

Prenatal Diagnosis of Rhombencephalosynapsis Associated With Multiple Fetal Anomalies and a Maternally Inherited EP300 Gene Variant: A Case Report



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INTRODUCTION

Rhombencephalosynapsis (RES) is a rare cerebellar malformation characterized by midline fusion of the cerebellar hemispheres with vermian agenesis, arising from disrupted dorsal–ventral hindbrain patterning [1]. While its etiology is often linked to ciliopathies or the SHH signaling pathway, many cases remain genetically unexplained. [2]. We report a unique case of RES associated with an EP300 variant, expanding the known phenotypic spectrum of this gene.

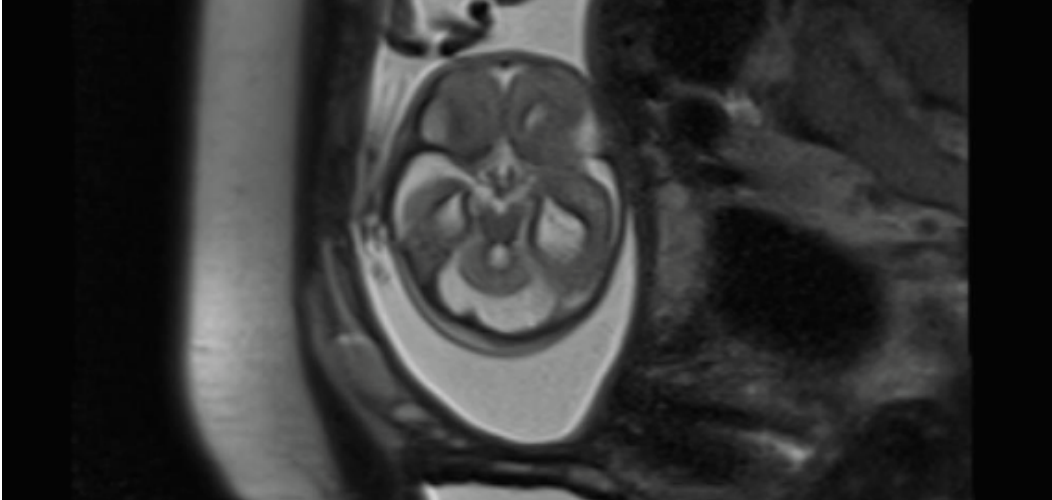
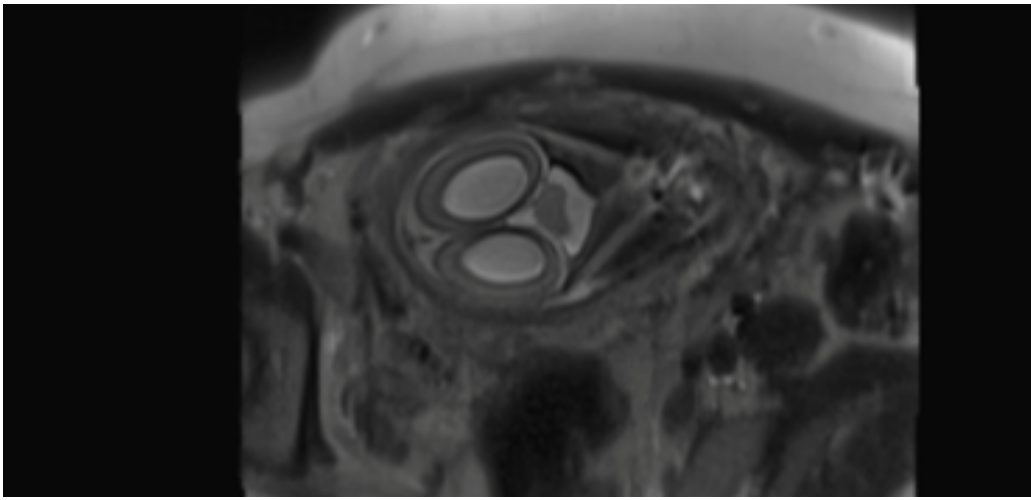
CASE PRESENTATION

A 26-year-old (G3P1) woman presented at 18 weeks of gestation



- 18 Week USG Findings :**
- Hypoplastic cerebellum (TCD: 15.69 mm)
 - Mild ventriculomegaly (LV:11 mm)
 - Protruding 14.6 × 4.99 mm parietooccipital myeloencephalocele
 - Grade 2 hyperechogenic bowel and a small mid-muscular VSD.

19- Week Fetal MRI
confirmed dorsal fusion of the cerebellar hemispheres with a continuous folial pattern, diagnosing RES.



There was no consanguinity between the parents. The mother had no known systemic illnesses and there were no pathological findings on the first-trimester screening test. Based on the findings, **fetal karyotype** and **WES** (whole-exome sequencing), **TORCH panel** was performed .

Genetic Findings (WES Result)

Identification of EP300 Variant
Whole-Exome Sequencing (WES) identified a heterozygous frameshift variant: **c.6584_6585del (p.Gln2195ArgfsTer14).**

EP300 Gene

c.6584_6585del (p.Gln2195ArgfsTer14)

Parental Segregation Analysis

Mother (Asymptomatic Carrier) × **Father (Wild-type)** → **Fetus (Lethal Phenotype, RES)**

Testing revealed the variant was inherited from the asymptomatic mother, while the father carried the wild-type gene.

Exclusion of Other Syndromes
Karyotype, TORCH panel, and analysis of known RES/ciliopathy-associated genes were all normal.

DISCUSSION

Clinical Overlap with Gómez-López-Hernández Syndrome

- The co-occurrence of RES, parieto-occipital myeloencephalocele, and ventriculomegaly initially suggested GLHS as a primary diagnosis.

Exclusion Based on Clinical Triad

- GLHS was excluded due to the absence of its hallmark clinical features: parietal alopecia and trigeminal anesthesia.

Typical vs. Atypical Syndromes

- EP300 mutations are classically associated with Rubinstein-Taybi and Menke-Hennekam syndromes, but this case's presentation was atypical for both.

Gene

While the progression from WES finding to MRI confirmation underscores the strength of genotype-phenotype correlation in this instance, suggests EP300 as a candidate in the complex molecular architecture of RES.

CONCLUSION

- This case highlights EP300's potential role as a transcriptional regulator in posterior fossa development; however additional case studies are needed to establish a definitive causal relationship. [3].**
- Furthermore highlights the importance of comprehensive genetic evaluation in patients with rhombencephalosynapsis.**

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3- Nibbeling, E. A. R., Duarri, A., Verschuuren-Bemelmans, C. C., Fokkens, M. R., Karjalainen, J. J., Smeets, C. J. L. M., de Boer-Bergsma, J. J., van der Vries, G., Dooijes, D., Bampi, G. B., van Diemen, C., Brunt, E., and 9 others. Exome sequencing and network analysis identifies shared mechanisms underlying spinocerebellar ataxia. Brain 140: 2860-2878, 2017.