Type 2A Pontocerebellar Hypoplasia, A Rare Cause of Psychomotor Delay: A Case Report

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ABSTRACT

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| **Aims: This case report aims to describe a child with type 2A pontocerebellar hypoplasia (PCH2), whose clinical features were suggestive but non-specific, emphasizing the diagnostic value of neuroimaging and genetic testing.**  **Presentation of Case: A 4-year-old girl, born at term from a consanguineous marriage, presented with feeding difficulties, neonatal hypotonia, psychomotor delay, epilepsy, and dyskinesia from 5 months of age. Examination revealed microcephaly, failure to thrive, spasticity, and clonus. Brain MRI showed hypoplasia of the cerebellar vermis. EEG indicated background slowing; visual evoked potentials were normal. Genetic testing revealed a homozygous mutation in the TSEN54 gene (17q25.1), confirming PCH2. She was treated with Levetiracetam, Clobazam, and Trihexyphenidyl.**  **Discussion: PCH2 is a rare autosomal recessive neurogenetic disorder linked to TSEN54 mutations. It typically presents neonatally with motor, feeding, and respiratory dysfunction, later progressing to severe neurological impairment. Diagnosis is based on clinical, radiological, and genetic findings. Due to its hereditary nature, genetic counseling is critical.**  **Conclusion: This case highlights the need to consider PCH2 in infants with early-onset neurological symptoms. Neuroimaging and genetic studies are essential for diagnosis. Multidisciplinary care and genetic counseling are key in managing such patients.** |

*Keywords: Pontocerebellar hypoplasia, TSEN54, Neonatalhypotonia, Pediatric neurology*

1. INTRODUCTION

Pontocerebellar hypoplasia type 2 (PCH2) is a rare neurodegenerative and genetic disorder with autosomal recessive inheritance, with limited treatment options (1). PCH2 was first described by Bart in 1979 and was later better characterized through genetic studies, particularly in 2009, which identified the mutation in the **TSEN54** gene (2). It is characterized by pontocerebellar hypoplasia associated with progressive neocortical atrophy. It is the most common form of pontocerebellar hypoplasia.The clinical presentation in the neonatal period is typically marked by dysphagia, respiratory distress, and feeding difficulties.The diagnosis is based on a combination of clinical and neuroradiological findings. The genetic study confirms the diagnosis by identifying a **p.A307S mutation in the TSEN54 gene**, which is present in **ninety percent of cases** (3). Our objective is to describe the clinical, radiological, and genetic features through a medical case report.

1. CASE PRESENTATION

A 4-year-old girl, born at term via non-instrumental vaginal delivery, with no history of perinatal asphyxia, from a consanguineous marriage. There is no known family history of similar cases. Since the neonatal period, she has presented with feeding difficulties and axial hypotonia. At the age of 5 months, she exhibited psychomotor delay (absence of head control, standing position, and speech), generalized epilepsy, and dyskinesia. At the age of 3 years, she experienced an episode of bacterial pneumonia.

Clinical examination revealed microcephaly, failure to thrive, spasticity, and clonus of the extremities. Brain MRI performed at 1 year of age showed hypoplasia of the cerebellar vermis. No follow-up dynamic MRI has been conducted. EEGs performed at 5 months, 1 year, 2 years, and 4 years demonstrated slowing of background activity relative to her age. Genetic analysis, conducted at the age of 2, identified a homozygous autosomal mutation in the **TSEN54** gene, located on the long arm of chromosome 17 at **17q25.1**, confirming the diagnosis of **pontocerebellar hypoplasia type 2A**. Therapeutically, the child is being treated with **Levetiracetam**, **Clobazam**, and **Trihexyphenidyl**.

