CASE REPORT

A Case of Gerstmann-Sträussler-Scheinker Syndrome

Momoko IRISAWA^{1*}, Makoto AMANUMA¹, Eito KOZAWA¹, Fumiko KIMURA¹,
and Nobuo ARAKI²

*Departments of ¹Radiology and ²Neurology, Saitama Medical School
38 Morohongo, Moroyama-cho, Iruma-gun, Saitama 350-0451, Japan*

(Received October 2, 2006; Accepted February 14, 2007)

Gerstmann-Sträussler-Scheinker syndrome (GSS syndrome) is a rare hereditary disorder caused by prion protein gene mutation. We present the case of a 31-year-old man, whose signs and symptoms gradually progressed from loss of attention while driving at onset to headache, dysarthria, night sweat, fatigue, and dysgraphia. Diffusion-weighted imaging (DWI) of the brain after admission showed high signal intensities in the bilateral caudate nuclei, bilateral thalami, and cerebral cortices that suggested transmissible spongiform encephalopathy. The patient was diagnosed with GSS syndrome on genetic study. Magnetic resonance (MR) imaging of the entire period of sickbed showed gradually changing signal intensities and cerebral atrophy. We present a series of images and discuss the reasons for the abnormal intensities in GSS syndrome that vary among reported cases.

Keywords: *Gerstmann-Sträussler-Scheinker syndrome, transmissible spongiform encephalopathy, MRI*

Introduction

Transmissible spongiform encephalopathy (TSE) is characterized by the deposition of scrapie prion protein (PrP^{Sc}), an abnormal form of a normal cellular protein (PrP^C). TSE exists in sporadic, genetic, and acquired forms.¹ It emerges as spongiform degeneration in the cerebrum and leads to certain death. Gerstmann-Sträussler-Scheinker syndrome (GSS syndrome) is a rare hereditary TSE, whose clinical features include cerebellar ataxia, myoclonus, and dementia. Patients often develop ataxia in their fifties and subsequent dementia and may become vegetative. We report a patient whose disease onset was characterized by abnormal behavior followed gradually by cerebral atrophy and whose final diagnosis on genetic study was GSS syndrome. Signal intensities on MR imaging of the brain from disease onset to the chronic phase changed gradually. Signal intensities of reported GSS syndrome are various and indefinite. We discuss the intensities and distribution of signals among reported cases.

Case

In May 2002, the family of a 31-year-old man remarked his loss of attention while driving a car. Afterward, headache, dysarthria, night sweat, fatigue, and dysgraphia gradually developed. In June, initial MR imaging of the brain was performed using a 1.5T machine (Vision, Siemens, Erlangen, Germany). T₂-weighted (T₂WI; repetition time/echo time [TR/TE] = 3500 ms/90 ms) and anisotropic diffusion-weighted images (DWI; TR/TE/ = 0.8 ms/123 ms) were obtained. MR imaging showed faint, high signal intensity in the right thalamus on DWI, which was difficult to identify because of high signal intensity of the thalami and callosal splenium caused by anisotropy (Fig. 1), and he was diagnosed as normal. In September and October, after experiencing hallucination and dystrophy, the man was admitted to our hospital. Physical examination revealed positive bilateral Babinski's reflex and left Chaddock's sign. Speech was slurred and slow. Gait was slightly wide based but not ataxic. Coordination was unstable but possible. Incomplete periodic synchronous discharge (PSD) was observed on electroencephalogram. Computed tomography (CT) of the brain after admission showed small calcifications in the left occipital lobe (Fig. 2). MR imaging was performed using 1.5T machines (Sonata and Quan-

*Corresponding author, Phone: +81-49-276-1265, Fax: +81-49-295-8003, E-mail: peach@saitama-med.ac.jp

Fig. 1. Magnetic resonance (MR) images of the brain at first visit to the hospital. (a) Diffusion-weighted image (DWI); high signal intensity of the right thalamus was difficult to identify because of high signal intensity of the thalami and callosal splenium from anisotropic image. (b) T₂-weighted image (T₂WI); faint high signal intensity is seen in the right thalamus.

Fig. 2. Computed tomography (CT) of the brain; small nodular calcifications are seen in the left occipital lobe.

