

Sporadic Creutzfeldt-Jakob Disease with Psychiatric Symptoms: A Case Report



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SUMMARY

Creutzfeldt-Jakob disease (CJD) is a fairly rare prion disease characterized by rapidly progressive dementia and neuropsychiatric symptoms. The diversity of the disease's clinical characteristics causes diagnostic difficulty. In some cases the initial findings of CJD are psychiatric symptoms. Herein we present a male patient that was diagnosed as CJD after dementia, ataxia, and myoclonus developed rapidly after the onset of psychiatric symptoms.

Keywords: Creutzfeldt-Jakob disease, psychiatric symptoms, dementia

INTRODUCTION

Creutzfeldt-Jakob disease (CJD) is a rare, progressive neurodegenerative disease, of which there are 4 types: sporadic, familial, iatrogenic, and variant. Most patients have the sporadic type. The incidence of CJD is 1/1,000,000 (Johnson 2005, Collins et al. 2006). Mean age at onset is 60 years. CJD begins with prodromal symptoms, such as anxiety, insomnia, lack of appetite, fatigue, and personality changes (Azorin et al. 1993, Kurne et al. 2005), followed by rapidly progressive cognitive impairment and severe dementia that may lead to akinetic mutism within months. Frequently, pyramidal, extrapyramidal, and cerebellar symptoms accompany CJD-associated dementia (Zerr et al. 2009, Van Everbroeck et al. 2004, Brown et al. 1994). Findings that support the diagnosis include signal changes in basal ganglia regions via T2-weighted, FLAIR, and diffusion-weighted cranial MRI, the presence of peracute wave discharges via electroencephalography (EEG), and protein 14-3-3 positivity in

cerebrospinal fluid (CSF) (Mittal et al. 2002, Finkenstaedt et al. 1996, Hsich et al. 1996, Wieser et al. 2006, Green 2002). - Histopathological examination should be performed for a definitive diagnosis (Brown et al. 1986). CJD is a disease of rapid progression and 90% of patients die approximately 1 year after the onset of symptoms (Glatzel et al. 2005, Will et al. 1984). Herein we present a CJD case of advanced age in which psychiatric symptoms occurred first, followed by rapidly progressive dementia and myoclonus.

Case

An 81-year-old male was brought to the emergency department with cutaneous saltation in both arms, general condition disorder, and loss of consciousness. The patient had poor hygiene, and anamnesis showed that he lived alone, became introverted upon the death of his wife 4 years earlier, and began to hallucinate 1 year earlier. His relatives reported that the patient reported burglars had entered his apartment and

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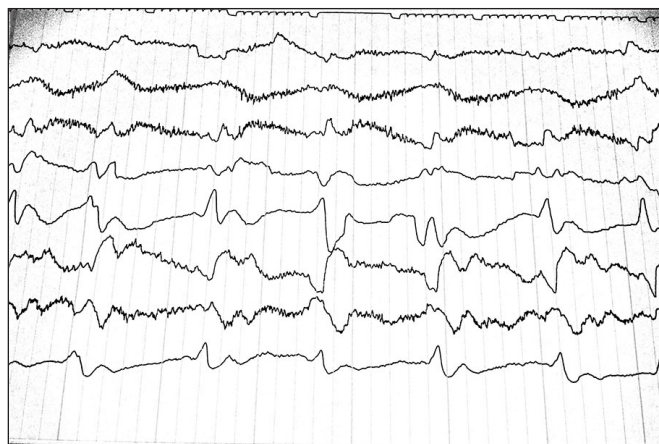
that the walls of his house were covered with blood, and that he appeared to be physically exhausted when he was visited 1 month earlier. The patient was able to remember past events, but occasionally could not remember the names of his relatives. He was able to feed himself, but had difficulty standing and walking due to imbalance, he spent most of each day in bed, and he did not regularly communicate with his relatives.

