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Case Report

Creutzfeldt-Jakob disease: Case report and literature review ☆

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ABSTRACT

Creutzfeldt-Jakob Disease (CJD) is a rare, rapidly progressive neurodegenerative disorder that presents significant diagnostic challenges. We report the case of a 50-year-old male with a four-month history of progressive neurological symptoms, including speech disturbances, hemiparesis, ataxia, and myoclonus. Initial brain MRI showed no significant abnormalities, but later imaging revealed characteristic hyperintensities in the frontal and paracentral regions, basal ganglia, and temporal cortex on T2 and FLAIR sequences. EEG showed periodic lateralized discharges, supporting the clinical suspicion of CJD. Although confirmatory tests like RT-QuIC and CSF biomarkers could not be performed due to financial constraints, the clinical presentation and imaging findings met the criteria for "probable" sporadic CJD. Unfortunately, the patient's condition rapidly deteriorated, and he passed away within four months. This case underscores the importance of early imaging and clinical awareness in diagnosing CJD, particularly in resource-limited settings, and highlights the need for further research into effective treatments for this fatal disease.

Introduction

Creutzfeldt-Jakob Disease (CJD) is a rare, rapidly progressing neurodegenerative disorder caused by prions—misfolded proteins that lead to brain damage. It can manifest in sporadic, hereditary, or iatrogenic forms. CJD is challenging to diagnose due to its swift progression and overlap with other neurodegenerative diseases. Clinical symptoms primarily include rapidly progressive dementia, myoclonus, visual disturbances, and both cerebellar and pyramidal/extrapyramidal signs. The disease typically advances quickly, leading to severe cognitive and functional decline, akinetic mutism in the late stages, and death

Magnetic resonance imaging (MRI), particularly diffusion-weighted imaging (DWI), is the most sensitive method for detecting the characteristic brain abnormalities associated with CJD, supporting the diagnosis and helping distinguish it from other conditions.

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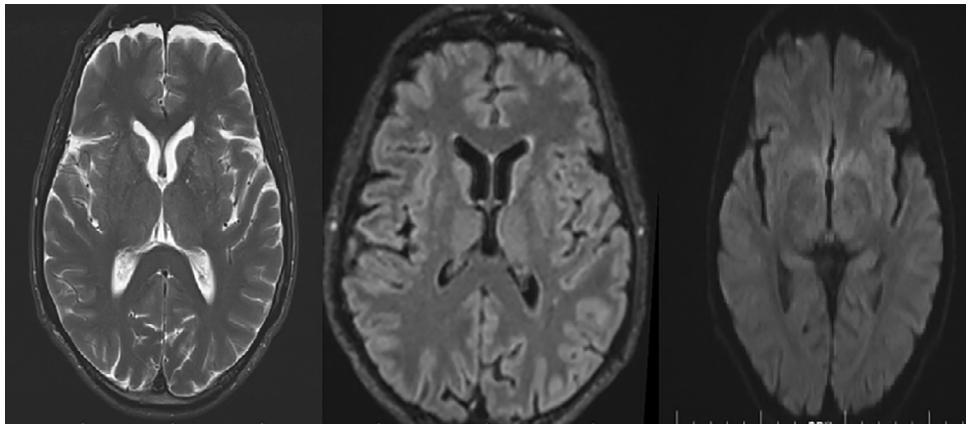

Fig. 1 – Brain MRI: Axial sections on T2-weighted, FLAIR, and Diffusion sequences.

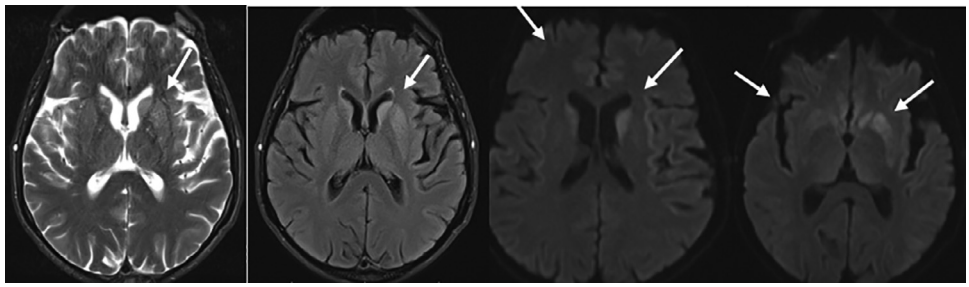

Fig. 2 – Axial T2-weighted, FLAIR, and Diffusion sequences: Hyperintense signal anomalies on FLAIR and T2 sequences with diffusion restriction involving the left parasagittal and paracentral frontal regions, the motor and premotor areas, the basal ganglia, and the bilateral temporal and insular cortical ribbon, with a more pronounced involvement on the left side.

