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Case Report

EEG–EMG polygraphic study of dystonia and myoclonus in a case of Creutzfeldt–Jakob disease☆

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ABSTRACT

We report on a patient with sporadic Creutzfeldt–Jakob disease (CJD) who showed dystonia, periodic myoclonus, and periodic sharp wave complexes (PSWCs) on EEG. The EEG–EMG polygraphic study revealed that dystonia appeared without relation to periodic myoclonus and PSWCs and that dystonia EMGs were strongly suppressed after periodic myoclonus EMGs. These findings suggest that dystonia has a pathogenesis different from that of periodic myoclonus and PSWCs, but dystonia and periodic myoclonus may be generated through the sensorimotor cortex in CJD.

1. Introduction

Periodic sharp wave complexes (PSWCs) on electroencephalography are characteristic of Creutzfeldt–Jakob disease (CJD) and are frequently associated with rhythmic myoclonic jerks which are time-locked to PSWCs [1–3]. Some patients with CJD also present dystonia during the course of the disease. Myoclonus and dystonia are concomitantly observed in a few patients with CJD, but their pathophysiology is obscure. We investigated the relations between electroencephalogram (EEG) findings, myoclonus, and dystonia in a patient with CJD and addressed pathogenetic mechanisms underlying these involuntary movements.

2. Case report

A 68-year-old woman was admitted to our hospital with a two-month history of behavioral change, visual hallucination, gait disturbance, and involuntary movements. She was akinetic, bedridden, and moderately disoriented and dysphasic. She showed hypertonic and dystonic postures of the left and right upper extremities. There were two patterns of dystonic postures in the left upper extremity: one showed shoulder abduction, elbow extension, and grasping (Fig. 1A) and the other showed shoulder flexion and abduction, elbow flexion, forearm pronation, and wrist flexion (Fig. 1B). Either pattern of dystonia could be seen. The right upper extremity showed elbow flexion and grasping (Fig. 1B). There was no myoclonus on admission. The deep tendon reflexes were normal, and plantar responses were flexor. Her blood test showed no elevation of antinuclear antibody, rheumatoid factor, or antithyroid antibodies. She was negative for HIV. Routine tests of cerebrospinal fluid (CSF) were not remarkable, and anti-HSV^{-1} antibodies of CSF were not elevated. A CSF neuron-specific enolase was elevated, 55 ng/ml (normal ≤30 ng/ml), but a CSF 14-3-3 test was negative. She had methionine homozygosity at codon 129 of the human prion protein gene. Diffusion-weighted magnetic resonance imaging (DWI-MRI) revealed hyperintensities involving the bilateral temporooccipital lobes, caudate heads, and anterior parts of the putamen (Fig. 1C). The hyperintensities were more remarkable on the right side of the brain. The patient was diagnosed as having sporadic CJD. A month later, the patient developed myoclonus of the upper and lower extremities which intermittently appeared at approximately 1 Hz. The myoclonus appeared focally or generally in synchronization. The patient's voluntary and involuntary activities gradually decreased to unresponsiveness state for the following 6 months. She deteriorated to a vegetative state and died 21 months after onset.

Electroencephalogram–electromyogram (EEG–EMG) polygraph recordings were performed using a conventional electroencephalograph. The filter bandpass was 0.5–120 Hz for EEGs and 50–120 Hz for EMGs on the same day 3 months after onset. The patient showed akinetic

