

Case Report

Probable sporadic Creutzfeldt–Jakob disease mimicking focal epilepsy

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ABSTRACT

Creutzfeldt–Jakob disease (CJD) presents with seizures as an early symptom in only approximately 3% of cases. These seizures often present as nonconvulsive status epilepticus (NCSE) or epilepsia partialis continua (EPC). Here, we describe a case of probable sporadic CJD (sCJD) in an 83-year-old man whose manifest an unusual presentation of left-hand tonic seizures without evolution to EPC, as well as brain MRI findings interpreted as peritonal changes, which led to an initial misdiagnosis of focal epilepsy.

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1. Introduction

Creutzfeldt–Jakob disease (CJD) arises from the accumulation of prion protein (PrP^{Sc}) in the brain, which leads to progressive and fatal neurodegeneration. Clinically, CJD predominantly manifests as progressive dementia accompanied by pyramidal, extrapyramidal, and visual signs. Psychiatric symptoms occasionally occur [1,2], and seizures are uncommon as an early symptom of sporadic CJD (sCJD). Nonspecific signs and symptoms point to the difficulty of distinguishing CJD from other diseases characterized by rapidly progressive cognitive impairment. The periodic sharp wave complexes (PSWC) on electroencephalography (EEG), hyperintensity on diffusion-weighted imaging (DWI) of brain magnetic resonance imaging (MRI) of the cerebral cortex (cortical ribboning) and striatum, and elevated 14-3-3 protein in CSF are helpful in the diagnosis of sCJD. However, atypical clinical presentations with ambiguous laboratory findings may still cause misdiagnosis.

2. Case report

An 83-year-old retired male farmer from eastern Taiwan presented with one month of a mild headache, behavioural changes, cognitive impairment, and irritability. According to the patient, his hypertension and

hyperlipidaemia are regularly being followed up, and he had no history of head injuries or epilepsy. His family described the patient as sometimes appearing absent-minded and exhibiting strange behavior, such as mistaking the newspaper for his clothing. The family also reported visual hallucinations and progressive memory impairment. Investigation results from prior consultation at a nearby regional hospital included an EEG revealing "seizure activity" and a brain MRI showing possible post-ictal changes. Two weeks after his first consultation, he came to our neurology outpatient department for a second opinion and was diagnosed with focal epilepsy. He was started on levetiracetam 1000 mg/day. Ten days later, the patient experienced a sudden onset of irritable mood followed by loss of consciousness and was brought to the emergency room (ER). In the ER, the patient regained consciousness and found his left hand weak with a Medical Research Council grade of 3/5. Acute stroke was suspected, but brain computed tomography showed no intracerebral haemorrhage. Based on the provisional diagnosis of seizure disorder with post-ictal left hand weakness, the patient was hospitalized. Considering that levetiracetam may have caused or exacerbated his irritability, his anti-seizure drug regimen was switched to gabapentin 1200 mg/day plus clobazam 20 mg/day.

To evaluate the seizure etiology, an examination of the patient's CSF was conducted and yielded a white blood cell count of 0 cells/ μ L, a protein level of 26.9 mg/dL, and a glucose level of 86 mg/dL (the serum glucose level was 122 mg/dL). The complete blood count and blood chemistry were normal, and the thyroid function was also normal. Venereal Disease Research Laboratory, Epstein Barr Virus serology, and tumor marker tests were all negative. The brain MRI showed gyriform hyperintensity bilaterally in the frontal, parietal, temporal, and occipital lobes, with the hyperintensity being more prominent on the right side

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in DWI (Fig. 1). The differential diagnosis of the brain MRI findings included peri-ictal changes, encephalitis, and hypoxic encephalopathy.

Despite the change in anti-seizure drugs, the patient remained agitated and experienced frequent focal tonic seizures of the left hand with impaired awareness. The stereotypic seizure was characterized by the patient making a fist with his left hand, which was sometimes followed by left arm stiffness; was associated with mental confusion; and had a duration ranging from 152 to 195 s. The seizure frequency was 18–30 seizures per day. An ictal EEG showed rhythmic epileptiform discharges arising from the right hemisphere and then spreading to the contralateral hemisphere (Fig. 2A, B). An interictal EEG showed right-sided lateralized periodic discharges (LPDs) with maximum amplitude in the right mid-frontal region (Fig. 2C). Treatment with zonisamide 200 mg/day was added to the anti-seizure drug regimen, and the gabapentin dose was increased to 1800 mg/day; however, no improvement was found, and the patient gradually developed clouding of consciousness and dysarthria. The follow-up EEG nine days later showed PSWC with right predominance and recurrence every 0.8–1.2 s (Fig. 2D). While the seizure frequency was reduced with the addition of levetiracetam 2500 mg/day, the level of consciousness worsened to lethargy, and the PSWC pattern was not attenuated. After two weeks of aggressive but ineffective treatment with anti-seizure drugs, pulse therapy was given for possible autoimmune encephalitis. However, the patient showed no clinical improvement. Elevated 14-3-3 protein in the CSF was confirmed, and the patient was later diagnosed with probable sCJD. Tests for both protease-resistant prion protein and prion protein gene (PRNP) were not performed. The patient died within three months of the onset of symptoms.

