

Bainbridge-Ropers Syndrome in a Brazilian Child Associated with Duplicated Pyelocaliceal System: A Case Report

Letícia Ferreira Beserra ^{1,*}, Guilherme Aresi da Silva ¹, Sarah Cavalcanti Guedes ¹, João Guilherme Bezerra Alves ^{1,*}

¹ Institute of Integral Medicine Prof. Fernando Figueira (IMIP), Boa Vista, Recife, Pernambuco, Brazil.

* Correspondence: joaoguilherme@imip.org.br.

Abstract: Bainbridge-Ropers syndrome (BRPS) is a rare neurodevelopmental disorder caused by pathogenic variants in *ASXL3*. We report the first Brazilian pediatric case of BRPS associated with a duplicated pyelocaliceal system, adding evidence to a possible, but still poorly understood, relationship between *ASXL3* mutations and urinary system developmental abnormalities. The patient presented typical BRPS features, including hypotonia, severe developmental delay, feeding difficulties requiring gastrostomy, seizures, and craniofacial dysmorphisms. Additionally, renal imaging revealed a duplicated pyelocaliceal system, with preserved renal function. Whole-exome sequencing identified a de novo truncating *ASXL3* variant. This case reinforces the expanding phenotypic spectrum of BRPS and highlights the importance of comprehensive systemic assessment, including increased vigilance and consideration of renal evaluation, in children with syndromic features and global developmental delay. Early genetic testing remains essential to diagnostic confirmation and management planning.

Keywords: Bainbridge-Ropers Syndrome; *ASXL3*; Developmental Delay; Renal Abnormalities; Pyelocaliceal Duplication.

Citation: Beserra LF, Silva GA, Guedes SC, Alves JGB. Bainbridge-Ropers Syndrome in a Brazilian Child Associated with Duplicated Pyelocaliceal System: A Case Report. Brazilian Journal of Case Reports. 2026 Jan-Dec;06(1):bjcr152.

<https://doi.org/10.52600/2163-583X.bjcr.2026.6.1.bjcr152>

Received: 2 December 2025

Accepted: 18 January 2026

Published: 20 January 2026



Copyright: This work is licensed under a Creative Commons Attribution 4.0 International License (CC BY 4.0).

1. Introduction

Bainbridge-Ropers syndrome (BRPS) is a rare genetic neurodevelopmental disorder caused by pathogenic variants in the *ASXL3* gene located on chromosome 18q12.1 [1,2]. First described in 2013 by Bainbridge et al. [3], BRPS is characterized by developmental delay, intellectual disability, feeding difficulties, hypotonia, behavioral abnormalities, and distinctive craniofacial features. Diagnostic confirmation relies on molecular testing, primarily whole-exome sequencing. Although over 100 cases have been described worldwide [8,9], BRPS likely remains underdiagnosed, especially in low- and middle-income countries where access to genetic testing is limited. Renal anomalies are not commonly associated with BRPS, but Xiao et al. [10] reported congenital renal dysplasia in a child with *ASXL3* pathogenic variants, suggesting that urinary tract abnormalities might represent part of an expanded phenotype.

To our knowledge, no pediatric cases of BRPS have been reported in Brazil. We present the first Brazilian child with molecularly confirmed BRPS and a duplicated pyelocaliceal system, contributing to the refinement of the BRPS phenotypic spectrum.

2. Case Report

A male child was born at term (38 weeks) by cesarean section in Pernambuco, Brazil, following an uneventful pregnancy. Birth weight was 3050 g and 49 cm, with Apgar 9 at

5 minutes. There was no parental consanguinity or family history of similar conditions. Despite exclusive breastfeeding, the child developed feeding difficulties at 3 months of age, including vomiting, low oral acceptance, and failure to thrive. Investigation for gastrointestinal malformations (esophagogram and endoscopy) was unremarkable. A cow's milk protein-free diet was attempted without improvement. Due to progressive malnutrition, gastrostomy was performed at the end of the first year of life.

During hospitalization, hypotonia, delayed neuromotor development, and dysmorphic features were noted: ptosis, hypertelorism, strabismus, crowded teeth, a high-arched and narrow palate, epicanthal folds, and downward-slanting palpebral fissures (Figure 1). The child later exhibited speech delay, intellectual disability, and emotional lability, according to the evaluation of the psychology service, where the Emotional Regulation Checklist (ERC) and the Child Behavior Checklist (CBCL/6-18) were applied.

Figure 1. Ptosis, hypertelorism, strabismus, crowded teeth, epicanthal folds, and downward-slanting palpebral fissures.



Karyotype was normal. Whole-exome sequencing identified a heterozygous variant at chr18:31,323,140 C>CTCTT in *ASXL3*, predicted to cause an alanine-to-leucine substitution at position 1112 followed by a frameshift and premature termination. Parental testing confirmed the variant was de novo. At 2 years and 6 months, the child developed generalized tonic-clonic seizures. Brain MRI was normal, while EEG showed diffuse and asymmetric baseline rhythm disorganization. An electroneuromyography and metabolic screening (lactate, CPK, aldolase, LDH, ammonia, glucose, electrolytes, and venous blood gas) showed results within normal limits. Seizure control was achieved with sodium valproate, levetiracetam, and nitrazepam. Despite this, the child continued to exhibit the

global developmental delay and intellectual disability although there was no noticeable loss of milestones. At 3 years of age, after three episodes of urinary tract infection, renal ultrasound revealed duplication of the left pyelocaliceal system. DMSA scintigraphy showed normal relative renal function and no scarring.