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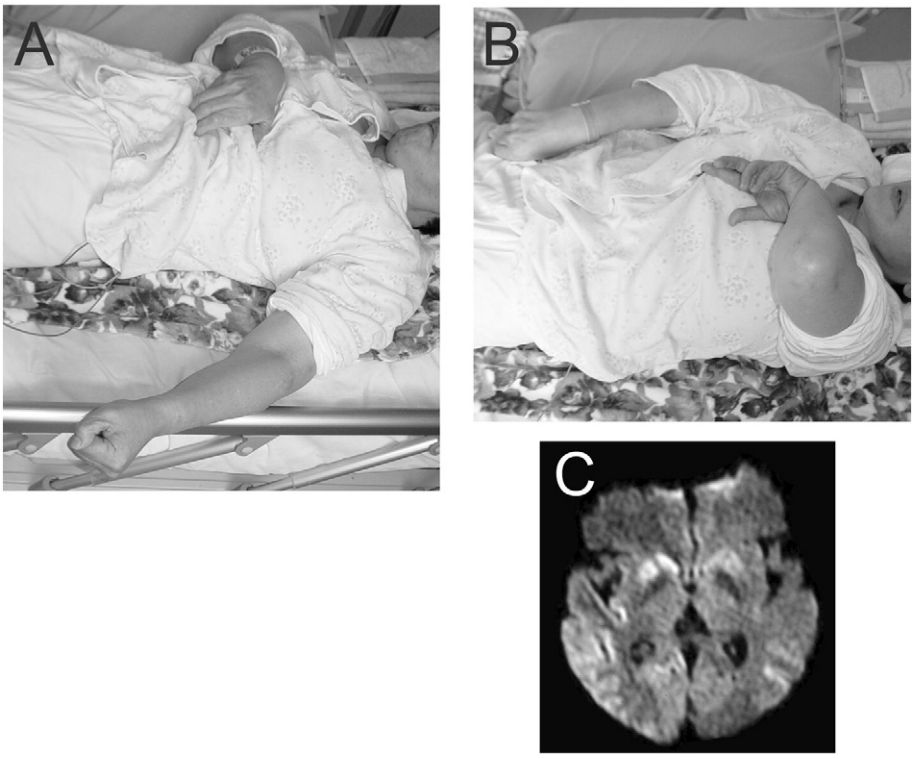

Fig. 1. Photos of the dystonia. There were two patterns of dystonic posture in the left upper extremity: (A) the shoulder abduction, elbow extension, and grasping, and (B) the shoulder flexion and abduction, elbow flexion, forearm pronation, and wrist flexion. The right upper extremity showed elbow flexion and grasping. DWI-MRI revealed hyperintensities involving the bilateral temporooccipital lobes, caudate heads, and anterior parts of the putamen (C). The hyperintensities were more remarkable on the right side of the brain.

mutism and had taken no antiepileptic medication. Myoclonus and dystonia were observed in the left upper extremity concomitantly or separately at this stage. Record 1 (Fig. 2A) showed PSWCs on EEGs and synchronized myoclonus EMGs in the wrist flexor and extensor muscles. The myoclonus EMGs were time-locked to PSWCs. Record 2 (Fig. 2B) showed PSWCs on EEGs, but there was only a trace of myoclonus EMGs. Record 3 (Fig. 2C) showed PSWCs and dystonia EMGs of the left upper extremity. There were a few positive and negative episodes of myoclonus superimposed on dystonia EMGs. Record 4 (Fig. 2D) showed dystonia without PSWCs in the initial recording part and dystonia and myoclonus with PSWCs in the later part. The dystonia EMGs were strongly suppressed in the periods following the positive myoclonus. Analysis of EEG and EMG activities with jerk-locked back-averaging method was not performed.

3. Discussion

Our case fulfilled the clinical diagnostic criteria of probable sporadic CJD [4]. The main symptoms, course of illness, and MRI findings were typical of sporadic CJD, and the initial symptoms of visual signs and myoclonus and methionine homozygosity at codon 129 of the human prion protein gene in our patient are in agreement with the elucidated

