**The Open Public Health Journal**
*DOI: 10.2174/0118749445439139260204094639, 2026, 19, e18749445439139*
**ISSN: 1874-9445**


**CASE REPORT** **OPEN ACCESS**

# Williams Syndrome Presenting with Recurrent and Persistent Vomiting: A Case Report

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**Abstract:**

***Introduction:*** Williams-Beuren syndrome (WS) is a rare genetic condition caused by a microdeletion on chromosome 7q11.23. Gastrointestinal symptoms are relatively common in WS, but recurrent, intractable, or cyclic vomiting as an initial or dominant presenting feature is uncommon and can significantly delay diagnosis.

***Case Presentation:*** We describe an 11-month-old male infant who presented to the emergency department with persistent vomiting and signs of dehydration. The child had been admitted to the hospital three times over the preceding two months for identical complaints, with vomiting recurring shortly after each discharge. On examination, he displayed the classic dysmorphic facial features of Williams syndrome, including a broad forehead, periorbital fullness, stellate iris pattern, wide mouth, and full lips. A grade 3/6 systolic murmur was audible. Laboratory evaluation revealed severe hypercalcemia (serum calcium 14.2 mg/dL). Echocardiography confirmed supravalvular aortic stenosis with the typical "hourglass" appearance. Initial management of the hypercalcemia with intravenous fluids, furosemide, and corticosteroids proved largely ineffective. Introduction of cinacalcet, a calcimimetic agent, resulted in a rapid and sustained normalization of serum calcium levels. The clinical diagnosis of Williams-Beuren syndrome was made on the basis of the characteristic phenotype and cardiovascular findings; fluorescent *in situ* hybridization (FISH) or chromosomal microarray confirmation was not performed in this acute setting.

***Conclusion:*** This case illustrates that Williams-Beuren syndrome should be considered in the differential diagnosis of infants presenting with unexplained, recurrent, or cyclic vomiting accompanied by hypercalcemia. Prompt recognition of the syndrome is essential, as targeted management-particularly the use of cinacalcet for refractory hypercalcemia-can lead to rapid clinical improvement and help prevent long-term complications.

**Keywords:** Williams syndrome (WS), Hypercalcemia, Gastrointestinal, Cyclic vomiting, Supravalvular aortic stenosis, Cinacalcet.



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*Cite as:* Mirrashidi F, Raesi R, Daneshi S. Williams Syndrome Presenting with Recurrent and Persistent Vomiting: A Case Report. Open Public Health J, 2026; 19: e18749445439139. http://dx.doi.org/10.2174/0118749445439139260204094639

Received: September 09, 2025
Revised: November 28, 2025
Accepted: December 09, 2025
Published: March 16, 2026



## 1. INTRODUCTION

Williams-Beuren syndrome (WS) is a rare multisystem genetic disorder resulting from a heterozygous microdeletion at chromosome 7q11.23, with reported prevalence estimates ranging from 1 in 7,500 to 1 in 20,000 live births [1-3]. The clinical phenotype is highly variable but classically includes distinctive elfin-like facial features, supravalvular aortic stenosis or other cardiovascular anomalies, mild to moderate intellectual disability, a characteristic behavioral phenotype (often hypersociability and relative strengths in language and music), and failure

to thrive during infancy [3-5]. Idiopathic infantile hypercalcemia is documented in up to half of affected infants and is frequently implicated in gastrointestinal disturbances, including vomiting, constipation, anorexia, and feeding difficulties [6, 7]. Although gastrointestinal symptoms are well recognized in WS, recurrent, cyclic, or treatment-refractory vomiting as the predominant or initial manifestation is uncommon and can substantially delay recognition of the underlying genetic diagnosis [8, 9]. We describe an 11-month-old male infant who presented with severe, persistent vomiting and dehydration that had prompted three hospital admissions over the preceding two months, with rapid recurrence after each discharge despite conventional antiemetic and rehydration measures. Physical examination revealed the typical dysmorphic facial features of WS and a grade 3/6 systolic murmur. Laboratory evaluation confirmed severe hypercalcemia, and echocardiography demonstrated supravalvular aortic stenosis with the characteristic hourglass appearance.

