Koolen-De Vries Syndrome

https://pubmed.ncbi.nlm.nih.gov/20301783/

Clinical characteristics:

Koolen-de Vries syndrome (KdVS) is characterized by congenital malformations, developmental delay / intellectual disability, neonatal/childhood hypotonia, epilepsy, dysmorphisms, and behavioral features. Psychomotor developmental delay is noted in all individuals from an early age. The majority of individuals with KdVS function in the mild-to-moderate range of intellectual disability. Other findings include speech and language delay (100%), epilepsy (~33%), congenital heart defects (25%-50%), renal and urologic anomalies (25%-50%), and cryptorchidism. Behavior in most is described as friendly, amiable, and cooperative.

Diagnosis/testing:

The diagnosis of KdVS is established in a proband who has either a heterozygous 500- to 650-kb deletion at chromosome 17q21.31 that includes

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or a heterozygous intragenic pathogenic variant in

KANSL1

. Note: The 17q21.31 deletion cannot be identified by analysis of G-banded chromosomes or other cytogenetic banding techniques.

Management:

Treatment of manifestations:

Supportive care, ideally through a multidisciplinary team of specialists, to improve quality of life, maximize function, and reduce complications is recommended. Speech therapy to support early feeding challenges and communication development; physiotherapy for gross and fine motor delays; educational programs directed to specific disabilities identified. Growth hormone therapy is indicated for those with growth hormone deficiency. Routine treatment of vision issues / strabismus; hearing loss; cardiac, renal, and urologic issues; epilepsy; scoliosis, hip dislocation, and positional deformities of the feet; multiple nevi.

Surveillance:

At each visit: measurement of growth parameters; evaluation of nutritional status and safety of oral intake; monitoring of developmental progress and educational needs; assessment for new manifestations, such as seizures and changes in tone; behavioral assessment; assessment of mobility and self-help skills. Annual full skin examination in those with lighter skin tones or skin types who are at greater risk for developing melanoma. Ophthalmology and hearing evaluations annually or as clinically indicated.

Genetic counseling:

KdVS, caused by a heterozygous deletion at chromosome 17q21.31 or a heterozygous intragenic

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pathogenic variant, is an autosomal dominant disorder. Almost all affected individuals represent simplex cases (i.e., a single affected individual in the family).The recurrence risk for future pregnancies is slightly greater than that of the general population because of the possibility of germline mosaicism in one of the parents. Once the KdVS-related genetic alteration has been identified in an affected family member, prenatal and preimplantation genetic testing are possible.