FOXP1 syndrome

https://pubmed.ncbi.nlm.nih.gov/37733892/

Clinical characteristics:

FOXP1 syndrome is characterized by delays in early motor and language milestones, mild-to-severe intellectual deficits, speech and language impairment in all individuals regardless of level of cognitive abilities, and behavior abnormalities (including autism spectrum disorder or autistic features, attention-deficit/hyperactivity disorder, anxiety, repetitive behaviors, sleep disturbances, and sensory symptoms). Other common findings are oromotor dysfunction (contributing to speech and feeding difficulties), refractive errors, strabismus, cardiac abnormalities, renal abnormalities, cryptorchidism, hypertonia, hearing loss, and epilepsy. To date, more than 200 individuals have been identified with FOXP1 syndrome.

Diagnosis/testing:

The diagnosis of FOXP1 syndrome is established in a proband with a heterozygous pathogenic variant in

identified by molecular genetic testing and supportive clinical findings.

Management:

Treatment of manifestations:

Supportive care to improve quality of life, maximize function, and reduce complications is recommended. This can include multidisciplinary care by specialists in pediatrics, developmental medicine or neurodevelopment, neurology, physiatry, occupational and physical therapy, speech-language pathology, psychiatry, psychology, ophthalmology, and medical genetics.

Surveillance:

Regular monitoring by the relevant specialists of existing manifestations, the individual's response to supportive care, and the emergence of new manifestations is recommended.

Genetic counseling:

FOXP1 syndrome is an autosomal dominant disorder typically caused by a

de novo

pathogenic variant. To date, most probands with FOXP1 syndrome whose parents have undergone molecular genetic testing have the disorder as the result of a

de novo

FOXP1

pathogenic variant. Rarely, a parent of an individual with FOXP1 syndrome has somatic and germline mosaicism for the

FOXP1

pathogenic variant or a complex chromosome arrangement involving

FOXP1

. Each child of an individual with FOXP1 syndrome has a 50% chance of inheriting the

FOXP1

pathogenic variant. Risk to future offspring of the parents of the proband is presumed to be low, as the proband most likely has a

de novo FOXP1

pathogenic variant. There is, however, a recurrence risk (~1%) to sibs based on the possibility of parental germline mosaicism; given this risk, prenatal and preimplantation genetic testing may be

considered.