



Correlation between clinical and radiologic features of patients with Gerstmann-Sträussler-Scheinker syndrome (Pro102Leu)

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ABSTRACT

Background and purpose: Gerstmann-Sträussler-Scheinker syndrome is a rare hereditary neurodegenerative disorder with clinical heterogeneity. This study is aim to demonstrate the clinical spectrum and radiologic characteristics of patients caused by Pro102Leu mutation in PRNP.

Materials and methods: We retrospect clinical manifestations of five patients from four Japanese families, and comprehensively analyzed their brain MRI, SPECT (N-isopropyl-p-[123I] iodoamphetamine), and PET (18F-2-fluoro-2-deoxy-D-glucose) images.

Results: All patients developed ataxia of lower limbs and trunk, gait disturbance, dysesthesia in legs, and lower limb hyporeflexia. In the early clinical stage before dementia began, no noticeable abnormalities could be observed from brain MRI, but SPECT and PET revealed mosaic-like pattern of blood flow and glucose metabolism of the brain. Predominant abnormalities were found in the occipital and frontal lobes on SPECT and PET analysis, respectively. In SPECT analysis, blood flow of the anterior cerebellar lobes was lower than that of the posterior cerebellar lobes.

Conclusions: Clinical symptoms resulting from failure of dorsal horn of spinal cord and spinocerebellar tracts were observed in all cases. Radiologic findings revealed individual differences of involved region in their brain, which could produce clinical diversity. We identified a downtrend of blood flow in the anterior cerebellar lobes, a projection field of the spinocerebellar tracts, which is an important feature of Gerstmann-Sträussler-Scheinker syndrome.

1. Introduction

Gerstmann-Sträussler-Scheinker syndrome (GSS), first reported in 1936, as a common inherited prion disease, is clinically and genetically heterogeneous [1,2]. According to a recent Japanese report, GSS102 accounts for 16.3% (93/572) of patients with inherited prion disease [3]. GSS102 is characterized clinically by prominent cerebellar signs accompanied by a slowly progressive dementia and pathologic findings of multifocal prion protein (PrP)-positive plaques [4,5]. Spinocerebellar degeneration is known as one of the disease features and has been recognized as associated with dementia. However, dementia

frequently appears later during the course of illness, which makes it difficult for neurologists to diagnose in the early stage.

Previously, we demonstrated that GSS102 mainly shows ataxia of the lower limbs and trunk, dysarthria, lower limb paresthesia, and decreased deep tendon reflexes in the early stage, followed by dementia in the advanced stage. On radiologic analysis, we have also described that SPECT imaging shows abnormalities earlier than MRI, manifesting predominantly as decreased blood flow in the occipital lobes but almost normal flow in the cerebellum [6]. In this study, we further examined the higher brain function of patients with GSS102, and evaluated the image findings of MRI, SPECT, and PET.

Abbreviations: GSS, Gerstmann-Sträussler-Scheinker syndrome; GSS102, GSS patients caused by Pro102Leu mutation in PRNP

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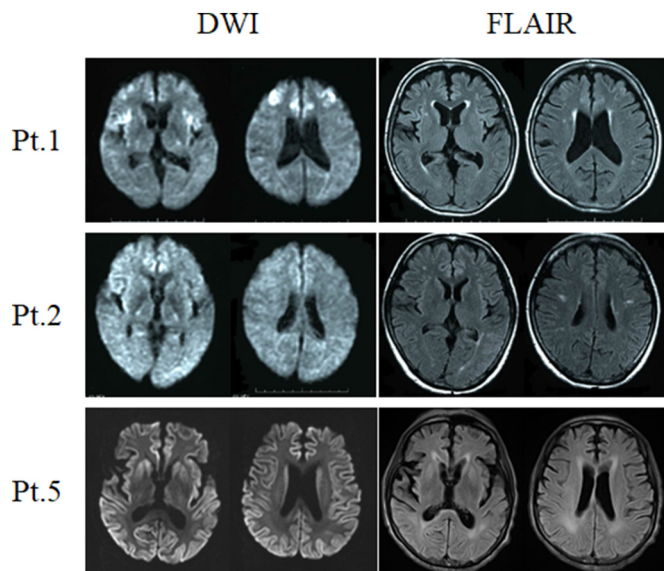


Fig. 1. Brain MRI. DWI and FLAIR image in Patients 1,2,5. They presented abnormal intensity of the cortex and no brain atrophy.

