

A case report of a Malaysian with WAGR syndrome

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Abstract

The Wilms tumour, aniridia, genital abnormalities and mental retardation (WAGR) syndrome is a rare genetic syndrome which is caused by contiguous gene deletion of PAX6 and the adjacent WT1 genes. The signs and symptoms of WAGR syndrome are related to the loss of multiple genes on the short (p) arm of chromosome 11. Here, we report the genetic cause in the case of a 4-year-old girl with global developmental delay, bilateral cataract and ptosis, everted lower lip, and tall nasal bridge. Genomic DNA subjected to microarray analysis using Agilent CGH microarray was carried out revealing loss of 535 probes at 11p14.3 to 11p13 with size of 10,417Kb. The array showed a deleted interval containing 49 RefSeq genes / 30 OMIM genes / 7 OMIM morbid: BDNF, FSHB, PAX6, WT1, CD59, LMO2 and CAT genes which are located within the known disease region “WAGR 11p13 deletion [OMIM #194072]”. Haploinsufficiencies in this region that include *WT1* and *PAX6* have been reported to cause major phenotypic characteristic of developmental delay and autistic features. Two studies found interstitial deletions at 11p13 including *PAX6* is associated with aniridia, cataract, ptosis and mental retardation. Our findings suggested this mutation is most likely responsible for the pathogenesis of WAGR syndrome in this patient. Additionally, probands below the age of 6 years old with *WT1* deletion were also found susceptible to childhood onset of Wilms tumor. While most cases result from a chromosomal deletion that occurs as a random event during gamete formation or in embryogenesis, some individuals may inherit an unbalanced translocation from an unaffected parent who carries a reciprocal translocation. Parental genetic screening is advised as risk for phenotypic abnormalities differs between familial or de novo mutation. Identification of mutation spectrum in this patient has crucial implications for understanding of a disease and its behaviour, leading to modifications of therapeutic recommendations, prognostic predictions and genetic counselling. Genetic etiology of WAGR syndrome cases in Malaysia are still scarcely reported. Hence, this case is reported for its rarity and for case collection to correlate between genotype and phenotype of WAGR syndrome in Malaysia.

Keywords: WAGR syndrome; Wilms tumour; congenital cataract

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