Case report

A 50-year-old male patient, with a history of well-controlled hypertension and active smoking (50 pack-years), was admitted for a presentation of complete anarthria evolving over four months. Upon admission, the patient was stable neurologically, respiratory-wise, and cardiovascularly, without hypoxia or hypoglycemia, and metabolic workup was unremarkable.

An initial brain MRI was performed and showed no significant abnormalities (Fig. 1). However, the patient experienced progressive clinical worsening after a month, developing right hemiparesis along with the onset of ataxia and myoclonus. This deterioration prompted a repeat brain MRI, which revealed abnormalities characterized by hyperintensities on FLAIR and T2 sequences with diffusion restriction involving the left parasagittal and paracentral frontal regions, the motor and premotor areas, the basal ganglia, as well as the bilateral cortical ribbon in the temporal and insular regions, with a predominance on the left side (Fig. 2).

An electroencephalogram (EEG) was also performed, showing generalized periodic activity in the form of periodic lateralized discharges with polyspikes and spike-wave complexes (Fig. 3).

The clinical presentation raised suspicion of a progressive neurological disorder. The diagnostic approach was based on a combination of imaging findings, clinical progression, and electroencephalogram (EEG) features.

Given the clinical picture and progression, symptomatic therapy was initiated, including antiepileptic drugs to manage myoclonus. Despite these measures, the patient's condition continued to deteriorate rapidly. Unfortunately, the patient succumbed to the disease three weeks after the repeat MRI.

Discussion

Creutzfeldt-Jakob disease (CJD) is a rare human neurodegenerative condition with an incidence of approximately 1 case per million people per year [1]. Previously called transmissible spongiform encephalopathies, it was first described by German neurologist Hans Gerhard Creutzfeldt in 1920 and shortly thereafter by Alfons Maria Jakob. Four types of CJD have been identified [2], with the sporadic form (sCJD) being the most common, accounting for 85%-90% of cases.

The sporadic form is caused by the spontaneous transformation of the prion protein or by somatic mutation [3], whereas the hereditary form is often associated with a mutation in the human prion protein gene. The iatrogenic form is rare and results from the administration of human pituitary hormones derived from cadavers [4], dura mater grafts,

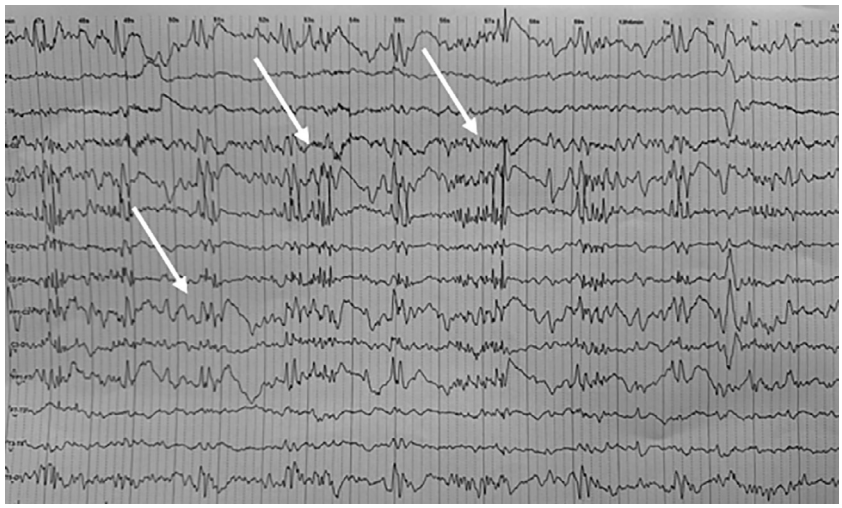

Fig. 3 – EEG shows generalized periodic activity (periodic lateralized discharges with polyspikes and spike-wave complexes).

corneal transplants, and the use of dura mater in radiological embolization procedures, among others.

CJD is a transmissible spongiform encephalopathy caused by prions. Prions are misfolded proteins formed in the neurons of the central nervous system (CNS). They disrupt signaling processes, damage neurons, and lead to degeneration in the affected brain, resulting in a spongy appearance. The CJD prion is dangerous because it promotes the refolding of natural prion proteins into the pathological state. The number of misfolded protein molecules increases exponentially, leading to large amounts of insoluble proteins in the affected cells [5].

CJD is clinically heterogeneous, with a common characteristic of rapid neuropsychiatric decline, and death typically occurring within one year of symptom onset [6]. Sporadic cases of CJD generally occur between the ages of 45 and 75, with the average age of symptom onset being between 60 and 65 years.