3. Discussion

3.1. Seizure and EEG findings

Epileptic seizures as the initial presenting feature of sCJD have been reported in only 3% of cases [3], with such seizures often presenting as nonconvulsive status epilepticus (NCSE) [4,5], myoclonus, and epilepsy partialis continua (EPC) [6–9]. Hence, our patient's presentation of early focal tonic seizures and no evolution to EPC is particularly rare, and this unusual presentation led to the misdiagnosis of focal epilepsy after it was combined with the radiographic findings interpreted as peri-ictal changes.

The PSWC EEG pattern is commonly seen in CJD cases, with a sensitivity and specificity of 64% and 91%, respectively [3]. Lateralized or focal periodic sharp waves have been reported, especially early in the course of CJD. Partial seizure activity and PLEDs in early CJD might indicate that PrP^{Sc} accumulation can have a focal or regional origin in the brain. Although the mechanism by which PrP^{Sc} causes neuronal damage and

seizures remains unknown, the rare seizure presentation and different phenotypes of CJD would be associated with the modulation of PRNP, which may influence the susceptibility to seizure, and variable PrP^{Sc} strains which show distinctive clinical and histopathological properties [10–12]. The relationships among different PrP^{Sc} strains, variable PRNP, and seizures should be studied further to increase our understanding of this topic.

3.2. Psychiatric symptoms

Psychiatric symptoms including paranoia, visual hallucinations, and aggression occasionally occur during the initial phase of sCJD [1,2]. However, mood and behaviour disturbances also occur in seizure disorders, as part of ictal clinical patterns or post-ictal psychosis. Thus, such psychiatric presentations can quickly be taken as compatible with a seizure disorder diagnosis if focal seizures present as an early symptom of sCJD [13]. Isolated visual disturbances at disease onset are the peculiar characteristic of the Heidenhain variant of CJD, which often shows occipito-parietal hyperintensity on DWI or FLAIR imaging [14]. In this case, the early symptoms of cognitive impairment, seizure, psychiatric symptoms, and visual hallucinations, combined with brain MRI showing diffuse hyperintensity bilaterally in the frontal, parietal, and temporal and occipital lobes, seemed less likely to indicate the Heidenhain variant.

3.3. MRI findings

The typical findings of brain MRI in sCJD are hyperintensity in the cerebral cortex (known as the cortical ribbon sign), striatum, or thalamus on DWI or FLAIR imaging [1,15]. Peri-ictally, brain MRI changes include hyperintense signal changes on FLAIR images and DWI due to vasogenic and cytotoxic edema. Peri-ictal MRI abnormalities and EEG findings often show topographic concordance, and the image changes entirely or partially resolve over weeks to months [16,17]. Our literature review yielded a case of NCSE erroneously diagnosed as CJD because similar MRI changes were seen in CJD and peri-ictal states [18]. In our case, we cannot conclusively state whether the MRI findings were due to seizure activity or CJD pathology. Nonetheless, this case illustrates that, in the context of sCJD with early seizures, peri-ictal changes interpreted from MRI may lead clinicians astray when making treatment decisions.

4. Conclusion

sCJD should be considered as a differential diagnosis if a patient presents with focal seizures and a rapid progression of cognitive dysfunction, even in cases in which brain MRI is initially interpreted as indicating peri-ictal changes.

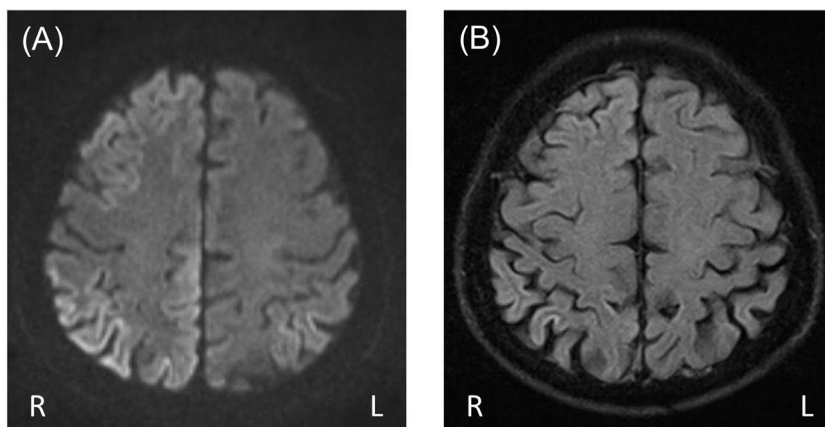


Fig. 1. (A) Diffusion-weighted MRI (DWI) showing gyriform hyperintensity bilaterally in frontal, parietal, temporal, and occipital lobes, with the hyperintensity being more prominent on the right side. (B) Fluid-attenuated inversion recovery (FLAIR) image showing hyperintensity in the right parietal and temporal cortex.

