ANKRD11 And KBG Syndrome

https://pubmed.ncbi.nlm.nih.gov/36564961/

Background:

KBG syndrome is a rare genetic disorder involving macrodontia of the upper central incisors, craniofacial, skeletal, and neurologic symptoms, caused either by a heterozygous variant in ANKRD11 or deletion of 16q24.3, including ANKRD11. Diagnostic criteria were proposed in 2007 based on 50 cases, but KBG syndrome remains underdiagnosed.

Methods:

Whole exome sequencing (WES) and array comparative genomic hybridization (array CGH) were conducted for genetic analysis and patient phenotypes were characterized based on medical records.

Results:

Eight patients from seven unrelated families were confirmed with KBG syndrome. All patients (8/8, 100%) had some degree of craniofacial dysmorphism and developmental delay or intellectual disabilities. Triangular face, synophrys, anteverted nostril, prominent ears, long philtrum, and tented upper lip, which are typical facial dysmorphism findings in patients with KBG syndrome, were uniformly identified in the eight patients participating in this study, with co-occurrence rates of 4/8 (50%), 4/8 (50%), 4/8 (50%), 4/8 (50%), 5/8 (62.5%), and 5/8 (62.5%), respectively. Various clinical manifestations not included in the diagnostic criteria were observed. Six patients had point mutations in ANKRD11, one had an exonic deletion of ANKRD11, and one had a 16q24.3 microdeletion. According to the ACMG guidelines, all mutations were classified as pathogenic. The c.2454dup (p.Asn819fs*1) mutation in Pt 4 was reported previously. The remaining variants (c.397 + 1G>A, c.226 + 1G>A, c.2647del (p.Glu883Argfs*94), and c.4093C>T (p.Arg1365Ter)) were novel.

Conclusion:

The clinical and molecular features of eight patients from seven unrelated Korean families with KBG syndrome described here will assist physicians in understanding this rare genetic condition.