Williams Syndrome (WS) — Symptoms and Treatment

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Williams Syndrome results from microdeletion in a region q11.23 of chromosome 7. It mostly results from de novo mutations and follows an autosomal dominant pattern. The affected individuals have a characteristic elfin facies. Common variable clinical abnormalities related to Williams Syndrome are cardiovascular diseases, connective tissue abnormalities, developmental delays, short stature, transient neonatal hypercalcemia, and mild to moderate intellectual disability. Fluorescent in situ hybridization (FISH) test is used to diagnose the syndrome. Treatment includes multidisciplinary approach.

Overview and Definition of Williams Syndrome

Williams syndrome, also known as Williams-Beuren syndrome (WBS), results from microdeletion in a small region of chromosome 7. It accounts for one in 10,000 live births. Microdeletion region in Williams syndrome is q11.23. This region contains more than 25 genes. The loss of multiple genes causes the characteristic features of this syndrome. Typical genes that are deleted in Williams syndrome are:

- CLIP2
- GTF2I
It is a developmental disability inherited in the autosomal dominant pattern. The mutations are mostly de novo. The learning disabilities and cognitive difficulties in people with William syndrome are due to the loss of several genes, especially CLIP2. The gene, ELN, which encodes for elastin protein is typically absent in this syndrome and results in cardiovascular disease and connective tissue abnormalities. The absence of genes LIMK1, GTF2I, and GTF2IRD1 cause difficulties regarding spatial visualization ability.

**Signs and Symptoms of Williams Syndrome**

Deletion of multiple genes in Williams Syndrome results in a wide range of physical and mental problems. Some of the commonly found signs and symptoms are:

- Connective tissue abnormalities
- Developmental delays
- **Short stature**
- Distinctive facial features (characteristic elfin facies)
- Broad forehead
- Short nose and broad nose tip
- Full cheeks
- Wide mouth with full lips
- Long philtrum
- Flattened nasal bridge
- Cardiovascular disease
- Supravalvular aortic stenosis
- Supravalvular pulmonary stenosis
- Insufficient elastin leading to hernias, bladder diverticula, full cheeks, and coarse voice
- Transient neonatal hypercalcemia
- Intellectual disability (mild to moderate)
- Difficulties regarding spatial visualization ability such as solving puzzles and drawing. However, these individuals do well in language and rote memorization
- Outgoing and engaging personality
- Attention deficit disorder (ADD)
- Problems related to anxiety and phobias
- Dental problems like hypodontia, diastema, and malocclusion
- Cocktail type personality which includes low IQ, higher verbal IQ and lack of social inhibition
“Distinctive facial appearance of persons with WBS (A) [5]. Young child with WBS at the age of 15 months (B) and 3 years (C). Note subtle characteristic facial features, including wide mouth, chubby cheeks, long philtrum, small nose, and delicate chin. The same patient is shown in Figs. 1B, 1C, and 1D (left; 21 years); another individual with WBS aged 28 years is shown in Fig. 1D (right).”


Other symptoms include:

- Failure to thrive
- Low muscle tone
- GI problems, such as colic
- Urinary difficulties
- Nocturnal enuresis
- Hyperacusis and phonophobia are often seen in affected individuals
- Higher prevalence of left-handedness
- Strabismus is found in around 75% of the cases

Diagnosis of Williams Syndrome

Diagnosis is made based on physical symptoms recognition and a genetic test. Developmental delays, stellate iris pattern, long philtrum, and puffiness around eyes are the initial signs which lead to testing for diagnosis.

**One of the following two types of tests are used:**

1. Microarray analysis
2. Fluorescent in situ hybridization (FISH) test

FISH involves probing the chromosome 7 to find two copies of elastin gene. The absence
Treatment of Williams Syndrome

The treatment is mainly aimed at improving the quality of life and alleviating other conditions associated with Williams syndrome. **For this, following tests are conducted:**

- Annual cardiology evaluation
- Ophthalmology evaluation
- Auditory exam
- Thyroid function tests
- Renal ultrasound
- Calcium at birth and during first few months
- Developmental and growth evaluation
- Examination for an inguinal hernia
- Blood pressure measurement
- Orthopedic assessment on joints and muscle tone
- Feeding and dietary assessments for treating constipation and urinary problems

Treatment includes:

- Cardiovascular issues are treated on an individual basis
- Hypercalcemia is treated along with avoidance of extra calcium and vitamin D
- Physical therapy for joint problems and low muscle tone
- Behavioral treatments
- Speech therapy to improve the social interactions of affected individuals

References


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