ECRONICON OPEN ACCESS

EC NEUROLOGY
Case Report

Rapidly Progressive Dementia and Hyperkinetic Syndrome, Report of a Case of Creutzfeldt-Jakob Disease, at the General Hospital of Mexico

Nancy Patricia Moreno-Aldama*

Neurology, with a Specialized on Degenerative Diseases and Movement Disorders, Hospital General de México Dr. Eduardo Liceaga, Mexico City, Mexico

***Corresponding Author:** Nancy Patricia Moreno-Aldama, Neurology, with a Specialized on Degenerative Diseases and Movement Disorders, Hospital General de México Dr. Eduardo Liceaga, Mexico City, Mexico.

Received: April 10, 2025; **Published:** May 15, 2025

Abstract

Creutzfeldt-Jakob disease is a fatal neuroselective and neurodegenerative condition, rare in daily clinical practice, a rare brain disorder that causes muscle spasms and dementia; establishing the clinical diagnosis represents a challenge for the treating physician. It should be clinically suspected of rapidly progressive dementia, concomitant with myoclonus, cerebellar involvement, visual disturbances, or psychiatric condition. We present the case of a 59-year-old patient who presented to the neurology service with cognitive impairment plus movement disorder, with a fatal outcome.

Keywords: *Creutzfeldt-Jakob Disease; Prions; Rapidly Progressive Dementia; Myoclonus; Chorea*

Background

The concept of Creutzfeldt-Jakob disease (CJD) transmissible dementia began in 1966 when Gajdusek, Gibbs, and Alpers transmitted Kuru's disease to the chimpanzee. Gibbs., *et al*. in 1968, based on the histopathological similarity between CJD and Kuru, managed to transmit CJD and defined its infectious character. In addition, CJD was found to have the dual condition of being simultaneously infectious and genetically conditioned. It is a subacute encephalopathy that produces a cognitive and neurological deterioration of rapid evolution towards death in the short term and that is expressed histopathologically by a spongiosis of the gray substance of the brain. The locus is located on the short arm of chromosome 20 [1]. They include hereditary Creutzfeldt-Jakob disease (CJD), Gerstmann-Straussler-Scheinker disease (EGSS), and familial fatal insomnia. The non-hereditary ones are CJD (sporadic, iatrogenic and variant) and Kuru [2].

Case Report

This is a 59-year-old woman, with a history of being hypertensive for 10 years in good control and attachment, without other risk factors. His current condition began in August 2021, with apparent urinary tract infection and weight loss of approximately 10 kilograms without dietary modification. By November of the same year, the patient presented fatigue and discomfort in a generalized way with the onset of behavioral alterations, performing repetitive activities in a fluctuating manner; in December the presence of vertigo and blurred vision without major symptoms; until January when she presents loss of coordination to take objects and make fine movements, however, later she begins with oscillatory movements of the gaze, for which she is valued specialty of otorhinolaryngology as a diagnosis of vertigo and is sent to the neurology consultation, It is decided to hospitalize her since the patient is in poor physical condition, Cognitive and with

sudden involuntary movement of the right hemibody, accompanied by alterations in the sleep pattern and mutism, so it is considered to be a rapidly progressive dementia associated with a hyperkinetic syndrome.

Within its laboratories, blood counts, serum electrolytes, liver profile, thyroid profile, glucose hemoglobin, coagulation times, tumor markers, viral panel, immunological, vitamin B12, which within normal parameters are performed. Its diagnostic approach continues, in which brain MRI is requested, which reports generalized atrophy, with data of bifrontal edges of right predominance (Image 1 and 2), is complemented with an electroencephalogram study (Image 3), suspecting a non-convulsive status epilepticus which is reported phase 1 of abnormal sleep. due to severe generalized dysfunction, periodic pattern of acute waves compatible with encephalopathic pattern and mild right frontal focal epileptic activity and finally lumbar puncture was performed, to send a sample for cytology which was reported colorless, transparent, without sediment, 0 leukocytes, 8 erythrocytes, glucose: 53 mg/dl, proteins 37.51 mg/dl, LDH: 42.4 IU/L chlorine: 130.82 mmol/l and a sample for protein 14-3-3 was sent, a result that was later obtained with a quantitative value of 56661 IU/ml.

