Clinical and Molecular Analyses of 24 Patients with Beckwith-Wiedemann Syndrome

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OBJECTIVES

Beckwith-Wiedemann syndrome (BWS) is a genetic disorder that results from abnormal expression of function of imprinting genes. Clinical manifestations vary greatly. To study the molecular genetic mechanism of BWS by Methylation Specific Multiplex Ligation-dependent Probe Amplification (MS-MPLA) and to analyze the relationship between genotype and phenotype, that will be helpful to improve the understanding of this disease.

METHODS

The copy number and methylation status of imprinted gene in chromosome 11p15.5 BWS region of peripheral blood were detected by MS-MLPA. The birth history, clinical phenotype and laboratory test results of the diagnosed patients were recorded and analyzed, and the relationship between different molecular genetic mechanisms and clinical phenotypes was analyzed.

RESULTS

24 patients were confirmed with BWS by MS-MLPA (10 males and 14 females; age range，1 day to 4 years). Among these 24 patients, 16 were identified with IC2 hypomethylation (67%), 2 with IC 1 hypermethylation (8%), 5 with pUPD (21 %), 1 with microdeletion in the region of chromosome 11p15.5 (4%). This diagnostic technique could not detect the inversion, translocation and mutation of gene *CDKN1C* in 11p15.5 region. Among these patients, abdominal wall defect were present in 13 patients, pre- or postnatal overgrowth in 9 patients, 6 patients with hypoglycemia, 15 with macroglossia, 5 showed ear creases, 7 showed facial nevus flammeus and hemihyperplasia was found in 8 patients. 5 cases were complicated with cardiovascular malformation (atrial septal defect), 6 cases with abdominal visceral organomegaly, 1 cases with severe abdominal rhabdomyosarcoma. Among them, patients with IC2 hypomethylation had higher incidence of macroglossia, abdominal wall defect and overgrowth, while patients with IC1 hypermethylation had higher incidence of facial nevus flammeus, ear crease and hemihyperplasia.

CONCLUSIONS

Macroglossia, umbilical hernia, excessive growth are the three main features of BWS, about 2/3 of the patients may show excessive growth, macroglossia, abdominal wall defecs. Facial nevus nevi, ear creases, hypoglycemia and abdominal visceral organomegaly are common clinical manifestations. This syndrome is associated with expression defect of imprinted genes in chromosome 11p15.5 BWS region, in which more than half of the patients are due to hypomethylation of IC2. When encountered great children, children with clinical giant tongue, umbilical herniation, excessive growth of limb asymmetry or other clinical manifestations, consideration should be given to the possibility of this disease, early detection of MS-MLPA. For children with high clinical suspicion but negative MS-MLPA result, mutation of gene CDKN1C or chromosome inversion and displacement in 11p15.5 region should be considered, and the related genetic tests should be further performed.

REFERENCE

Katrin O. Silver-Russell Syndrome and Beckwith- Wiedemann Syndrome: Opposite Phenotypes with Heterogeneous Molecular Etiology. Mol Syndromol 2016;7:110–121

NOTHING to DISCLOSE

WL, RL, BW, WZ, ZZ,MZ,FL