American Journal of Psychiatry and Neuroscience
2025, Vol. 13, No. 4, pp. 132–137
https://doi.org/10.11648/j.ajpn.20251304.13

Case Report

From Genetics to Psychiatry: Long-Term Psychiatric Management of Williams Syndrome with a Rare Variant of Congenital Adrenal Hyperplasia

Farsana Banu, Murugavel Veeramani*, Akshay Ajith, Syam Unnikrishnan

Department of Psychiatry, ESIC Medical College and Hospital, Chennai, India

Abstract

This case report presents a 19-year-old male with an exceptionally rare co-occurrence of Williams-Beuren Syndrome (WBS) and 17α-hydroxylase deficiency, a form of congenital adrenal hyperplasia (CAH). Diagnosed with CAH in infancy due to hypertension, hypokalaemia, and ambiguous genitalia, and later confirmed to have WBS via fluorescence in situ hybridization (FISH), the patient exhibited global developmental delays, intellectual disability, recurrent seizures, and poor medication adherence. Psychiatric referral at age 18 was prompted by escalating aggression, self-injurious behaviour, and functional decline. A multidisciplinary intervention was initiated, combining behavioural therapy based on the Antecedent-Behaviour-Consequence (ABC) framework, low-dose risperidone, psychoeducation for caregivers, and vocational rehabilitation. Over six months, the patient demonstrated marked improvement in aggression, seizure control, and compliance with daily routines. He remained seizure-free on sodium valproate and began contributing to household income through structured vocational engagement. This case underscores the importance of integrated psychiatric care in managing syndromic intellectual disability, particularly when compounded by rare endocrine disorders. The estimated statistical frequency of this genetic overlap is approximately 1 in 500 million, posing unique diagnostic and therapeutic challenges. The report highlights the need for early genetic evaluation, coordinated interdepartmental care, and family-centered interventions to optimize outcomes. It also emphasizes the utility of structured behavioural frameworks and low-dose antipsychotics in managing irritability and aggression in syndromic populations. In resource-limited settings, sustained caregiver involvement and interdisciplinary collaboration are critical to improving quality of life and long-term prognosis. This case advocates for enhanced training in syndromic psychiatry and integrated care models to address the complex needs of individuals with overlapping genetic and endocrine conditions.

Keywords

Williams-Beuren Syndrome, 17α-hydroxylase Deficiency, Congenital Adrenal Hyperplasia, Intellectual Disability, Behavioural Therapy, Risperidone, Multidisciplinary Care, ABC Model

*Corresponding author: murugavelveeramani@gmail.com (Murugavel Veeramani)

Received: 29 October 2025; **Accepted:** 7 November 2025; **Published:** 9 December 2025

1. Introduction

The coexistence of multiple rare genetic and endocrine disorders in a single individual presents a unique diagnostic and therapeutic challenge. This case report describes a 19-year-old male with Williams syndrome and 17 alpha-hydroxylase deficiency—a rare form of congenital adrenal hyperplasia (CAH)—who has experienced a complex clinical trajectory marked by intellectual disability, behavioural disturbances, and multisystem involvement.

Williams syndrome is a genetic disorder caused by a microdeletion at chromosome 7q11.23, affecting the elastin gene [1]. WBS is usually sporadic, caused by de novo deletions, although autosomal dominant inheritance has also been reported. The syndrome has an estimated prevalence of 1 in 7,500 to 20,000 live births [2, 3]. It is characterized by distinctive facial features, cardiovascular anomalies (most commonly supra-valvular aortic stenosis), a variety of gastrointestinal and endocrine symptoms, intellectual disability, and a unique behavioural phenotype including hyper sociability and anxiety [4].

17 alpha-hydroxylase deficiency, on the other hand, is a rare autosomal recessive form of CAH, accounting for less than 1% of all CAH cases [5]. It results from mutations in the CYP17A1 gene, leading to impaired synthesis of cortisol and sex steroids, and excess mineralocorticoids [6]. Clinically, it manifests as hypertension, hypokalemia, sexual infantilism, and ambiguous genitalia in genetic males [7].

The coexistence of Williams-Beuren Syndrome (WBS) and 17 alpha-hydroxylase enzyme deficiency type of Congenital Adrenal Hyperplasia (CAH) is exceptionally rare, with an estimated statistical frequency of 1 in 500 million. This case report presents a unique genetic overlap, detailing the comprehensive clinical presentation, diagnostic challenges, interdisciplinary management, and long-term outcomes. It underscores the critical importance of a multidisciplinary approach in caring for patients with overlapping genetic and endocrine disorders. Early diagnosis, coordinated care, and tailored behavioural and pharmacological interventions are essential to improving quality of life and functional independence in such complex cases.

