CMMB
https://doi.org/10.31689/rmm.2025.32.3.303
CASE REPORTS

Sporadic Creutzfeldt-Jakob Disease with Rapid Cognitive Decline and Cortical Ribboning: A Case Report

Razvan-Gabriel PRICOPE [1*], Andreea-Eliza CAZACU [2]

Abstract

Background: Creutzfeldt-Jakob disease (CJD) is a rare, rapidly progressive, and universally fatal neurodegenerative disorder caused by the accumulation of misfolded prion proteins. Early-stage diagnosis is often delayed due to its initially non-specific presentation and broad differential diagnosis.

Case Presentation: We describe a 75-year-old male who presented with new-onset dizziness and a pressure-like headache. Neurological examination revealed subtle left-sided ataxia, mild anomic aphasia, and possible left-leg neglect. Initial investigations, including non-contrast cranial CT and carotid angiography, were unremarkable. Cognitive screening using the Montreal Cognitive Assessment (MoCA) scored 17/30. Persistent neurological deficits prompted further evaluation, including lumbar puncture, electroencephalography, and magnetic resonance imaging of the brain. CSF analysis showed a mildly elevated white cell count and was positive for 14-3-3 protein. Although RT-QuIC testing was uninterpretable due to CSF blood contamination, markedly elevated total tau (>1765 pg/mL) with normal phosphorylated tau (pTau181) supported a diagnosis of prion disease. MRI demonstrated asymmetric cortical diffusion restriction and characteristic cortical ribboning. EEG revealed a diffuse encephalopathic pattern without periodic discharges. With the rapid evolution of cognitive dysfunction, cerebellar ataxia, and extrapyramidal signs, the clinical, radiological, and biochemical findings fulfilled diagnostic criteria for probable sporadic CJD.

Conclusion: This case underscores the importance of a multimodal diagnostic approach in suspected CJD. In the absence of definitive RT-QuIC results or characteristic EEG changes, early recognition of MRI patterns and CSF biomarkers remains pivotal for timely diagnosis, appropriate counseling, and care planning.

Keywords: Creutzfeldt-Jakob Disease, cortical ribboning, rapid cognitive decline, sporadic prion disease, MRI

[1]Praxis am Bahnhof, 8630 Rüti, Switzerland
[2]Spital Lachen, 8853 Lachen, Switzerland

***Corresponding author:**
Răzvan-Gabriel PRICOPE, Praxis am Bahnhof 8630 Rüti, Switzerland
E-mail: razvprc@gmail.com

INTRODUCTION

Creutzfeldt-Jakob disease (CJD) is a rare, rapidly progressive, and invariably fatal neurodegenerative disorder caused by the pathological accumulation of misfolded prion proteins (PrP^Sc). Clinically, it is characterized by rapidly progressive dementia, cerebellar ataxia, myoclonus, and extrapyramidal signs, with a median survival of 6 to 12 months from symptom onset[1,2]. The sporadic form (sCJD) represents the most prevalent subtype, accounting for approximately 85–90% of all cases globally[3].

Early diagnosis of CJD remains a significant clinical challenge. Initial symptoms are often vague and nonspecific—such as dizziness, headache, or subtle cognitive impairment—frequently mimicking more common neurological conditions like vascular dementia, encephalitis, or metabolic encephalopathies. Given the disease's aggressive trajectory, early and accurate recognition is essential to guide clinical management and avoid unnecessary interventions.

Currently, the diagnostic approach relies on a combination of clinical assessment and ancillary investigations. These include brain magnetic resonance imaging (MRI), particularly diffusion-weighted imaging (DWI) and fluid-attenuated inversion recovery (FLAIR) sequences; cerebrospinal fluid (CSF) analysis for biomarkers such as 14-3-3 and total tau protein; real-time quaking-induced conversion (RT-QuIC) assays; and electroencephalography (EEG)[4,5].

In this report, we present a case of sCJD that initially manifested with non-specific symptoms before evolving into a characteristic clinical and radiological picture. This case illustrates the importance of maintaining a high index of suspicion and employing a multimodal diagnostic strategy to facilitate early identification of this rare but devastating disease.