His relatives reported that they observed him making involuntary movements, including cutaneous saltation in both hands. Due to discomfort, increased agitation, and nightmares the patient was taken to a doctor, and donepezil and quetiapine treatment was initiated with a pre-diagnosis of dementia. The patient's condition gradually declined and he was brought to emergency service after 2 weeks, because he could not get out of bed, did not communicate with his relatives, and involuntary movements in both arms significantly increased.

Upon examination the patient was very sleepy, and cooperation and orientation could not be evaluated. He opened his eyes to painful stimuli and voluntary motor movements were present. His Glasgow coma scale (GCS) score was 9. Cranial nerve examination findings were normal. Both elbows, wrists, and knees were rigid. Deep tendon reflexes were increased in both extremities. Base skin reflex was bilaterally unresponsive. There were highly frequent myoclonic movements in both upper extremities and the head. Myoclonic movements increased with sound and tactile stimuli. The patient was admitted to the neurologic intensive care unit and underwent etiologic examination. Both the patient's and family's histories were unremarkable.

Hematological and biochemical findings were normal. Together with EEG generalized attenuation of background activity, repetitive periodic discharges consisting of high amplitude sharp and tri-phasic waves of $1.5\text{--}2\text{ Hz s}^{-1}$ were noted. Minimal signal increase in the putamens and bilateral caudate head, and diffusion restrictions in diffusion sequences at these levels were observed via T2-weighted cranial MRI. Microbiological and biochemical findings in CSF obtained via lumbar puncture were normal. CSF 14-3-3 protein was positive. CSF neuron-specific enolase was 40 ng mL^{-1} (normal value $<20\text{ ng mL}^{-1}$).

Based on World Health Organization (WHO) diagnostic criteria (17), the patient, who first had psychiatric symptoms followed by subacute dementia, myoclonus, and pyramidal, and extrapyramidal findings, was diagnosed as CJH (17), which was supported by typical imaging, EEG, and CSF findings (Table 1). High fever and pneumonia developed during the patient's follow-up and he did not respond to supportive therapy. The patient died on d 19 of hospitalization. The patient's relatives declined a brain biopsy for determining the cause of death.



Sporadic CJD

Table. Diagnostic criteria for Creutzfeldt-Jakob disease (CJD)

Possible:

Progressive dementia, and ≥ 2 of the following 4 clinical features:

- i) Myoclonus
- ii) Visual or cerebellar signs
- iii) Pyramidal/extrapyramidal signs
- iv) Akinetic mutism
- v) Non-supportive EEG

Probable:

Rapidly progressive dementia, and ≥ 2 of the following 4 clinical features:

- i) Myoclonus
- ii) Visual or cerebellar signs
- iii) Pyramidal/extrapyramidal signs
- iv) Akinetic mutism;

and a positive result for ≥ 1 of the following laboratory tests:

- a) Typical EEG (periodic sharp wave complexes) during an illness of any duration, and/or;
- b) CSF positive for 14-3-3 protein in patients with disease duration <2 years;
- c) Diffusion-weighted or fluid attenuated inversion recover MRI high signal abnormalities in the caudate nucleus and/or putamen;

and routine investigations do not indicate an alternative diagnosis.

Definite:

Diagnosed via standard neuropathological techniques, and/or immunocytochemically and/or Western blot-confirmed protease-resistant PrP, and/or the presence of scrapie-associated fibrils.

DISCUSSION

CJD is the most common human prion disease. The sporadic form accounts for 80%–90% of cases (Brown et al. 1994, Will and Matthews 1984). The disease affects both genders equally and develops in those of middle-advanced age (Zerr et al. 2009, Brown et al. 1986, Glatzel et al. 2005). Deterioration in cognitive functions and rapidly progressive dementia occur following a prodromal period characterized by psychiatric symptoms. In addition to dementia, cerebral findings are most frequently observed, including pyramidal and extrapyramidal symptoms, and ataxia. Myoclonus frequently accompanies the advanced stages of the disease (Collins et al. 2006, Van Everbroeck et al. 2004, Brown et al. 1994). As the presented case had subacute progressive dementia that began with psychiatric findings, and he had concomitant neurologic findings, the differential diagnosis included central nervous system infection, lesions in the intracranial space, and dementia. Additionally, as rapidly progressive dementia was noted and the clinical findings were inconsistent with Alzheimer disease, Lewy body dementia was excluded. Furthermore,