2. Case Description

A boy in his early twenties, who is a known case of William syndrome (Figure 1) and 17 alpha hydroxylase enzyme deficiency, belonging to a lower socioeconomic status, has been under regular follow up in multiple departments in our tertiary healthcare hospital since birth. He was referred to the psychiatry department 1 year back from neurology, due to aggressiveness and self-injurious behaviour. When he was 15 years of age, his mother started to notice his aggressive behaviour. He would refuse to get up from bed and go to special school. He would throw things at family member and say inappropriate words when asked to do things which he didn't like, for example going to school, doing small household chores or eating food he didn't like. His self-care, social interactive and academic skills were in further decline. This aggressive and adamant behaviour continued to worsen over the years. He completely stopped going to special school and taking medications. It got harder for his parents to bring him to the hospital for follow ups and because of not taking anti epileptics he ended up suffering from recurrent seizures.

A developmental history indicated that he had a normal full term vaginal birth with birth weight around 3 kg. He didn't walk until 18 months of age. He started speaking single words only after 1-year-old of age. He was not able to do toilet training until 4 years of age. His parents described him as a slower learning compared to their other children in his house.

Binet Kamat test done at the age of 6 gave a score of 44, indicating moderate intellectual disability.

About the family history, he was the fifth in birth order and the third surviving child of second-degree consanguineous parents. (Figure 2) The first two siblings, both with ambiguous genitalia, died in the neonatal period due to low birthweight and was suspected to have congenital adrenal hyperplasia (CAH). Subsequently, the mother received antenatal dexamethasone for each pregnancy. The third child, a female with clitoromegaly, was diagnosed with CAH and started on hydrocortisone early, achieving puberty at 15 years. The fourth child, a male, is healthy. There is no family history of CAH, genetic syndromes nor psychiatric illnesses.

Figure 1. *Salient features of Williams syndrome (A-Elfin facies, B-Micro dentition and C-Kyphosis).*

About his past medical history, at around one month age, he presented with multiple episodes of vomiting; he was hypertensive, had hypokalemia, hypernatremia and decreased serum 17-hydroxyprogesterone. A diagnosis of 17 alpha hydroxylase enzyme deficiency type of Congenital Adrenal Hyperplasia was made. He was started on oral steroids and antihypertensives.

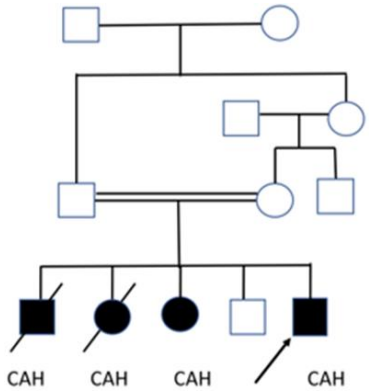

Figure 2. *Pedigree chart.*

By age 3, abdominal ultrasound revealed small kidneys and right kidney mal-rotation. He also had recurrent seizures for which he was started on Tab. Sodium Valproate. Around age 4, he was diagnosed with aortic stenosis with bicuspid aortic valve and underwent Balloon Aortic Valvotomy. A decade later, he developed severe supra-annular aortic stenosis and Open Aortic Valvotomy with Gore-Tex patch repair was done. Around the age of 10, Williams syndrome was suspected based on characteristic facies and congenital anomalies and then confirmed via fluorescence in situ hybridization (FISH). Around the age of 12, bilateral orchidopexy was performed for undescended testes. Delayed pubic hair development suggested late onset of secondary sexual characteristics.

On examination, he has short stature with scoliosis and is underweight (Height: 140 cm, Weight: 34 kg, BMI: 17.3 kg/m ^{3}). He has elfin facies, characterized by a broad forehead, low hairline, widely spaced eyes, low set ears and micro dentition. Facial, pubic and axillary hair are absent. His skin shows generalized hyperpigmentation which has increased over the years.

Cardiovascular examination revealed an ejection systolic murmur (grade 3/6), suggesting a residual aortic stenosis. On central nervous system examination, hypotonia with muscle power of grade 4/5 was present.

On Mental State Examination, he was ill kempt with shabby clothes. Rapport was established with difficulty, with sustained eye contact and was in touch with surroundings. Speech had decreased tone, tempo, volume and amount and affect was irritable. However, he is occasionally overly friendly with an inappropriate smile. Higher mental functions revealed he was attentive but concentration was not sustained. General fund of intelligence is lacking. Concrete abstract thinking, Impaired personal and social judgment was present with absent insight.

