



CASE REPORT

Creutzfeldt-Jakob Disease: A Case Report Emphasizing the Differential Diagnosis

Shu-Ping Chao*, Yu-Hsuan Han

Department of Neurology, Taipei Medical University-Wan Fang Medical Center, Taipei, Taiwan

ARTICLE INFO

Article history:

Received: Dec 30, 2011

Revised: Jan 16, 2012

Accepted: Jan 17, 2012

KEY WORDS:

Creutzfeldt-Jakob disease;
dementia;
rapid progressive dementia

Creutzfeldt-Jakob disease (CJD) has various clinical presentations in cognitive, behavior, sensory or motor dysfunction.¹ A male patient (80 years old) presented himself with forgetfulness, personality change and sleep disorder initially. Afterwards, he started to show many other neurological symptoms such as visual manifestation, dyspraxia, dysarthria, and myoclonic jerks. Magnetic resonance imaging (MRI) of the brain revealed the findings of cortical ribbon sign as well as basal nuclear hyperintensity lesion in both fluid attenuated inversion recovery images (FLAIR) and diffusion-weighted images (DWI). The results of electroencephalography (EEG) showed bi-lateral periodic sharp wave complexes. Deterioration in the clinical condition was rapid and relentless, progressing to a completely dependent state within 2 months. In this case report, we have illustrated clinical, laboratory, neurophysiologic, and imaging findings and details of the diagnostic procedures of the condition. We suggest that making the diagnosis of CJD is difficult early in the course of CJD.

Copyright © 2012, Taipei Medical University. Published by Elsevier Taiwan LLC. All rights reserved.

1. Introduction

Creutzfeldt-Jakob disease (CJD) is a fatal prion-related neurodegenerative disorder.^{1,2} When a patient has rapid progressive dementia, myoclonic jerk and characteristic electroencephalographic (EEG) findings, the diagnosis of CJD is commonly considered. However, the initial presentations of CJD patients are frequently nonspecific, so the diagnosis of CJD can be difficult. Doctors from diverse disciplines may be the physicians first consulted during the early phase of the disease. We report an 80-year-old male patient who had rapid progressive cognitive dysfunction and gait disturbance. We made the diagnosis of probable CJD based on his history and clinical presentation, as well as electroencephalography (EEG), and cerebrospinal fluid (CSF) findings according to the World Health Organization (WHO) criteria.³

2. Case report

An 80-year-old male patient was admitted to our hospital because of progressively worsening of insomnia, confusion and unsteady gait for 6 weeks. The patient had been in his usual state of health until about 6 weeks before admission, when he started to have emotional lability, insomnia and memory impairment. Later, he also showed the symptoms and signs of persecutory delusion,

agitation, restlessness, intermittent inattention, personality change, and visual and auditory hallucinations.

Four weeks before admission, the patient consulted a neurologist at a clinic at Taiwan Adventist Hospital. The findings of neurological examination revealed memory impairment (especially immediate memory), tremor of hands bilaterally, positive signs of glabellar and palmomental reflexes. The results of routine laboratory tests were within normal range. The results of serum vitamin B₁₂ and folic acid levels as well as thyroid function were normal. The result of a Venereal Disease Research Laboratory (VDRL) test was non-reactive. Computed tomography scanning of the brain showed an atrophied right eye with calcifications in bilateral globes. The score of Mini-Mental State Examination was 20/30, and that of the Clinical Dementia Rating 2. He received sertraline 25 mg q.d., alprazolam 0.5 mg h.s., and quetiapine 12.5 mg q.i.d. for insomnia. The patient's family members also confirmed that there was continuous worsening in his difficulty in standing, taking small steps, unsteady gait and confusion.

Two weeks before admission, the patient visited our neurology outpatient clinic. On examination, he had symptoms of cognitive deterioration in his slow responses, relative change in circadian cycle, and delusion. He was scheduled to have additional outpatient laboratory tests. The findings of magnetic resonance imaging (MRI) of the brain without contrast showed linear hyperintensity in both fluid attenuated inversion recovery images (FLAIR) and diffusion-weighted images (DWI) at bilateral frontoparietal, and temporal cortex, and small similar lesion at right caudate nucleus (Figure 1). Later, he was reported to have spontaneous jerky movements of limbs (more pronounced on the left side) without loss of consciousness as well as bladder and bowel incontinence.

* Corresponding author. Shu-Ping Chao, Department of Neurology, Taipei Medical University-Wan Fang Hospital Medical Center, 111, Section 3, Hsing Long Road, Taipei 116, Taiwan.