tum, Siemens, Erlangen, Germany): Sonata: T₁WI (TR/TE = 522 ms/12 ms), T₂WI (TR/TE = 4000 ms/87 ms), and DWI (TR/TE/b factor = 4100 ms/78 ms/1000 s/mm²) and Quantum: T₁WI (TR/TE = 567 ms/13 ms), T₂WI (TR/TE = 3800 ms/91 ms), and DWI (TR/TE/b factor = 4100 ms/88 ms/1000 s/mm²). The bilateral caudate nuclei, bilateral thalami (ventral medial nucleus), and cortices showed high intensity on DWI (Fig. 3). Similar faint, high intensity in the same sites were also identified on T₂WI and fluid-attenuated inversion-recovery (FLAIR) imaging (Fig. 3). Single photon emission computed tomography (SPECT) obtained with ^{99m}Tc-ECG (Neurolight® Daiichi Radioisotope Labs, Ltd.) revealed decreased blood flow that was predominant in the occipital lobes. Family history was unremarkable. From genetic study, he was diagnosed with GSS syndrome with Leu mutation in codons 102 and in a prion protein. After admis-

sion, dementia gradually progressed and speech gradually decreased. As the disease progressed, he showed apparent myoclonus. In December, he left our hospital per family wishes. He was followed as an out-patient at our hospital, and underwent periodic MR imaging. Through the disease's clinical course, there were gradual changes in locations and characteristics of abnormal signal intensities on MR imaging (Fig. 4). On DWI, high intensities of the thalami and caudate nuclei gradually decreased starting 10 months after initial examination, whereas intensities in the cerebral and insular cortices remained high (Fig. 4b). Intensities on DWI and T₂WI of the cerebral and insular cortices gradually increased and then gradually decreased, showing the highest intensity at 12 months after initial examination (Fig. 4c, g). On T₂WI, intensities in the deep white matter of the cerebrum gradually increased starting 10 months

Fig. 3. Magnetic resonance (MR) images of the brain 4 months after initial examination. (a, b) Diffusion-weighted image (DWI); brain cortices, bilateral thalami, and bilateral caudate nuclei appear high intensity. (c) T₂-weighted image (T₂WI); faint high signal intensity in bilateral thalami and caudate nuclei. (d) Fluid-attenuated inversion-recovery (FLAIR) image; similar high intensity to T₂-weighted image in bilateral thalami and caudate nuclei are shown.

after initial examination (Fig. 4f). On DWI and T₂WI, intensities of the bilateral globus pallidus gradually decreased starting 12 months after initial examination (Fig. 4c). The abnormal signal intensity in the bilateral globus pallidus was slightly high on T₁WI (Fig. 4k, l). The bilateral thalami also showed slightly high intensity on T₁WI starting 12 months after initial examination (Fig. 4k, l). Intact at the early stage, the bilateral hippocampus gradually decreased in volume as disease progressed. Gradual cerebral atrophy was observed throughout the period of sickbed (Fig. 4). In March 2003, after developing fever, appetite loss, and decline in activity, he was again admitted to our hospital because of pneumonia. Fever remained after inflammation was reduced. He developed akinetic mutism 25 months after initial examination.

Discussion

MR imaging findings in our patient showed high intensities in the bilateral caudate nuclei, thalami, and cerebral cortices on DWI in the early stage, within 4 months after initial examination. A similar signal pattern is reported in patients with Creutz-

feldt-Jakob disease (CJD).²⁻⁶ In patients with CJD, this abnormal intensity corresponds with spongiform changes and astrocytic glioses.^{4,5} Because GSS syndrome is also included in the TSE category that includes CJD, the similar signal abnormality may be described by the same mechanism. Furthermore, Finkenstaedt's group⁶ reported abnormal signal intensity on T₂WI and proton-density image (PDI). The signal abnormality on T₂WI and PDI also corresponded with spongiform degeneration.

In our case, the bilateral thalami and caudate nuclei showed strong high intensity on DWI in the early stage that decreased 10 months after initial examination. On the other hand, the intensities of the cerebral and insular cortices on DWI gradually increased up to 12 months after initial examination and then decreased. Nitirini and associates⁴ reported that the high signal intensity on DWI in some regions of the brain in patients with CJD has been attributed to the severity of spongiform degeneration and to gliosis. The gradual decrease in intensity in the basal ganglia, thalami, and cerebral cortices on DWI in our patient may have reflected the termination in spongiform degeneration. The

Fig. 4. Consequence of magnetic resonance (MR) imaging 4 to 17 months after initial examination. (a–d) Diffusion-weighted imaging (DWI) 4 to 17 months after initial examination. (e–h) T₂-weighted imaging (T₂WI) 4 to 17 months after initial examination. (i–l) T₁-weighted imaging (T₁WI) 4 to 17 months after initial examination. DWI shows areas of high intensity in the cerebral cortex, thalami, and caudate nuclei 4 months after initial examination (a). Areas of high intensity of the bilateral thalami and caudate nuclei are obscured at 10 months after initial examination on DWI and T₂WI (b, f). Signal intensity of the cerebral and insular cortices on DWI and T₂WI gradually increase up to 12 months after initial examination and decrease afterward (c, g). Intensity of deep white matter of cerebrum starts to increase gradually on T₂WI at 10 months after initial examination (f). Intensities of the bilateral globus pallidus gradually decreased on DWI and T₂WI starting at 12 months after initial examination (c, g). The bilateral globus pallidus show slightly high intensity on T₁WI at 12 months and 17 months after initial examination (k, l). The bilateral thalami show slightly high intensity on T₁WI at 12 months and 17 months after initial examination (k, l). Progressive cerebral atrophy is seen.

decreased intensity on DWI in the bilateral thalami and caudate nuclei preceding changes in intensity in the cerebral and insular cortices suggests the possibility of degeneration or gliosis in the bilateral thalami and caudate nuclei preceding that in the cerebral and insular cortices. Because we have not conducted biopsy, we cannot pathologically prove what happened to the cerebral nuclei and cortices

and what factors played a role in the changes in signal intensity over time. Patterns of signal change in the cerebral nuclei and cortices are not reported previously, but may be a clue to characterize MR imaging findings in GSS syndrome.

