WILLIAMS SYNDROME

Aaron Goldberg, MD
UCI/CHOC Pediatric Residency Program
Learning Objectives

◦ Understand the genetic basis of Williams syndrome
◦ Be able to identify key clinical features of Williams Syndrome
◦ Know how Williams syndrome is diagnosed
◦ Know the basics of screening and health care supervision for children with Williams Syndrome
The Genetics

- 1 in approximately 10,000 live births

- Microdeletion of the long arm of chromosome 7 (7q11.23)
  - Includes 26 to 28 genes
  - Elastin gene lost in nearly all cases

- Most cases result from spontaneous microdeletion, with small number of cases having autosomal dominant inheritance
Facial Features: “Elfin facies”

Ears:
- Hyperacusis (sensitive to certain frequencies)
- Progressive sensorineural hearing loss
- Recurrent ear infections

Eyes:
- Starry pattern on iris (above)
- Strabismus
Heart, Hypercalcemia, Hyperflexible, Hemias

- Cardiovascular abnormalities (80%)
  - Supravalvar aortic stenosis (most common) or peripheral pulmonic stenosis
  - Hypertension (50%)

- Hypercalcemia
  - Idiopathic
  - Results in extended period of colic/irritability
  - Usually starts in infancy and resolves before 3 years old

- Joint hypermobility and/or contractures

- Umbilical and inguinal hemias
Growth

- Slightly lower to normal birth weight
- Slow weight gain
  - Feeding difficulties due to hypotonia, which typically resolve as child gets older
- Early puberty
- Overall growth delay, resulting in short stature
Development, Cognitive and Behavioral

- “Cocktail party” personality
  - Loquacious, gregarious, excel socially
- Developmental delay (predominantly language and motor)
  - Language – first words at 3 years old
  - Motor – 6 months delayed in young children
- Moderate intellectual disability (IQ 50-60)
- Impaired visuospatial constructive cognition
- Unusually good musical ability (20% with absolute or perfect pitch)
Diagnosis

- First identify physical and clinical features
- Confirm with either:
  - Chromosomal microarray (looks at all chromosomes)
  - FISH (Fluorescence in Situ Hybridization) probes targeted at identifying if 2 copies of elastin gene
Health Screening and Surveillance

- Plot growth parameters on Williams Syndrome-specific growth chart (each visit)
- Check blood pressure in both arms (each visit)
  - If aortic stenosis present, 3 limb BP and echo with cardiology every 3 months in 1st year, then every 1-2 years
- Check for inguinal hemia (each visit in first year, then annually)
- Evaluate for hypotonia, hyperreflexia, cerebellar signs, joint laxity (each visit in first year, then annually)
- In first year of life, discuss potential feeding issues, hypercalcemia (avoid Vitamin D), constipation (treat aggressively)
- Vision and hearing screening yearly
- Serum calcium levels every 4 months in 1st year of life, then every 4-6 mo until 2yo, then every 2 years
  - EKG yearly for prolonged QT surveillance
- Thyroid function tests yearly until 3yo, then every 2 years
- Renal/bladder ultrasound at diagnosis (possible malformations) and urinalysis yearly
**William Ferrell is Elf (a mnemonic)**

<table>
<thead>
<tr>
<th>William Syndrome Feature</th>
<th>How it fits in the mnemonic</th>
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<tbody>
<tr>
<td>Elfin facies</td>
<td>Will Ferrell is an Elf</td>
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<tr>
<td>Hypersocial/friendly</td>
<td>This is his character’s personality in the movie</td>
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<tr>
<td>Short stature</td>
<td>Elves are short</td>
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<tr>
<td>Cardiac (supravalvar aortic stenosis)</td>
<td>He had a big loving heart</td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>As an elf, he drank A LOT of milk</td>
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</tbody>
</table>

Bonus: William is 7 letters = chromosome 7
References


Morris CA, Braddock SR. Health Care Supervision for Children With Williams Syndrome. Pediatrics. 2020;145(2)