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Original Investigation | Neurology

"Bainbridge-Ropers Syndrome: An Overview"

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Key Points

Question:
What are the genetic basis and clinical characteristics of Bainbridge-Ropers Syndrome (BRS)?

Findings:
Genetics & Pathophysiology:
Caused by **ASXL3 gene mutations (18q12.1)**, primarily **loss-of-function variants in exons 11 & 12**.
Implicated in **chromatin remodelling**, leading to neurodevelopmental defects.
Clinical Features:
Feeding difficulties, hypotonia, intellectual disability, behavioral issues, dysmorphic facial features, and **musculoskeletal abnormalities**.
Wide phenotypic variability: symptom severity **does not strongly correlate** with mutation type.

Meaning:
Despite a shared genetic cause, **BRS presents with diverse symptoms**, influenced by genetic and environmental factors.
Further research is needed to establish **genotype-phenotype correlations**.

Abstract

Importance:
Bainbridge-Ropers syndrome (BRS) is a rare neurodevelopmental disorder associated with heterozygous pathogenic variants in the ASXL3 gene, located at 18q12.1. Despite increasing knowledge, BRS's Underlying genetic mechanisms and clinical spectrum remain poorly understood.

Aim of the study:
This review aims to provide an overview of BRS, focusing on its clinical features, genetic etiology, and current research and medical conditions. By consolidating the existing literature and highlighting gaps in knowledge, this review aims to deepen understanding of this challenge and inform future research.

Materials and Methods:
Embase and Google Scholar repositories were used to identify relevant studies published between 2000 and 2024. Inclusion criteria were limited to studies that provided original research data on patients with BRS and included clinical descriptions, genetic analyses, and clinical outcomes.

Results:
As of now, 108 cases of BRS have been published in the literature. The majority of reported variants are loss-of-function mutations found in exons 11 and 12. Clinically, the syndrome is commonly associated with feeding difficulties, hypotonia, distinctive facial features, severe intellectual disability, behavioral difficulties, and musculoskeletal features.
Phenotypic analysis revealed a wide range of clinical manifestations of BRS, including varying degrees of mental retardation, motor delay, and dysmorphic facial features. However, symptom severity did not directly correlate with specific ASXL3 mutations.

Discussion:
The identification of ASXL3 mutations as the major cause of BRS has unveiled a great deal about the molecular pathways that lead to this disorder. Abnormal gene expression due to the involvement of this gene in chromatin remodeling could be associated with the neurodevelopmental defects of BRS.

Conclusion and Relevance
Despite the common genetic etiology, the phenotypic diversity observed in BRS highlights the complex interplay between genetic and environmental factors. Further studies are needed to draw any meaningful conclusions about specific location genotype-phenotype correlations.

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