HNRNPH2-NDD

https://pubmed.ncbi.nlm.nih.gov/36108116/

Clinical characteristics:

Most individuals with HNRNPH2-related neurodevelopmental disorder (HNRNPH2-NDD) have symptoms early in life, before age 12 months. The major features of HNRNPH2-NDD are developmental delay / intellectual disability, motor and language delays, behavioral and psychiatric disorders, and growth and musculoskeletal abnormalities. Minor features include dysmorphic facies, gastrointestinal disturbances, epilepsy, and visual defects. Although HNRNPH2-NDD is an X-linked condition, there is not enough information on affected females versus affected males to make any generalizations about phenotypic differences between the two sexes.

Diagnosis/testing:

The diagnosis of

HNRNPH2

-NDD is established in a proband with suggestive clinical findings and a heterozygous or hemizygous pathogenic (or likely pathogenic) variant in

HNRNPH2

identified by molecular genetic testing.

Management:

Treatment of manifestations

: Feeding therapy or gastrostomy tube placement for those with poor weight gain; standard treatment for developmental delay / intellectual disability, behavioral problems, epilepsy, movement disorders, abnormal tone, constipation, sleep apnea, cortical visual impairment, hearing loss, musculoskeletal anomalies, cardiac defects, and pubertal anomalies.

Surveillance

: At each visit: measurement of growth parameters; evaluation of nutritional status, feeding issues, and safety of oral intake; assessment of developmental progress and educational needs; behavioral assessment; assessment for new manifestations (seizures, change in tone, movement disorders, developmental regression); monitoring for evidence of sleep disturbance and signs/symptoms of sleep apnea; orthopedic assessment, including for scoliosis (until skeletal maturity or in older individuals who are nonambulatory). Assess for hip dysplasia in infancy or at each visit in individuals who are nonambulatory. At each visit in childhood and adolescence: assessment for signs/symptoms of puberty. At least annually or as clinically indicated: hearing evaluation (in childhood); ophthalmologic evaluation.

Genetic counseling:

HNRNPH2

-NDD is inherited in an X-linked manner. Most affected individuals have the condition as the result of a

de novo

pathogenic variant. If the mother of the proband has an

HNRNPH2

pathogenic variant, the chance of the mother transmitting it in each pregnancy is 50%. Females who inherit the pathogenic variant are at high risk of being affected. Males who inherit the pathogenic variant have a variable phenotype ranging from severe manifestations to mild developmental delay with autistic features and psychiatric diagnoses. A male with a mosaic *HNRNPH2* pathogenic variant that includes the germline may transmit the *HNRNPH2* pathogenic variant to daughters but not to sons. Prenatal and preimplantation genetic testing are possible if the familial pathogenic variant has been identified.