Single Photon Emission Computed Tomography (SPECT)
Findings of a Patient with a Novel Prion Mutation

Kosuke Matsuzono, Ryuta Morihara, Kota Sato, Nozomi Hishikawa,
Toru Yamashita, Kentaro Deguchi and Koji Abe

Abstract

We experienced a unique case of familial prion disease with a prion gene mutation that caused pan-autonomic failure, sensory neuropathy and mild cognitive impairment. No abnormal sites of intensity were observed on diffusion-weighted magnetic resonance image (MRI) over six to 11 years or fluid attenuated inversion recovery MRI at six or nine years. However, \(^{99m}\)Tc-ethylcysteinate dimer single photon emission computed tomography (SPECT) showed a decreased cerebral blood flow in the bilateral parietal and occipital lobes at nine years, which then expanded at 11 years, corresponding to mild atrophy in these areas on MRI. In some cases of prion mutations, particularly the slowly progressive type, SPECT may show abnormalities, while MRI does not.

Key words: prion disease, SPECT, MRI, sensory neuropathy, autonomic disease

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Introduction

Creutzfeldt-Jakob disease (CJD) is a rare, but severe neurological disease. Many reports have documented the magnetic resonance image (MRI) findings of CJD; however, only a few reports have described the features on single photon emission computed tomography (SPECT) (1, 2). For example, Mathews et al. reported that the cerebral blood flow (CBF) is remarkably decreased in the parietal and occipital cortices in cases of the Heidenhain variant of CJD (3), and Matsuda et al. reported the usefulness of brain SPECT with \(^{123}\)I-IMP for making an early diagnosis of CJD (4). In this report, we discuss the unique SPECT findings in a CJD case of familial prion disease with a new prion gene mutation consisting of a 2-bp deletion (CT) in codon 178 and highlight the characteristic clinical features of pan-autonomic failure, sensory neuropathy and mild cognitive impairment as the initial symptoms of this disorder.

Case Report

A 37-year-old Japanese woman began to experience urinary retention of up to 2 L at 26 years of age. At 30 years of age, she exhibited syncope for five minutes due to orthostatic hypotension. At 31 years of age, she began to display memory disturbances. After 31 years of age, she suffered from frequent vomiting and diarrhea. However, she continued to live on her own 11 years after symptom onset. Her mother and little brother had also developed dementia, urinary disturbances and orthostatic hypotension with frequent vomiting and diarrhea at 47 and 29 years of age, respectively. Her mother died one year after disease onset. In addition, the patient’s grandfather developed dementia with a urinary disturbance and orthostatic hypotension at 52 years of age and died at 62 years of age, although no medical documents were recorded. We subsequently found a 2-bp deletion (CT) in codon 178 in the prion gene of the current patient that caused the addition of variable 25 amino acids at the C-terminal from the mutation site to the premature stop codon at codon 195 (5). Although we were unable to analyze the gene of the patient’s mother due to her death, the prion gene of her father was normal. We previously reported this familial case of a prion gene mutation involving a 2-bp deletion (CT) in codon 178 (5). The affected family members exhibited a unique phenotype consisting of severe
Figure. FLAIR MR images obtained at six (A), nine (B) and eleven (C) years after onset and a DW MR image obtained at eleven years after onset (D). Note the lack of cerebral atrophy or sites of abnormal intensity at six (A) and nine (B) years, with slight atrophy of the bilateral anterior, parietal and occipital lobes at eleven years (C). 99mTc-ECD SPECT showing a CBF decrease in the bilateral parietal and occipital lobes according to an easy Z-score imaging system (eZIS) analysis at nine years after onset (E), subsequently expanding to the bilateral anterior lobes (arrowheads) at eleven years (F).
pan-autonomic failure, sensory neuropathy and mild cognitive impairment caused by this novel prion gene mutation.

