Radiology Case Reports 16 (2021) 3950–3954

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Prenatal diagnosis of zellweger syndrome by fetal MRI: a case report ☆,☆☆

Joana Diaz, MD, MPH[a], *Larry Matsumoto, MD*[c], *Jennifer Kucera Neville, MD, MS*[a,b,*]

[a] *Department of Radiology, University of South Florida Morsani College of Medicine, 2 Tampa General Circle, Tampa, FL STC 6102, USA*

[b] *Department of Radiology, Johns Hopkins All Children's Hospital, University of South Florida, St. Petersburg, FL, USA*

[c] *Department of Maternal Fetal Medicine, Sarasota Memorial Hospital, Sarasota, FL, USA*

ARTICLE INFO

Article history:
Received 16 September 2021
Accepted 20 September 2021

Keywords:
Pediatric
Fetal MRI
Neuroradiology
Pediatric radiology

ABSTRACT

Zellweger Syndrome (ZS) is a rare peroxisomal disorder also referred to as cerebrohepatorenal syndrome. ZS is an autosomal recessive disease often manifesting in the neonatal period with profound dysfunction of the central nervous system, liver and kidneys. Prenatal diagnosis of this syndrome is infrequent with imaging findings on fetal MRI rarely illustrated in the literature. This case highlights the pivotal role fetal MRI can play in identifying subtle features of the disease that are difficult to visualize on prenatal ultrasound. It is important for pediatric radiologists to be familiar with the most common imaging features of ZS on fetal MRI to expedite the diagnosis and help facilitate appropriate prenatal counseling.

Introduction

Zellweger Syndrome (ZS) is an autosomal recessive disorder with an estimated incidence of approximately 1 in 50,000 to 1 in 100,000 with a dismal prognosis and average lifespan of approximately 1 year [1,2]. ZS is classified as a peroxisomal biogenesis disorder with the most severe phenotype. The pathophysiology of the spectrum of ZS is caused by a mutation in one of 13 different PEX genes which leads to a deficiency of functional peroxisomes which assist in the breakdown of very long chain fatty acids. Biochemical testing can be performed to evaluate for a defective PEX gene [2]. The clinical presentation of ZS is highly variable with the most common features being liver dysfunction, developmental delay and other neurological abnormalities, and adrenocortical dysfunction.

Prenatal diagnosis of ZS has been historically difficult due to the limits of ultrasound itself as well as the single or late manifestation of its most common fetal features [3]. With advances in fetal MRI, it is now more feasible to prenatally diagnose ZS on imaging. The most common prenatal ultrasound features include fetal hypokinesia, renal hyperechogenicity, and cerebral ventricular enlargement [3]. Definitive diagnosis may be confirmed with Whole Exome Sequencing (WES), Trio Analysis (Trio-WES), using tissue from the proband and par-

☆ Funding Sources for Manuscript: None
☆☆ Declaration of competing interest: None
* Corresponding author. Joana Diaz
E-mail address: jodiazleyva@gmail.com (J. Diaz).
https://doi.org/10.1016/j.radcr.2021.09.055