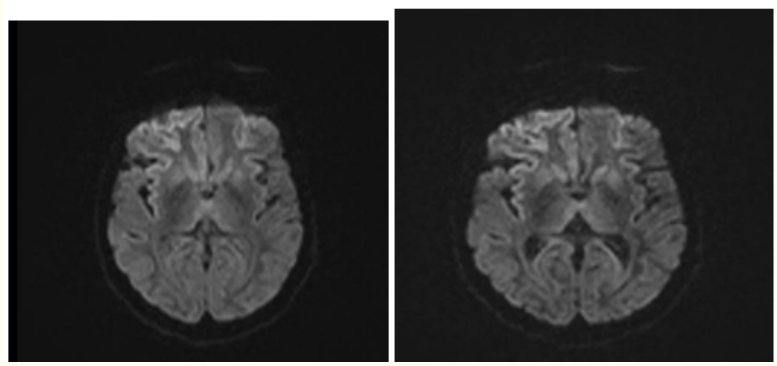

Image 1 and 2

During her hospital stay, the patient with a torpid evolution, with symptomatic management, based on anticonvulsants, baclofen and atypical antipsychotic, was discharged by maximum therapeutic range, dying one month at home.

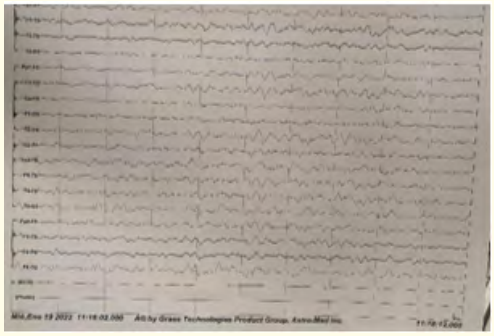

Image 3

Discussion

The first studies that allowed the identification of the infectious protein were carried out by Prusiner in 1982 in scrapie, which is the spongiform encephalopathy of sheep, where he identified the prion protein as PrPSc, which stands for proteolysis-resistant scrapie protein. The prion would lack RNA or DNA molecules [1]. Its distribution in tissues is very irregular, being expressed mainly in the central nervous system and lympho-reticular tissue, being found in very low concentration in accessible tissues (blood, urine) [3]. They have long incubation periods and progress inexorably to death once clinical symptoms appear. Three categories of human prion diseases are recognized: Sporadic: sporadic Creutzfeldt-Jakob disease (sCJD), sporadic fatal insomnia, and protease-sensitive prionopathy. Genetic: genetic Creutzfeldt-Jakob disease (gCJD), fatal familial insomnia (FFI), and Gerstmann-Straussler-Scheinker syndrome (GSS). Acquired: Kuru, iatrogenic Creutzfeldt-Jakob disease (iCJD) and variant Creutzfeldt-Jakob disease (vCJD). sCJD is the best known and accounts for more than 90% of sporadic prion diseases [4].

These human prion diseases share certain common neuropathological features including neuronal loss, proliferation of glial cells, absence of an inflammatory response, presence of small vacuoles within the neuropil that produces a spongiform appearance, and presence of protease-resistant prion protein. One of these strains is associated with atypical amyloid deposition, a neuropathological feature not found in typical bovine spongiform encephalopathy (BSE) [4].

The average age of onset of the disease is approximately 62 years, although rare cases have been reported in young adults and those over 80 years of age. There is no gender predilection. Other risk factors that have been variably identified for CJD include residence on a farm, family history, and medical history of psychosis [4].

The 2 most common symptoms of CJD are: Dementia, myoclonus. People with CJD also often have other symptoms that may include: Behavioral changes. Mood swings, such as depression. Trouble walking or problems with balance. Sleeping much more or much less than usual. These symptoms are similar to those that occur with other, more common types of dementia, such as Alzheimer's disease. But in CJD, symptoms worsen much faster [5].

Impairment of concentration, memory, and judgment are common early signs. Mood swings such as apathy and depression are common; Euphoria, emotional lability, and anxiety occur less frequently. Sleep disorders, particularly hypersomnia, but also insomnia, are also common and can be a sign of presentation. Some patients have psychotic features, especially visual hallucinations [4].

