# Kleefstra Syndrome

*https://pubmed.ncbi.nlm.nih.gov/20945554/*

Clinical characteristics:

Kleefstra syndrome is characterized by intellectual disability, autistic-like features, childhood hypotonia, and distinctive facial features. The majority of individuals function in the moderate-to-severe spectrum of intellectual disability although a few individuals have mild delay and total IQ within low-normal range. While most have severe expressive speech delay with little speech development, general language development is usually at a higher level, making nonverbal communication possible. A complex pattern of other findings can also be observed; these include heart defects, renal/urologic defects, genital defects in males, severe respiratory infections, epilepsy / febrile seizures, psychiatric disorders, and extreme apathy or catatonic-like features after puberty.

Diagnosis/testing:

The diagnosis of Kleefstra syndrome is established in a proband who has a heterozygous deletion at chromosome 9q34.3 that includes at least part of

EHMT1

(~50%) or a heterozygous intragenic

EHMT1

pathogenic variant (~50%).

Management:

Treatment of manifestations:

Ongoing routine care by a multidisciplinary team specializing in the care of children or adults with intellectual disability. Referral to age-appropriate early-childhood intervention programs, special education programs, or vocational training; speech-language therapy, physical and occupational therapy, and sensory integration therapy; specialized care for those with extreme behavior issues, movement disorders, sleep disorders, and/or epilepsy; standard treatment for vision, hearing, cardiac, renal, urologic, and other medical issues.

Surveillance:

Monitoring as needed of cardiac and renal/urologic abnormalities.

Genetic counseling:

Kleefstra syndrome, caused by a deletion at 9q34.3 or pathogenic variants in *EHMT1*, is inherited in an autosomal dominant manner. Almost all cases reported to date have been *de novo*; rarely, recurrence in a family has been reported when a parent has a balanced translocation involving the 9q34.3 region or somatic mosaicism for an interstitial 9q34.3 deletion. Except for individuals with somatic mosaicism for a 9q34.3 deletion, no individuals with Kleefstra syndrome have been known to reproduce. Prenatal testing may be offered to unaffected parents of a child with a 9q34.3 deletion or an *EHMT1* pathogenic variant because of the increased risk of recurrence associated with the possibility of germline mosaicism, somatic mosaicism including the germline, or a balanced chromosome translocation.