ANKRD11 And KBG Syndrome

https://pubmed.ncbi.nlm.nih.gov/29565525/

Clinical characteristics:

KBG syndrome is typically characterized by macrodontia (especially of the upper central incisors), characteristic facial features (triangular face, brachycephaly, synophrys, widely spaced eyes, broad or bushy eyebrows, prominent ears, prominent nasal bridge, bulbous nose, anteverted nares, long philtrum, and thin vermilion of the upper lip), short stature, developmental delay / intellectual disability, and behavioral issues. Affected individuals may have feeding difficulties (particularly in infancy), skeletal anomalies (brachydactyly, large anterior fontanelle with delayed closure, scoliosis), hearing loss (conductive, mixed, and sensorineural), seizure disorder, and brain malformations. There is significant variability in the clinical findings, even between affected members of the same family.

Diagnosis/testing:

The diagnosis of KBG syndrome is confirmed in a proband by detection of either a heterozygous

pathogenic variant in

ANKRD11

or deletion of 16q24.3 that includes

ANKRD11

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Management:

Treatment of manifestations:

Surgical corrections and/or speech therapy for palatal anomalies; nasogastric tube feeding in infants; pharmacologic treatment for gastroesophageal reflux disease; pressure-equalizing tubes and/or tonsillectomy/adenoidectomy for chronic otitis media; consideration of amplification for hearing loss; consideration of growth hormone therapy for short stature and medication to arrest puberty for premature pubertal development; standard treatment of seizure disorder, undescended testis in males, congenital heart defects, strabismus / refractive errors, and developmental disabilities.

Surveillance:

Routine monitoring of hearing, vision, growth, pubertal status (in prepubertal individuals), and cognitive development.

Agents/circumstances to avoid:

Ototoxic drugs should be avoided because of the risk for hearing loss.

Pregnancy management:

Pregnancy management should be tailored to the specific features in the affected woman. For example, involvement of a cardiologist and maternal fetal medicine physician for a pregnant woman with a history of a congenital heart defect; control of seizures during pregnancy for those with a seizure disorder.

Genetic counseling:

Recurrence risk for sibs of a proband with KBG syndrome depends on the genetic alteration:

Deletion of 16q24.3 (~75% of reported pathogenic variants are

de novo

and the remainder are inherited in an autosomal dominant manner.)

ANKRD11

sequence variants (~66% of reported pathogenic variants are

de novo

and the remainder are inherited in an autosomal dominant manner.)

Prenatal testing and preimplantation genetic testing are possible if the causative genetic alteration has been identified in an affected family member.