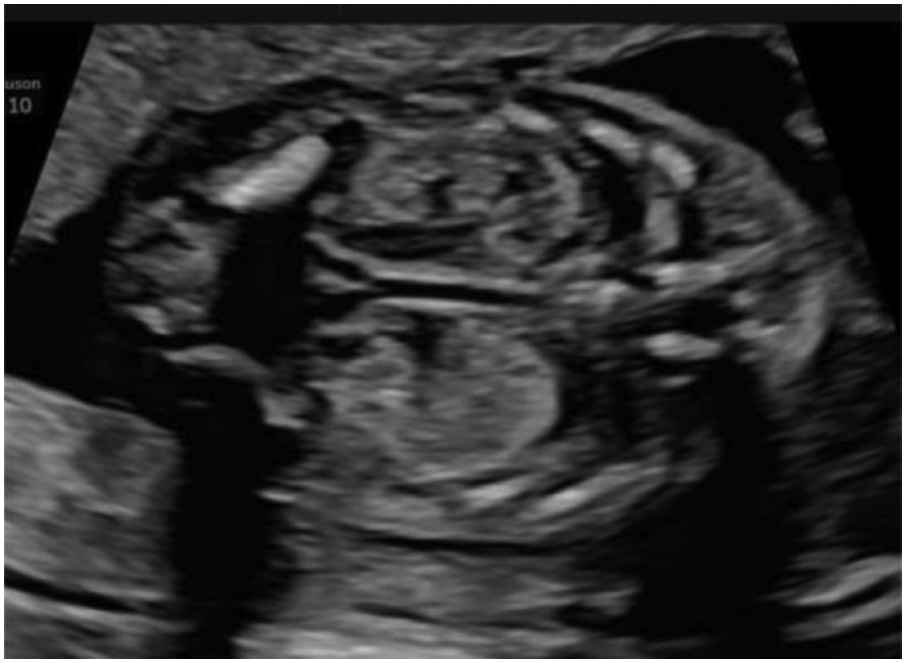

Fig. 1 – Prenatal grayscale ultrasound at 19 wk gestational age (GA) in the coronal plane reveals hyperechoic, enlarged kidneys bilaterally, measuring 2.1 AP x 1.2 transverse cm on the left and 2.2 AP x 1.1 transverse cm on the right. The normal range for GA should not exceed 1.5 cm in AP diameter.

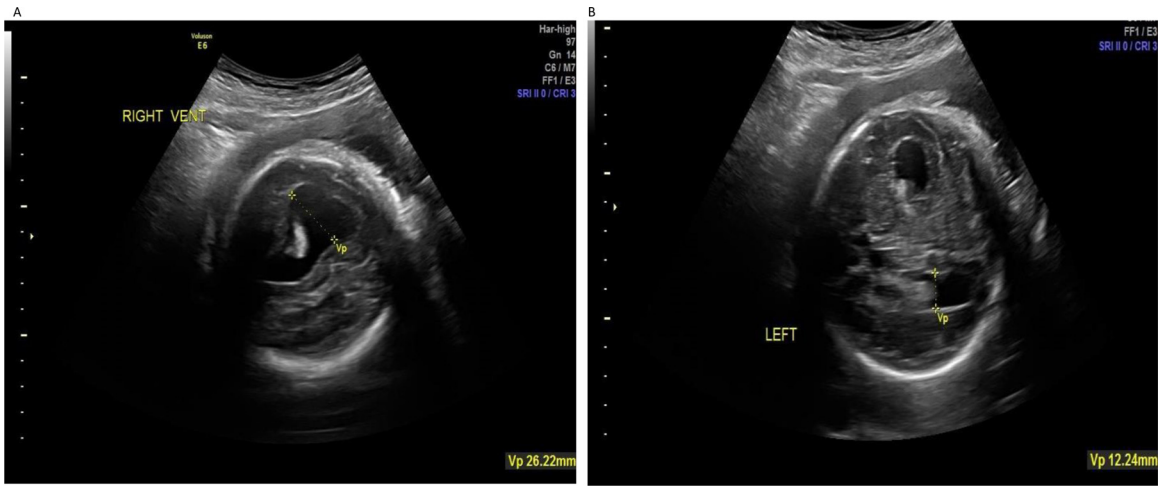

Fig. 2 – (A) Prenatal US at 34 wk GA at the level of the lateral ventricles demonstrates vetriculomegaly with asymmetricsevere enlargement of the right lateral ventricle at 2.6 cm compared with multiple priors which revealed normal caliber ventricles. (B) Prenatal US at the level of the bilateral ventricles demonstrating mild enlargement of the left lateral ventricle. Measuring 1.2 cm. GA, gestational age.

ents. Pathogenic variants of the PEX gene will not be detected using traditional karyotyping or microarray.