3. Discussion and Conclusion

Since its original description in 2013, the phenotypic spectrum of BRPS has expanded substantially. Classic manifestations include severe developmental delay, feeding difficulties, failure to thrive, hypotonia, craniofacial dysmorphisms, and behavioral changes—all observed in this patient. Feeding problems are highly prevalent and frequently require gastrostomy, consistent with previously published reports [5–7].

Renal anomalies are not typically associated with BRPS; however, the duplicated pyelocaliceal system identified in this child mirrors the case described by Xiao et al. [10], who suggested a potential link between *ASXL3* expression in renal tissue and urinary tract development. More recently, Woods et al. [11] reported renal abnormalities in 15% of 64 individuals harboring pathogenic or likely pathogenic variants in the *ASXL3* gene. Reported abnormalities included vesicoureteral reflux, duplicated collecting systems, dysplastic kidneys, and hydronephrosis. The biological plausibility of this association is supported by molecular evidence demonstrating that *ASXL3* is expressed in the kidney and urinary tract, among other tissues, and functions as an epigenetic regulator involved in embryogenesis and organ development.

Our case provides additional evidence supporting a possible association between *ASXL3* variants and congenital renal abnormalities. Although a causal relationship cannot yet be established, the accumulation of clinical reports may help clarify whether renal screening should be incorporated into the routine evaluation of patients with BRPS. To our knowledge, this is the first pediatric case of BRPS reported in Brazil. Limited access to genetic testing may contribute to underdiagnosis in the region. Early recognition of syndromic features and timely genomic evaluation are essential for achieving an accurate diagnosis and guiding multidisciplinary management.

In conclusion, this case contributes to the growing understanding of BRPS and highlights urinary system developmental abnormalities as a potential component of the syndrome's phenotype. Further studies are required to elucidate the biological role of *ASXL3* in renal morphogenesis.

Funding: None.

Research Ethics Committee Approval: Written informed consent was obtained from the patient's legal guardian for participation in the study and for the explicit use of the child's clinical images in the publication. The journal made a specific and stringent request for express authorization regarding image publication, which was fully complied with by the authors. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. If required for verification, the signed informed consent form (TCLE) is available upon request from the corresponding authors or from the Brazilian Journal of Case Reports (BJCR).

Acknowledgments: None.

Conflicts of Interest: All other authors declare no conflicts of interest.

References

1. Balasubramanian M, Willoughby J, Fry AE, et al. Delineating the phenotypic spectrum of Bainbridge-Ropers syndrome: 12 new patients with de novo, heterozygous, loss-of-function mutations in *ASXL3* and review of published literature. *J Med Genet.* 2017;54:537–543. doi:10.1136/jmedgenet-2016-104360.
2. Trujillano L, Valenzuela I, Costa-Roger M, et al. Comprehensive clinical and genetic characterization of a Spanish cohort of 22 patients with Bainbridge-Ropers syndrome. *Clin Genet.* 2025;107(6):646–662. doi:10.1111/cge.14701.
3. Bainbridge MN, Hu H, Muzny DM, et al. De novo truncating mutations in *ASXL3* are associated with a novel clinical phenotype with similarities to Bohring-Opitz syndrome. *Genome Med.* 2013;5:11. doi:10.1186/gm415.

4. Aşık A, Fıncıoğulları EC, Avcı Durmuşoğlu E, et al. Dentofacial findings and management of two pediatric patients with Bainbridge-Ropers syndrome: a case report. *Am J Med Genet A*. 2025;197(8):e64090. doi:10.1002/ajmg.a.64090.
5. Cuddapah VA, Dubbs HA, Adang L, et al. Understanding the phenotypic spectrum of ASXL-related disease: Ten cases and a review of the literature. *Am J Med Genet A*. 2021;185(6):1700–1711. doi:10.1002/ajmg.a.62156.
6. Woods E, Holmes N, Albaba S, Evans IR, Balasubramanian M. ASXL3-related disorder: molecular phenotyping and comprehensive review providing insights into disease mechanism. *Clin Genet*. 2024;105(5):470–487.
7. Schirwani S, Albaba S, Carere DA, et al. Expanding the phenotype of ASXL3-related syndrome: a comprehensive description of 45 unpublished individuals with inherited and de novo pathogenic variants. *Am J Med Genet A*. 2021;185(11):3446–3458. doi:10.1002/ajmg.a.62465.
8. Xiao TS, Arce GC, Marron AR, Benitez GA, Schwanecke R. Bainbridge-Ropers syndrome in a Texan boy: a case report and review of the literature. *Cureus*. 2022;14(12):e32902. doi:10.7759/cureus.32902.
9. Zhang R, He XH, Lin HY, Yang XH. Bainbridge-Ropers syndrome with ASXL3 gene variation in a child: literature review. *Zhonghua Er Ke Za Zhi*. 2018;56(2):138–141.
10. Ikekwe JC, Osuagwu FC, LePlatte D, Ghaziuddin M. Comorbid psychiatric aspects of Bainbridge-Ropers syndrome. *Prim Care Companion CNS Disord*. 2021;23(3):20m02783. doi:10.4088/PCC.20m02783.
11. Woods E, Holmes N, Denommé-Picho AS et al. An International ASXL3 Natural History Study: Deep Phenotypic Analyses Including Detailed Reports of a Milder Phenotype, Novel Associations, and Clinical Recommendations. *Am J Med Genet A*. 2025;197(11):e64157. doi: 10.1002/ajmg.a.64157.