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Case Report: Radiogenomic Insights into Corpus Callosum Dysgenesis with Hypoplastic Septum Pellucidum

Case Report

Baby NM*

Department of Radiology, Government Medical College, Ernakulam, Kerala, India

***Corresponding author:** Nikita Mary Baby, Senior Resident, Department of Radiology Government Medical College, Ernakulam, Kerala, India. E-mail Id: nikita92.nmb@gmail.com

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Abstract

This case report presents a radiogenomic approach to a patient with MRI findings of Corpus Callosum Dysgenesis (CCD) and Hypoplastic Septum Pellucidum (HSP). By meticulously observing and documenting radiological data, we integrate these findings to identify the causative genetic mutations, predict the neurodevelopmental course, and guide treatment planning. This case and approach highlight the potential to leverage radiogenomics using routine MRI findings to improve therapeutic strategies.

Keywords: Corpus Callosum Dysgenesis; Hypoplastic Septum Pellucidum; Radiogenomics; Genetic Mutations; Neurodevelopmental Disorders; Magnetic Resonance Imaging (MRI).

Introduction

Corpus Callosum Dysgenesis (CCD) with Hypoplastic Septum Pellucidum (HSP) is a complex neurodevelopmental condition with diverse clinical manifestations. Radiogenomics, by integrating imaging findings with genetic analysis, enhances the understanding of genotype-phenotype correlations. Careful observation and documentation of radiological features serve as the cornerstone for identifying underlying genetic mutations. This report focuses on the radiogenomic evaluation of CCD and HSP, emphasizing the role of MRI in guiding genetic testing and personalized care. As noted by Rudas et al., "Corpus callosum malformations are frequently associated with other brain anomalies, including ventricular enlargement and cortical dysgenesis, which underscores the importance of early genetic evaluation" (Rudas et al., 2024)[1].

Case Presentation

Patient Information

- **Age:** 7 years
- **Gender:** Female

A 7-year-old female presented with significant developmental delays affecting cognitive, motor, and language functions.

Developmental History

The patient displayed an abnormal developmental trajectory from infancy, with delayed milestones such as late walking and persistent poor coordination. Early intervention therapies were initiated but showed limited improvement. Social challenges were also noted, including reduced engagement and difficulty communicating with peers.

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Family History

The family history was largely unremarkable for neurological conditions, except for the patient's maternal grandmother, who had developmental delays. This raised the possibility of a hereditary or carrier genetic condition.

The primary concerns included:

- Cognitive impairments: Difficulty with attention, memory, and language acquisition.
- Motor delays: Poor coordination, balance issues, and impaired fine motor skills.
- Speech delays: Challenges in articulation and comprehension.

Neurological Examination

Key findings from the neurological examination included:

- Hypotonia: Decreased muscle tone.
- Motor incoordination: Balance difficulties and fine motor impairments. No seizures or other overt neurological deficits were observed.

Imaging Findings

MRI Brain

Structural MRI revealed:

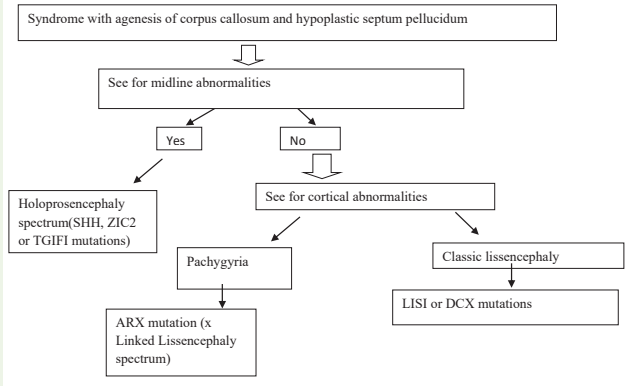
- Agenesis of the corpus callosum.
- Hypoplasia of the septum pellucidum.
- Mild ventricular enlargement.
- Pachygyria

CT Scan

CT confirmed the absence of the corpus callosum and provided additional details on ventricular morphology.CT scan was performed to rule out any associated corpus callosal lipoma.

Radiogenomic approach

The imaging findings indicate a disrupted neuronal migration and midline development.



Genetic Analysis

Genetic Testing

Whole-exome sequencing revealed a pathogenic missense mutation in the ARX gene (c.1234T>G), a mutation known to be associated with X-linked lissencephaly and CCD. This genetic finding correlated directly with the radiological abnormalities observed.

