Williams syndrome: Infant with significantly large deletion at 7q11.23 and unique clinical presentation

Katie Farkouh[1], Robert Roger Lebel[2], Jennifer Black[2], Scott Smith[3]

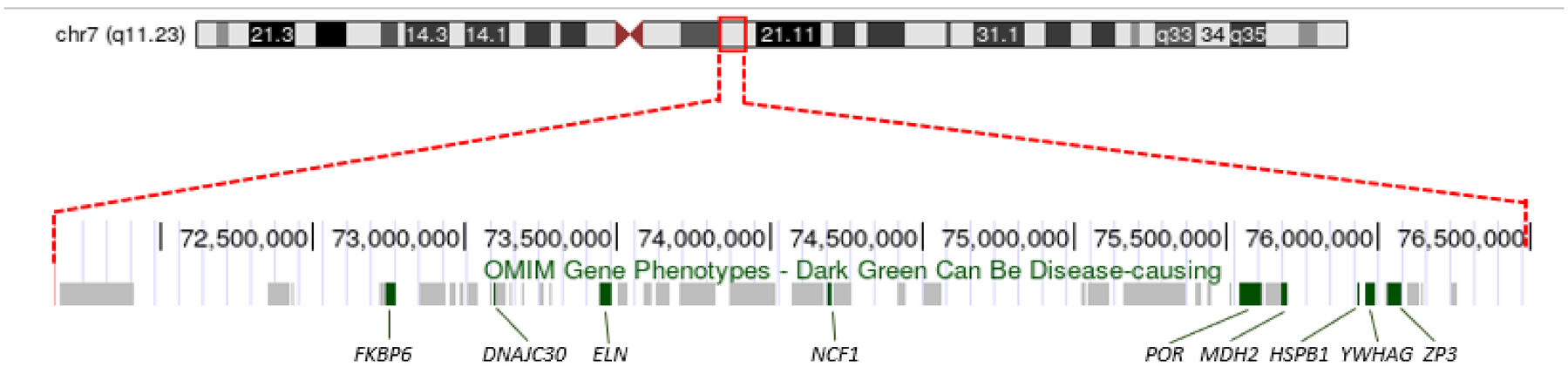
[1] Norton College of Medicine, SUNY Upstate Medical University, Syracuse, NY. [2] Center for Development, Behavior and Genetics, Pediatrics, SUNY Upstate Medical University, Syracuse, NY. [3] Department of Pathology, SUNY Upstate Medical University, Syracuse, NY.

Background

- Williams syndrome (WS) is usually caused by a heterozygous 1.55 to 1.84-Mb deletion at 7q11.23.[1]
- Clinical features include cardiovascular disease (hypertension, supravalvular aortic and pulmonary stenosis), distinct facial features (round face, full cheeks, thick lips, anteverted nares, stellate iris, small chin), endocrine abnormalities (hypercalcemia), developmental delays, connective tissue abnormalities, and unique personality characteristics.
- This typical 7q11.23 deletion contains several genes that can explain the WS phenotype: the *ELN*, *LIMK1*, GTF2I, *BAZ1B*, *CLIP2*, and *GTF2IRD1* genes are responsible for connective tissue abnormalities and cardiovascular disease, visuospatial construction, developmental and intellectual delays, hypercalcemia, cerebellar abnormalities, and craniofacial features, respectively.[1]

FIGURE 1. Features of our patient not typical of a child with WS

Genetics



Typical Williams deletion (1.5-1.8 Mb)

This patient (3.47 Mb)

Clinical Presentation

- 22-month-old female patient with an unusually large deletion (3.47 Mb) at 7q11.23 as well as a 707 kbp duplication at 2q33.3 of uncertain clinical significance.
- Medical history is significant for supravalvular aortic and pulmonary stenosis, hypercalcemia, milestone delays, dysmorphic facies, and growth abnormalities.
- She also has unique nephrologic abnormalities including non-functioning left multicystic dysplastic kidney (MCDK), chronic kidney disease, and right ureteropelvic junction stenosis with severe hydronephrosis and renal dysplasia.
- The cardiovascular, endocrine, developmental, and facial abnormalities seen in our patient are consistent with the typical characteristics of WS.
- However, her renal abnormalities are unique and differ from typical WS presentations.

Discussion and Conclusions

Most patients with WS exhibit a heterozygous 1.5-1.8 Mb deletion, with only 2-5% of patients possessing atypical deletion sizes. While the usual deletion spans about 26 to 28 genes[2], this patient's large deletion of 3.47 Mb involves 42 genes. Other cases of large, atypical deletions did not present with renal abnormalities like those in our patient. We consider her unique urogenital phenotype to be the result of the loss of genes not typically involved in the WS. Additionally, her 707 kbp duplication may influence her phenotype in unknown ways. Consistent follow-up is necessary to ensure optimal health for our patient and this multisystemic disorder.

References

1. Kozel, B. A., Barak, B., Kim, C. A., Mervis, C. B., Osborne, L. R., Porter, M., & Pober, B. R. (2021). Williams syndrome. *Nature reviews. Disease primers*, *7*(1), 42.
2. Lugo, M., Wong, Z. C., Billington, C. J., Jr, Parrish, P. C. R., Muldoon, G., Liu, D., Pober, B. R., & Kozel, B. A. (2020). Social, neurodevelopmental, endocrine, and head size differences associated with atypical deletions in Williams-Beuren syndrome. *American journal of medical genetics. Part A*, *182*(5), 1008–1020.