Familial Cases with *MECP2* Mutations

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Abstract

Objective: To investigate the rate of Chinese familial cases with *MECP2* mutations, the clinical and molecular characteristics of the familial cases, and its hereditary mechanism.

Method: Familial cases with *MECP2* mutation were identified by PCR, direct sequencing of the gene *MECP2* in patients with Rett syndrome (RTT) and their mothers, as well as array comparative genomic hybridization (aCGH) in patients with non-specific X-linked mental retardation (XLMR). Clinical information was collected. X-chromosome inactive (XCI) patterns of the female patients and their mothers carrying *MECP2* mutation were analyzed.

Result: Seven Chinese familial cases with *MECP2* mutation were detected among 426 families. The rate was 1.6% (7/426). Three probands were females with mutation of c.397C>T, p.R133C (2 cases); c.916C>T, p.R306C. Four probands were males with mutation of c.1164-1207 del44bp, p.P389X; c.1409G>A, p.R470H; c.441C>G, p.D147E and *MECP2* duplication. Three female patients meet the diagnosis criteria of RTT, while the males were diagnosed with non-specific XLMR and *MECP2* duplication syndrome. All mutated *MECP2* genes were inherited from their mothers. One mother had mild learning disorder, while others were asymptomatic. XCI studies showed all female patients have a random XCI. Five mothers had a skewed XCI. Two mothers had a random XCI pattern.

Conclusion: Familial cases with *MECP2* mutation were rare. The clinical manifestation between male and female patients was different. All the mutated genes were inherited from the asymptomatic or with mild learning disorder mothers. Different XCI pattern and different pathogenic gene spectrum in male and female may contribute the different phenotype between the mothers and their children.

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