

Case Report

Epilepsia Partialis Continua as the First Presenting Symptom in Probable Sporadic Creutzfeldt-Jacob Disease: A Case Report and Literature Review

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Keywords

Epilepsia partialis continua · Sporadic Creutzfeldt-Jacob disease · Magnetic resonance diffusion-weighted image · Simple focal motor seizures

Abstract

We present the case of a middle-aged man suffering from epilepsy partialis continua 3 weeks before the start of cognition decline, visual disturbance, and pyramidal dysfunction. The epilepsy partialis continua was difficult to control, and the underlying cause was uncertain even after thorough surveys for infection, inflammation, autoimmunity, and neoplasm. However, progressive signal intensity changes were noted over the involved cortical gyri, bilateral caudate, and putamen on serial magnetic resonance diffusion-weighted images, which were compatible with sporadic Creutzfeldt-Jacob disease. Therefore, we tested for 14-3-3 protein in the cerebrospinal fluid, and the results were positive. Multifocal myoclonus jerks, severe mental decline, akinetic mutism, and typical periodic sharp wave complexes on electroencephalogram developed late in his disease course. He died under the hospice care, and his total disease duration was approximately 5 months. This case highlights that epilepsy partialis continua can be the first presenting symptoms of sporadic Creutzfeldt-Jacob disease, and that magnetic resonance imaging abnormalities can be helpful to identify the disease.

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Introduction

Sporadic Creutzfeldt-Jacob disease (sCJD) is a fatal neurodegenerative disease, and the typical clinical course is characterized by rapid mental decline, behavioral changes, visual disturbance, myoclonus, and finally akinetic mutism. The early presentations can be varied and include cognitive impairment, limb or gait ataxia, mental change, or visual problems [1]. Making a prompt diagnosis of sCJD in the early stage is not easy if the affected patient has an atypical presentation. The incidence of seizures among patients with CJD in one cohort report was 14% [2], and the seizures tended to occur late in the disease when critical medical conditions developed. Epilepsia partialis continua (EPC) is an uncommon type of simple focal motor status epilepticus with varied etiologies, and it is rare in patients with sCJD. The current case at first presented medication-resistant EPC without change of cognition, and clinical surveys to identify underlying etiology were all unremarkable. However, there were consistent findings on early and follow-up magnetic resonance diffusion-weighted images, which helped to make an early identification of probable sCJD.

Case Report

A 62-year-old man with subclinical Hashimoto's thyroiditis had numbness and subsequent intermittent rhythmic jerking-tremors in his left hand. The jerking-tremors marched to his left arm or leg occasionally; however, he could manage his antique business without difficulty. Unfortunately, the twitches progressed for 3 weeks, and he visited our emergency room (ER) when weakness and stiffness of his left limbs developed. At the ER, he was able to detail his history clearly with intact cognition. An initial electroencephalogram (EEG) revealed independent epileptic foci in the right frontal-parietal and occipital areas (Fig. 1a–c). Brain magnetic resonance (MR) diffusion-weighted images (DWI) at the ER revealed non-enhancing bright signal in bilateral frontoparietal, right insular, and occipital cortices, with faint bright signal in bilateral caudate nuclei and putamen (Fig. 2a–d). Hematological, biochemical, infectious, inflammatory, neoplasm, and autoimmune surveys were all normal except for elevated levels of antithyroid-peroxidase and antithyroglobulin antibodies. Cerebrospinal fluid (CSF) examinations showed normal cell counts and all other standard parameters. After admission, different seizures with gaze shift and right arm elevation were seen occasionally. These seizures were partially controlled with valproate and topiramate after failing to respond to other anti-seizure drugs. A slow verbal response, spastic weakness over his left limbs, and blurred vision developed on the third day of admission. His recent and remote memory rapidly deteriorated after 1 week, and his Mini-Mental State Examination score was 6 in the second week. Follow-up MR-DWI 2 weeks after admission revealed progression of hyperintensity in the right frontotemporal, bilateral occipital-parietal cortices, bilateral caudate and putamen (Fig. 2e–h). As the specific imaging findings were compatible with sCJD, we tested his CSF for 14-3-3 protein after reporting the case to the Taiwan Center for Disease Control. The Western blot test for CSF 14-3-3 was positive. Two months after the onset of EPC, he developed akinetic mutism with irregular startle myoclonus, and his EEG showed generalized periodic sharp wave complexes (Fig. 1d). Frequent generalized convulsive seizures were observed after he became comatose. He received hospice care and died 3 months after discharge. The total duration of his illness was approximately 5 months.

Discussion

The early presentations of sCJD can be varied, and include cognitive impairment, limb or gait ataxia, mental decline, and visual problems [1]. Making a prompt diagnosis of sCJD in the early stage is not easy if the patient has unusual clinical manifestations. Seizures are uncommon in the early stage of sCJD. In a retrospective study on seizures in patients with CJD, epileptic seizures most frequently occurred in the late stage of the disease with an average of 12 days between the onset of seizures and death [2]. Most of the seizures were non-convulsive focal seizures or general tonic-clonic seizures, and they usually occurred late in the disease course. The occurrence of EPC as the first symptom before the occurrence of dementia is uncommon, and only five cases have been documented in Western countries [3–7]. EPC, a rare form of focal status epilepticus, is defined as clonic muscular twitches repeated at regular short intervals in one part of the body for a period of time [8]. The flexion-extension twitches affected rhythmically and regularly at the distal and proximal parts of the right upper limb in our patient were typical of EPC. In addition, the patient's EEG showed the evolving rhythmic epileptic activities in the corresponding regions. EPC is typically resistant to medications, and the causes are diverse. The treatment and prognosis depend on the identification of the underlying etiology.