vascular dementia was not considered because the symptoms indicative of vascular dementia were not observed via cranial MRI and there were no associated risk factors. Central nervous system (CNS) infections were excluded based on anamnesis, cranial imaging, and CSF evaluations. A pre-diagnosis of CJH was considered, but because the patient didn't have a family history we didn't consider a familial prion disease. Variant CJH was also not a diagnostic consideration because the patient was of advanced age at onset and had EEG findings characteristic of sporadic CJH.

Anxiety, fatigue, personality changes, and lack of appetite can be observed in the early stages of CJD. The literature includes case reports of psychiatric symptoms as the initial findings in CJD. Psychiatric findings are rarely observed during the early stage of CJD, but are common during the later stages (Wall et al. 2005, Azorin et al. 1993, Dervaux and Laine 2003, , Solvason et al. 2002, Keshavan et al. 1987). In general, patients are initially diagnosed with depression and followed-up by a psychiatrist. Patients with psychotic characteristics, such as paranoid delusions and visual hallucinations, have been reported (Keshavan 1987). Although psychiatric symptoms occur more frequently in variant type CJH, there are case reports starting with typical depression findings in CJH (Solvason ve ark. 2002). In the presented case psychotic symptoms, including paranoid delusions and visual hallucinations, followed such symptoms of depression as change in personality, introversion, and poor self-care/hygiene.

As the presented case had rapidly progressive dementia and neurological findings, he underwent EEG based on a pre-diagnosis of CJH. EEG findings, including generalized attenuation of background activity, and repetitive periodic discharges consisting of high amplitude sharp and triphasic waves of 1.5-2 Hz s⁻¹, supported the diagnosis of CJH. EEG findings may be normal during the early stages of CJD. High periodic, biphasic, or triphasic synchronized bilateral sharp wave complex rates on slow wave backgrounds are typical EEG findings of late stage CJD (Wieser ve ark. 2006) . The specificity and sensitivity of EEG for CJD were reported to be 74%-94% and 64%-67%, respectively (Zerr et al. 2000).

The caudate nucleus in cranial MRI, increased signal intensity in the putamen in T2-weighted images, and diffusion limitations in diffusion-weighted images are typical of CJH. Studies reported that diffusion-weighted MRI had high specificity and sensitivity for the disease (Shiga et al. 2004, Young et al. 2005) . Observation of diffusion limitation, even during the early stage of CJD is very important for early diagnosis (Ukisu et al. 2005, Bahn and Parchi 1999). In the presented case similar imaging findings with defined characteristics were found.

CSF 14-3-3 protein positivity is noted in 93% of CJD patients. Although CSF 14-3-3 protein is highly sensitive for the disease, it does not have high specificity, but its positivity

does support the diagnosis of CJD. Another finding supporting the diagnosis of CJD is an elevated CSF neuron-specific enolase value (Hsich et al. 1996, Green 2002). In the presented case CSF 14-3-3 protein was positive and the neuron-specific enolase value was high. In the presented case sporadic CJH was considered as a possible diagnosis based on WHO diagnostic criteria, including onset with psychiatric symptoms, followed by subacute progressive dementia, pyramidal, extrapyramidal, and cerebral findings, and characteristic EEG findings (WHO 1998). MRI and CSF findings in the presented case supported the diagnosis of CJD.

CJD can begin with psychiatric symptoms. Patients of advanced age, especially those with a negative psychiatric history, should undergo detailed examination in order to identify any organic pathology that could play an etiological role, and should be closely monitored due to the possible development of neurological findings. CHJ should be a consideration in cases with rapidly progressing dementia and accompanying focal neurological signs, and in such cases EEG and cranial imaging should be performed.

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