



(CASE REPORT)



A case of delayed diagnosis of Williams-Beuren syndrome

Bouchra Aabbassi ^{1,*} and Fatiha Manoudi ²

¹ Child, health and development Research Laboratory, Faculty of Medicine and Pharmacy of Marrakesh, Morocco.

² Psychiatric department, UHC Mohamed VI, Marrakesh, Morocco.

World Journal of Advanced Research and Reviews, 2023, 18(03), 410–412

Publication history: Received on 29 April 2023; revised on 08 June 2023; accepted on 12 June 2023

Corresponding author: aabbassi40@gmail.com

Article DOI: <https://doi.org/10.30574/wjarr.2023.18.3.1087>

Abstract

Williams or Williams-Beuren syndrome (SWB) is a rare, sporadic and non-hereditary genetic disease, relating to a chromosomal microdeletion at 7q11.23. It is a disorder that affects multiple systems. We deploy a case of a girl in whom the diagnosis of SWB was made by the child psychiatrist at the age of six despite having consulted the front line many times long before. Many children with this disease, as all rare diseases, do not benefit from early diagnosis due to poor doctors' knowledge of this entity. the purpose of this article is to highlight the delay in the diagnosis of this entity by childhood practitioners, which can delay treatment and sometimes worsen the prognosis of evolution.

Keywords: Williams syndrome; Williams-Beuren syndrome; Child psychiatrist; Diagnosis; Case report

1. Introduction

Williams or Williams-Beuren syndrome (SWB) is a rare, sporadic and non-hereditary genetic disease, relating to a chromosomal microdeletion at 7q11.23. It is a disorder that affects multiple systems. It is essentially characterized by facial dysmorphism, cardiovascular malformations and a specific neuropsychological profile. However, it remains unknown to clinicians. Many children with this disease, like all rare diseases, do not benefit from early diagnosis. This leads to a real diagnostic delay and a rather disjointed care circuit. This will not be without consequences for the child. We deploy a case of a girl in whom the diagnosis of SWB syndrome was made by the child psychiatrist at the age of six despite having consulted front-line clinicians many times long before.

2. Case report

A. is six years old child who consults in child psychiatry, accompanied by her two parents for school learning difficulties. She is still in the middle section of kindergarten. Parents who have consulted several pediatricians since the age of three for global psychomotor retardation. The little girl benefited from rehabilitation sessions in psychomotricity and speech therapy but “with timid progress”, says the father. Apart from these complaints, A. had no personal or family history of organic or psychiatric illness. Nevertheless, a deafness assessment was carried out three years ago to explore the origin of the oral language delay. The current psychiatric evaluation finds a jovial girl, with familiar contact, with an endearing gaze, her language is still poorly articulated. She is motorally unstable but without noticeable clumsiness. Regarding learning, the girl does not yet have access to reading or writing. The drawing is reduced to scribbles. Furthermore, we find no signs of depression, anxiety or environmental dysfunction. The parents seem committed and invested in their little girl to the point of postponing any decision to have a second child for fear of abandoning their girl. She has a face with a small chin, a wide and full-lipped smile, a wide forehead and a flat nasal bridge. These dysmorphic and behavioral traits are reminiscent of the Williams-Beuren syndrome. Genetic counseling confirms the diagnosis. Somatic evaluation

* Corresponding author: Bouchra Aabbassi

revealed slight weight loss and supra-ventricular aortic stenosis without functional repercussions. The neurocognitive assessment concluded to a mild to moderate intellectual disability. So multidisciplinary care was proposed: regular pediatric follow-up combined with developmental child psychiatry follow-up, parental guidance, individual psychotherapy, speech therapy focused on expressive language and writing, psychomotricity sessions. The girl was able to join an association for children carrying Williams Beuren. She is currently in the first year of elementary school. Apart from difficulties in managing her emotional outbursts, she progresses in school.

3. Discussion

SWB is a developmental anomaly described for the first time in 1961. The genetic cause was identified in 1993: it is a microdeletion of the chromosomal region 7q11.23 leading to the loss of an allele of 26 to 28 genes on one of the two chromosomes 7 [1, 2]. One of these genes is for elastin and other genes involved in hypercalcemia, growth retardation, intellectual disability and behavioral disorders. It has been estimated that the prevalence of WBS is approximately 1/75001/20,000 [2,3]. The clinical manifestations include:

- Cardiovascular disease: elastin defect arteriopathy, supra-ventricular aortic stenosis, stenosis of the branches of the pulmonary artery, arterial hypertension.
- An evocative facial morphology: a broad forehead, bitemporal narrowing, periorbital fullness, an iris with star and/or lace patterns, a short, upturned nose with a bulbous tip, a long philtrum, a wide mouth, full lips and mild micrognathia. This dysmorphism is inconstant; which can explain the deviations in the clinical assessment.
- Retarded growth of weight and height
- Neonatal hypercalcemia in 15% of cases
- Digestive disorders such gastroesophageal reflux in early childhood or colonic diverticulosis at any age
- Moderate intellectual disability
- A specific cognitive profile characterized by great difficulties in the visual and spatial domain contrasting with an apparently correct language
- A rather specific behavior or hypersociable type, approaching others easily. Children have a hypersensitivity to noise and a disposition for music, great language faculties, as well as a good auditory memory.
- Anxiety remains the most common psychiatric comorbidity in 54% of patients. Psychotic symptoms are exceptional but may occur in adolescence [2].

