Abstract

Objectives: Sepiapterin reductase deficiency (SRD) causes central nervous system symptoms due to dopamine and serotonin depletion because sepiapterin reductase plays an important role in tetrahydrobiopterin biosynthesis. SRD cannot be detected by newborn screening because of the absent hyperphenylalaninemia. To diagnose SRD biochemically, confirmation of reduced monoamine metabolites and elevated sepiapterin in the cerebrospinal fluid (CSF) has been considered necessary, because a past study showed no elevation of urine sepiapterin. Recently, however, the elevation of urine sepiapterin in SRD was reported.

Methods: We developed a fast method to measure sepiapterin and creatinine simultaneously using high-performance liquid chromatography with fluorescence and ultraviolet detection. Urine sepiapterin and creatinine were measured in three SRD patients, two SRD carriers, four SRD siblings, and 103 non-SRD patients.

Results: In the three SRD cases, concentrations of urine sepiapterin were 1086, 914, and 575 μmol/mol creatinine (upper limit: 101.7 μmol/mol creatinine), and were markedly higher than those in other groups. CSF sepiapterin concentration was also measured in one SRD case and it was 4.1 nmol/L (upper limit: 0.5 nmol/L).

Conclusions: The simultaneous determination of urine sepiapterin and creatinine appears helpful for the diagnosis of SRD. This assay system can also be used to measure sepiapterin in the CSF.

Key words: developmental delay; involuntary movement; neurotransmitter disorders; neurometabolic disorders; high-performance liquid chromatography