Standard therapy for hypercalcemia (intravenous hydration, loop diuretics, and corticosteroids) was largely ineffective, but serum calcium levels normalized rapidly and remained stable after initiation of cinacalcet. The clinical diagnosis of Williams-Beuren syndrome was made on the basis of the characteristic phenotype and cardiovascular findings. Reporting this case is justified for several reasons. First, severe hypercalcemia presenting primarily as cyclic, refractory vomiting is an atypical and diagnostically challenging initial manifestation of WS, often leading to prolonged gastrointestinal investigations and repeated hospitalizations-particularly in settings where prompt genetic testing is not readily available. Second, the literature on management of infantile hypercalcemia in WS is limited, and published experience with cinacalcet in this specific context remains scarce. Third, by documenting the diagnostic pathway, biochemical course, and therapeutic response to cinacalcet, this report provides useful clinical detail, supports earlier consideration of WS in similar presentations, and contributes to the small body of evidence that may help inform treatment decisions in future pediatric cases with comparable features.

## 2. CASE PRESENTATION

An 11-month-old male infant was admitted to the emergency department with persistent vomiting and signs of dehydration. Over the previous two months, he had required three separate hospitalizations for identical symptoms. Each episode responded temporarily to intravenous fluids and supportive care, but vomiting recurred within days of discharge. This report has two primary objectives: first, to describe an uncommon initial presentation of Williams-Beuren syndrome in infancy-namely, recurrent and refractory vomiting attributable to severe hypercalcemia-and second, to document a therapeutic experience in which conventional measures (hydration, diuretics, and corticosteroids) failed to control the hypercalcemia, whereas cinacalcet resulted in rapid and sustained normalization of serum calcium.

### 2.1. Past Medical History

The pregnancy and perinatal period were uncomplicated. There was no family history of genetic syndromes, metabolic disorders, or consanguinity. Since birth, the infant's weight and length had consistently tracked below the 5th percentile. The parents reported recurrent episodes of irritability, poor feeding, and difficulty maintaining weight gain.

### 2.2. Physical Examination

On admission, the infant was irritable and moderately to severely dehydrated, with dry mucous membranes, reduced skin turgor, sunken fontanelle and eyes, and delayed capillary refill. Cardiovascular examination disclosed a grade II/VI systolic ejection murmur, loudest at the upper right sternal border, suggestive of supravalvular aortic stenosis (later confirmed by echocardiography). The abdomen was soft, non-distended, and without hepatosplenomegaly or palpable masses.

Characteristic dysmorphic facial features were evident, including a broad forehead, periorbital fullness, stellate iris pattern, short upturned nose with a broad nasal tip, full cheeks, wide mouth with full lips, and a small chin. Growth parameters remained below the 5th percentile for both weight and length, and the infant exhibited mild feeding difficulty and persistent irritability.

### 2.3. Laboratory Investigations

Laboratory evaluation on admission revealed the following:

Serum calcium: 14.5 mg/dL (reference range: 8.5–10.5 mg/dL)

Phosphorus: 4.4 mg/dL (reference range: 4.0–6.5 mg/dL)

Albumin: 4.1 g/dL (reference range: 3.5–5.0 g/dL)

Parathyroid hormone (PTH): 23 pg/mL (reference range: 10–65 pg/mL)

25-hydroxyvitamin D: 24 ng/mL (reference range: 20–50 ng/mL)

Creatinine: 0.4 mg/dL (reference range: 0.2–0.5 mg/dL)

Thyroid-stimulating hormone (TSH): 1.5 mIU/L (reference range: 0.5–5.0 mIU/L)

Urine calcium/creatinine ratio: 0.9 (age-adjusted upper limit of normal: <0.6)

### 2.4. Imaging

Renal ultrasonography showed no evidence of nephrocalcinosis or nephrolithiasis. Echocardiography demonstrated supravalvular aortic stenosis with the characteristic hourglass configuration and mild concentric left ventricular hypertrophy, consistent with the cardiovascular phenotype of Williams-Beuren syndrome.