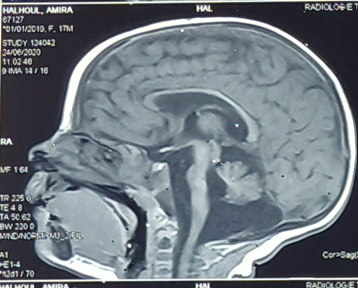


Figure : Sagittal section of a brain MRI showing cerebellar hypoplasia



Figure : Transversal section of a brain MRI showing vermian hypoplasia

1. discussion

Pontocerebellar Hypoplasia Type 2 is a rare and severe neurodegenerative disorder, primarily affecting psychomotor development.This autosomal recessive condition is characterized by the underdevelopment and degeneration of key structures in the brainstem and cerebellum, leading to profound neurological impairment, without signs of either spinal or peripheral involvement (4).

PCH2 typically presents with severe psychomotor delay, microcephaly, and early-onset extrapyramidal movement disorders such as chorea, dystonia, or dyskinesia. Neonatal symptoms often include feeding difficulties, respiratory issues, and clonus, which progress to more severe symptoms such as spasticity, epilepsy, and motor impairments. The clinical presentation can vary significantly, which has led to the identification of two distinct groups: one with dyskinesia/dystonia and severe infratentorial hypoplasia, and another with neonatal onset and polyhydramnios, hyperekplexia, and a more rigid, akinetic presentation. These differences highlight the complexity of the disease and underscore the importance of recognizing its varied manifestations (5) (6) (4) (7). Epilepsy is a frequently observed symptom, with a risk that increases with age, and can be very difficult to distinguish clinically from dyskinesias (8).

Imaging plays a crucial role in the diagnosis of PCH2, with MRI scans typically showing severe hypoplasia or flattening of the pons, cerebellar vermis, and hemispheres. The cerebellar structures often appear "wing-like," which can serve as a distinctive imaging feature. However, it is important to note that the severity of the neuroimaging findings does not always correlate with the clinical outcomes. This discrepancy emphasizes the importance of a comprehensive diagnostic approach that includes clinical, genetic, and radiological data (5) (9) (10).

Pontocerebellar hypoplasia type 2 is caused by mutations in the TSEN54 gene, located on chromosome 17, which is involved in the maturation of transfer RNAs (tRNAs). Mutations in this gene disrupt normal cellular processes, leading to cerebellar and pontine hypoplasia. The autosomal recessive inheritance pattern of PCH2 is commonly seen in consanguineous families, which further underscores the importance of genetic counseling and early diagnosis in affected populations (11).

In addition to the primary neurological manifestations, patients with PCH2 may experience other complications, such as episodes of rhabdomyolysis and, rarely, Reye-like syndrome (12). These complications highlight the need for comprehensive management strategies that address not only the central nervous system involvement but also other organ systems potentially affected by the disorder.

The differential diagnosis of pontocerebellar hypoplasia type 2A (PCH2A) includes other forms of PCH, particularly type 1, which is distinguished by associated spinal cord involvement, as well as types 4 and 6, which share some clinical and radiological features but differ in genetic origin and disease progression (13)(14). The CASK-related syndrome should also be considered, as its clinical presentation may mimic that of PCH2A, with a combination of microcephaly, hypotonia, epilepsy, and neurodevelopmental delay. However, it is differentiated by the potential presence of ophthalmological abnormalities (15)(16). Certain congenital malformations of the cerebellum or brainstem may resemble PCH2, but they are usually associated with other radiological findings, such as cysts or anomalies of the corpus callosum (15).

Treatment is symptomatic and focuses on managing dystonia, dyskinesia, and seizures, as well as feeding the patient through a percutaneous endoscopic gastrostomy tube.

This case highlights the importance of clinical examination during the neonatal period, as well as the need for early MRI and genetic counseling in cases of developmental delay.

1. Conclusion

Pontocerebellar hypoplasia type 2A is often fatal in early childhood. Potentially life-threatening complications include sleep apnea, rhabdomyolysis, and malignant hyperthermia. In the parents of an affected child, the risk of having another affected child is 25%, highlighting the importance of genetic counseling with targeted genetic testing in the parents. Despite recent advances, several questions remain unanswered, warranting further research, particularly regarding therapeutic possibilities.

Consent

As per international standards, parental written consent has been collected and preserved by the author(s).

Ethical approval

ETHICAL APPROVALAs per international standards or university standards written ethical approval has been collected and preserved by the author(s)

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

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