CASE PRESENTATION

A 75-year-old male with no prior history of neurological or psychiatric illness presented to the emergency department with a one-week history of dizziness and a persistent, pressure-like bifrontal headache. He was hemodynamically stable and in good general condition. Neurological examination revealed subtle left-sided upper limb ataxia, suspected left-leg neglect, and mild anomic aphasia. The initial National Institutes of Health Stroke Scale (NIHSS) score was 2.

Non-contrast cranial computed tomography (CT) and CT angiography of the cervical and intracranial vessels were unremarkable, with no evidence of hemorrhage, early ischemic changes, or significant vascular stenosis. Initial laboratory tests revealed normochromic normocytic anemia and a mild vitamin B12 deficiency, but no electrolyte imbalances or signs of systemic infection. Electrocardiography demonstrated normal sinus rhythm.

Given the persistent focal neurological findings, empiric antiplatelet and statin therapy were initiated for presumed cerebrovascular etiology. While the headache and dizziness resolved spontaneously within 48 hours, mild cognitive impairment, left-sided ataxia, and possible myoclonic jerks of the left hand persisted.

Neurocognitive assessment using the Montreal Cognitive Assessment (MoCA) yielded a score of 17/30, indicating significant cognitive impairment. Electroencephalography revealed mild generalized slowing and intermittent triphasic waves over the frontal regions, but no epileptiform activity or periodic sharp wave complexes.

Cerebrospinal fluid analysis showed a mildly elevated leukocyte count (6 cells/μL) with normal glucose and protein levels. Empirical treatment with intravenous acyclovir and corticosteroids was initiated for suspected viral or autoimmune encephalitis, but discontinued after comprehensive infectious and autoimmune panels — including HSV, VZV, NMDA-R, and LGI1 antibodies — returned negative.

Brain magnetic resonance imaging with diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) mapping demonstrated asymmetric cortical diffusion restriction with a marked right hemispheric predominance, as well as signal abnormalities in the right caudate head and mildly in the lateral putamen, without contrast enhancement (Figure 1), (Figure 2). These findings raised the differential diagnosis of postictal changes, infectious encephalitis (e.g., Creutzfeldt-Jakob disease), or vascular etiologies, while metabolic causes were considered less likely.

Over the subsequent days, the patient's neurological condition deteriorated. He developed marked spatial neglect, dysphasia, ideomotor apraxia, and extrapyramidal features including left-predominant rigidity and bradykinesia. Gait instability and bilateral cerebellar signs (abnormal finger-nose and heel-shin testing, positive Romberg sign) were also noted. Deep tendon reflexes were symmetrical, and plantar responses were flexor bilaterally.

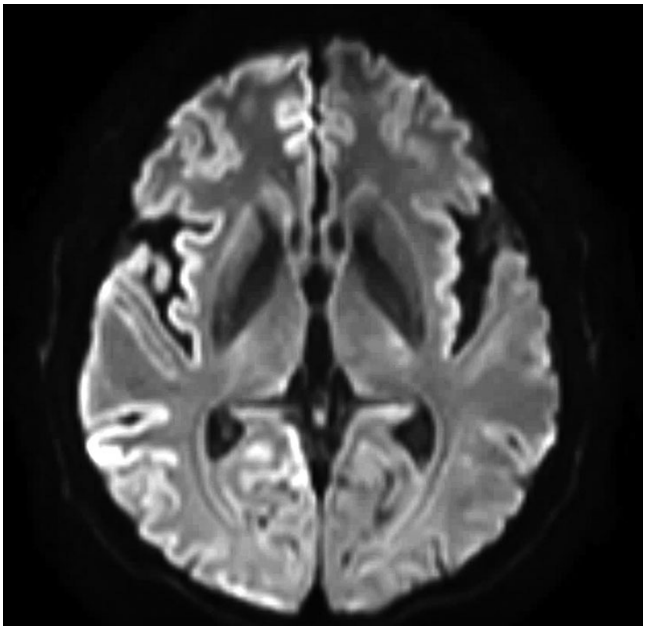

Figure 1. Diffusion-weighted MRI (DWI) shows marked cortical diffusion restriction with right hemispheric predominance, especially in the frontal and temporal lobes. Hyperintensities in the right caudate nucleus and lateral putamen suggest a "cortical ribboning" pattern typical of sporadic Creutzfeldt-Jakob disease.