Myoclonus, especially caused by startles, is present in more than 90% of patients at some point in the disease, but may be absent at the time of presentation, even when dementia is profound. Sporadic CJD (sCJD) should always be considered in a patient with a combination of rapidly progressive dementia and myoclonus [4].

Cerebellar manifestations, including nystagmus and ataxia, occur in approximately two-thirds of patients and are the presenting symptoms in 20 to 40%. In particular, iatrogenic CJD (iCJD) related to human gonadotropin and growth hormone treatment, as well as dura grafts, has a propensity to manifest as a largely isolated cerebellar syndrome early in the disease course [4].

Signs of corticospinal tract involvement develop in 40% to 80% of patients, including findings such as hyperreflexia, extensor plantar responses (Babinski's sign), and spasticity. Extrapyramidal signs such as hypokinesia, bradykinesia, dystonia, and rigidity may also be present. Atypical features: include cranial nerve abnormalities and peripheral nervous system involvement. Alterations in pupillary responses, trigeminal neuropathy, and vestibulocochlear dysfunction have been reported in isolated cases, but are not characteristic [4].

Diagnostic criteria for vCJD have been developed and validated based on clinical features and diagnostic test results. While a definitive diagnosis requires neuropathological confirmation, it is reasonable to make the diagnosis in life using the probable criteria described below, as these appear to be very sensitive and specific. However, an autopsy should be performed for definitive diagnosis [6].

In the absence of a tonsil biopsy, a diagnosis of probable vCJD requires [6]:

- A progressive neuropsychiatric disorder; and
- A duration of illness > 6 months; and
- Routine investigations that do not suggest an alternative diagnosis; and
- No history of potential iatrogenic exposure; and
- No family history of transmissible spongiform encephalopathy; and
- Four of five of the following clinical features: early psychiatric features, persistent painful sensory symptoms, ataxia, movement disorder (myoclonus or chorea or dystonia), dementia; and
- Bilateral pulvinar signal on magnetic resonance imaging (MRI); and
- Absence of periodic acute wave complexes (PSWCs) on electroencephalography (EEG).

The Centers for Disease Control and Prevention (CDC) outlines two criteria for probable CJD [4]:

- Neuropsychiatric disorder with a positive real-time tremor-induced conversion test (RT-QuIC), or
- Progressive dementia and
- At least two of the following four clinical features:
- Myoclonus.
- Visual disorder of the cerebellum.
- Pyramidal or extrapyramidal dysfunction.
- Akinetic mutism.
- Supporting findings on one or more of the following tests:
- A typical electroencephalogram (EEG; e.g. periodic acute wave complexes [PSWCs]) during an illness of any duration.
- Positive 14-3-3 cerebrospinal fluid (CSF) test with a clinical duration to death of less than two years.
- Magnetic resonance imaging (MRI) showing hyperintensity in the caudate/putamen nucleus and/or in at least two cortical regions (temporal, parietal, and occipital) on diffusion-weighted (DWI) or fluid-attenuated inversion recovery (FLAIR) imaging.
- Routine investigations should not suggest an alternative diagnosis.

Magnetic resonance imaging is superior to computed tomography (CT) in detecting abnormalities in patients with CJD. A CT scan of the head is usually normal and serves primarily to exclude other diagnoses. However, serial CT scans performed over several months may show rapid ventricular enlargement and progressive cortical atrophy in some patients. PET scans using amyloid tracers (^{18}F-florbetaben) can cross-react with prion proteins [4].

In MRI, the hyperintense signal on DWI, FLAIR, and T2-weighted images involving the cerebral cortex and caudate striatum, head, and putamen is the most common pattern in MRI in patients with sporadic CJD. In particular, the superior frontal gyrus, the superior parietal lobe, the cingulate gyrus and the insular cortex are frequently affected; isolated limbic involvement is rare; and the perirolandic cortex is usually safe [4].

