Disorders of dopamine metabolism in pediatric neurotransmitter disease in Japan; Segawa disease, sepiapterin reductase deficiency and tyrosine hydroxylase deficiency

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Background: Segawa disease (SD), sepiapterin reductase (SR) deficiency and tyrosine hydroxylase (TH) deficiency are very rare inherited diseases characterized by dopa-responsive dystonia. Dysfunction of GTP cyclohydrolase I and SR due to mutations of the enzyme-coding gene, *GCH1*and *SPR,* respectively, reduces the production of neopterin and biopterin, and this induces a shortage of dopamine in the central nervous system (CNS). TH deficiency also induces a shortage of dopamine in the CNS. Method: We examined 137 patients who suffered dystonia and/or other involuntary movements, from January 2012 to December 2016. We measured the neopterin and biopterin content in these patients. Genetic analysis of *GCH1*, *SPR and TH* were also performed in 50, 2 and 1 patients, respectively. Results: Twenty-two patients had mutations in *GCH1*and were diagnosed with SD. Of the remaining 87, 2 patients had mutations in *SPR*and *TH,*and were diagnosed as having SR deficiency and TH deficiency, respectively. SD patients comprised 18 females and 4 males. The average age of patients who underwent genetic analysis was 19.35 years (Range: 7 to 62). Most of the patients who were diagnosed as adults showed dystonic symptoms from a very young age. No common mutation was observed in SD patients. In this study, we examined patients from 32 of the 47 prefectures in Japan (total population of these areas was 106,058,400 in 2016). The calculated incidence rate of SD was 4.1/100,000,000 per year in this study. The prevalence rate of SD was considered to be 1.6/1,000,000 when the average of duration of this disease was 40 years. Conclusion: Over the course of five years, we genetically diagnosed patients with SD, SR deficiency and TH deficiency. No common mutation was observed. In SD the incidence rate was 4.1 per hundred million people per year and the prevalence rate was 1.6 per million people in Japan.