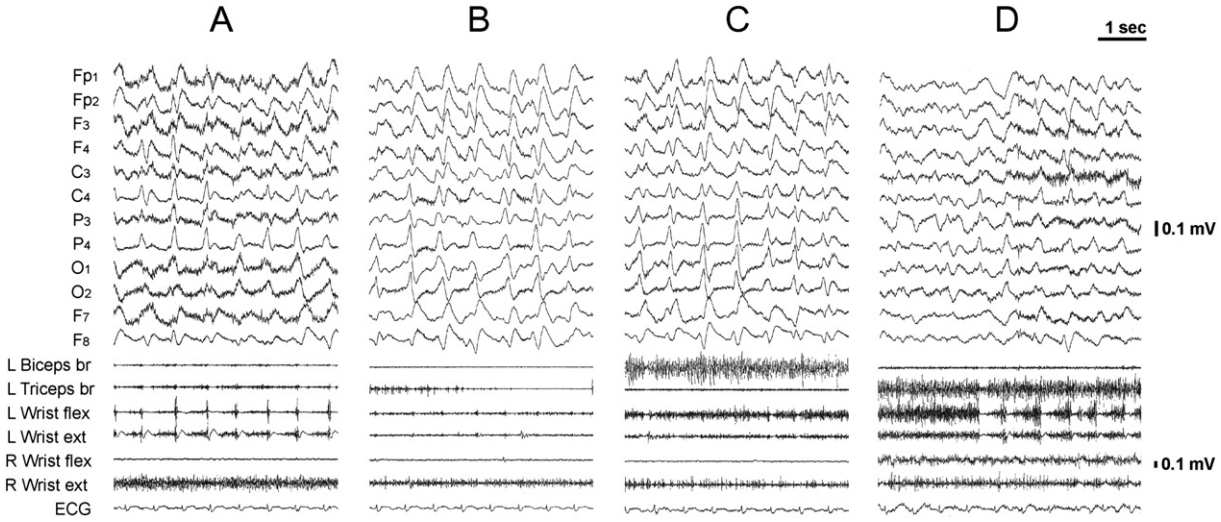

Fig. 2. EEG and EMG polygraphs. (A) Record 1 showed PSWCs on EEGs and synchronized myoclonus on EMGs. (B) Record 2 showed PSWCs, but no myoclonus. (C) Record 3 showed PSWCs and dystonia of the left upper extremity. (D) Record 4 showed dystonia without PSWCs in the initial recording part and dystonia and concomitant myoclonus with PSWCs in the later part. In Record 4, the positive myoclonus was superimposed on dystonia, and the dystonic contractions were strongly suppressed in the periods following the positive myoclonus.

genotype–phenotype correlation [5]. Myoclonus occurs in approximately 90% of patients with CJD; it appears at a relatively advanced stage of CJD and disappears in the terminal stage [1,3]. Myoclonus in CJD can be classified as rhythmic or irregular and positive or negative [2,6], and polygraphic study reveals that positive EMG bursts of periodic myoclonus are always time-locked with PSWCs [2,6]. A pacemaker which drives PSWCs is estimated to be located in subcortical structures, possibly the brainstem or thalamus, and an afferent volley from the pacemaker may excite the neocortex to form PSWCs [6,7].

Our case had periodic myoclonus, dystonia, and PSWCs, separately and simultaneously in the middle of the course of illness. The EEG–EMG polygraphic recordings disclosed that PSWCs are necessary for the occurrence of periodic myoclonus but are not always associated with it. Periodic sharp wave complexes have been suggested to be generated in the cortical and subcortical sources [6,7], while periodic myoclonus in CJD is estimated to be of cortical origin, probably sensorimotor cortices [6–8]. Therefore, it is probable that myoclonus may appear with PSWCs only in the period during which the excitability level of the sensorimotor cortex is high. Dystonia appeared without relation to periodic myoclonus and PSWCs in our patient, suggesting that the pathophysiology of dystonia is different from that of both myoclonus and PSWCs. The pathophysiology of dystonia remains obscure, but the studies on neural activity in the basal ganglia motor circuit in patients with dystonia have disclosed that altered temporal and spatial patterns of neural activity underlie dystonia [9,10].

Our records demonstrated the superimposition of periodic myoclonus on dystonic contractions and strong inhibition following each positive myoclonus. Similar periodic pauses time-locked to PSWCs were documented during active tonic contraction in CJD [6], and the decrease in excitability of the primary sensorimotor cortices was suggested to underlie it [6,7,11]. One of the possible mechanisms is estimated to be phasic refractoriness of cortical structures following periodic myoclonus [6,7,11]. Based on the similarity, it is suggested that the pauses of dystonic neural activity following myoclonus may occur in the sensorimotor cortex. This suggests that dystonic neural activity may pass through the sensorimotor cortex in CJD.

In conclusion, the EEG–EMG polygraphic findings in our patient suggest that periodic myoclonus is generated by a combination of the drive of PSWCs and the high excitability level of the sensorimotor cortex. Dystonia has a different pathogenesis from that of periodic myoclonus and PSWCs, but dystonia and periodic myoclonus may be generated through the sensorimotor cortex in CJD.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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