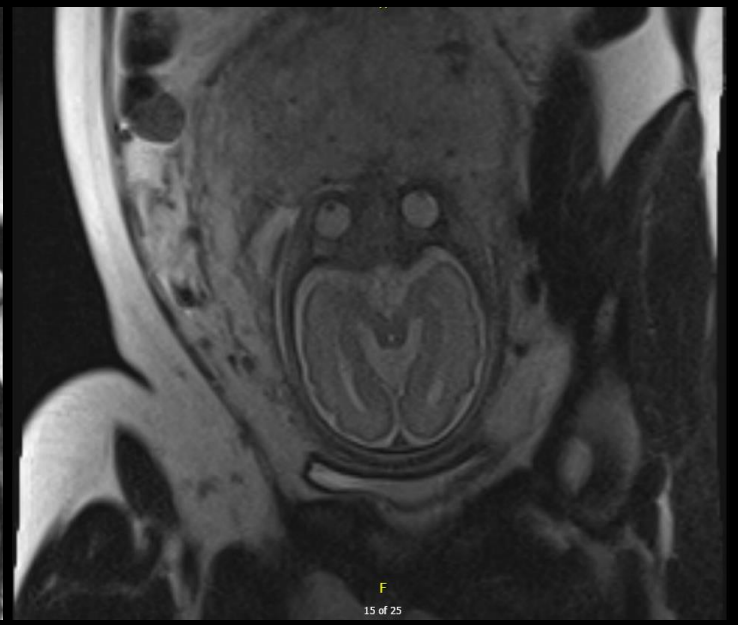
This was the modality chosen!

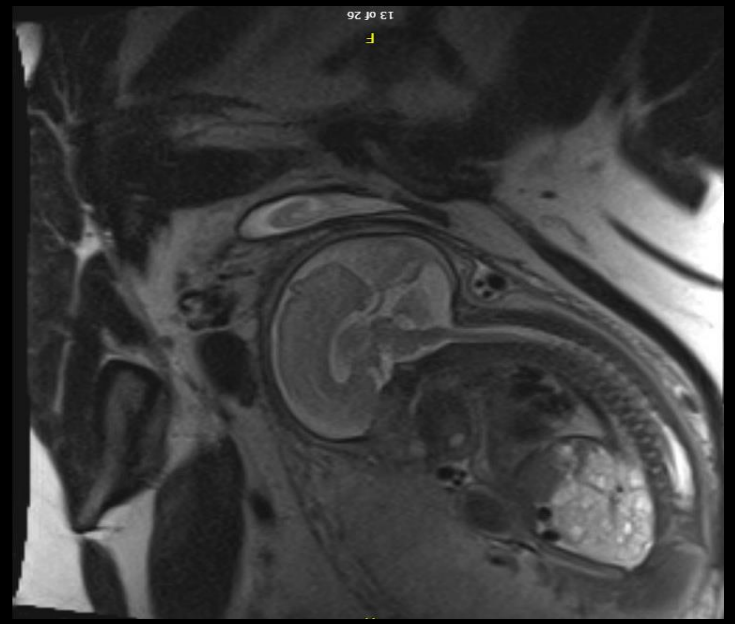
AMSER

Findings (unlabeled)

