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Novel syndrome resulting from multiple genomic lesions

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Although genomic testing can be useful for clinical diagnosis, most patients have no obvious genomic changes despite a strong indication of a genetic condition. In a paper published in the March issue of *Cold Spring Harbor Molecular Case Studies*, researchers from the US, Turkey, and the Netherlands describe a rare new syndrome likely arising from the dual contribution of two genomic abnormalities previously individually associated with clinical pathologies.

Two male siblings with similar phenotypic features, namely neurocognitive, craniofacial, and gonadal malformations, did not conform to previously described syndromes. To aid diagnosis, researchers performed whole exome sequencing and cytogenetic testing on the patients and their parents. Initially, the researchers homed in on a coding mutation shared by both patients on the X Chromosome and inherited from their mother. However, testing in zebrafish did not reveal any developmental defects similar to those seen in the patients.

The researchers next looked for large-scale changes in the patients' genomes. Both patients have a terminal duplication of Chromosome 16q and a terminal deletion of Chromosome 5p, encompassing 114 and 50 genes, respectively. The breakpoints of the lesions do not disrupt any transcripts, but previous reports of syndromes with molecular breakpoints overlapping a single chromosomal abnormality are associated with some of the same clinical features as the patients in this study.

The researchers suggest that both genomic regions contribute to the complex clinical presentation of the patients, likely as a result of changes to gene copy numbers. "We anticipate that the unbiased dissection of large copy number variants similar in size to those identified in this study will become possible with the increased throughput of genome editing technologies in model organisms," the researchers write.

More information: Aysegul Ozanturk et al. A t(5;16) translocation is the likely driver of a syndrome with ambiguous genitalia, facial dysmorphism, intellectual disability, and speech delay, *Molecular Case Studies* (2015). DOI: 10.1101/mcs.a000703