Case report

A 36-year-old pregnant healthy female (G3P1011) presented with a prenatal screening ultrasound at 19.5 weeks which demonstrated enlarged, hyperechoic kidneys as the sole abnormality (Fig. 1). Amniocentesis was performed due to the prenatal US findings in combination with the patient's late maternal age. Initial amniocentesis was negative. Follow-up ultrasounds at 23 and 29 weeks did not demonstrate any new abnormalities.

Follow-up US at 34 weeks demonstrated a new finding of asymmetrically dilated lateral ventricles with the right measuring up to 2.6 cm and the left measuring up to 1.2 cm, at

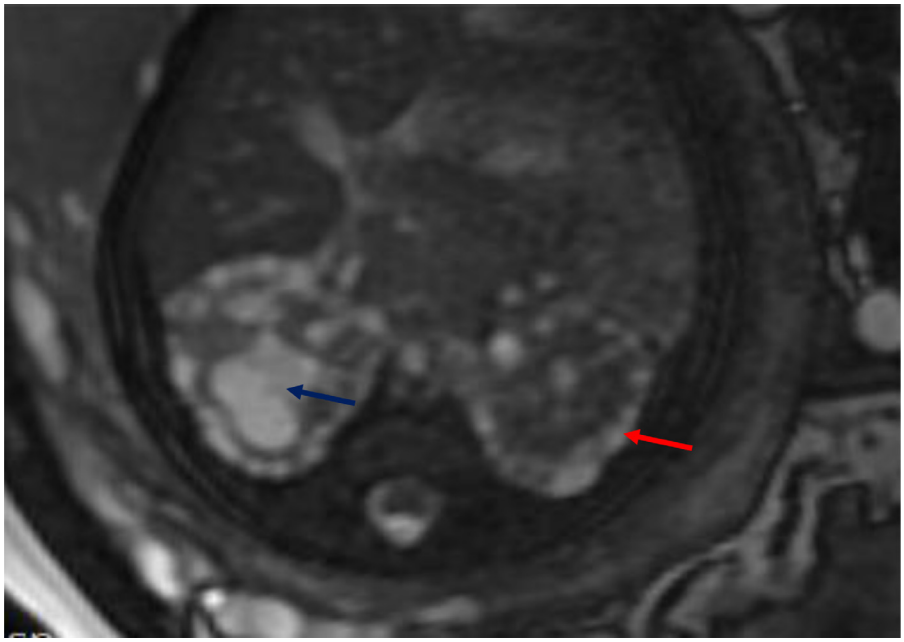

Fig. 3 – Axial T2 FIESTA fetal MRI at 35 wk GA at the level of the kidneys demonstrate enlarged kidneys with innumerable tiny cysts along the cortex (red arrow). Hydronephrosis is also seen within the right kidney (blue arrow). GA, gestational age. "Color version available online."