E-mail: Shu-Ping Chao <99362@wanfang.gov.tw>

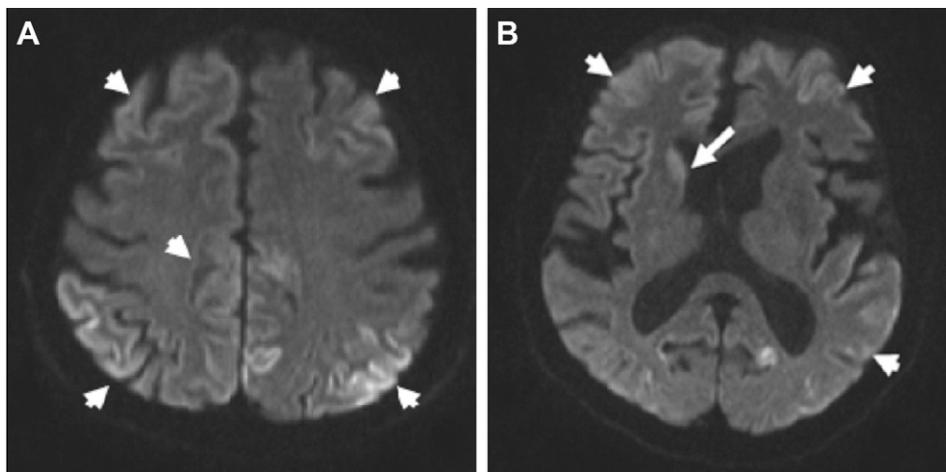


Figure 1 Axial diffusion-weighted imaging showing high-signal intensity in the cortical regions of bilateral cerebral hemispheres (A and B, arrowheads) and the head of right caudate nucleus (B, arrow).

Personal and past histories showed that the patient was a retired professor and had lived in Los Angeles for 7 years. He had a history of hypertension, and retinal detachment with bilateral blindness. He did not have any family members with the similar condition. The patient had not had fever, low blood pressure, hypoxia, trauma, toxin exposure, poor nutrition, or body weight loss in recent months.

At admission, neurological examination revealed his somnolence, blunted affect at times, inability to communicate and to follow verbal commands, extremely dysarthric speech, difficulty in swallowing, movement of all his extremities in response to painful stimuli, asterix over left upper extremity as well as intermittent myoclonus over four extremities (especially left side) emerging spontaneously. His stretch reflexes were brisk with flexor plantar response.

The patient had normal findings in complete blood counts, renal and liver function, serum glucose, electrolytes, ammonia, vitamin B₁₂, folic acid, prostate-specific antigen, carcinoembryonic antigen, erythrocyte sedimentation rate, and thyroid function tests. The results of tests for thyroid autoantibody and VDRL were negative. Chest radiography revealed the picture of cardiomegaly. Scalp EEG showed bi-lateral periodic sharp wave complexes (predominantly in right hemisphere), interspersed with background activity slowing and low voltage (Figure 2). CSF analysis was normal, except elevated protein of 62 mg/dL. CSF culture was negative. Over the next 2 weeks, the patient became mute and more difficult to arouse, with persistent myoclonus of the extremities, and then became bed-bound completely.

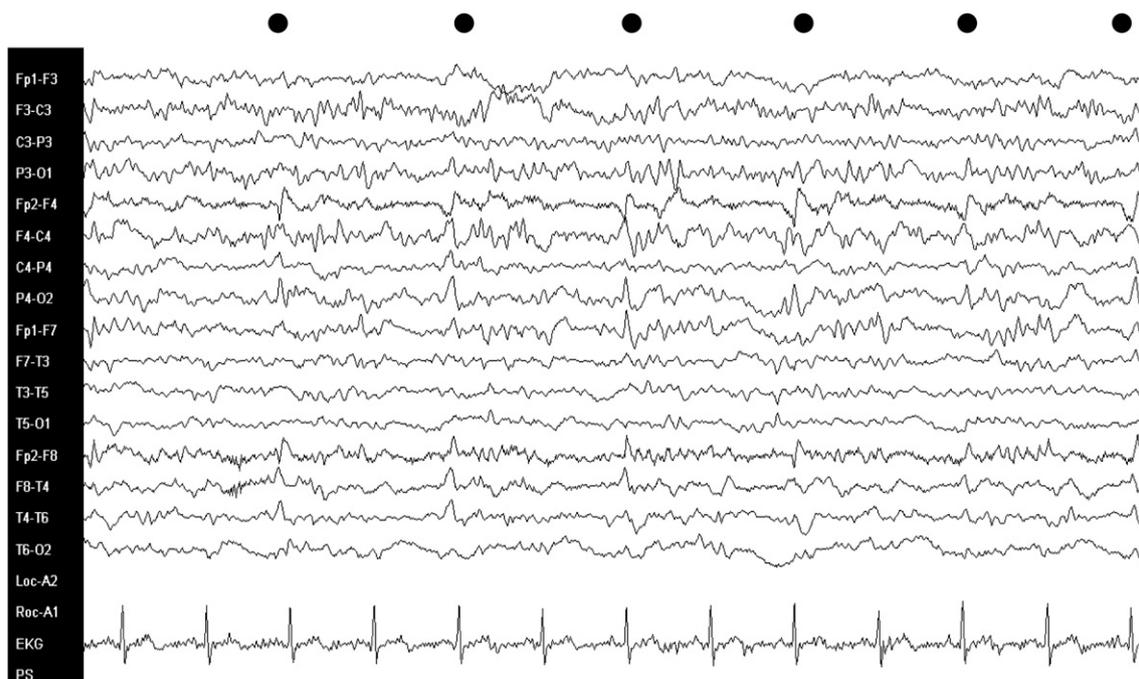


Figure 2 Electroencephalography in double banana montage showing bilateral periodic generalized sharp complexes at intervals of 1.5 seconds to 2.0 seconds (dots), interspersed with background activity slowing and low voltage. Left channels Fp1-O1 (channel 1–4 and 9–12); right channels Fp2-O2 (channel 5–8 and 13–16).

