Kabuki Syndrome 2

Alternative Names
KABUK2

Record Category
Disease phenotype

WHO-ICD
Congenital malformations, deformations and chromosomal abnormalities > Other congenital malformations

Incidence per 100,000 Live Births
2-5

OMIM Number
300867

Mode of Inheritance
X-Linked Dominant

Gene Map Locus
Xp11.3

Description
KABUK2 is a subset of Kabuki syndrome caused by mutations in the KDM6A gene. It is a multi-system disorder characterized by distinct facial features such as arched and sparse eyebrows, long palpebral fissures, eversion of the lateral third of the lower eyelid, a flat and broad tip of the nose and large prominent ears. The distinctive faces of affected patients is similar to the stage makeup used in traditional Japanese Kabuki theatre, from which the name of the disorder is derived. Kabuki patients also suffer from intellectual disability, growth deficiency, skeletal anomalies, abnormal dentition and cardiovascular defects. Skeletal abnormalities include joint laxity, scoliosis and persistence of fetal fingerpads while neurologic issues include hypotonia, seizures and behavioral difficulties.

Despite the significant morbidity, the prognosis of Kabuki syndrome is positive. Life expectancy may however be affected by cardiovascular or immunological defects. The condition was initially reported in Japan and has an overall estimated prevalence of about 1 in 32,000 live births.

The disorder is diagnosed based on clinical findings and molecular analysis of the KDM6A gene. Prenatal diagnoses can also be carried out if the pathogenic variant has been identified in the family. There is currently no cure for Kabuki syndrome and treatment is focused on symptomatic care. Depending on their symptoms, patients may require antiepileptic medication, behavioral therapy, physical therapy and educational aids. Periodic visual and auditory evaluations are advised.

Molecular Genetics
KABUK2 follows an X-linked dominant pattern of inheritance. As mentioned above, it is caused by mutations in the KDM6A gene. This gene encodes an enzyme responsible for demethylating the Lysine-27 residue of histone H3. By regulating the transcription of HOX genes, KDM6A plays a key role in anterior-posterior development. KDM6A mutations implicated in Kabuki syndrome include deletions and transitions that result in frameshift and premature truncation of the protein. Recent reports have also identified heterozygous KMT2A gene mutations in some patients affected with the disorder. This gene encodes an enzyme responsible for catalyzing the methylation of the Lysine-4 residue of histone H3. Similarly to KDM6A, it is also involved in the expression of HOX genes.

Epidemiology in the Arab World
Saudi Arabia
Monies et al. (2017) evaluated the findings of 1000 diagnostic panels and exomes carried out at a next generation sequencing lab in Saudi Arabia. One

patient, a 4-year-old female, suffered from skeletal dysplasia, ribs fusion, ear deformity, cleft palate, absent uterus and vagina and choanal atresia. The phenotype resembled a CHARGE-like presentation, however, a multigene panel for dysmorphology/skeletal dysplasia identified a de-novo heterozygous mutation (c.3248G>A, p.R1083Q) in exon 4 of the patient's KMT2A gene, associated with Kabuki syndrome. This case highlighted the benefit of molecular testing in the diagnosis of overlapping clinical syndromes.

References

Monies D, Abouelhoda M, AlSayed M, Alhassnan Z, Alotaibi M, Kayyali H, Al-Owain M, Shah A, Rahbeeni Z, Al-Muhaizea MA, Alzaidan HI, Cupler E, Bohlega S, Faqeih E, Faden M, Alyounes B, Jaroudi D, Goljan E, Elbardisy H, Akilan A, Albar R, Aldhalaan H, Gulab S, Chedrawi A, Al Saud BK, Kurdi W, Makhseed N, Alqasim T, El Khashab HY, Al-Mousa H, Alhashem A, Kanaan I, Algoufi T, Alsaleem K, Basha TA, Al-Murshedi F, Khan S, Al-Kindy A, Alnemer M, Al-Hajjar S, Alyamani S, Aldhekri H, Al-Mehaidib A, Arnaout R, Dabbagh O, Shagrani M, Broering D, Tulbah M, Alqassmi A, Almugbel M, AlQuaiz M, Alsaman A, Al-Thihli K, Sulaiman RA, Al-Dekhail W, Alsaegh A, Bashiri FA, Qari A, Alhomadi S, Alkuraya H, Alsebayel M, Hamad MH, Szonyi L, Abaalkhail F, Al-Mayouf SM, Almojalli H, Alqadi KS, Elsiesy H, Shuaib TM, Seidahmed MZ, Abosoudah I, Akleh H, AlGhonaium A, Alkharfy TM, Al Mutairi F, Eyaid W, Alshanbary A, Sheikh FR, Alsohaibani FI, Alsonbul A, Al Tala S, Balkhy S, Bassiouni R, Alenizi AS, Hussein MH, Hassan S, Khalil M, Tabarki B, Alshahwan S, Oshi A, Sabr Y, Alsaadoun S, Salih MA, Mohamed S, Sultana H, Tamim A, El-Haj M, Alshahrani S, Bubshait DK, Alfadhel M, Faquih T, El-Kalioby M, Subhani S, Shah Z, Moghrabi N, Meyer BF, Alkuraya FS. The landscape of genetic diseases in Saudi Arabia based on the first 1000 diagnostic panels and exomes. Hum Genet. 2017 Aug;136(8):921-939. PMID: 28600779.

Related CTGA Records

Lysine-Specific Methyltransferase 2A (OMIM 159555)

External Links

http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=2322

https://ghr.nlm.nih.gov/condition/kabuki-syndrome#

https://www.ncbi.nlm.nih.gov/books/NBK62111/

Contributors

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