Electroencephalogram: A characteristic EEG pattern of periodic synchronous three-phase or biphasic PSWC is seen in 67 to 95 percent of patients with sCJD at some point during the course of the disease. This finding provides supportive but not definitive evidence for CJD. Typical sCJD PSWCs are characterized by the following characteristics: Strictly periodic brain potentials, most lasting 100 to 600 milliseconds and an intercomplex interval of 500 to 2000 milliseconds. Generalized and/or lateralized complexes. At least five repetitive intervals with a duration difference of <500 milliseconds are required to exclude semiperiodic activity [4].

The detection of the protein 14-3-3 in cerebrospinal fluid should be considered an adjunct rather than a diagnostic test for the diagnosis of prion diseases, as studies have reported conflicting results regarding its sensitivity and specificity. A systematic review reported an overall sensitivity of 92% and a specificity of 80% in the diagnosis of SCJD. A specificity of 80% in a disease with a prevalence as low as that of CJD means that most positive tests will represent false positives. A negative test does not exclude diagnosis [4].

Tau protein: Some studies have found that an elevated tau level (>1150 picograms/mL) has superior accuracy and specificity compared to protein 14-3-3 as a diagnostic test for CJD, although both tests produced a significant number of false results. Negative and false positive results [4].

Neuropathology: While neuropathology provides a definitive diagnosis of CJD, a brain biopsy is not required in most patients and should be performed primarily for the purpose of excluding an alternative treatable etiology rather than providing definitive evidence of prion disease. In particular, a brain biopsy is generally not necessary in the context of a positive RT-QuIC result, given its high specificity for sCJD, unless an alternative diagnosis is considered [4].

Early symptoms of vCJD are nonspecific; Depression and other psychiatric illnesses are commonly considered to be the initial diagnosis. Once neurological symptoms appear, the differential diagnosis is usually expanded to include sporadic CJD (CJD), Alzheimer's disease, paraneoplastic disease or malignancy, viral encephalitis, frontotemporal dementia, demyelination, vasculitis, subacute sclerosing panencephalitis, cerebrovascular disease, multiple system atrophy, Huntington's disease, Wilson's disease, and autoimmune limbic encephalitis. Magnetic resonance imaging (MRI) findings, laboratory studies, and lumbar puncture usually help exclude many of these diagnoses and provide evidence of vCJD [6].

There is no effective treatment for CJD, which is uniformly fatal. Supportive and symptomatic treatment: An effective treatment for human prion diseases, which are universally fatal, has not been identified. Care for patients with prion disease is supportive and includes: Early and effective communication with family. Referral to social services to coordinate care needs, arrange hospice assessment, and counsel families on end-of-life and financial matters. Remission is adequate at the time of diagnosis [4].

Myoclonus may respond to benzodiazepines (e.g. clonazepam) as well as certain anti-seizure medications, such as levetiracetam and valproate. Treatment with cholinesterase inhibitors or N-methyl-D-aspartate receptor antagonists (NMDAs) is not expected to be useful in CJD and is not administered [4].

Death usually occurs within one year of the onset of symptoms, with a median duration of the disease of six months. The mean duration of vCJD disease is longer than that of CJD (14 vs. 4 to 5 months) [4,6-15].

Conclusion

This case is of importance, since she is a female patient in the sixth decade of life, an age younger than what the reported epidemiology establishes, and she is a patient referred to our service by otorhinolaryngology for suspecting a vertiginous syndrome, without considering the context in a comprehensive way of the patient. calling his attention to the first contact with the patient of the presence of a hyperkinetic syndrome characterized by right hemichorea, so that in the first instance with a history of cognitive alterations, it is considered that it is a

Huntington's disease, so it is decided to admit him due to poor general conditions and for the study protocol, During his thorough evaluation it was determined that it is a dementia rapidly progresses together with psychiatric alterations, myoclonus and choreic movements of the right hemibody, protocol is initiated ruling out metabolic causes finding paraclinical studies within normal parameters, which did not justify his current state, due to the myoclonic movements, it is decided to perform an electroencephalogram study where a characteristic pattern of triphasic or biphasic is found synchronous and as a diagnostic part, an imaging study was completed where the presence of borders in the frontal lobes bilaterally was striking, with the set of these studies and in the face of a rapidly progressive dementia ruling out other possible causes, Creutzfeldt-Jakob disease was suspected, given this diagnostic suspicion and the torpid evolution of the patient, a study of the cerebrospinal fluid was completed in which tau protein 14 -3-3 was requested that although it does not specify, it is very sensitive to this condition, obtaining a very high quantitative value; The last step was the taking of a brain biopsy, however this could not be carried out due to two circumstances; Our hospital does not have an authorized center for handling samples of this type of material and the patient died at home.

