

Familial Creutzfeldt-Jakob disease presenting as *epilepsia partialis continua*

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ABSTRACT – Creutzfeldt-Jakob disease (CJD) is a rare disorder caused by prions that can affect any part of the central nervous system. It is characterized by a long incubation period, but once symptoms start there is a progressive neurological decline. Clinical features include dementia, ataxia and myoclonus (startle), among others. We report a biopsy-proven case of familial CJD (fCJD) presenting with continuous focal seizures, *epilepsia partialis continua* (EPC), as the initial presentation. CJD is an unusual neurological disorder with an incidence of approximately one case per million population (Prusiner 2001). The disorder is due to neuronal degeneration resulting from the accumulation of a pathological isoform (PrP) of the prion protein (PrPc). Patients with fCJD have mutations in the gene encoding PrPc (PRNP) (Vercueil 2006, Collins *et al.* 2004). This fCJD represents 10-15% of CJD cases making the sporadic form more common 85-95% (Parry *et al.* 2001). During the course of the disease myoclonus has been reported in 88% of cases, and epileptic seizures (partial seizures, generalized status epilepticus) in 8% (Vercueil 2006). Periodic sharp wave complexes (PSWC) are uncommon in fCJD and occur in about 10% of patients (Wieser *et al.* 2006).

Key words: *epilepsia partialis continua*, epilepsy, prion disorders, Creutzfeldt-Jakob

Our case illustrates a rare and uncommon initial presentation of CJD that should be considered in patients presenting with progressive decline in function and EPC.

Case study

A 49-year-old, right-handed white woman presented to Penn State Hershey Medical Center as a transfer from an outside facility with complaints of left upper extremity weakness, continuous, rhythmical, left upper extremity jerking activity and spasticity. All her complaints had initially started

one month prior to presentation to our facility apart from the rhythmical left upper limb jerking activity which had started seven days prior to presentation. There were no reported cognitive complaints including memory. She had poor coordination of her left hand, associated with distal weakness and spasticity. A worsening gait dysfunction over a one month period rendered her recently wheelchair-bound. She had a medical history of hypertension, arthritis and hypothyroidism. There was no neurological history. There was no history of corneal transplants or cadaveric growth hormone

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use. She had two children and lived with her husband. She was otherwise healthy prior to the onset of symptoms. Family history revealed an aunt who died secondary to a progressive illness affecting her memory but had not sought medical attention.

On examination, she was noted to be hypophonic with fluent speech, alert and oriented to self, place, date and time. She had no memory, visual spatial or executive function problems. Motor examination revealed weakness in her left upper extremity, distally associated with spasticity. There was continuous rhythmical jerking activity of her left upper extremity. There was no startle myoclonus.

Reflexes were brisk in her left biceps, brachioradialis and triceps. There was no Hoffman's sign and no pathological spreading of reflexes. Babinski was elicited in her left foot.

Laboratory testing including chemistry panels, complete blood count, liver profile, antineutrophil cytoplasmic antibodies, antinuclear antibodies, Sjogren syndrome antigen A and B, copper studies, anti-tpo antibodies, thyroid stimulating hormone were within reference range.

A sample of CSF with testing of white blood cells, glucose, and protein showed values within reference range.

CSF neuron specific enolase was 156 ng/mL (normal less than 20), CSF lyme and HSV pcr were not detected, CSF paraneoplastic antibodies (anti-hu, yo and ri) were not present and CSF 14-3-3, tau, S100b were not obtained given a brain biopsy was performed.

MRI of the brain, with and without contrast (*figure 1*), prior to lumbar puncture showed increased signal intensity on T2-weighted, diffusion weighted and FLAIR sequences involving bilateral caudates, putamens and thalami pulvina with no enhancement. Repeat brain MRI ten days after admission was performed because of an abrupt clinical deterioration consistent with status epilepticus, which showed a new, increased T2 signal and restricted diffusion in the bilateral occipital lobes, the right greater than left.

She progressively declined developing nonconvulsive status epilepticus, ventilator-acquired pneumonia, diabetes insipidus and adrenal insufficiency. Anticonvulsants used were pentobarbital, levetiracetam, lamotrigine, zonisamide and phenytoin. Her initial EEG showed findings consistent with periodic lateralized epileptiform discharges (PLED) (*figure 2*) with nearly continuous spike wave discharges seen arising predominantly from the right