### 2.5. Hospital Course

During the three previous admissions over the preceding two months, the patient had received

intravenous hydration, pantoprazole, famotidine, and oral laxatives, resulting only in transient symptomatic relief. Upper gastrointestinal endoscopy performed during one of the earlier admissions was normal. On the current admission, hypercalcemia persisted despite aggressive management with intravenous fluids, loop diuretics (furosemide), dietary calcium restriction, and short-term corticosteroids. Given the constellation of dysmorphic facial features, congenital heart disease, and refractory hypercalcemia, a clinical diagnosis of Williams-Beuren syndrome was established. Genetic confirmation *via* fluorescent *in situ* hybridization (FISH) or chromosomal microarray analysis was not feasible due to limited local resources. Cinacalcet, a calcimimetic agent, was initiated at a dose of 0.25 mg/kg/day. The patient showed rapid clinical improvement, with vomiting resolving within 48 hours and serum calcium normalizing from 14.5 mg/dL to within the reference range (≤10.5 mg/dL), corresponding to a minimum reduction of 27.6% in the first 48 hours. Calcium levels remained stable in the normal range thereafter. The infant was discharged in stable condition and remained asymptomatic during outpatient follow-up over the subsequent three months. To enhance clarity and readability, the biochemical course was illustrated with revised figures that provide a cleaner visualization of serum calcium trends over time, together with clearer labeling and incorporation of effect-size information to better demonstrate the magnitude and rapidity of the therapeutic response to cinacalcet.

## 3. DISCUSSION

Williams-Beuren syndrome (WS) is a multisystem genetic disorder with a highly variable phenotype. Core clinical features include distinctive elfin-like facial dysmorphism, congenital cardiovascular anomalies (most commonly supravalvular aortic stenosis), mild to moderate intellectual disability, a characteristic hypersociable behavioral profile, and failure to thrive in infancy [10, 11]. The diagnosis is usually established by demonstrating the characteristic microdeletion at 7q11.23 using fluorescence *in situ* hybridization (FISH) or chromosomal microarray analysis [10, 12]. Hypercalcemia occurs in 5–50% of infants with WS and frequently manifests with nonspecific symptoms such as irritability, vomiting, constipation, polyuria, dehydration, and poor feeding [1, 13, 14]. The underlying mechanisms remain incompletely understood but are thought to involve increased sensitivity to vitamin D, dysregulation of calcium homeostasis, and impaired renal calcium handling [15, 16]. In the majority of cases, hypercalcemia is transient and responds to conservative measures; however, severe or persistent hypercalcemia may necessitate pharmacologic therapy [6, 7].

Although gastrointestinal symptoms are relatively common in WS, recurrent, cyclic, or treatment-refractory vomiting as the predominant initial presentation is uncommon and can significantly delay recognition of the syndrome [17]. Such cases often prompt extensive gastrointestinal investigations (endoscopy, imaging, motility studies), repeated hospitalizations, and prolonged diagnostic uncertainty, particularly in resource-limited settings where genetic testing is not immediately accessible. The coexistence of dysmorphic facial features and congenital heart disease should prompt clinicians to consider a syndromic etiology rather than pursuing isolated gastrointestinal pathology [17, 18]. Standard initial management of hypercalcemia includes aggressive intravenous hydration, loop diuretics (furosemide), dietary calcium restriction, and, in some cases, short-term glucocorticoids or bisphosphonates [6, 19]. In refractory cases, cinacalcet-a calcimimetic agent that acts as an allosteric agonist of the calcium-sensing receptor-has been reported to effectively reduce serum calcium levels in patients with WS [20, 21]. In the present case, conventional measures were insufficient, but cinacalcet administration resulted in rapid normalization of serum calcium and complete resolution of vomiting, with sustained biochemical and clinical stability over three months of follow-up. Williams-Beuren syndrome is associated with considerable long-term morbidity arising from cardiovascular complications, neurodevelopmental impairment, endocrine disturbances (including hypercalcemia and hypogonadism), and other organ system involvement. Early recognition, multidisciplinary care (involving cardiology, endocrinology, developmental pediatrics, and genetics), and tailored interventions are essential to optimize outcomes and prevent avoidable complications [10, 22].