The patient was admitted under psychiatric care for evaluation and management of persistent aggression and behavioural disturbances. A detailed behavioural analysis was conducted using the Antecedent-Behaviour-Consequence (ABC) framework to identify specific triggers, problematic behaviours, and their outcomes. Events that could serve as positive reinforces—such as his favorite food, watching television, receiving praise, and going outdoors—were identified, along with negative reinforces like the time-out method. His parents were educated about these behavioural cues and trained to implement reinforcement strategies to manage noncompliance and aggression at home. Alongside behavioural interventions, the patient was initiated on a low dose of T. Risperidone 1 mg to reduce irritability. Over a six-month period, there was a marked reduction in aggressive outbursts and improved compliance with daily routines. Psychoeducation sessions were conducted for the parents, focusing on understanding the patient's syndromic conditions, the importance of regular medical follow-ups, and adherence to prescribed treatments.

With sustained psychiatric and neurological support, the patient has remained seizure-free with Tab. Sodium Valproate 400 mg for over a year. He continues to attend monthly follow-up appointments and is actively involved in vocational rehabilitation. He now performs basic mechanical tasks at a nearby shop, earning a modest income and contributing meaningfully to his family's financial needs.

3. Discussion

Individuals with intellectual disability (ID) are disproportionately affected by multi-morbidity, encompassing physical, psychiatric, and social challenges that often worsen during their life span [8]. Despite this their care pathways remain fragmented across disciplines. Historically, management strategies have been isolated with each department operating within its own framework, often without coordinated input from other specialties. This piecemeal approach not only undermines continuity of care but also obscures the complex interplay between neurodevelopmental, psychiatric, medical, and social determinants of health.

Intellectual disability and behavioural disturbances are core neurodevelopmental features seen in children with genetic syndromes such as Williams–Beuren Syndrome (WBS). In the present case, the patient demonstrated global developmental delays in early childhood, with poor academic performance that prompted formal cognitive assessment. The Binet Kamat Test of Intelligence revealed moderate intellectual disability, consistent with previous studies, which report that approximately 75% of individuals with WBS fall within the borderline to mild intellectual disability range [9].

Congenital adrenal hyperplasia is never associated with systemic structural abnormalities and is usually not associated with neurodevelopmental disorders unless in cases of salt-wasting adrenal crisis-induced brain damage [10]. Hence, when this patient got diagnosed with Aortic stenosis, intellectual disability, and renal anomalies, these had to be considered manifestations of another syndrome. When the child grew up, dysmorphic facies in a background of intellectual disability and severe Aortic stenosis, William syndrome was suspected and then diagnosed through Fluorescent in situ hybridization. Fluorescent in situ hybridization is one of the most commonly used laboratory tests to detect the 7q11.23

microdeletion seen in Williams [4].

The family history reveals consanguinity and multiple affected siblings, including neonatal deaths with ambiguous genitalia and a sister with CAH. This pattern suggests autosomal recessive inheritance of CAH and highlights the importance of genetic counselling. Antenatal dexamethasone was administered in subsequent pregnancies, reflecting awareness of prenatal interventions. However, the recurrence of CAH and syndromic features in this child underscores the need for comprehensive genetic evaluation and counselling for future reproductive planning.

Standardized tools like the PAS-ADD (Psychiatric Assessment Schedule for Adults with Developmental Disabilities) have identified mental health problems in 24% of adults with Williams syndrome [11]. This was observed in the current case, where the patient was described as overly friendly with an inappropriate smile during mental status examination. However, this sociability is often accompanied by behavioural dysregulation, irritability, and emotional outbursts.

Health seeking behaviour is very poor among adults with Intellectual disability, hence family members and their understanding play a major role in their care [12]. A systematic review done on this topic, showed that family-centered care is the best way for developing care plans for children with intellectual disability [13]. Psychoeducation sessions for caregivers emphasized the importance of medication adherence, regular follow-ups, and understanding the syndromic nature of the patient's condition.

Pharmacological management with low-dose risperidone (1 mg) led to a significant reduction in irritability and aggression over six months. Risperidone is commonly used in syndromic intellectual disability for managing irritability and aggression, with evidence supporting its efficacy and tolerability in low doses [14].

Teaching strategies for school going patients include using tape recorders, computers or even phonetic methods which plays to their strength of language skills over visuospatial skills. Furthermore, positive reinforcement, minor environmental modifications, and specific educational interventions help in managing any behavioural disturbances that is coupled with intellectual disability. The ABC framework for assessing behavioural disturbances proved efficient in alleviate overall aggression and impulsivity [15, 16]. Here in this the child, a diagnosis of two rare genetic disorders is made. Even in this complicated case psychiatry can play a role.

Although the management of cases with multiple genetic syndromes is possible, it remains difficult especially in low resource settings. A combined approach involving health care professionals, social workers and teachers are necessary for increasing the survivability and quality of life of such cases.

4. Conclusions

Our case report highlights how structured multidisciplinary involvement particularly psychiatric expertise can enhance diagnostic clarity, therapeutic outcomes, and long-term quality of life for individuals with intellectual disability. We should develop active inter-disciplinary training for faculties and residents to improve treatment outcomes.

