Phenotypic and Genotypic Correlation of Joubert Syndrome with Occipital Encephalocele- A case report

Authors: Nalluri Hima Bindu,Vemavarapu Gayathri, Deb Jarita

Institution-Birthright by Rainbow Hospitals, HYDERABAD.

Abstract No 5250

Introduction

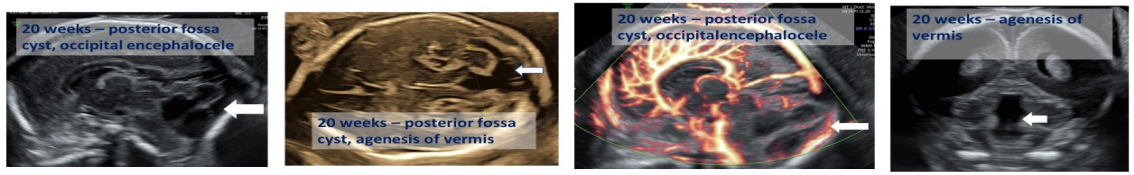
Encephalocele, is usually a congenital neural tube defect where brain tissue and overlying meninges herniate out through a defect in the cranium.
Joubert syndrome is an autosomal recessive cerebellar and brain stem malformation giving a distinctive 'molar tooth' appearance on axial images. It is characterized by aplasia or hypoplasia of the cerebellar vermis.
Another entity called Joubert syndrome and related disorders (JSRD) is used to describe individuals with Joubert syndrome who have additional findings, including occipital encephalocele.

Case Report

Presenting a case to highlight the Phenotypic and Genotypic Correlation of Joubert Syndrome in a case of occipital encephalocele with posterior fossa cyst.
A 26 year old G3P2L2 visited our facility for Nuchal Translucency scan at 12 weeks 6 days.
They are a non consanguineous couple.
Their first child is Alive and healthy. In the second pregnancy, agenesis of vermis was diagnosed at 34 weeks of gestation. The child passed away 15 days after birth.
Nuchal Translucency scan – Small occipital encephalocele (3mm) and a posterior fossa cyst. There were no other significant findings.
16 weeks – Confirmed the above findings.

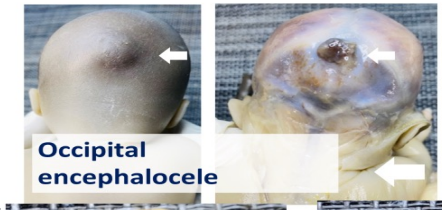
She under went Amniocentesis for Chromosomal Microarray and Whole Exome sequencing
Chromosomal Microarray- No significant copy number variants.
Whole exome sequencing - compound heterozygous for CPLANE 1 gene on Exon 17 and Exon 43, likely pathogenic variants for Joubert syndrome 17 (OMIM 614615) and Oro-Facio-Digital syndrome VI (OMIM 277170) respectively.
The fetus was also heterozygous for MKS1 gene on Exon 18, variant of uncertain significance for Meckel syndrome.

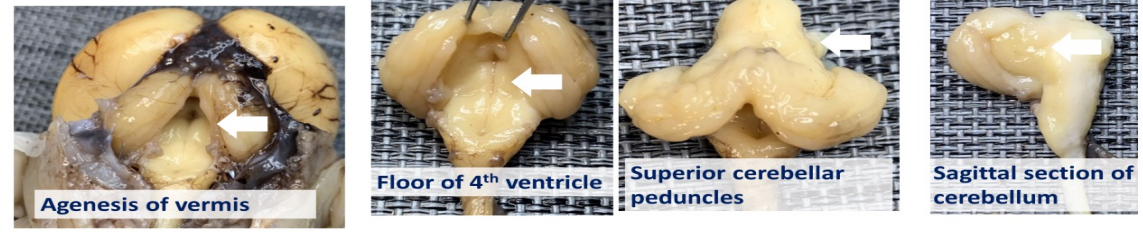
On Anomaly scan at 20 weeks there was agenesis of vermis, posterior fossa cyst and occipital encephalocele.



Case Report Continued

The couple opted for Medical Termination of pregnancy and submitted the fetus for Autopsy.
Fetal Autopsy confirmed agenesis of vermis, posterior fossa cyst and occipital encephalocele.





Discussion

Occipital encephaloceles (OE) are the most common form of encephaloceles (85%) and are manifested as a swelling of different sizes over the occipital bone in the midline.
The diagnosis is by neuroimaging corroborated by postnatal evaluation/ fetal autopsy.
Encephaloceles may be associated with chromosomal defects, mainly trisomy 13 or 18, are found in about 10% of cases.
Cerebral and non-cerebral defects and genetic syndromes are found in >60% of cases.
Common known associations include

- Chiari malformations, Dandy-Walker malformations
- Meckel-Gruber syndrome
- Walker Warburg Syndrome
- Amniotic Band Syndrome

Compound heterozygous mutations in CPLANE 1 gene is a rare association leading to the expression of the disease as Joubert syndrome.
Its combination with MKS1 gene in heterozygous state causing occipital encephalocele needs further evaluation.

Conclusion

Careful correlation phenotypic and genotypic features is necessary in the era of whole exome sequencing.This approach will enable appropriate counselling for future pregnancies.

References-

1 Radswiki T, Ashraf A, Yap J, et al. Encephalocele. Reference article, Radiopaedia.org

2. Parisi M, Glass I. Joubert Syndrome. 2003 Jul 9 [updated 2017 Jun 29]. In: Adam MP, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2023. PMID: 20301500.

3.Markovic I, Bosnjakovic P, Milenkovic Z. Occipital Encephalocele: Cause, Incidence, Neuroimaging and Surgical Management. Curr Pediatr Rev. 2020;16(3):200-205. doi:10.2174/1573396315666191018161535. PMID: 31656152; PMCID: PMC8193807.

4. Matos Cruz AJ, De Jesus O. Encephalocele. [Updated 2023 Feb 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562168/

5. The Fetal Medicine Foundation. (n.d.). The Fetal Medicine Foundation. https://fetalmedicine.org/education/fetal-abnormalities/brain/encephalocele