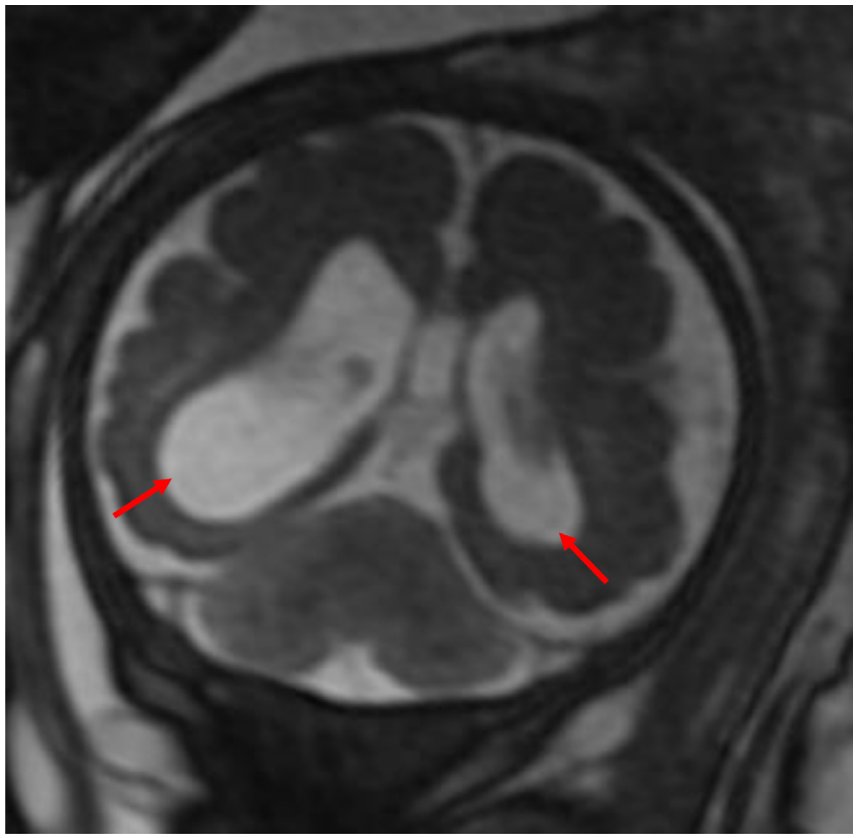

Fig. 4 – Coronal T2 FIESTA fetal MRI at 35 wk GA at the level of the bilateral ventricles confirm ventriculomegaly with asymmetric enlargement of the right greater than left ventricle (red arrow). GA, gestational age. "Color version available online."

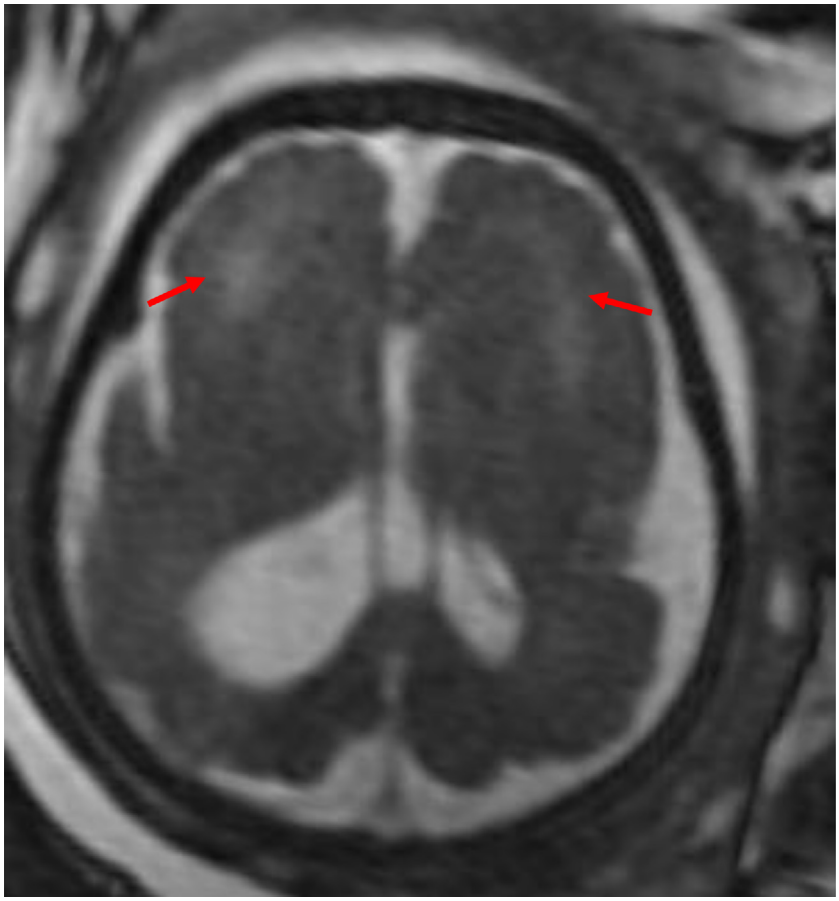

Fig. 5 – Axial FIESTA T2 fetal MRI at 35 wk GA demonstrating bilateral white matter signal abnormality within the bifrontal lobes (red arrows). GA, gestational age. "Color version available online."