Low signal intensity in the basal ganglia on T₂WI on MR imaging is reported as a characteristic finding in GSS syndrome^{7,8} and is attributed to abnor-

mally increased amounts of iron deposition, such as that seen in chronic inflammatory and degenerative disease.⁸ This finding, observed in the bilateral globus pallidus in our patient, gradually decreased its intensity starting 12 months after initial examination. According to Finkenstaedt's group,⁶ no signal abnormality is observed in some part of patients with CJD, and this can be explained by iron deposition. Loss in signal intensity on T₂WI from iron deposition may mask the increase in signal intensity from spongiform degeneration. In our case, as stated, gradual decrease of high signal intensity in the bilateral caudate nuclei, thalami, and cerebral cortices correlated with reduction in spongiform degeneration. Thus, abnormal signal intensity in the globus pallidus may have been masked in the early stage, when high spongiform degeneration is suspected.

The bilateral thalami came to show slightly high intensity on T₁WI at 12 months after initial examination, indicating the shortening of T₁ and T₂ relaxation time by a mineral factor, such as manganese or zinc. Wong and colleagues⁹ reported a maximum decrease in copper of 50% and an overwhelming 10 times increase in manganese observed in the brain of patients with sporadic CJD compared with that of the normal person. Normal prion proteins work for acid resistance in combination with copper. However, when copper is low, prion protein is inclined to combine with manganese. This quite convincingly explains the high intensity on T₁WI.

There were some nodular calcifications in the left periventricular white matter. However, to our knowledge, there is no report of calcification in patients with TSE, so we suppose the calcification in our patient has nothing to do with the entity.

Proton magnetic resonance spectroscopy (¹H-MRS) has been reported useful in detecting subtle, ongoing neural changes in patients with GSS syndrome, even in the early stage.¹⁰ Unfortunately, this study was not carried out in our case.

Conclusions

We have reported a case of GSS syndrome that

demonstrated various signal intensities attributable to various factors, including spongiform degeneration, gliosis, iron deposition, and mineral factors.

References

1. Knight RSG, Will RG. Prion diseases. *J Neurol Neurosurg Psychiatry* 2004; 75 Suppl 1:i36–42.
2. Samman I, Schulz-Schaeffer WJ, Wohrle JC, Sommer A, Kretzschmar HA, Hennerici M. Clinical range and MRI in Creutzfeldt-Jakob disease with heterozygosity at codon 129 and prion protein type 2. *J Neurol Neurosurg Psychiatry* 1999; 67: 678–681.
3. Fukushima R, Shiga Y, Nakamura M, Fujimori J, Kitamoto T, Yoshida Y. MRI characteristics of sporadic CJD with valine homozygosity at codon 129 of the prion protein gene and PrP^{Sc} type 2 in Japan. *J Neurol Neurosurg Psychiatry* 2004; 75: 485–487.
4. Nitrini R, Mendonca RA, Huang N, LeBlanc A, Livramento JA, Marie SK. Diffusion-weighted MRI in two cases of familial Creutzfeldt-Jakob disease. *J Neurol Sci* 2001; 184:163–167.
5. Bahn MM, Parchi P. Abnormal diffusion-weighted magnetic resonance images in Creutzfeldt-Jakob disease. *Arch Neurol* 1999; 56:577–583.
6. Finkenstaedt M, Szudra A, Zerr I, et al. MR imaging of Creutzfeldt-Jakob disease. *Radiology* 1996; 199:793–798.
7. Wimberger D, Uranitsch K, Schindler E, Kramer J. Gerstmann-Sträussler-Scheinker syndrome: MR findings. *J Comput Assist Tomogr* 1993; 17:326–327.
8. Farlow MR, Yee RD, Dlouhy SR, Conneally PM, Azzarelli B, Ghetti B. Gerstmann-Sträussler-Scheinker disease. I. Extending the clinical spectrum. *Neuroradiol* 1989; 39:1446–1452.
9. Wong BS, Chen SG, Colucci M, et al. Aberrant metal binding by prion protein in human prion disease. *J Neurochem* 2001; 78:1400–1408.
10. Konaka K, Kaido M, Okuda Y, et al. Proton magnetic resonance spectroscopy of a patient with Gerstmann-Sträussler-Scheinker disease. *Neuroradiol* 2000; 42:662–665.