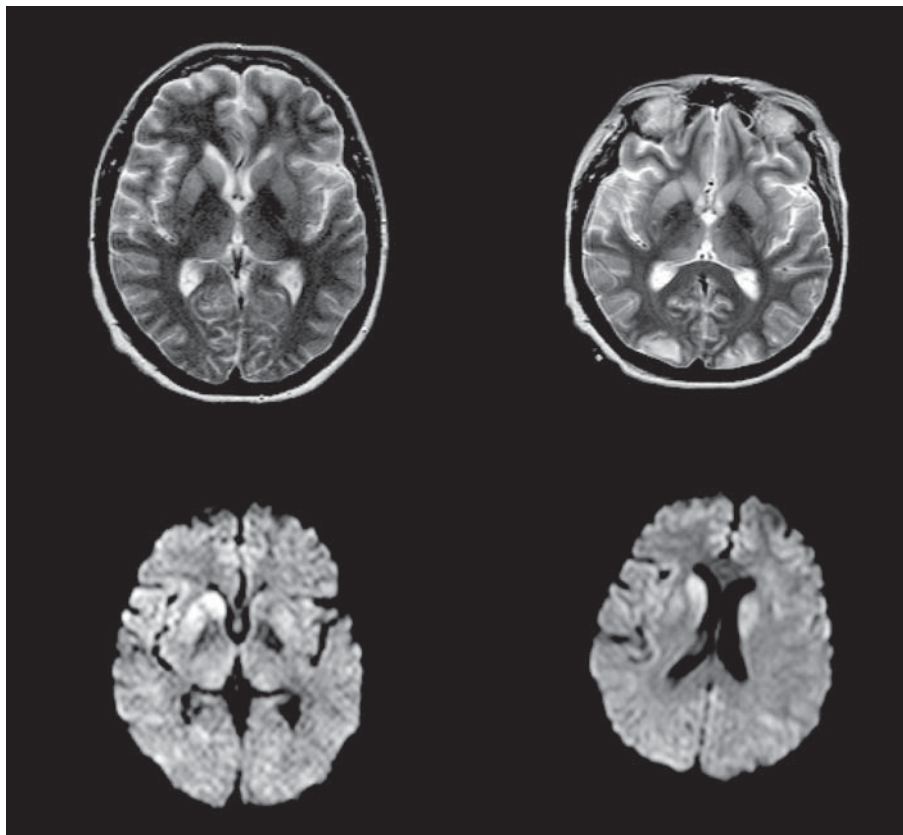


Figure 1. MRI of the brain, with and without contrast, shows abnormal bilateral signal intensity on T2-weighted images (upper) and diffusion weighted images (lower) involving bilateral caudate, bilateral putamens, bilateral thalamic pulvina, and occipital regions with no enhancement.

