

Prenatal diagnosis of Kabuki Syndrome

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Introduction

Kabuki Syndrome (KB) was first described in the early 1980s in Japan. KB is characterized by distinct facial dysmorphism, growth retardation, psychomotor developmental delay and a wide spectrum of other manifestations affecting various body systems. Facial dysmorphism may be enough to raise suspicion of KS, after which genetic diagnostics (a pathogenic or a likely pathogenic variant in KMT2D or KDM6A) must be found to ultimately confirm KS.

Case report

A 25-year-old primigravida without risk factors showed at the first trimester scan a thickened nuchal fold (>p99) (Figure A) and a high risk (1/72) for Down Syndrome. A chorionic villus sampling was performed. Quantitative fluorescence polymerase chain reaction (QF-PCR) and comparative genome hybridization (CGH) array were normal.

Echocardiography at 16 weeks was correct but at 26 weeks a mild right hydrothorax was diagnosed (Figure B). At 28 weeks it was not observed and the follow up was normal.



Figure A



Figure B

The patient was referred to the Genetics Unit and a facial dysmorphism consist of long parpebral features (Figure C), eversion of the lower eyelid (Figure D) and macrodontia (Figure E) was reported. Short stature and a slight intellectual disability were observed and Kabuki Syndrome was suspected.



Figure C



Figure D



Figure E

Sequencing gene panels for RASopathies and chromatinopathies were executed and Exome sequencing revealed a mutation in ANKRD11c.7327C > T in the fetus, classified as a Probably pathogenic variant. A parental segregation study revealed that the pregnant women had a de novo mutation in ANDRD11. Mutations affecting the transcriptional regulator Ankyrin Repeat Domain 11 (ANKRD11) are mainly associated with the multisystem developmental disorder known as KBG syndrome but have also been identified in individuals with Cornelia de Lange syndrome (CdLS) and other developmental disorders caused by variants affecting different chromatin regulators.

At 38.5 weeks a 3310g female was born after a vaginal delivery and shown the same features as her mother.

This clinical case highlights the importance of assessment by a multidisciplinary team. This collaborative effort enabled the clinical diagnosis of the fetus based on the mother's features.