Abbreviations

WBS	Williams Beuren Syndrome
CAH	Congenital Adrenal Hyperplasia
FISH	Fluorescence in Situ Hybridization
ABC	Antecedent Behavior Consequence
PAS-ADD	Psychiatric Assessment Schedule for Adults with Developmental Disabilities

Author Contributions

Farsana Banu: Conceptualization, Writing – original draft

Murugavel Veeramani: Supervision, Writing – review & editing

Akshay Ajith: Writing – review & editing

Syam Unnikrishnan: Conceptualization, Supervision

Funding

This work is not supported by any external funding.

Data Availability Statement

Not applicable.

Conflicts of Interest

The authors declare no conflicts of interest.

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Biography

Farsana Banu, M.D (Psychiatry), is a dedicated psychiatrist currently serving as a Senior Resident at ESIC Medical College, Chennai. A gold medalist in MD Psychiatry from JIPMER, Puducherry, she has demonstrated excellence in both clinical practice and academic pursuits. Her medical journey began with an MBBS from Kerala University of Health Sciences, followed by specialized training in diverse psychiatric domains including peri-partum psychiatry, de-addiction, psychosexual health, Neuropsychiatrist and child and adolescent psychiatry. She had actively contributed to research, with studies exploring psychotic symptoms and cognitive impairment, as well as the link between sunshine hours and suicide rates. She has participated in numerous national and international CMEs and webinars, reflecting her commitment to continuous learning. Passionate about teaching, she has mentored MBBS and PG students in both theory and clinical settings.

Murugavel Veeramani, MBBS, DPM, DNB (Psychiatry), is a dedicated psychiatrist with over eleven years of clinical experience. Currently, he serves as an Assistant professor in the Department of Psychiatry at ESIC Medical College and Hospital, KK Nagar, Chennai. He completed his MBBS from Chengalpattu Government Medical College, followed by a Diploma in Psychological Medicine (DPM) from the Institute of Mental Health, Madras Medical College. He further specialized with a DNB in Psychiatry at the Schizophrenia Research Foundation (SCARF), Chennai. He has worked across general hospital and rehabilitation settings, with a special focus on de-addiction psychiatry and geriatric mental health. His therapeutic expertise includes cognitive behavioural therapy, motivational enhancement therapy and neuromodulation techniques like ECT and tDCS. He has contributed to academic forums through presentations and publications, and actively engages in psychiatric education.

Akshay Ajith, MBBS, is currently pursuing his MD in Psychiatry as a first-year resident at ESIC Medical College and Hospital, Chennai. He completed his MBBS from Government Medical College, Thiruvananthapuram, where he developed a strong interest in Psychiatry and excelled in multiple quiz competitions in Psychiatry and other medical subjects. After graduation, he gained valuable clinical experience working as a Medical Officer in private clinics and hospitals. Now, eight months into his postgraduate training, he has actively contributed to academic activities by conducting Psychiatry quizzes for undergraduates and engaging in research and conference presentations. He has also been recognized with Best Poster Awards at medical conferences as a first-year resident. As part of his residency duties, Dr. Akshay is involved in the management of Psychiatry and De-addiction wards, and regularly assists in administering Electroconvulsive Therapy (ECT) under the supervision of his professors. Through these experiences, he continues to develop his clinical acumen and commitment to becoming a compassionate and skilled psychiatrist.

Syam Unnikrishnan, D. M (Neurology)., Post Graduate Degree in Palliative care (Cardiff University, UK)., is a distinguished neurologist with over three decades of clinical, academic, and research experience. Currently serving as Head of Neurology at ESIC Medical College, Chennai, he has held key positions across premier institutions including NIMHANS, SGPGIMS, and SCTIMST. His expertise spans neuro-rehabilitation, epilepsy in women, and community-based palliative neurology. A prolific researcher and speaker, he has contributed to numerous international conferences and peer-reviewed journals. He has more than 450 citations and 216 research index score. Dr. Syam is also a Commonwealth Scholar and recipient of the Award of Excellence in Social Service. His work reflects a deep commitment to compassionate, inclusive neurological care.

Research Fields

Farsana Banu: Perinatal mental health, De-addiction psychiatry, Child psychiatry, Consultation liaison psychiatry, neuropsychiatry

Murugavel Veeramani: De-addiction psychiatry, Dementia, Consultation liaison psychiatry, Psychopharmacology, Neuropsychiatry, non-invasive brain stimulation.

Akshay Ajith: De-addiction psychiatry, Consultation liaison psychiatry, Psychopharmacology, Neuropsychiatry, schizophrenia

Syam Unnikrishnan: neuro developmental disorders, neuro-rehabilitation, neuropsychiatric disorders, epilepsy in women, and community-based palliative neurology