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Correlation between periodic sharp wave complexes and diffusion-weighted magnetic resonance images in early stage of Creutzfeldt-Jakob disease: A report of two cases

Masahiro Mizobuchi [a,*], Chiharu Tanaka [a], Kazuya Sako [a], Atsuko Nihira [a], Takenori Abe [a], Atsushi Shirasawa [b]

[a] *Department of Neurology, Nakamura Memorial Hospital, Sapporo, Japan*
[b] *Miyuki Giken Co., Ltd, Tokyo, Japan*

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Summary We evaluated the correlation between the periodic sharp wave complexes (PSWC) on EEG and the spreading lesions on diffusion-weighted (DW) magnetic resonance images (MRI) in two cases of Creutzfeldt-Jakob disease (CJD). In Case 1, DW-MRI showed increased signal intensity in bilateral caudate, bilateral parietal, and right temporo-occipital cortex at 7 weeks after onset. EEG showed PSWC of 1 Hz frequency at 8 weeks after onset. Source localization analysis of the PSWC was conducted by low resolution electromagnetic tomography (LORETA), and localized the source in the cortex of bilateral parietal lobes and mesial frontal lobe, predominantly on the right side. At 10 weeks after onset, the PSWC source spread to bilateral parietal and frontal lobes, and the same spread was also observed for the lesion depicted on DW-MRI. In Case 2, DW images showed high signal intensity in the right parietal cortical lesion at 4 weeks after onset. PSWC of 2 Hz frequency were seen in the routine EEG, and the source was localized in bilateral frontal lobes and right parietal lobe at 7 weeks after onset. The lesions on DW images also spread to bilateral frontal and parietal lobes. Nine weeks after onset, the source of PSWC extended to the right frontal lobe and bilateral parietal lobes, while the lesions on DW images progressed to the right temporal lobe and bilateral fronto-parieto-occipital lobes. Spreading DW-MRI lesions may correlate with the appearance of PSWC.

Introduction

Creutzfeldt-Jakob disease (CJD) is a fatal disease manifesting slowly progressive dementia, hallucination, ataxia, myoclonus, pyramidal tract sign and

* Corresponding author at: Nakamura Memorial Hospital, Minami-1, Nishi-14, Chuoku, Sapporo 060-8570, Japan.
Tel.: +81 11 231 8555; fax: +81 11 231 8387.
E-mail address: mizo@med.nmh.or.jp (M. Mizobuchi).

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extrapyramidal tract sign. A definite diagnosis depends on histopathological examination of biopsies or autopsy specimens. However, the transmissible nature of CJD limits the use of these high-risk methods. A probable diagnosis [1] is made according to symptoms and course of illness together with paroxysmal sharp wave complexes (PSWC) as characteristic EEG findings,[2] elevated 14-3-3 protein in the spinal fluid [3] and abnormal cortical intensity on diffusion-weighted (DW) magnetic resonance images (MRI).[4] Among these examinations, detection of lesion on DW-MRI is the most useful finding in the early stage of CJD.[5,6] However, a diagnosis is sometimes difficult in cases with focal or localized MRI lesions in the early stage of this disease.[7,8]

The first EEG finding of CJD is often localized frontal intermittent rhythmical delta activity (FIRDA) that appears immediately after onset.[9] The activity evolves to typical PSWC after a few weeks. PSWC are characterized by generalized synchronized high voltage sharp wave, with frequencies of 1—2 Hz.[10] Although PSWC usually show "generalized" waves, they sometimes exhibit lateralized or localized distributions in early stages of CJD.[10] Although PSWC is included as one of the criteria of clinical diagnosis of CJD, the mechanism of PSWC is not fully understood.

In this study, we followed two patients with CJD from the early stage and evaluated DW-MRI findings in association with the localization of PSWC on EEG determined by low resolution brain electromagnetic tomography (LORETA),[11] which is a source localizing method.

Patients and methods

Patients

Two cases with a clinical diagnosis of probable CJD were analyzed.

Case 1 was a 75-year-old woman who manifested slowly progressive cognitive decline with dizziness and unstable gait. Four weeks after onset, she experienced visual hallucination of something moving or dancing. She had a past history of primary biliary cirrhosis but no other diseases. Seven weeks after onset, she was admitted to our hospital because of unstable gait. At admission, neurological evaluation revealed moderate cognitive disturbance of orientation and memory, and visual illusion and visual agnosia were suspected. She also had ataxic gait with limb ataxia. Cerebrospinal fluid examination showed normal cell counts, sugar and protein, and moderately elevated neuron specific enolase (99.6 ng/dl) and 14-3-3 protein (55 ng/ml; normal range: below 25 ng/ml). No abnormal mutation was detected in prion protein gene. At week 2 after admission, vivid visual hallucination worsened, and myoclonus in four extremities was evident at 4 weeks. She could not speak and required a gastric tube for nutrition at 8 weeks after admission, and developed akinetic mutism and ataxic respiration at 16 weeks.

Case 2 was a 70-year-old man. Approximately 1 month before admission to our hospital, he felt occasional dizziness followed by slow progression of left leg weakness. One week later, his gait became unstable and an abnormal MRI lesion was detected in a local hospital. Two weeks after onset, he developed visual illusion and hallucination (for example, upper half of the human body wandering in the room), and left hemi-myoclonus. Left hand weakness and dysarthria gradually progressed. He was admitted to our hospital at 4 weeks after onset. He presented with mildly disturbed consciousness with dysarthria and incomprehensible, meaningless speech. Left hemiparesis with myoclonus and bilateral Chaddock signs were observed. Cerebrospinal fluid examination showed normal cell counts, sugar and protein, with mildly elevated neuron specific enolase (59.5 ng/dl) and 14-3-3 protein (+). No abnormal mutation was detected in prion protein gene. Seven weeks after admission, he could not speak and showed akinetic mutism with generalized myoclonus.

EEG sampling

Routine digital EEG was recorded every week from weeks 7 to 11 week after onset in Case 1, and from weeks 5 to 9 after onset in Case 2. Nineteen electrodes were placed following the international 10—20 method, and EEG was recorded (EEG2100, Nihon Koden, Tokyo) at a sampling rate of 200 Hz.

MRI

MRI was conducted using a 1.5 T system (Magnetome Symphony, Siemens). Routine T2-weighted image, proton image and DW image were acquired. Axial images of 5-mm slice thickness were obtained with the following conditions: SE, TR 3000 and TE 99 for T2-weighted image; SE, TR 3000 and TE 12 for proton image; and EPI, TR 5600, TE 176 and B factor 1000 for DW image.

Digital EEG analysis

Each digital EEG recording was examined visually to detect PSWC by an electroencephalographer who