The unique findings on the patient's early and serial MR-DWI helped to identify the underlying cause. There were increased changes in signal intensity over the cortical gyri without gyral swelling or gadolinium enhancement, and progressively increased signal intensity over bilateral caudate and putamen. In cases of status epilepticus, the involved gyri are often swollen with increased vascularity and without signal intensity changes over both caudate and putamen, even in patients with general convulsive status epilepticus. One multicenter international study evaluated the MRI scans of 436 patients with sCJD cases and 141 controls, and the results showed that alterations in signal intensity were correlated with distinct sCJD molecular subtypes [9]. The authors found MR-DWI studies could provide adequate diagnostic accuracy for suspected cases of sCJD. If high signals in DWI appear in at least two cortical regions or both caudate nuclei and putamen, sCJD should be highly suspected. Another retrospective observation study of 37 cases of sCJD found that the increased extent and degree of signal intensity on DWI were correlated with disease duration and the degree of spongiform change. Signal intensity changes in the basal ganglia are a consistent finding and can be used as a noninvasive biomarker for CJD [10]. The change in signal intensity in DWI of sCJD patients can precede the onset of typical clinical manifestations and provide evidence for an early diagnosis [10].

As there was no neuropathological proof in our patient, the diagnosis of sCJD was based on his worsening clinical features, the para-clinical tests including periodic sharp wave complexes on EEG, a positive immunoassay for 14-3-3 protein in his CSF, and characteristic MR findings. Interestingly, the DWI hyperintensity changes at bilateral dorsal striatum and corresponding cortical gyri appeared early in his disease course.

The reason why EPC started in the early stage is unclear. In a review of the literature, we found five reported cases of sCJD with early clinical presentations of EPC. Three had subtle numbness and subsequent EPC at the same limb as the leading symptoms [4, 6, 7], and one case with familial CJD showed consistent DW signal intensity changes over bilateral dorsal striatum nuclei before changes in signal intensity over cortical gyri [7]. To the best of our knowledge, this is the first case to demonstrate the evidence of EPC and sCJD on serial examinations during the disease course.

Conclusions

EPC can be a leading presentation of sCJD. The distinctive MR-DWI features compatible with sCJD can be helpful in the early identification of probable sCJD.

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Fig. 1. **a** The EEG revealed independent epileptic foci at right central, frontal, and occipital areas. **b, c** When the patient was admitted, his EEG revealed continuing rhythmic focal epileptic discharges arising from right frontal and parietal areas, which evolved and accelerated with higher amplitude and frequency and lasted 2 min. **d** When the patient developed akinetic mutism, the EEG showed generalized periodic sharp wave complexes.

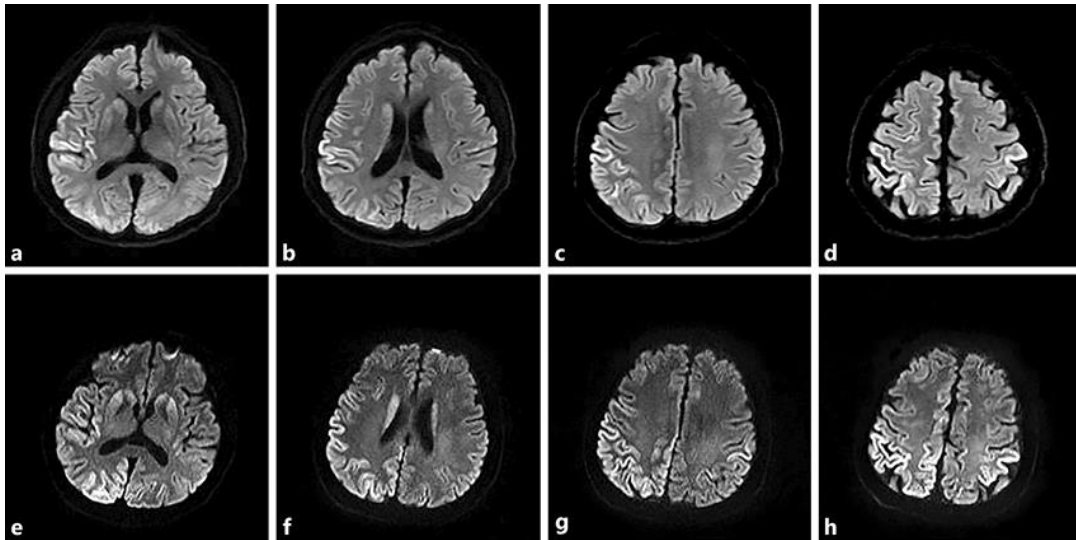


Fig. 2. a–d The brain MR-DWI when the patient presented with EPC at the ER showed restriction diffusion with bright signals at bilateral high frontoparietal, right insular, and right occipital cortical gyri, and a faint bright signal at bilateral caudate nuclei and putamen. e–h The MR-DWI 2 weeks after admission revealed progression of hyperintensity right frontotemporal, bilateral occipital-parietal cortical gyri, bilateral caudate and putamen with thalamus sparing.