2. Materials and methods

We retrospectively studied five GSS patients from four families with genetically confirmed heterozygous Pro102Leu mutation in the *PRNP* gene. Additionally, 4 patients harbored homozygous methionine at codon 129 in *PRNP*, while heterozygous substitution from methionine to valine (Met129Val) was detected in patient 3. Besides, all patients shared a homozygous glutamate at codon 219. All patients were born in Kagoshima Prefecture, locating in the southern part of Japan. The protocol of the following study was reviewed and approved by the Institutional Review Board of Kagoshima University. All patients and family members provided written, informed consents to participate in this study.

2.1. Cognitive and electrophysiological studies

Neurologic examination was performed mainly in our hospital. To evaluate cognitive abnormalities, three methods were applied, consisting of the Mini Mental State Examination (MMSE), the Wechsler Adult Intelligence Scale-Revised (WAIS-R) test, and the Trail Making Test (TMT). Three of the five patients underwent electrophysiologic studies, including nerve conduction study (NCS), needle electromyography (needle EMG), short latency somatosensory evoked potential (SSEP), and electroencephalogram (EEG).

Table 1

Clinical summary of 5 GSS patients with Pro102Leu mutation.

Patient No.	1	2	3	4	5
Year/sex	73/F	62/F	61/F	60/M	59/M
Duration from onset	1y3m	1y11m	2y0m	0y9m	> 2y
Onset symptom	Dysesthesia in lower limbs	Ataxic gait	Ataxic gait	Dysarthria	Character change
Clinical features at initial examination					
MMSE	29	25	24	27	Unable
Dysarthria	–	+	+	+	+
Ataxia in upper limbs	–	+ / –	+	+	+
Ataxia in lower limbs	+	+	+	+	+
Weakness of lower limbs	+	+	+	+	+
Pyramidal sign	+	+	+	–	+
Extra-Pyramidal sign	–	–	–	–	–
Areflexia in lower limbs	+	+	+	+	+
Dysesthesia in lower limbs	+	+	+	+	Unknown
Vibration in lower limbs	normal	normal	normal	normal	Unable
WAIS-R (VIQ/PIQ/IQ)	83/84/82	76/64/69	91/100/95	84/82/81	N.E.
TMT A	92	80	27	55	N.E.
TMT B	140	incomplete	40	119	N.E.
Codon129	Met/Met	Met/Met	Met/Val	Met/Met	Met/Met
Codon219	Glu/Glu	Glu/Glu	Glu/Glu	Glu/Glu	Glu/Glu
Brain MRI abnormality	+	+	–	–	+
SPECT abnormality	+	+	+	+	+
PET abnormality	+	+	+	+	+
Electrophysiological study					
EEG PSD	–	–	–	–	N.E.
NCS	normal	normal	normal	normal	normal
Needle EMG	normal	normal	normal	N.E.	N.E.
SSEP latency in lower limbs	normal	normal	normal	N.E.	N.E.

MMSE: Mini Mental State Examination.

WAIS-R: Wechsler Adult Intelligence Scale-Revised.

VIQ: Verbal Intelligence Quotient.

PIQ: Performance Intelligence Quotient.

IQ: Intelligence Quotient.

N.E.: Not Exam.

TMT: Trail Making Test.

EEG: electroencephalogram.

PSD: periodic synchronous discharge.

NCS: nerve conduction study.

EMG: electromyography.

SSEP: short latency somatosensory evoked potential.

Bold value means abnormal value.

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