CENTOGENE
THE RARE DISEASE COMPANY

CASE STUDY

Unraveling a Clinically Relevant Uniparental Disomy With CentoXome®

At CENTOGENE, we are committed to revolutionizing rare disease patient care – continuously striving to provide you and your patients with the best possible medical solutions every step of the way.

The first step: Choosing the right genetic test to efficiently establish or confirm a diagnosis and guide appropriate medical care and prognosis. Keep reading to learn more about how CentoXome, our enhanced Whole Exome Sequencing (WES) solution, is helping physicians around the world to diagnose patients promptly and with the highest levels of certainty.

Clinical Overview

6-month-old male

Birth weight, length, and occipitofrontal circumference within normal range; failure to thrive from 1 month of age, motor delay, and global development delay; mild hypotonia, horizontal nystagmus, apparent ocular proptosis; facial dysmorphic features, skeletal system abnormality, mild hirsutism, and fair skin

Parents are healthy and non-consanguineous; the index is the fourth child, with three healthy older siblings

Clinical suspicion of hereditary skeletal dysplasia, osteopetrosis

Previous Genetic Testing Performed

Normal karyotype (46, XY) results from an external lab

Testing Strategy

The physician opted for CentoXome Trio to rule out hereditary skeletal dysplasia, osteopetrosis and to establish a diagnosis to guide the best early medical intervention as the infant's condition was deteriorating. As testing with CentoXome detects nearly all types of genetic variants in a single test, CENTOGENE enhanced WES offered a fast and optimal testing solution.

Diagnosis of Osteopetrosis Type 4

CentoXome Trio identified a homozygous variant of uncertain significance (NM_001287.5:c.761G>T) with very strong evidence in the gene *CLCN7*, resulting in possible genetic diagnosis of osteopetrosis type 4, of autosomal recessive inheritance. The Trio analysis enabled the confirmation that the mother was a carrier of the variant (heterozygote). In the father, no clinically relevant variants were detected for the described clinical presentation. Additionally, because CENTOGENE's CentoXome enables the screening for uniparental disomy (UPD), the analysis revealed a maternal UPD for the entire chromosome 16, which was confirmed by chromosomal microarray analysis.

Testing Impact

CentoXome Trio revealed relevant findings that led to a diagnosis and the start of an effective treatment. This would have not been possible with a routine WES analysis, because UPD is rarely evaluated. The UPD screening with CentoXome identified a maternal UPD as causing the homozygosity of the deleterious recessive variant – enabling a correct diagnosis and better clinical management. The family received genetic counseling, and the patient got a tailored treatment strategy and a bone marrow transplant, which can be curative if performed before complications and sequelae from the disease occur.

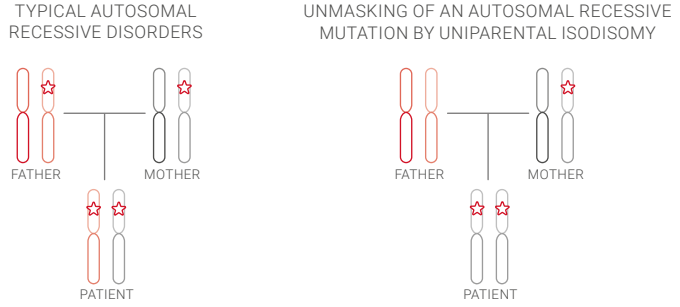

Figure 1: Isodisomy can generate homozygosity of a deleterious recessive variant from a heterozygous carrier-parent. The affected region can be confined to a portion of the chromosome (segmental) or can span the entire chromosome (complete) and is an identical copy of one parental allele (isodisomy) or distinct alleles from the same parent (heterodisomy).

CentoXome can provide superior assessment of nearly all types of genetic variants in a single test, including a reliable screening for UPD, and accelerate medical solutions for your patients

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