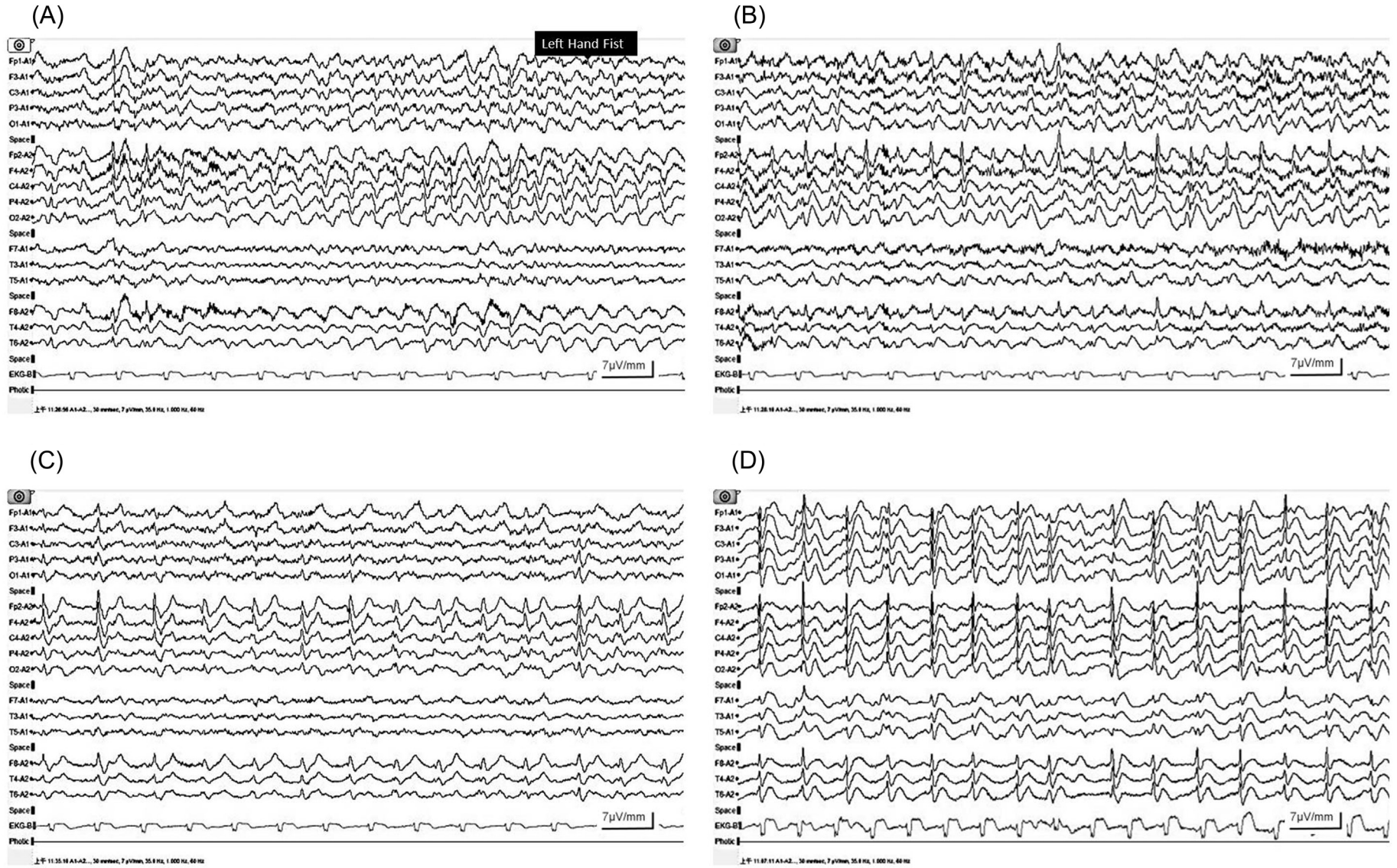


Fig. 2. (A) Ictal EEG showing rhythmic discharges arising from the right hemisphere, and (B) then spreading to the contralateral hemisphere. (C) Interictal EEG showing right-sided lateralized periodic discharges (LPDs) with maximum amplitude in the right mid-frontal region. (D) Follow-up EEG nine days later showed periodic sharp wave complexes (PSWC) with right predominance and recurrence every 0.8–1.2 s.

Disclosure

The authors report no conflict of interest.

Ethical statement

This is a retrograde study, and ethics approval (NYMUH IRB No. 2017A024) was obtained according to our institutional standards.

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