The higher cognitive function test battery of the minimal mental state examination (MMSE) (at nine and 11 years after onset), frontal assessment battery (FAB) and Montreal cognitive assessment (MoCA) (at nine years after onset) were examined in this case of a 37-year-old Japanese woman. In addition, an electroencephalogram (EEG) was obtained at nine years, MRI was performed at six, nine and 11 years after onset, and SPECT with \(^{99m}\)Tc-ethylcysteinate dimer (\(^{99m}\)Tc-ECD SPECT) was performed at nine and 11 years after onset. The results of \(^{99m}\)Tc-ECD SPECT were subsequently analyzed using easy Z-score imaging system (eZIS), although the computer software programs differed at nine and 11 years, with a decrease in the CBF indicated by a change from green to red at nine years and blue to green at 11 years. We subsequently evaluated the relationships between the results of these examinations.

The cognitive function of the present patient showed a mild decline to 27/30 on the MoCA at nine years after onset. Meanwhile, the MMSE score decreased to 22/30 at 11 years after onset. EEG showed only normal \(\alpha\) waves, without periodic synchronous discharge and fluid attenuated inversion recovery (FLAIR) MR images showed neither cerebral atrophy nor abnormal intensity at six years after onset (Figure A). It was difficult to identify differences on the FLAIR images obtained at six and nine years after onset (Figure B). In contrast, the FLAIR image obtained at 11 years after onset showed mild atrophy of the bilateral anterior, parietal and occipital lobes (Figure C), whereas diffusion-weighted images (DWI) of MRI showed no abnormal sites of intensity from six to 11 years after onset (Figure D). Furthermore, \(^{99m}\)Tc-ECD SPECT showed a decrease in CBF in the bilateral parietal and occipital lobes at nine years after onset (Figure E); these areas had expanded in the bilateral anterior lobes at 11 years after onset (Figure F, arrowheads). Notably, the areas of CBF decrease observed at nine years corresponded to the areas of mild atrophy detected on FLAIR MR images at 11 years.

**Discussion**

Only limited medical tests are currently available for diagnosing CJD. Periodic sharp wave and slow wave complexes (PSWCs) are sometimes found on electroencephalograms. However, PSWCs are not detected in the early stage, and neither variant nor familial CJD patients usually show PSWCs, similar to that seen in the present case (6, 7). In contrast, MRI is more useful for detecting CJD with high signal intensity on DWI in the cerebral cortex (1, 8). Shiga et al. reported a sensitivity of DWI of 92.3%, with a specificity of 93.8% (2). Although SPECT is also useful for diagnosing early-stage CJD (9), the diagnostic advantages and relationship between MRI and SPECT in cases of CJD have not been clarified. In the present case, no MRI abnormalities were noted six to 11 years after onset (Figure A-D), while a CBF decrease was only found in the bilateral parietal and occipital lobes on SPECT at nine years after onset (Figure E), which had subsequently progressed at 11 years (Figure F). The present case was very slowly progressive, with a unique prion gene mutation; therefore, such slow progression may not be visualized as high intensity on DWI, although MRI was not performed before six or after 11 years after onset. In addition, there were no symptoms due to parietal or occipital lobe dysfunction, perhaps because that CBF decrease was not severe.

It is unclear whether the CBF pattern differs among CJD subtypes. Matsuda et al. reported that the CBF was decreased in various parts of the cerebral cortex, including the frontal, temporal, parietal and occipital lobes, in six sporadic CJD cases, with the CBF decrease in the occipital lobe being milder than that observed in the other regions. The authors also reported that the CBF was preserved in the thalamus and cerebellum in five sporadic cases (4). In addition, we previously reported the SPECT findings in one case of the V180I mutation, in which the CBF was decreased in the left parietal and frontal lobes at 17 months after disease onset and subsequently spread to the bilateral basal ganglia, right parietal and frontal lobes, except for the occipital lobe, at 23 months after onset (9). Although the decrease in CBF was primarily found in the cerebral cortex, not in the thalamus or cerebellum, in most sporadic CJD and our previous V180I case, the initial CBF decrease in the bilateral occipital lobes was unique in the present case.

Our present case is unique in that the clinical phenotype of severe pan-autonomic failure and sensory neuropathy is rare as a prion disease and the SPECT images showed positive findings, while MRI showed no abnormalities.

**The authors state that they have no Conflict of Interest (COI).**

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**References**