However, poor doctors' knowledge of this entity can make the delay of diagnosis until an advanced age. In this case, the characteristic behavioral profile is a good clue to orient clinicians to diagnosis, towards the 5-6 years old. The positive diagnosis is confirmed by chromosomal analysis called FISH test [4]. The standard karyotype is often normal. The announcement of the diagnosis is an essential step in the care process: the explanation of the diagnosis, the planning of the care and follow-up, with the description of the multidisciplinary team that will provide it. Information on the natural history and prognosis of the SWB syndrome, on the treatments prescribed, their possible adverse effects; on the need for regular follow-up and on the planning of the examinations necessary for diagnosis, monitoring of the disease or screening for possible complications. It is also essential to emphasize that the parents are not the cause of this trouble; it is an accidental disease that can occur in any family. This information reassures the parents and frees them from the unconscious pressure of guilt towards their child, as was the case with our patient. Our patient's parents were more engaged and collaborative in caring for their child after the announcement. They even thought about having a new child in the same year of follow-up, while the couple was reluctant to this idea before. However genetic counseling is essential. The risk of recurrence is very low, if it is verified that the genetic anomaly appeared "de novo" [3]. We emphasize the importance of early diagnosis in the favorable evolution of the child in terms of development and quality of life. This is why the knowledge of this entity by child practitioners is a first step in improving follow-up. Currently, there is no cure for Williams syndrome. In childhood, the essential is to treat cardiac diseases and hypertension, of hypercalcemia by suppressing the supply of vitamin D, a diet low in calcium, and /or injectable pamidromete. The management of nephrocalcinosis, or hypercalcaemia and/or hypercalciuria requires specialized opinion from nephropediatrics. ophthalmological follow-up. The educational care of children must be done in a multidisciplinary framework involving paediatricians, psychomotrician, speech therapist and psychologist. A neuro-psychological and behavioral assessment is essential to guide the individual management of learning disabilities, as well as attention and anxiety disorders which are frequent. Each stage of development or each difficult phase requires support. It is an ongoing process. The support of child and parents by the multidisciplinary team is essential, and the patient association can be extremely useful. A child who is well taken care of and accompanied on the various learning paths, supported by the educational and medical teams as well as by the family, has every chance of becoming an adult assuming an independent life. Individual and family psychotherapy, whether supportive or more structured, finds its place in the child's therapeutic arsenal. Psychotropic drugs are often necessary for behavioral disorders, especially in cases of attention deficit or anxiety disorders. Relaxation techniques can also help with anxiety [3,4]. On the developmental level, somatic and psychiatric

follow-up must be programmed at an annual rate until adulthood. In particular neuropsychological and/or psychiatric evaluations looking for behavioral disorders, environmental and school adaptation difficulties, anxious or depressive comorbidity and more rarely, but not exceptionally, psychotic derivation as recently described on literature in entering adolescence[5,6]. The prognosis of SWB is linked to the degree of organic damage and psychiatric comorbidities. Fortunately for our patient, the medical case was manageable despite the diagnosis delay.

4. Conclusion

The clinical case that we present, although it is a syndrome known in the scientific literature, it remains however ignored by practitioners. SWB is a rare disorder but which involves the vital and developmental prognosis of the affected child, hence the importance of reconsidering this entity and thinking about it in the face of specific somatic but also behavioral signs.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflicts of interest in relation to this article.

Statement of informed consent

Informed consent was obtained from the parent of the adolescent included in the study.

References

- [1] Zhou Jianrong Ying Zheng, Guiying Liang et al. Atypical deletion of Williams–Beuren syndrome reveals the mechanism of neurodevelopmental disorders. *BMC Medical Genomics* 2022,15:79
- [2] Ferrero Giovanni Battista, Biamino Elisa , Sorasio Lorena et al. Presenting phenotype and clinical evaluation in a cohort of 22 Williams–Beuren syndrome patients. *European Journal of Medical Genetics*, 2007;50: 327-337
- [3] Mervis Carolyn, John Angela. Cognitive and behavioral characteristics of children with Williams syndrome: implications for intervention approaches. *Am J Med Genet C Semin Med Genet.* 2010; 154C(2):229–48.
- [4] Royston Rachel, Waite Jane, Howlin Patricia. Williams syndrome: recent advances in our understanding of cognitive, social and psychological functioning. *Curr Opin Psychiatry.* 2019; 32(2):60–6.
- [5] Benali Adeslam, Oueriagli Fadoua, Laffinti Amine mahmoud, et al. Syndrome de Williams et état psychotique aigu : Une comorbidité très rare. *Research fr* 2015; 2:1405.
- [6] Salgado Henrique, Martins-Correia Luis. Williams syndrome and psychosis: a case report. *J Med Case Rep.* 2014; 8:49.

Author's Short biography

**Bouchra AABBASSI**

Professor of child and adolescent psychiatry

Member of the “Child, health and development Research Laboratory”, Faculty of Medicine and Pharmacy of Marrakesh, Morocco.

Child and adolescent psychiatric department, UHC Mohamed VI, Marrakesh, Morocco