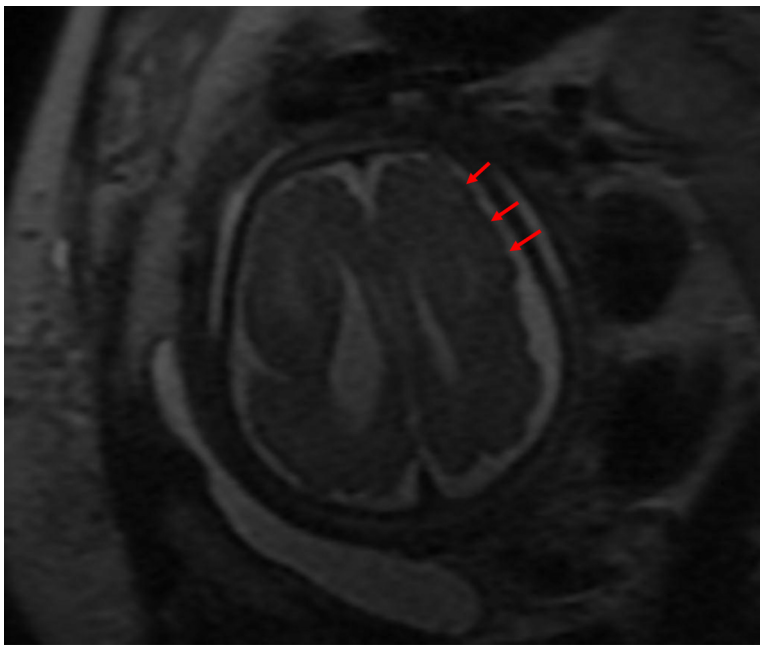

Fig. 6 – Coronal SSFSE T2 fetal MRI demonstrates questionable pachygyria in the left frontal cortex (red arrows). "Color version available online."

