



## Case Report

# Creutzfeldt-Jakob disease: A Case Report and Differential Diagnoses

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### Abstract

Sporadic Creutzfeldt-Jakob disease is a neurodegenerative disorder of unknown origin that leads to rapidly progressive dementia and is considered rare. It is uniformly fatal, with most patients passing away within a year. Patients with this disease may experience myoclonus, visual disturbances, and impairments in cognitive and functional abilities, as well as cerebellar and pyramidal/extrapyramidal signs<sup>1</sup>. However, these symptoms are nonspecific, making it challenging to diagnose the disease during the patient's lifetime due to low awareness and clinical suspicion.

The application of diffusion-weighted MR imaging can aid in the timely diagnosis and monitoring of the advancement of sporadic Creutzfeldt-Jakob disease. On diffusion-weighted images, the appearance of ribbon-like areas of hyperintensity in the cerebral cortex corresponds to the Sporadic Creutzfeldt-Jakob disease.

We present a case report of a 70-year-old man who presented with symptoms of rapidly progressive anxiety and dementia that had been ongoing for 8 weeks. After undergoing a series of comprehensive diagnostic tests and continuous monitoring, the patient was diagnosed with sporadic Creutzfeldt-Jakob disease based on the 2017 Euro-CJD criteria. The key clinical findings in the case were rapidly progressive dementia, blurry vision, extrapyramidal signs such as cogwheel rigidity, deteriorating health, and abnormal hyperintensity signals observed on diffusion-weighted MRI.

**Keywords:** Sporadic Creutzfeldt - Jakob disease; Prion Disease; Rapidly Progressing Dementia; Anxiety

### Background

CJD is a human prion disease and a progressive neurodegenerative disorder that leads to uniform fatality. The worldwide annual incidence rate of this disease is 1-2 per million. The defining characteristics of CJD include the accumulation of abnormal prion proteins in the brain, neuronal loss, gliosis, and spongiform changes [1]. The rarity of the disease and low clinical suspicion or insufficient knowledge poses significant challenges in diagnosing CJD during the patient's lifetime.

Creutzfeldt-Jakob Disease (CJD) is a type of human spongiform encephalopathy that can be transmitted through

different means, including familial inheritance, iatrogenic exposure, or sporadic occurrences [2]. The sporadic variant of CJD is identified by the rapid progression of dementia and myoclonus and is responsible for about 85% of all cases of prion disease in humans. The remaining cases are attributed to the infectious and inherited types of prion diseases.

Sporadic Creutzfeldt-Jakob disease (sCJD) is the most common form of CJD, accounting for 85% to 90% of cases, while the remaining cases are attributed to familial, iatrogenic, and variant forms [3]. The onset age of sCJD, which ranges between 60 and 80 years, has a mean value of 65 years. Although sCJD is uncommon in patients aged less than 30 or over 80 years, the underlying etiology remains unknown, and both genders are equally susceptible to the disease [3].

The clinical presentation of this disease is mainly characterized by multifocal neurological findings such as myoclonus, visual disturbances, cerebellar, and pyramidal/extrapyramidal signs, along with rapidly progressive dementia [4]. As the disease progresses, cognitive and functional impairment advance swiftly towards akinetic mutism in the later stage, and eventually, death typically occurs within 12 months of the disease onset.

## Case

Our case of study was a 70-year-old, retired English teacher, right-hand-dominant. Mr. A, presents with a progressive history of over six weeks of constellation of unusual features.

He was referred to the neurology department for further evaluation of rapidly progressive dementia, which had been ongoing for 8 weeks. The initial symptoms included anxiety, blurry vision, memory loss, anorexia, unintentional weight loss, and a general feeling of being unwell.

His medical history did not contribute towards the diagnosis. Although he had a long-standing history of health anxiety for himself and his wife, who has had cancer twice and a family history of Huntington's disease, he is generally in a stable condition. His medical record showed that he underwent CABG-2014 and had a history of Angina and GORD. No iatrogenic risks for prion disease or exposure to human-derived hormones were found, and neither did he have a history of high-risk surgical procedures. Additionally, there was no record of any neurological illness or family history of dementia.

Since November 2022, a gradual increase in anxiety was noted in the patient, that was uncharacteristic for him, but he attempted to prevent it from impacting his daily routine. Mild dementia was discernible from his speech pattern. Visual changes occurred abruptly six weeks ago, when he entered his kitchen and perceived that everything appeared 'different.' The patient was unable to provide a detailed explanation, but he sensed that things were not 'normal' and experienced discomfort as he perceived objects moving. Initially, this was suspected to be related to anxiety.

