DISORDERS OF DOPAMINE METABOLISM IN PEDIATRIC NEUROTRANSMITTER DISEASES (PNDs) IN JAPAN;

SEGAWA DISEASE, SEPIAPTERIN REDUCTASE (SR) DEFICIENCY, AND TYROSINE HYDROXYLASE (TH) DEFICIENCY

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Introduction

- Segawa disease, 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.

Patiens and Methods

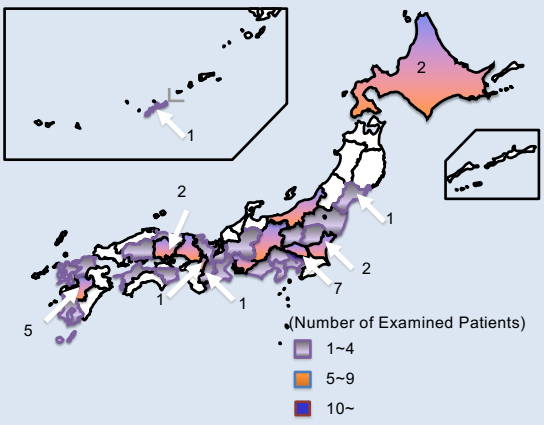
- We examined 137 patients who suffered dystonia and/or other involuntary movements, from January 2012 to December 2016.
- We measured the neopterin and biopterin content in these patients.
- Genetic analysis of *GCH1*, *SPR and TH* were also performed in 50, 2 and 1 patients, respectively.

Result 1

- Twenty-two patients had mutations in *GCH1* and were diagnosed with Segawa Disease.
- Of the remaining 87, two patients had mutations in *SPR* and *TH,* and were diagnosed as having SR deficiency and TH deficiency, respectively.
- Segawa Disease 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 Segawa Disease patients.

Result 2

(1) Number of examined patients were shown in the map of Japan. Number of Segawa disease patients detected in this study were shown and pointed in each prefecture. All patients were ethnically East Asian.



- 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 Segawa Disease was 4.1/100,000,000 per year in this study .
- The prevalence rate of Segawa Disease was considered to be 1.6/1,000,000 when the average of duration of this disease was 40 years.

Conclusions

1. Over the course of five years, we genetically diagnosed 22 patients with Segawa disease, 1 SR deficiency and 1 TH deficiency.
2. No common mutation was observed.
3. The calculated incidence rate of Segawa disease was 4.1/100,000,000 per year in this study.
4. The prevalence rate was considered 1.6/1,000,000 when the average of duration of this disease was 40 years.