## 4. LIMITATIONS

A principal limitation of this case report is the absence of molecular confirmation of the 7q11.23 microdeletion. Fluorescence *in situ* hybridization (FISH) and chromosomal microarray analysis were not available locally, and referral for genetic testing was not pursued during the acute admission due to resource constraints. The diagnosis of Williams-Beuren syndrome was therefore established on clinical and echocardiographic criteria alone, relying on the presence of the characteristic facial phenotype and supravalvular aortic stenosis. This clinical diagnostic strategy is consistent with established diagnostic guidelines for WS in resource-limited settings and has been applied in several previously published cases where molecular testing was not immediately feasible. Nevertheless, the lack of genetic verification means that other phenotypically overlapping conditions cannot be completely excluded, and the ability to offer precise recurrence risk counseling or detailed genotype-phenotype correlation is restricted. In future cases, molecular confirmation is strongly recommended whenever diagnostic facilities permit, as it provides greater diagnostic certainty and supports more accurate prognostic assessment.

## CONCLUSION

This case draws attention to an unusual presentation of Williams–Beuren syndrome (WS), in which recurrent vomiting was the main clinical problem and only later was shown to be related to marked hypercalcemia. Gastrointestinal symptoms are known to occur in WS, but

vomiting as an isolated and dominant feature, without early cardiac or developmental abnormalities, is uncommon and can easily delay diagnosis. As a result, many infants undergo repeated hospital admissions and extensive gastrointestinal testing before a syndromic cause is suspected. When distinctive facial features are accompanied by a systolic murmur suggestive of supravalvular aortic stenosis and hypercalcemia that does not respond to routine treatment, WS should be considered even if genetic testing is not immediately available. This point is especially relevant in regions with limited access to molecular diagnostics. Our experience also adds to the small number of reports describing the use of cinacalcet in WS-related hypercalcemia. In this patient, standard measures-such as intravenous fluids, loop diuretics, dietary calcium restriction, and short-term corticosteroid therapy-did not achieve adequate biochemical control. After cinacalcet was introduced, serum calcium levels normalized quickly, vomiting resolved, and the child remained clinically stable during three months of follow-up. This response supports previous observations that cinacalcet may be a useful and well-tolerated option when first-line therapies are ineffective in children with WS. Early identification of WS is therefore important. A timely diagnosis makes it possible to treat acute metabolic disturbances promptly and to arrange appropriate long-term follow-up for cardiac, endocrine, developmental, and nutritional issues. Physicians in pediatrics, gastroenterology, endocrinology, and emergency care should keep WS in mind when an infant presents with otherwise unexplained recurrent vomiting together with hypercalcemia. Earlier recognition can reduce unnecessary investigations, prevent complications, and ultimately improve outcomes in this multisystem genetic condition.

## CLINICAL IMPLICATIONS

This case reminds clinicians that persistent vomiting together with high serum calcium in infancy should not be dismissed, even when early laboratory and gastrointestinal studies appear unrevealing. Although Williams–Beuren syndrome (WS) is rare, it deserves consideration when vomiting is recurrent or difficult to manage, particularly if there are subtle facial differences or mild cardiac findings in the background. Keeping WS in mind at this stage can shorten the diagnostic process and spare the child from unnecessary or invasive investigations. The favorable outcome seen after starting cinacalcet is also clinically meaningful. In children whose hypercalcemia does not improve with fluids, dietary measures, or other standard treatments, cinacalcet may provide effective biochemical control and symptom relief. Its use in this setting has the potential to reduce hospital admissions and improve daily functioning for affected infants and their families. Since WS involves multiple organ systems, ongoing follow-up with cardiology, endocrinology, and developmental services remains an important part of care.

## WHAT THIS CASE ADDS

This case describes an unusual early presentation of Williams–Beuren syndrome in which severe hypercalcemia led to recurrent, treatment-resistant vomiting and repeated hospital admissions for gastrointestinal evaluation. It also reports the effective use of cinacalcet in an infant after standard measures, including hydration, diuretics, and dietary calcium restriction, failed to control serum calcium levels, thereby contributing to the limited pediatric data on this therapy. In addition, the case highlights the practical importance of recognizing characteristic facial features and basic echocardiographic findings in supporting the diagnosis, particularly in settings where rapid genetic testing is not readily available.