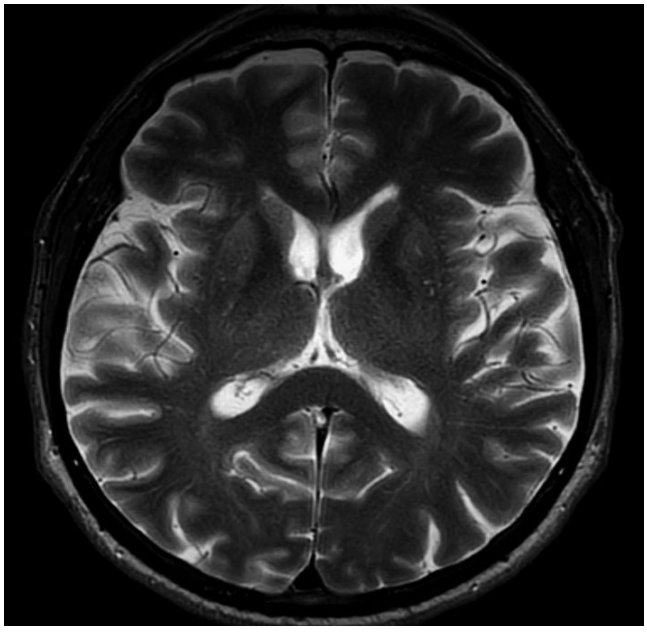

Figure 2. Axial T2-weighted MRI shows preserved gray-white matter contrast without significant atrophy or signal changes. The absence of abnormalities supports the specificity of DWI hyperintensities typical in prion disease.

Further CSF testing revealed elevated total tau protein (>1765 pg/mL) with a normal phosphorylated tau (pTau181) concentration, effectively excluding Alzheimer's disease and supporting a diagnosis of prionopathy. The 14-3-3 protein was positive, consistent with neuronal injury. However, real-time quaking-induced conversion (RT-QuIC) testing was inconclusive due to blood contamination of the CSF sample. No oligoclonal bands were detected.

In light of the rapidly progressive cognitive decline, cerebellar and extrapyramidal signs, characteristic MRI findings, and supportive CSF biomarkers, the patient fulfilled the diagnostic criteria for sporadic Creutzfeldt-Jakob disease according to both Centers for Disease Control and Prevention and European diagnostic guidelines.

DISCUSSION

Creutzfeldt-Jakob disease, particularly its sporadic form, remains a formidable diagnostic challenge due to its protean manifestations and the absence of a definitive premortem test. The disease typically begins insidiously, often mimicking more common neurological or psychiatric conditions such as vascular dementia, autoimmune encephalitis, or metabolic encephalopathies[1,4]. In this case, the patient's early presentation with vertigo and headache delayed clinical suspicion, illustrating the diagnostic ambiguity in the initial stages of the disease.

However, the subsequent rapid deterioration—marked by progressive cognitive decline, cerebellar ataxia, myoclonus, and extrapyramidal rigidity—served as critical red flags. These features, particularly when combined, should prompt consideration of prion disease. The hallmark of sCJD is its swift progression, typically culminating in severe disability or death within one year of onset[3].

Neuroimaging proved essential in this case. MRI findings demonstrated the classic "cortical ribboning" appearance — diffusion restriction in the cerebral cortex on DWI and corresponding hypointensity on ADC maps — which is considered highly specific to CJD[5,6]. The patient also showed hyperintensity in the basal ganglia, another supportive radiologic marker. Importantly, these changes can precede clinical symptoms, making MRI a crucial early diagnostic tool. Asymmetric cortical involvement, particularly in the frontal and temporal lobes, correlated well with the patient's neurocognitive decline.

