WHITE-SUTTON SYNDROME: A CASE REPORT

[1]Maria Carolina da Silva Campos; [2]Fernanda Singh Vieira; [3]Mariana Tavares de Souza Monteiro Bizarro; [3]Luciano Santana de Oliveira; [1]Suely Rodrigues dos Santos

1. Hospital Universitário Gaffrée e Guinle - Universidade Federal do Estado do Rio de Janeiro – UNIRIO; 2. Universidade Federal do Estado do Rio de Janeiro – UNIRIO; 3. Laboratório de Citogenética, Departamento de Genética e Biologia Molecular– Instituto Biomédico – Universidade Federal do Estado do Rio de Janeiro - UNIRIO

INTRODUCTION

White-Sutton syndrome (WHSUS) is a neurodevelopmental disorder characterized by a large spectrum of cognitive dysfunction, motor delay, speech and language acquisition, hypotonia, autism spectrum disorder (ASD), and other behavioral problems. The diagnosis is confirmed when a pathogenic variant in the *POGZ* gene is found in gene sequencing. Phenotype is shared with other syndromes such as intellectual disability (ID) and ASD, therefore, clinically, WHSUS is not usually identified.

CASE PRESENTATION

The patient was referred to the genetics outpatients of Hospital Universitário Gaffrée e Guinle (HUGG) at the age of 11. He is the first child of a non-young and non-consanguineous couple. After uneventful pregnancy, he was born by caesarean section (full term) without perinatal complications except neonatal jaundice, no phototherapy. Anthropometric measurements of birth and on examination at the age of 11 are described in table 1. He evolved with developmental delay (DD), especially speech (he was nonverbal until the age of 3) and learning disabilities. In addition to centripetal obesity, he presented ocular and nipple hypertelorism, hypogenitalism (micropenis), and flat feet (Figure 1). Normal EEG, abdominal ultrasound and cranial MRI. Karyotype, fragile X PCR and CGh array were normal but Whole Exome Sequencing (WES) detected a mutation in the *POGZ* gene, in heterozygosity, a probably pathogenic variant, associated with WHSUS.

Figure 1: In A, patient with ocular hypertelorism, posterior rotated ears and synophrys; In B it is possible to see slight prognatism.

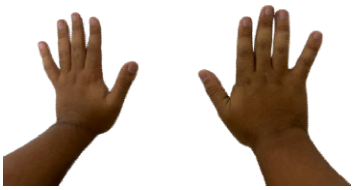

Figure 2: Patient`s hands showing brachydactily.

Table 1 shows the anthropometric measurements of the patient at birth and in physical examination at the age of 11.

	Feature	Measures	Percentile
Anthropometric measurements of the patient	Birth Weight	3435g	50-90
	Birth Size	49.5cm	10-50
	Birth OFC	34cm	10-50
	Weight at 11yo	70.95	>97
	Size at 11yo	150	85
	OFC at 11yo	53cm	~50

Legend: OFC: Occipito-Frontal Circumference; yo: yers old; g: grams; cm: centimeters; >: greater than; ~: approximately

RESULTS AND DISCUSSION

Recently described (2020), WHSUS is an autosomal dominant disease, and is related to mutations in the *POGZ* gene. Most cases result from a new mutation, and there is no consensus regarding clinical diagnostic criteria. In our case, the variant found is a nonsense mutation first described so far. There is a genotype/phenotype correlation, as showed in table 2, except seizures and refractive errors. We emphasize the importance of the diagnosis in patients with ASD/ID to provide genetic counseling for the family. Despite the advanced maternal age, in this case, the risk of recurrence is low. Prenatal or preimplantation genetic testing is possible. There are few cases related.

Table 2 shows the physic-developmental characteristics found in our patient in comparison with cases already described in literature.

CLINICAL FEATURE/PHENOTYPE	CASE PRESENTED	LITERATURE DESCRIPTION
Intellectual disability/ Learning dificulty	+	+
Speech delay	+	+
Motor delay	+	+
Hypotonia	-	+
Behavioral disorders	+ Hyperactivity; Aggressiviness	+
Epilepsy	-	+
Ophtalmopogical changes	-	+
Hearing loss	+	+
Sleep disorders	+	+
Gastrointestinal disorders	-	+
Genitourinary anomalies	+ Hypogenitalism; Micropenis	+
Musculoskeletal anomalies	+ Brachydactyly	+
Hyperphagia	+	-

Legend: + refers to presence of the feature and – refers to absence of the feature.

**This study was approved by HUGG Ethics Committee (6.786.609). **The reproduction of the images was authorized by the patient/guardian.*