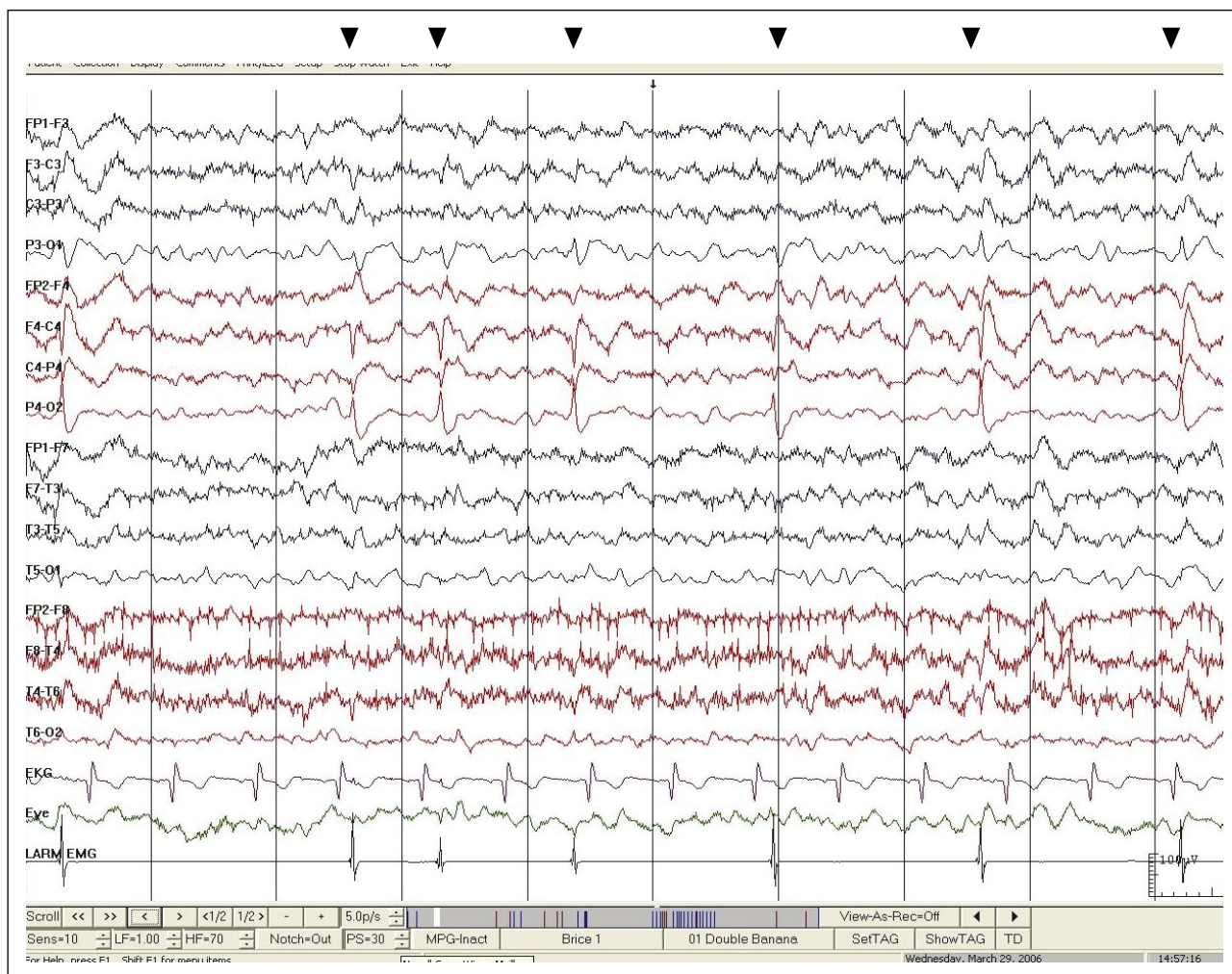


Figure 2. Initial EEG in bipolar montage showing generalized cerebral background slowing in the theta and delta ranges, and periodic focal sharp and spike wave discharges seen arising predominantly from the right centroparietal region with negative phase reversal at C4-P4 consistent with PLED. The right hemispheric focal sharp waves correspond to the patient's left upper extremity myoclonus.

centroparietal region, waxing and waning in periodicity and never absent for longer than 20 seconds at the very most. Each spike was followed by a slow wave with the same distribution and correlated with the patient's left upper extremity myoclonus. Six weeks after admission, her EEG (*figure 3*) showed generalized periodic spike and sharp wave complexes (PSWC). A biopsy of the dura and right frontal lobe were submitted to the National Prion Disease Pathology Surveillance Center. Results showed that the sequencing of the prion protein (PrP) gene was consistent with the diagnosis of *vCJD* associated with the E200K-129M mutation in the PrP gene.

After a protracted and complicated hospital course the patient was discharged with home hospice. Anticonvulsants were continued and she required tracheostomy and percutaneous endoscopic gastrostomy tube placement. She died three weeks later, at her home. The total duration

of her illness from the start of her symptoms to death was two months and three weeks.

Discussion

Our patient presented with atypical clinical features of prion disease that included absence of dementia, startle myoclonus and EPC as initial, presenting findings. Patients with *CJD* who have presented with epilepsy show complex partial seizures and generalized status epilepticus (Vercueil 2006, Parry *et al.* 2001, Lee and Haight 2000). Other findings include periodic lateralizing epileptiform discharges (PLED), PSWC, nonconvulsive status epilepticus (Lee and Haight 2000) and refractory, nonconvulsive status epilepticus (Shapiro *et al.* 2004). EPC, although rare, can present as an initial manifestation of *CJD* (Laurent 2006, Parry *et al.* 2001, Lee and Haight 2000).



Figure 3. EEG bipolar montage obtained six weeks after admission showing generalized. PSWC with triphasic morphology occurring at a rate of approximately 1 hertz per second. The intervening background consists of generalized low voltage slowing.

The presence of a right centroparietal focus seen on the electroencephalogram (EEG) in our patient correlated with the left upper extremity myoclonic continuous jerking. The anatomical and physiological origin of EPC has been under much discussion, and in which both cortical and sub-cortical mechanisms have been proposed (Cockerell *et al.* 1996). It has been hypothesized that the periodicity of the epileptiform discharges may derive from intrinsic mechanisms in affected neurons that become electrotonically coupled because of prion-induced membrane fusion (Traub and Pedly 1981, Wieser *et al.* 2006). Antiepileptic drugs (AEDs) must be used to prevent the spread of EPC.

The use of ancillary tests including MRI, EEG and CSF analysis, facilitates the diagnosis but there are problems with specificity and sensitivity (Tyler 2003). A definite diagnosis can be made at autopsy or pre-mortem biopsy, and demonstration that brain tissue of patients with CJD could transmit the disorder to primates. Given that our

patient presented in an atypical way, brain biopsy was obtained to provide a definite diagnosis of CJD.

The differential diagnoses for EPC include Rasmussen's encephalitis, strokes, astrocytoma, hemangioma, lymphoma, multiple sclerosis, non-ketotic diabetes mellitus, renal encephalopathy and certain medications such as penicillin and cefotaxime (Parry *et al.* 2001).

In conclusion, CJD may present in several ways including ataxia, parkinsonism, dementia, spasticity, sensory disturbance and myoclonus, typically startle. Continuous focal seizure activity seen in EEG tracings, correlating with the patient's myoclonus (EPC), is an uncommon, initial presentation for CJD. This possibility should be considered when clinicians encounter patients with history of a rapidly progressive, neurological decline associated with movement disorders. □

Disclosures. The authors report no conflict of interest.

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