3. Discussion

CJD should be considered in the differential diagnosis for patients with rapidly progressive dementia, myoclonic jerk, and characteristic EEG findings. WHO criteria for probable sporadic CJD are: (1) exclusion of alternative diagnoses with routine investigations; (2) rapid progressive dementia; (3) at least two of the following four clinical features — myoclonus, visual disturbance or cerebellar dysfunction, pyramidal or extrapyramidal feature, and akinetic mutism; (4) a typical EEG pattern (periodic sharp-wave complex), and/or CSF positive for 14-3-3 by immunoblot; and (5) a clinical duration of less than 2 years before death.³ Our patient met the WHO criteria for probable CJD.

Myoclonic jerk may be seen in various conditions, such as vascular, infectious, hypoxic, metabolic, degenerative, paraneoplastic or autoimmune disease.⁴ Cognitive decline and myoclonus can be present in subacute sclerosing panencephalitis and neurosyphilis, and some autoimmune disease, such as Hashimoto's encephalitis. However, our patient's blood screening and CSF examination results were all negative, ruling out these disorders listed.⁵ Patients with hypoxic encephalopathy and adult-onset lipid-storage diseases may mimic the symptoms,¹ but our patient did not have the histories of these diseases. Mild myoclonus may occur in Alzheimer's disease, but with a slow clinical course.⁶ However, our patient had a rapid clinical course.

The DWI abnormalities reported for CJD include regions of asymmetric high-signal intensity in the brain cortex (cortical ribbon sign), thalamus, caudate, and putamen nuclei with a distribution pattern that does not correspond to that of the arterial circulation.⁵ The intensity was increased along the course of the disease on serial scans.⁵ But cortical ribbon sign in DWI maybe presented in chronic herpes encephalitis and syndrome of mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes.⁷ The medical history as well as results of CSF analysis and brain MRI ruled out those disorders in our patient.

Characteristic EEG findings in CJD consist of lateralized periodic bursts of spike-wave complexes (PSW) in early stage and generalized in the middle and late stages.⁴ EEG is often used as diagnostic tool, but characteristic EEG findings are not always seen and periodic EEG activity is not specific in CJD. EEG in patients with lithium toxicity or other toxic encephalopathies may show PSW without rhythmicity.⁴ Rhythmic PSW with much longer interburst intervals may be seen in patients with subacute sclerosing panencephalitis or Hashimoto's encephalitis.⁴

In conclusion, CJD is a progressive neurological condition with fatal outcome. The early features of CJD vary and are nonspecific. Our patient's clinical presentation and EEG findings provided clues for diagnosis according to WHO CJD criteria.³ MRI of the brain in the early stages may give the clinician a hint to be aware of the possibility of CJD, although it is not included in diagnostic criteria. It is important for physicians to be cognizant of the clinical and investigative features of CJD in order to make a differential diagnosis. Early diagnosis is still a challenge in the early stages of CJD.

References

1. Rosenbloom MH, Alireza Atri A. The evaluation of rapidly progressive dementia. *Neurologist* 2011;**17**:67–74.
2. Geschwind MD, Haman A, Miller BL. Rapid progressive dementia. *Neurol Clin* 2007;**25**:783–807.
3. World Health Organization. *Global surveillance, diagnosis and therapy of human transmissible spongiform encephalopathies: report of a WHO consultation*. WHO/EMC/ZOO/97.3. Geneva: WHO; 1998.
4. Sadowski M, Verma A, Wisniewski T, Bradley WG, Daroff RB, Fenichel G, Jankovic J. Infections of nervous system: prion diseases. In: *Neurology in clinical practice*. 5th ed. USA: Butterworth-Heinemann; 2008. p. 1567–81.
5. See SJ, Pan A, Seah A, Teo J, Chan LL, Wong MC. Care reports of two biopsy-proven patients with CJD in Singapore. *Ann Acad Med Singap* 2004;**33**:651–5.
6. Heinemann U, Gawinecka J, Schmidt C, Zerr I. Differential diagnosis of rapid progressive dementia. *Eur Neurol Rev* 2010;**5**(2):21–8.
7. Ukisu R, Kushihashi T, Tanaka E, Baba M, Usui N, Fujisawa H, Takenaka H. Diffusion-weighted MR imaging of early-stage Creutzfeldt-Jakob disease: typical and atypical manifestations. *RadioGraphics* 2006;**26**:S191–204.