HNRNPU-related disorder

https://pubmed.ncbi.nlm.nih.gov/35274911/

Clinical characteristics:

HNRNPU

-related neurodevelopmental disorder (

HNRNPU

-NDD) is characterized by developmental delay and intellectual disability – typically moderate to severe – with speech and language delay and/or absent speech. Affected individuals may also display autistic features. There may be feeding difficulties during the neonatal period as well as hypotonia, which often remains lifelong. Dysmorphic features have been described but they are nonspecific. Affected individuals are likely to experience seizures (most commonly tonic-clonic or absence) that may be refractory to treatment. Nonspecific brain MRI findings include ventriculomegaly and thinning of the corpus callosum. Less common findings include cardiac abnormalities, strabismus, undescended testes in males, renal anomalies, and skeletal features, including joint laxity, polydactyly, and scoliosis. Rarely, abnormal breathing patterns, including hyperventilation and apnea, may be present and can lead to sleep disturbance.

Diagnosis/testing:

The diagnosis of

HNRNPU

-NDD is established in a proband with suggestive findings and a heterozygous pathogenic variant in

HNRNPU

identified by molecular genetic testing.

Management:

Treatment of manifestations

: Standard treatment of seizures with anti-seizure medications (sodium valproate is often used and is frequently effective); consider instituting the ketogenic diet and/or newer generation anti-seizure medications in those with refractory seizures. Feeding therapy; consider a temporary or permanent feeding tube for those with persistent feeding issues. Consider supplemental oxygen, CPAP, or BiPAP in those with sleep apnea. Standard treatment for tone abnormalities, intellectual disability, behavioral problems, hyperventilation / abnormal breathing patterns, congenital heart defects, strabismus, hearing loss, renal anomalies, undescended testes, and limb defects.

Surveillance

: At each visit: measurement of growth parameters; evaluation of nutritional status and safety of oral intake; monitor for evidence of constipation, new seizures, hyperventilation, apnea, and changes in tone; assessment of developmental progress and behavior. Annually or as clinically indicated: ophthalmologic and audiologic evaluations.

Agents/circumstances to avoid:

Activities and agents that may induce seizures.

Genetic counseling:

HNRNPU

-NDD is expressed in an autosomal dominant manner and typically caused by a

de novo

HNRNPU

pathogenic variant. The risk to other family members is hypothesized to be low. Presumed parental germline mosaicism has been reported in one family with two affected sibs. Once the

HNRNPU

pathogenic variant has been identified in an affected family member, prenatal testing and preimplantation genetic testing are possible.