What makes this case interesting is the manifestation of two syndromes, which, although they are known within the approach to prion disease, the presence of a hemichorea syndrome plus a rapidly progressive dementia, forces us to perform a discarding algorithm, which in the end the two syndromes can be justified with Creutzfeldt-Jakob disease.

Ethical Responsibilities Right to Privacy and Informed Consent

The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

Data Confidentiality

The authors state that they have followed their workplace's protocols on the publication of patient data.

Protection of People and Animals

The authors state that the procedures followed conformed to the ethical standards of the committee for responsible human experimentation and in accordance with the World Medical Association and the Declaration of Helsinki.

Conflict of Interest

The authors declare that they have no conflict of interest.

Bibliography

1. Cartier-Rovirosa L. "Prion disease, human spongiform encephalopathy and Creutzfeldt-Jakob disease". *Revista Médica de Chile* 147.9 (2019): 1176-1183.

2. Legua-Koc S., *et al*. "Creutzfeldt-Jakob disease: 5-year experience in a tertiary hospital in Chile". *Revista Médica de Chile* 149.9 (2021): 1285-1291.

3. Pitarch Fabregat J., *et al*. "Visual disturbance as an initial manifestation of Creutzfeldt-Jakob disease". *Medicina Clínica* 157.11 (2021): e335-e336.

4. Gómez Roldós A., *et al*. "Refractory status epilepticus in genetic Creutzfeldt-Jakob disease with E200K mutation". *Neurología (English Edition)* 35.9 (2020): 712-714.

5. Mantilla Flórez YF., *et al*. "Creutzfeldt's disease Jakob. Presentation of a case and review of the literature". *Revolution Medicines* 27.2 (2019): 103-111.

6. Ramírez M., *et al*. "Challenges in the diagnosis of Creutzfeldt-Jakob disease: a clinical case". *Revista Médica de Chile* 144.6 (2016): 806-811.

7. García-Ortega YE., *et al*. "Creutzfeldt-Jakob disease". *Medicina Interna de México* 35.5 (2019): 795-801.

8. Garnés Sánchez CM., *et al*. "Electroencephalographic and polysomnographic findings in a patient with familial Creutzfeldt-Jakob disease". *Neurology* 33.9 (2018): 625-628.

9. Briones-Torres CA., *et al*. "Study of 14-3-3 and Tau proteins as biomarkers in patients with neurodegenerative diseases of undetermined origin. Experience in the Clinical Pathology Laboratory of Médica Sur". *Revista de Investigación Médica Sur* 21.3 (2014): 116-119.

10. Mercado-Flores M., *et al*. "Magnetic resonance imaging findings in rapidly progressive dementia, probable Creutzfeldt-Jakob prion disease sporadic form". *Annals of Radiology Mexico* 14.3 (2015): 292-298.

11. Pérez-Pérez J., *et al*. "Atypical presentation in brain resonance imaging of Creutzfeldt-Jakob disease: a case report". *Neurología Argentina* 14.2 (2023):98-103.

12. González-Ramos S., *et al*. "Clinical-epidemiological characterization of Creutzfeldt-Jakob disease in a hospital center". *Revista Científica Estudiantil HolCien* 12.3 (2023): 210-215.

13. Rodríguez-Melgarejo P., *et al*. "Experience with Creutzfeldt-Jakob disease from a single reference center in Mexico: Analysis of a case series". *Gaceta Médica de México* 158.6 (2022): 321-326.

14. Tian H., *et al*. "Recent advancements in the diagnosis of Creutzfeldt-Jakob disease: a review". *Journal of the Neurological Sciences* 420 (2021): 117242.

15. Lee JM., *et al*. "Clinical and imaging findings in a patient with Creutzfeldt-Jakob disease and temporal lobe involvement". *Clinical Neurology and Neurosurgery* 206 (2021): 106711.

Volume 17 Issue 5 May 2025