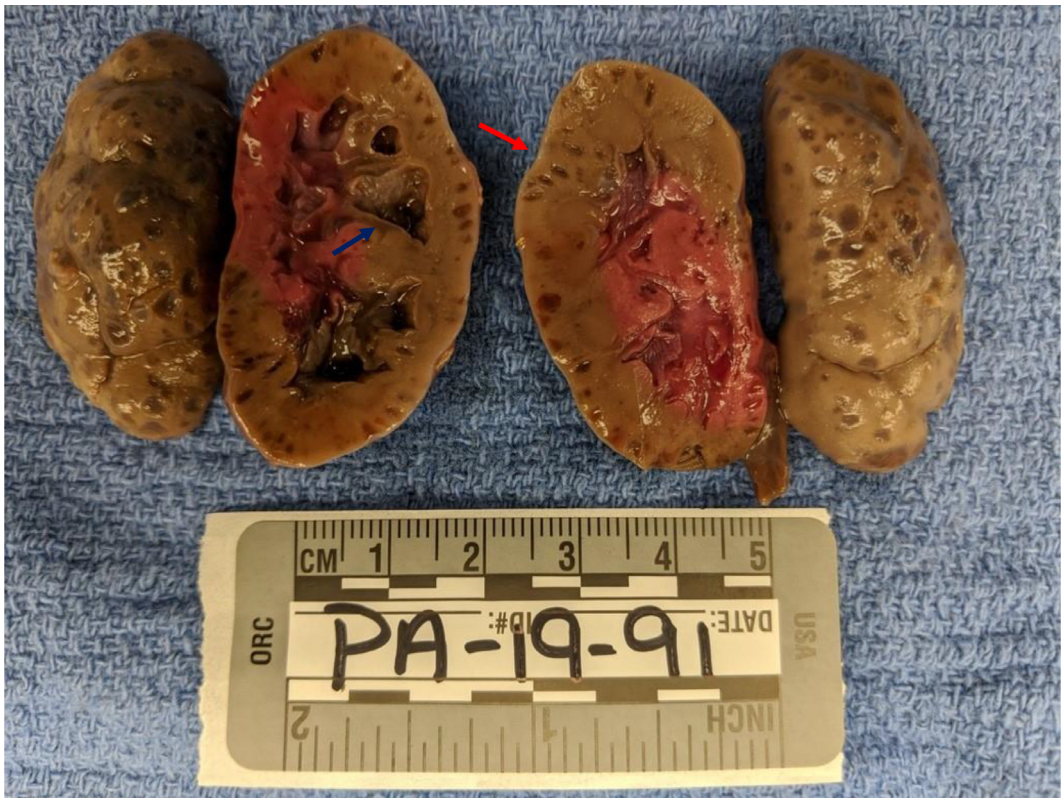

Fig. 7 – Gross pathology of the kidneys shows the multifocal cortical cysts (red arrow) and right hydronephrosis (blue arrow). "Color version available online."

which point a syndromic diagnosis was suggested (Fig. 2). The patient was referred for fetal MRI.

The fetal MRI at 34 weeks confirmed bilateral renal enlargement and also demonstrated numerous cortically based small cysts. Right sided hydronephrosis was also present (Fig. 3). Ventriculomegaly with asymmetric enlargement of the right lateral ventricle compared with the left (Fig. 4) was confirmed [4]. Bifrontal white matter signal abnormality was noted and there was the suggestion of focal pachygyria or other migrational anomaly (Figs. 5 and 6). The brainstem appeared normal without kinking or definite molar tooth configuration. No cephalocele was seen. There was also subjective decreased fetal motion during the scan. These features suggested a potential diagnosis of a syndrome such as Zellweger, with other differential diagnoses including disorders in the ciliopathy or dystroglycanopathy families. A repeat amniocentesis was sent for specific PEX-1 analysis using the Trio-WES, which supported the diagnosis of Zellweger syndrome.

Given the dismal prognosis of Zellweger syndrome, the patient opted for termination by intracardiac injection. The fetus underwent autopsy, which confirmed the imaging findings. Renal gross pathology demonstrates cortical cysts with pathologic confirmation of tubular dysplasia (Fig. 7).

Discussion

This case highlights the pivotal role fetal MRI can play in a potentially devastating diagnosis. This is an example of a case where fetal MRI may provide more detailed imaging features than ultrasound, and drastically alter patient management. It is important for pediatric radiologists to be familiar with the imaging features of Zellweger syndrome to better facilitate prenatal counseling and guide appropriate clinical management.

Authorship

All authors had access and role in writing the manuscript.

REFERENCES

[1] Klouwer FC, Berendse K, Ferdinandusse S, Wanders RJ, Engelen M. Poll-The BT. Zellweger spectrum disorders: clinical overview and management approach. Orphanet J Rare Dis 2015;10:151 Published 2015 Dec 1. doi:10.1186/s13023-015-0368-9.

[2] Pfeifer CM, Martinot CA. Zellweger syndrome: depiction of MRI findings in early infancy at 3.0 Tesla. Neuroradiol J 2017;30(5):442–4. doi:10.1177/1971400917700670.

[3] Mochel F, Grébille AG, Benachi A, Martinovic J, Razavi F, Rabier D, et al. Contribution of fetal MR imaging in the prenatal diagnosis of Zellweger syndrome. AJNR Am J Neuroradiol Feb 2006;27(2) 333-6. PMID: 16484405; PMCID: PMC8148762.

[4] Salomon LJ, Bernard JP, Ville Y. Reference ranges for fetal ventricular width: a non-normal approach. Ultrasound Obstet Gynecol 2007;30:61–6. doi:10.1002/uog.4026.