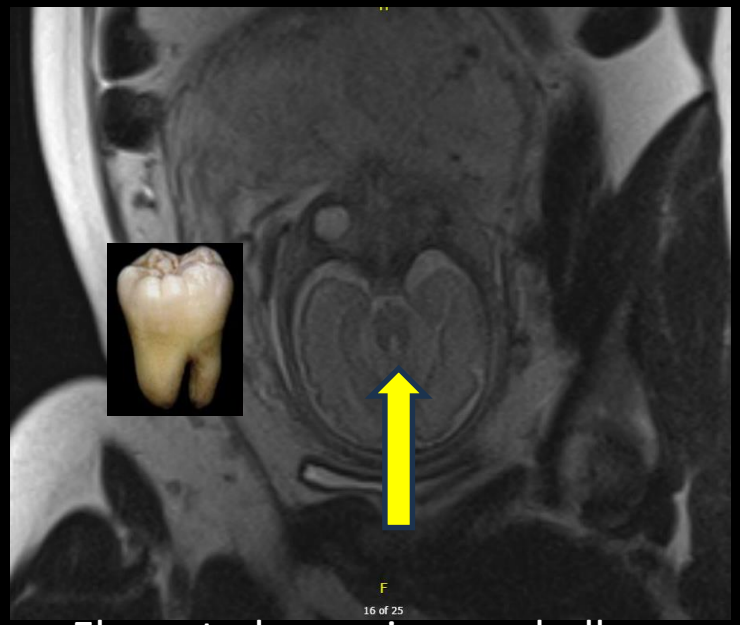




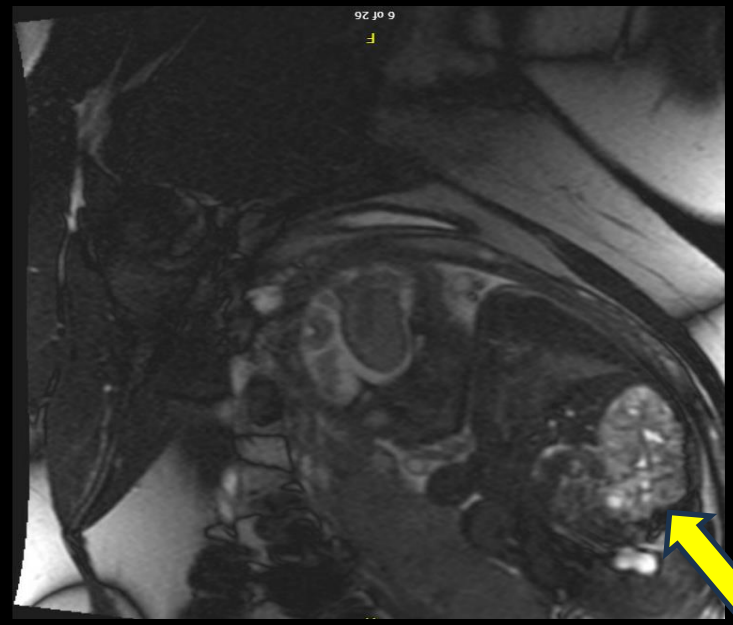


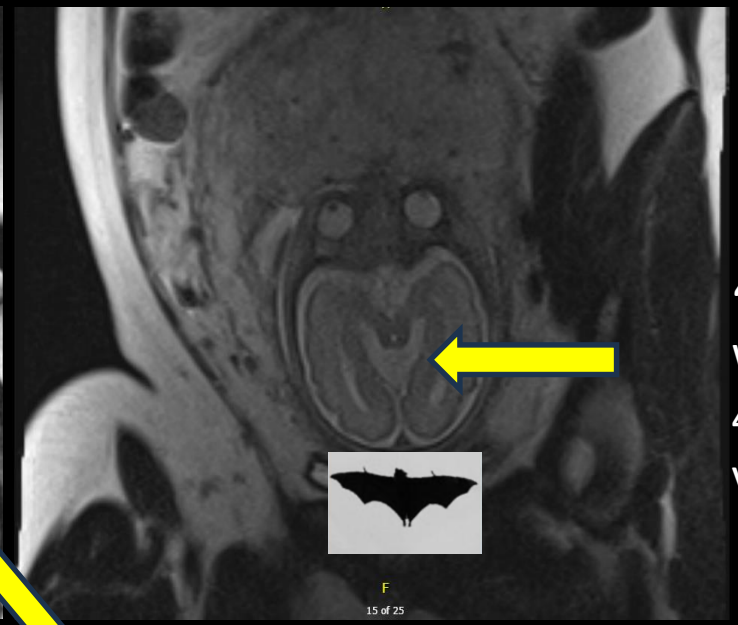


Fetal MRI Findings at 29 weeks gestational age

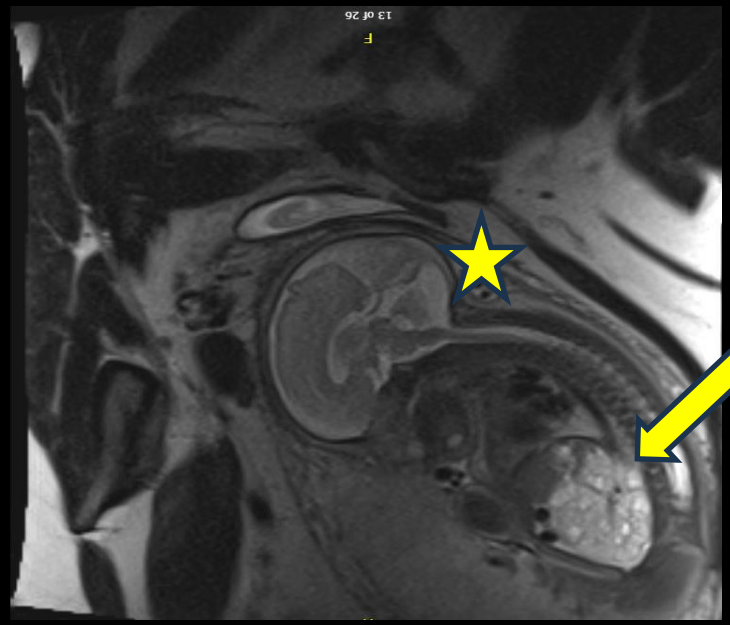


Elongated superior cerebellar peduncles and aplastic vermis, “molar tooth sign”





“Bat Wing” 4th ventricle



Bilateral enlarged multicystic kidneys

Prominent posterior fossa

Final Dx:
Joubert Syndrome and Related Disorders

Case Discussion

- Etiology: Joubert syndrome is a ciliopathy, a class of disorders caused by genetic mutations that produce dysfunctional cilia. It is inherited primarily in an autosomal recessive manner, with over 30 identified genes such as AHI1, **TMEM67 (this case)**, and CC2D2A being implicated in the disease.