## FUTURE PERSPECTIVES

Metabolic and gastrointestinal signs often appear early in WS, offering a chance for earlier detection. Clinicians would benefit from strategies that bring together lab tests, physical traits, and heart evaluations to identify patients promptly. Making rapid genetic tests, like microarray or FISH, more accessible-especially in under-resourced areas-could help confirm diagnoses sooner and allow treatment to start earlier. At the same time, long-term studies are needed to better understand how cinacalcet affects infants and young children with syndromic hypercalcemia, including both safety and effectiveness. Clear, practical treatment guidelines, including dosing and follow-up recommendations, could further improve care. Finally, educating general pediatricians and emergency physicians about the subtler presentations of syndromes like WS is essential for timely recognition and effective management in daily practice.

## AUTHORS' CONTRIBUTIONS

The authors confirm contribution to the paper as follows: F.S.M., and R.R.: Wrote the main manuscript text; S.D.: Designing the study and Supervision. All authors reviewed the manuscript.

## LIST OF ABBREVIATIONS

WS = Williams Syndrome / Williams-Beuren Syndrome

PTH = Parathyroid Hormone

TSH = Thyroid-Stimulating Hormone

FISH = Fluorescence *In Situ* Hybridization

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

## HUMAN AND ANIMAL RIGHTS

Not applicable.

## CONSENT FOR PUBLICATION

Written informed consent for publication of clinical information and images was obtained from the patient's legal guardians, and a signed copy is retained in the patient's medical record.

## STANDARDS OF REPORTING

CARE guidelines were followed.

## AVAILABILITY OF DATA AND MATERIALS

All data generated or analyzed during this study are included in this published article.

## FUNDING

None.

## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

## ACKNOWLEDGEMENTS

Declared none.

## REFERENCES

[1] Morris CA, Mervis CB. Williams syndrome. Cassidy and Allanson's Management of Genetic Syndromes,. Wiley 2021; pp. 1021-38. http://dx.doi.org/10.1002/9781119432692.ch63

[2] Morris CA. Introduction: Williams syndrome. Am J Med Genet C Semin Med Genet 2010; 154C(2): 203-8. http://dx.doi.org/10.1002/ajmg.c.30266

[3] Pober BR. Williams–Beuren Syndrome. N Engl J Med 2010; 362(3): 239-52. http://dx.doi.org/10.1056/NEJMra0903074 PMID: 20089974

[4] Lopes FDT. Deciphering the genetic basis of intellectual disability through unbiased genomic approaches. Thesis University of Minho 2017.

[5] Delio M, Pope K, Wang T, *et al*. Spectrum of elastin sequence variants and cardiovascular phenotypes in 49 patients with Williams–Beuren syndrome. Am J Med Genet A 2013; 161(3): 527-33. http://dx.doi.org/10.1002/ajmg.a.35784 PMID: 23401415

[6] Sindhar S, Lugo M, Levin MD, Danback JR. Hypercalcemia in Patients with Williams-Beuren Syndrome. J Pediatr 2016; 178: 254-260.e4. http://dx.doi.org/10.1016/j.jpeds.2016.07.037 PMID: 27592092

[7] Tersteeg S, Bakhutashvili V, Crook M, Ferris HA. Incidental diagnosis of williams syndrome in an adult with recurrent hypercalcemia. JCEM Case Reports 2023; 2(1): luad164. http://dx.doi.org/10.1210/jcemcr/luad164 PMID: 38169967

[8] Martens MA, Wilson SJ, Reutens DC. Research Review: Williams syndrome: A critical review of the cognitive, behavioral, and neuroanatomical phenotype. J Child Psychol Psychiatry 2008; 49(6): 576-608. http://dx.doi.org/10.1111/j.1469-7610.2008.01887.x PMID: 18489677

