CENTOGENE

CASE STUDY

CentoXome MOx Diagnosed Niemann-Pick Disease Type C1

Demonstrating the power of CENTOGENE's multiomic approach for a fast and conclusive diagnosis

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

Diagnostic genetic testing can help pinpoint the cause of persistent, often debilitating symptoms, in patients suffering with suspected rare, metabolic, or neurodegenerative diseases. The extreme heterogeneity of these diseases poses a serious diagnostic challenge. The emerging use of a multiomic approach has been shown to improve diagnostic power.

Clinical Overview

5-year-old male

Global developmental delay, delayed speech and language development, general developmental regression, psychomotor deterioration, drooling, dysphagia, dystonia, rigidity, tonic seizures, and bowel and urinary incontinence

Family history: affected sister and consanguineous parents

Clinical suspicion of neuronal ceroid lipofuscinosis

Previous Testing Performed

- No previous biochemical or genetic testing
- Magnetic Resonance Imaging (MRI) showed abnormality of the cerebral white matter and cerebral cortical atrophy; Electromyography (EMG) results were normal

Testing Strategy

Based on the complex and heterogeneous symptoms, the physician opted for CentoXome MOx as a first-line test. CentoXome MOx is our multiomic Whole Exome Sequencing (WES) test, combining the power of genomic and biochemical testing to determine the pathogenicity of clinical variants, resulting in a higher diagnostic yield.

Diagnosis of Niemann-Pick Disease Type C1

CentoXome MOx identified a homozygous missense variant in the *NPC1* gene that was classified as likely pathogenic based on increased biomarker concentration (see table below) plus data from the CENTOGENE Biodatabank, the world's largest data repository for real-world rare and neurodegenerative diseases. This *NPC1* variant was not present in HGMD® or ClinVar, but was documented in the CENTOGENE Biodatabank after it was identified by our lab in a homozygous state in two previous patients with overlapping phenotypes and elevated biomarker concentration. Pathogenic variants in the *NPC1* gene are associated with autosomal recessive Niemann-Pick disease type C1 and type D (OMIM®: 257220). Niemann-Pick disease type C is a lysosomal lipid storage disease characterized by progressive clinical manifestations that vary with age of onset, often with severe neurological symptoms.

Biochemical Testing

Name of Biomarker	Result	Reference	Interpretation
Lyso-SM-509	1.9 ng / ml	≤ 0.9 ng / ml	Pathologic

Variant

Gene	Variant	Zygosity	Final Classification
NPC1	NM_000271.4:c.575A>G	Homozygous	Missense; Likely Pathogenic (class 2)

Table 1: Result Summary

Testing Impact

CentoXome MOx established a fast, definitive diagnosis of Niemann-Pick disease type C1 using a single patient sample. In one step, CentoXome MOx integrated both deep exomic and biochemical data, interpreted by our medical experts using insights from our extensive Biodatabank, which was a critical cornerstone for the classification of the detected *NPC1* variant as likely pathogenic. The diagnosis enabled optimized symptomatic treatments for the patient with a focus on improving his quality of life. The family received genetic counselling and general supportive care.