He begins to get very depressed and low. He was more tired and apathetic. He started to struggle to navigate around his house (He could not find the living room from the kitchen for example) and furniture began to change room size, shape, and position. Objects started to vanish in front of him. Colors were breaking up into patterns and there were times when he could not see moving objects.

He attended his GP and was admitted to hospital for assessment. During his first visit, his son reported a sudden and

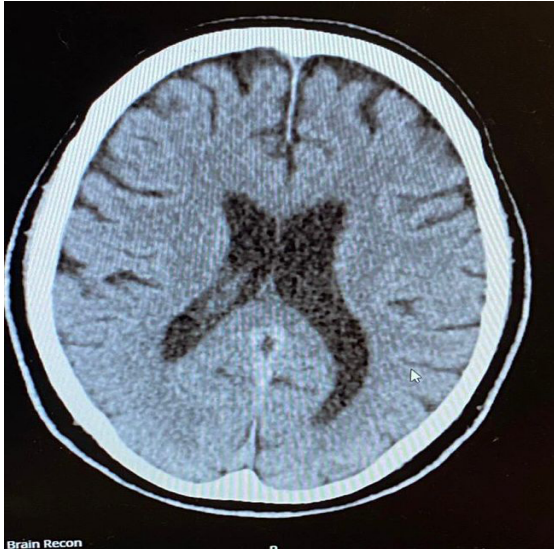
acute worsening of his cognitive problems over the previous 4 days. The patient was experiencing difficulties with short-term memory and daily functional activities such as finding his way around the house. His wife also noted that the patient had emotional lability and exhibited signs of mistrust towards his own family. The patient's vision was deteriorating, and he was experiencing increased drowsiness. The patient's family members denied the presence of myoclonic jerks, tremors, gait unsteadiness, or visual, auditory, or sensory hallucinations in him earlier.

The patient's physical examination revealed significant findings of perseveration, anomie aphasia, alexia, agnosia, and apraxia. Normal muscle tone was observed in all four extremities, and the cranial nerves appeared to be grossly normal. The patient had normal sensation and coordination, and symmetric reflexes were noted, with no Babinski reflexes detected. The patient's gait was slow but non-ataxic. Blood work was conducted, including a basic metabolic profile, CBC, thyroid studies, liver studies, vitamin B1, vitamin B12, and folate levels, lactic acid, Erythrocyte Sedimentation Rate (ESR), Rapid Plasma Reagin (RPR), Human Immunodeficiency Virus (HIV), Angiotensin-Converting Enzyme (ACE) levels, and ceruloplasmin, which were all within normal ranges. Pyruvate kinase, Purkinje cell antibody screen, Anti-Hu antibody, Anti-Jo antibody serum tests were also conducted, and the results were normal.

An MRI and a CT scan were performed on him and were reported as normal as shown in Figure 1 & Figure 2. He was scheduled to be seen by a neurologist but was discharged over the weekend on 10 December.



**Figure 1:** Normal MRI Scan of Mr. A



**Figure 2:** Images of CT scan Showing Normal Structure

It was observed that his walking had deteriorated while in the hospital, and he was hesitant to mobilize. Driving was ceased due to safety concerns. He became quieter and experienced additional unusual perceptual changes, such as difficulty perceiving height and depth. He encountered challenges using cutlery and was unable to perform self-care activities, such as washing himself. Jerky movements were noted during his sleep, although he did not exhibit REM sleep behavior disorder.

On the 21st of December, an incident occurred with the TV suddenly coming on and startling him, which led to him toppling over. As a result, he was distressed and had to be taken to the hospital, where he was admitted through A&E. His health continued to decline, and little voluntary speech was observed. Jerky myotonic sounding movements had now developed, and he could no longer feed himself. Assistance from two nurses was required for him to mobilize, and sedation was necessary for him to sleep. Visual hallucinations had also developed, mostly involving objects or distortion of object shape (visual illusions / misperceptions). At times, he began to refuse things.

During his 2nd admission, another MRI was performed, which revealed evolving and progressive cortical changes

involving parietal, temporal & occipital lobes, including posterior cingulate gyri, as well as much more florid right caudate changes highly suspicious of CJD. Following the MRI, the case was discussed with the Edinburgh Research & Surveillance unit. The plan was made to perform a lumbar puncture and send the sample for analysis to the center, which revealed slightly raised proteins (Figure 3).