[9] Teixeira MCTV, Monteiro CR, Velloso RL, Kim CA, Carreiro LR. Behavioral and cognitive phenotype of children and adolescents with Williams-Beuren Syndrome. Pró-Fono Revista de Atualização Científica 2010; 22(3): 215-20. http://dx.doi.org/10.1590/S0104-56872010000300010 PMID: 21103708

[10] Kozel BA, Barak B, Kim CA, *et al*. Williams syndrome. Nat Rev Dis Primers 2021; 7(1): 42. http://dx.doi.org/10.1038/s41572-021-00276-z PMID: 34140529

[11] Meyer-Lindenberg A, Mervis CB, Faith Berman K. Neural mechanisms in Williams syndrome: A unique window to genetic influences on cognition and behaviour. Nat Rev Neurosci 2006; 7(5): 380-93. http://dx.doi.org/10.1038/nrn1906 PMID: 16760918

[12] Souza DH, Moretti-Ferreira D, Rugolo LMSS. Fluorescent *in situ* hybridization (FISH) as a diagnostic tool for Williams-Beuren syndrome. Genet Mol Biol 2007; 30(1): 17-20. http://dx.doi.org/10.1590/S1415-47572007000100005

[13] Helfrich AM, Philla KQ. Late-onset hypercalcemia in Williams-Beuren syndrome: importance of early and frequent screening and intervention. J Pediatr Endocrinol Metab 2015; 28(3-4): 425-8. PMID: 25332293

[14] Thom RP, Pober BR, McDougle CJ. Psychopharmacology of Williams syndrome: Safety, tolerability, and effectiveness. Expert Opin Drug Saf 2021; 20(3): 293-306. http://dx.doi.org/10.1080/14740338.2021.1867535 PMID: 33369485

[15] Lameris ALL, Geesing CLM, Hoenderop JGJ, Schreuder MF. Importance of dietary calcium and vitamin D in the treatment of hypercalcaemia in Williams-Beuren syndrome. J Pediatr Endocrinol Metab 2014; 27(7-8): 757-61. http://dx.doi.org/10.1515/jpem-2013-0229 PMID: 24572979

[16] Hsu SC, Levine MA. Perinatal calcium metabolism: Physiology and pathophysiology. Semin Neonatology 2004; 9(1): 23-36. http://dx.doi.org/10.1016/j.siny.2003.10.002

[17] Boechler M, Fu YP, Raja N, *et al*. Gastrointestinal manifestations in Williams syndrome: A prospective analysis of an adult and pediatric cohort. Am J Med Genet A 2024; 194(12): e63827. http://dx.doi.org/10.1002/ajmg.a.63827 PMID: 39073239

[18] Staiano A, Martinelli M. Motility problems in developmental disorders: cerebral palsy, down syndrome, william syndrome, familial dysautonomia, and mitochondrial disorders. In: Faure C, Thapar N, Di Lorenzo C, Eds. Pediatric Neurogastroenterology: Gastrointestinal Motility and Functional Disorders in Children. New York (NY): Springer 2012; pp. 285-92.

[19] Walker MD, Shane E. Hypercalcemia. JAMA 2022; 328(16): 1624-36. http://dx.doi.org/10.1001/jama.2022.18331 PMID: 36282253

[20] Tenhola S, Hendy GN, Valta H, *et al*. Cinacalcet treatment in an adolescent with concurrent 22q11. 2 deletion syndrome and familial hypocalciuric hypercalcemia type 3 caused by AP2S1 mutation. J Clin Endocrinol Metab 2015; 100(7): 2515-8. http://dx.doi.org/10.1210/jc.2015-1518 PMID: 25993639

[21] Chin A, Topor LS. Hypercalcemia. In: Srivastava T, Alon US, Eds. Endocrine Conditions in Pediatrics: A Practical Guide. Cham, Switzerland: Springer Nature 2020; pp. 39-46. http://dx.doi.org/10.1007/978-3-030-52215-5_6

[22] Carrasco X, Castillo S, Aravena T, Rothhammer P, Aboitiz F. Williams syndrome: Pediatric, neurologic, and cognitive development. Pediatr Neurol 2005; 32(3): 166-72. http://dx.doi.org/10.1016/j.pediatrneurol.2004.09.013 PMID: 15730896