The symptomatology of CJD initially includes memory loss and confusion [7]. Coordination problems and ataxia may appear later in the disease. While dementia, ataxia, and myoclonus are the most characteristic signs, other neurological abnormalities, such as psychiatric disorders, seizures, neuropathy, abnormal movements, and visual disturbances (e.g., diplopia and decreased visual acuity), can also be present [8].

Extrapyramidal signs, such as hyperreflexia, extensor plantar responses, and spasticity, are observed in about 40% of cases [9].

Pathological studies of brain tissue to detect protease-resistant PrPsc (PrPres) remain the gold standard for diagnosing prion diseases. However, a probable diagnosis of CJD can be established using non-invasive tests, which are generally sufficient. According to the Centers for Disease Control and Prevention (CDC) diagnostic criteria for CJD, our patient meets the criteria for “probable” CJD [10].

MRI is the modality of choice for evaluating patients suspected of having CJD and for ruling out other differential diagnoses, such as autoimmune encephalitis, hypoxia, and hypoglycemia [11]. The most sensitive sequence for identifying characteristic changes is diffusion-weighted imaging (DWI), which shows hyperintensities more pronounced than those observed in T2/FLAIR sequences and ADC maps. It can detect hyperintense areas in typical sites for this pathology, such as the cerebral cortex, with frequent involvement of the insula, cingulate gyrus, and superior frontal gyrus. The deep gray matter is also affected, with the most common locations being the striatum (caudate and putamen) and the thalamus.

Electroencephalography (EEG) is a key diagnostic tool in the evaluation of CJD, particularly in its sporadic form. It reveals characteristic abnormalities in the advanced stages of the disease, although its utility varies according to the subtype of CJD.

The classic EEG pattern of sporadic CJD is characterized by periodic triphasic complexes. These complexes appear as periodic, symmetrical, and stereotyped generalized waveforms. They occur most frequently every 0.5-2 s and are typically associated with clinically observed myoclonus. These abnormalities are more common in the advanced stages of the disease [12].

Diffuse slowing of brain activity may also be found, although it is not specific and can be observed in other metabolic or neurodegenerative encephalopathies.

Other tests include the RT-QuIC (Real-Time Quaking-Induced Conversion) test. This test relies on the ability of pathological prions (PrP^Sc) to catalyze the misfolding of normal prion proteins (PrP^C) into pathological forms. This reaction leads to amplified conversion, detected in real-time by fluorescence. It is a noninvasive test, requiring cerebrospinal fluid (CSF) as a sample, thereby avoiding the need for a brain biopsy.

It has a sensitivity of 87%-91% and a specificity of 98%-100% [3]. The detection of the 14-3-3 protein in CSF should be considered a complementary test rather than a diagnostic one for prion diseases [13]. CSF Tau protein levels (>1150 picograms/mL) provide higher accuracy and specificity compared to the 14-3-3 protein as a diagnostic test [14]. However, these tests could not be performed on our patient due to financial constraints.

Other studies on CSF, such as S100 proteins, neuron-specific enolase, and beta-thymosin [3], have been reported in some series, but due to their low specificity and sensitivity, they are not performed routinely.

The detection of prions in tissues outside the CNS, such as the skin, spleen, and nasal mucosa, has not yet yielded conclusive results sufficient to recommend these techniques for diagnostic confirmation [15].

CJD can initially be mistaken for psychiatric disorders, such as acute delusional episodes, as behavioral and personality changes can be significant and mask the specific neurocognitive features of the disease. However, as the disease progresses, neurological signs become more pronounced. It can also be challenging to distinguish CJD from other dementias, such as Alzheimer's disease, dementia with Lewy bodies, and corticobasal degeneration, which are also associated with myoclonus and exhibit a more rapid progression. Nonetheless, the specific MRI findings, particularly using diffusion sequences, and CSF analysis help establish the diagnosis [16]. Before making the diagnosis, metabolic disorders such as hypoglycemia, infectious, vascular, and autoimmune conditions should be excluded.

Currently, there is no curative treatment, and care is primarily focused on symptom relief. The progression of CJD is fulminant, leading to death within one year in 85% of patients [17]. In our patient, death occurred four months after the onset of the disease.

Conclusion

This case illustrates the importance of early recognition and the role of advanced imaging in diagnosing Creutzfeldt-Jakob Disease (CJD). Diffusion-weighted MRI and EEG findings were key in supporting the diagnosis, even without confirmatory laboratory tests. Despite the absence of specific treatments, prompt diagnosis is critical for managing symptoms and providing appropriate care. This case highlights the need for ongoing research and awareness to improve outcomes for patients with CJD.

Patient consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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