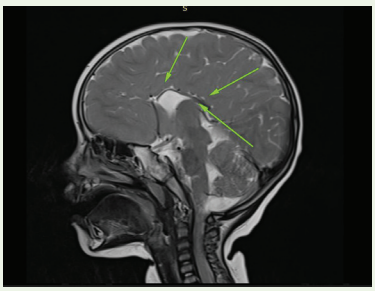


Figure 1: MRI demonstrates a dysgenetic corpus callosum with severe volume reduction, most pronounced in the rostrum and splenium. Additionally, the fornix and hippocampal commissure, part of the limbic system, are hypoplastic, along with the cingulate gyrus

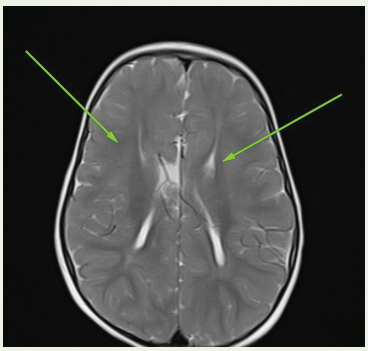


Figure 2: MRI shows bilateral lateral ventricles with parallel orientation, contrasting the normal bow-tie (racing car) configuration. Areas of pachygyria seen, characterized by broad, thickened gyri, indicating abnormal cortical development.

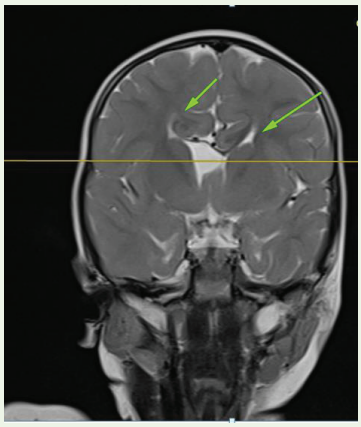


Figure 3: Coronal MRI illustrates the "Viking helmet" appearance of the lateral ventricles with steer-like frontal horn morphology.

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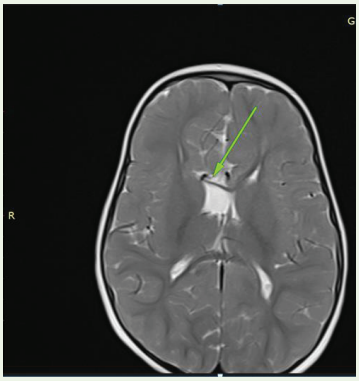

Figure 4: MRI reveals hypoplasia/absence of the septum pellucidum, with asymmetrically dilated frontal horn of the right lateral ventricle, resulting in a focal midline shift of 3mm to the left.

Discussion

Radiogenomic Correlation

The ARX mutation identified in this case aligns with hallmark radiological features, including corpus callosum agenesis, hypoplastic septum pellucidum, and pachygyria. As Al-Gazali et al. note, "ARX mutations are involved in a wide range of brain malformations, including lissencephaly and agenesis of the corpus callosum" (Al-Gazali et al., 2008)[2].

Value of Detailed MRI Observation

Careful analysis and documentation of MRI findings, such as recognizing CCD, hypoplasia of the septum pellucidum, and cortical malformations, prompted targeted genetic testing. Radiological features serve as a reliable guide for narrowing down potential genetic etiologies and streamlining the diagnostic process.

Impact on Treatment

Integrating radiogenomic insights enhances management by tailoring interventions:

- **Therapies for Cognitive and Motor Development:** Early intervention programs focusing on motor coordination and cognitive deficits.
- **Seizure Surveillance:** Anticipatory monitoring given the association of ARX mutations with epilepsy.
- **Genetic Counseling:** Recommendations for family planning and testing for carrier status.

Prioritizing Risk-Specific Interventions

Radiogenomic data can predict potential comorbidities, allowing for early intervention:

- **ARX-related CCD**: Focus on motor milestones due to hypotonia and cognitive rehabilitation for attention and memory deficits.
- **CCD with lissencephaly**: Intensive focus on seizure control, respiratory support, and multidisciplinary therapies for severe developmental delays.
- **CCD with pachygyria**: Tailored developmental programs addressing moderate delays with a better outlook for independence.

Conclusion

Radiogenomic evaluation begins with meticulous MRI analysis, serving as a bridge to genetic insights. **Only when a radiologist reports a case with radiogenomics in mind can they help the geneticist successfully derive the causative mutation.** Adopting a radiogenomic approach to a case is crucial to avoid missing subtle associated radiological findings that may otherwise be overlooked in the presence of more obvious and gross abnormalities (satisfaction of search error). Similarly, reporting negative findings helps exclude alternative genetic causes.

In this case, observing and documenting subtle imaging features like pachygyria and mild ventricular enlargement led to the identification of an ARX mutation. Likewise, documenting the absence of midline abnormalities associated with the holoprosencephaly spectrum helps exclude other genetic causes, refining the diagnosis and guiding personalized care. **An astutely reported MRI brain is a crucial tool for a genetic laboratory to narrow down genetic mutations in a child with developmental delay**. This approach underscores the potential of radiologists to enhance the understanding and management of complex neurodevelopmental disorders.

Acknowledgements

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Conflicts of Interest: The author declares no conflicts of interest related to this case report.

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