NEOPTERIN AND BIOPTERIN METABOLISM IN SEGAWA DISEASE

H. Shintaku, H. Fujoka, T. Sakaguchi, S. Kudoh
Department of Pediatrics, Osaka City University Graduate School of Medicine, Osaka, Japan
shintakuh@med.osaka-cu.ac.jp

Background: Segawa Disease is characterized as childhood-onset dystonia plus syndrome with marked diurnal fluctuation and caused by partial defects of guanosine 5'-triphosphate cyclohydrolase I (GTPCH). Administration of levodopa is markedly improved the symptom of dystonia (Dopa-responsive dystonia: DRD). In this study, we measured neopterin and biopterin level in DRD patients to confirm biochemical diagnosis and tried to distinguish Segawa Disease from DRD.
Patients and methods: Eleven Japanese patients from 8 families were diagnosed as DRD patients due to heterozygous mutations in GCH1 gene, which codes for GTPCH (DRD (+/-)). Eleven non-dystonic controls were also measured. Neopterin and biopterin concentrations in plasma and CSF were measured in the patients and controls by using HPLC apparatus.
Results: The DRD patients had two missense mutations (A190V, T106I) and two frameshift mutations (K107fs, M211fs), one nonsense mutation (K239X), and a deletion of exons 2 and 3. Student's t test was used to compare values. It indicated that plasma neopterin level of DRD (+/-) (8.84±4.84 nM) was lower than those of controls (19.25±5.83 nM) ($p=0.0002$). Plasma biopterin level of DRD (+/-) and controls showed no significant difference ($p=0.2866$). Significant differences between DRD (+/-) and controls were also shown in CSF neopterin level ($p=0.0014$) and CSF biopterin level ($p<0.0001$). Data were expressed as average±SD.
Conclusion: The decrease in plasma neopterin concentration was related to DRD with GTPCH deficiency. It may be a useful diagnostic classification of DRD.