**Figure 3:** Second MRI Scan Revealing Progressive Cortical Changes

It was suspected that the man had sporadic CJD, given the absence of iatrogenic or familial factors. The disease progressed rapidly and aggressively, with a complex visual onset. These are typical features of the Heidenhain subtype of sporadic CJD. This subtype is known to be associated with an extremely rapid deterioration, and the prognosis for the man was estimated to be two weeks or less, as CJD tends to accelerate over time.

The probable case by Euro-CJD criteria 2017 was met by the patient (Figure 4) [5]. Evolving complex visual symptoms (Alice in Wonderland) were observed for 6-8 weeks. Highly suggestive MRI imaging of evolving right cortical signal change with right caudate hyperintensity on DWI was detected. CSF protein exhibited a borderline rise, but it remained within known limits.



**Definite:**

Progressive neuropsychiatric syndrome and neuropathological or immunocytochemical, or biochemical confirmation

**Probable:**

I + two of II and typical EEG\*  
or  
I + two of II and typical brain MRI†  
or  
I + two of II and positive CSF 14-3-3  
or  
progressive neuropsychiatric syndrome and positive RT-QuIC in CSF or other tissues  
**+ exclusion of other causes in complete diagnostic workup**

**Possible:**

I + two of II + duration <2 years

<b>I</b> Rapidly progressive cognitive impairment
<b>II</b> A. Myoclonus B. Visual or cerebellar disturbance C. Pyramidal or extrapyramidal signs D. Akinetic mutism

**Figure 4:** Euro-CJD criteria 2017

It was communicated to him that his condition was indicative of CJD. Extensive discussions were held with him and his family regarding the course and prognosis of the disease.

The management relied on controlling symptoms, providing palliative care, and nursing care. It was probable that he would require 24-hour care. I suggested using levetiracetam at a dosage of 500 mg BD to control or improve his myoclonus. As his swallowing worsened, the total 24-hour dose was administered through a subcutaneous driver. Basic nursing care, contact with body fluids, skin, or mucous membranes did not pose any risk of transmission.

One week later, he was found to have developed cogwheel rigidity. Despite medical management, his symptoms continued to worsen and he passed away two weeks following his admission. Postmortem brain autopsy revealed the presence of abnormal protease-resistant prion protein detected through Western Blot analysis.

## Discussion

The diagnosis of sCJD could only be confirmed by verifying pathologic prion protein deposition in the brain [6]. However, it is possible to support the diagnosis through periodic sharp wave complexes on EEG, determination of 14-3-3 protein in the CSF, and abnormal signal changes in caudate nuclei and/or putamen on diffusion-weighted or fluid attenuated inversion recovery (FLAIR) MRI [7].

Rapidly progressive dementia, myoclonus, visual disturbances, cerebellar ataxia, and pyramidal/extrapyramidal signs are commonly observed on neurological examination in

sCJD, and can be caused by various diseases, indicating their non-specificity [8]. Thus, differentiated diagnosis between sCJD and other mimicking disorders requires a broad and updated knowledge base and diagnostic skills.

Probable sCJD was diagnosed in this case, based on the Euro-CJD criteria 2017 (Figure 1), while the patient was alive.5 Key findings of rapidly progressive dementia, visual disturbances (blurry vision), extrapyramidal signs (cogwheel rigidity), and hyperintensity signals in bilateral parietal and temporal lobes and thalami on diffusion-weighted MRI were observed [9].

Myoclonus and akinetic mutism were not observed initially, and they are frequently absent during the early stages. Although this is not a specific finding, protein 14-3-3 was not detected in the CSF. The EEG showed only a diffusely slow and disorganized background without typical periodic sharp wave complexes, which may not be visible during the early or later stages of sCJD [10].

A post-mortem brain autopsy was performed on this patient, and the presence of abnormal protease-resistant prion protein was confirmed by Western Blot analysis, thereby confirming the diagnosis of definite sCJD by CDC criteria [11].

Significant improvement has been observed in the diagnosis of sCJD in recent years due to the development of refined brain-imaging techniques and specific CSF assays. The disease's phenotypic spectrum is now better understood, and subtype-specific early diagnosis potential has increased. However, the revision of current diagnostic criteria is necessary to facilitate such diagnosis. Despite these advances, a safe and effective treatment for sCJD is yet to be discovered.

## Conclusion

While no generally accepted treatment is currently available for sCJD, an early and accurate diagnosis is crucial because some treatable differential diagnoses, such as viral or bacterial encephalitis, may be mistaken for it. Early diagnosis enables patients and their families to prepare for the expected disease course, establish care goals, and potentially request palliative care consultation.

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