- Pathophysiology: The abnormal cilia alter organogenesis in the developing fetus, leading to widespread developmental anomalies in the brain, eyes, kidneys, and liver. Affected patients will have characteristic malformations in the cerebellar vermis and brainstem. They may also have concurrent anomalies in the kidneys (i.e., cystic renal disease), liver (i.e., hepatic fibrosis and as part of COACH syndrome), and eyes (i.e., coloboma, retinal dystrophy). Later presentations of Joubert syndrome can include nephronophthisis, hepatic fibrosis, and retinal degeneration. When there is renal, liver and/or ocular involvement, the more accurate term to be used is Joubert syndrome and related disorders.

Case Discussion

Differential at 16 weeks gestational age for cystic kidneys in isolation:

- Autosomal Recessive Polycystic Kidney Disease (ARPKD)
- Autosomal Dominant Polycystic Kidney Disease (ADPKD)
- Multicystic Dysplastic Kidney (MCDK)
- Beckwith-Wiedemann Syndrome (BWS)
- Cystic Renal Dysplasia

Differential at 29 weeks gestational age for enlarged posterior fossa in isolation:

- Dandy-Walker Malformation
- Blake's pouch cyst
- Megalencephaly and Mega Cisterna Magna
- Arachnoid cyst

Differential for neurologic anomalies with cystic kidneys:

- Joubert Syndrome
- Meckel-Gruber Syndrome
- Bardet-Biedl Syndrome
- Zellweger Spectrum Disorders
- Trisomy 13 (Patau Syndrome)

Case Discussion

- Epidemiology: The prevalence of Joubert syndrome is approximately 1 in 100,000.
- Clinical Presentation: Affected individuals usually present with ataxia and have dysmorphic facies, global developmental delay, hypotonia, rapid breathing and oculomotor apraxia. There is a significant range in the degree of cognitive impairment, with IQ ranging from 30 to 80.
- Management: There is limited data available on the long-term outcomes, though persistent neuromotor developmental delay is a feature of surviving individuals , and associated retinal dysplasia appears to portend a poorer prognosis. These patients should never receive any agent that causes respiratory depression, as individuals with Joubert syndrome are exquisitely sensitive to these effects. Genetic counseling is recommended.

Case Discussion

Imaging:

- Fetal MRI w/o contrast is the best modality to diagnose Joubert syndrome in utero. It may demonstrate:
  - A “bat wing” 4th ventricle.
  - Prominent, thickened, elongated superior cerebellar peduncles, producing the characteristic “molar tooth” sign.
  - The cerebellar vermis may be dysplastic or aplastic, producing an enlarged posterior fossa.
  - An abnormal inferior olivary nucleus
  - The absence of fiber decussation in the superior cerebellar peduncles and pyramidal tracts, though best appreciated with diffusion tensor imaging performed post natal.
  - Minor lateral ventriculomegaly (6-20% of cases) and corpus callosal dysgenesis (6-10% of cases), though only present in the minority of cases.

References:

- Scortegagna F, Corrêa DG, Pacheco FT, Nunes RH, da Rocha AJ. Joubert syndrome with the decaying molar tooth sign: report of 2 cases. Acta Neurol Belg. 2024 Sep 6. doi: 10.1007/s13760-024-02635-5. Epub ahead of print. PMID: 39240439.
- Yen VTH. Prenatal diagnosis of Joubert syndrome: A case report. Radiol Case Rep. 2024 Jul 29;19(10):4369-4374. doi: 10.1016/j.radcr.2024.07.009. PMID: 39165313; PMCID: PMC11334561.
- Montero Torres JA, Flores Escobar B, Guzman Martinez J, Barrera Martínez RA, Hernández Cortez FP. Radiological features of Joubert syndrome and clinical case presentation. Radiol Case Rep. 2024 Jul 18;19(10):4167-4172. doi: 10.1016/j.radcr.2024.06.065. PMID: 39101024; PMCID: PMC11293500.
- https://radiopaedia.org/articles/joubert-syndrome-1?lang=us