Electroencephalography, though traditionally associated with the detection of periodic sharp wave complexes in CJD, did not show this hallmark in our patient. Instead, non-specific triphasic waves consistent with metabolic encephalopathy were observed. This is not unusual—EEG findings in CJD evolve over time and can initially lack specificity[7]. Serial EEGs may be more informative but are often impractical given the rapid disease course.

Cerebrospinal fluid analysis further supported the diagnosis. The detection of elevated total tau (>1765 pg/mL) and 14-3-3 protein is suggestive of extensive neuronal damage and has become a cornerstone in non-invasive diagnosis[8,9]. Although 14-3-3 protein has limited specificity, especially in conditions like encephalitis or stroke, total tau concentrations exceeding 1200 pg/mL are strongly associated with sCJD. The normal p-Tau181 level helped differentiate this case from Alzheimer's disease, which typically presents with disproportionately elevated phosphorylated tau.

Real-time quaking-induced conversion, currently the most specific test for prion diseases, offers over 90% sensitivity and specificity[10]. Unfortunately, the assay result in this case was invalid due to CSF sample contamination with blood, underscoring a known limitation of the test. Despite this, the clinical profile, MRI features, and CSF biomarkers met the CDC and WHO criteria for a diagnosis of sCJD[3,9].

Ultimately, no curative treatment exists for CJD. Management is supportive and focused on symptom relief and family counseling. However, accurate early diagnosis is essential for guiding prognosis, avoiding unnecessary investigations, and enabling timely end-of-life planning. This case underscores the importance of integrating clinical acumen with neuroimaging and biomarker analysis to arrive at a confident diagnosis, even in the absence of definitive histopathological confirmation.

CONCLUSION

This case highlights the diagnostic challenges posed by Creutzfeldt-Jakob disease, particularly in its early stages when symptoms may mimic more common neurological conditions. A multidisciplinary diagnostic approach—integrating clinical observation, neuroimaging, EEG findings, and CSF biomarkers—is crucial for achieving a timely and accurate diagnosis. While the prognosis of sCJD remains poor and no curative treatment exists, early recognition is vital for optimizing palliative care, facilitating informed discussions with patients and families, and avoiding unnecessary investigations or interventions. Greater awareness and clinical suspicion among healthcare professionals can help reduce diagnostic delays and improve the quality of end-of-life care for affected patients.

Ethics Statement and Conflict of Interest Disclosures

Financial support and sponsorship: All authors have declared that no financial support was received from any organization for the submitted work.

Ethics Consideration: The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national laws. Written informed consent was provided by the patient participant in this study.
This study was approved by the Institutional Research Board and Ethics Committee.

Conflict of interest: No known conflict of interest correlated with this publication.

Availability of data and materials: The data used and/ or analyzed throughout this study are available from the corresponding authors upon reasonable request.

Competing interests: The authors declared that they have no competing interests.

The use of generative AI and AI-assisted technologies: The authors did not use in this article generative AI and AI-assisted technologies.

REFERENCES

1. Zerr, I., Kallenberg, K., Summers, D. M., et al. Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease. Brain, 132(10), (2009), 2659–2668.
2. Mead, S. Prion disease genetics. European Journal of Human Genetics, 14(3), (2006), 273–281.
3. Centers for Disease Control and Prevention (CDC). Diagnostic criteria for Creutzfeldt-Jakob Disease (CJD), 2023 update. CDC Guidelines, (2023).
4. Geschwind, M. D. Rapidly progressive dementia. Continuum: Lifelong Learning in Neurology, 22(2), (2016), 510–537.
5. Vitali, P., Maccagnano, E., Caverzasi, E., et al. Diffusion-weighted MRI hyperintensity patterns differentiate CJD from other rapid dementias. Neurology, 76(20), (2011), 1711–1719.
6. Shiga, Y., Miyazawa, K., Sato, S., et al. Diffusion-weighted MRI abnormalities as an early diagnostic marker for Creutzfeldt-Jakob disease. Neurology, 63(3), (2004), 443–449.
7. Wieser, H. G., Schindler, K., Zumsteg, D. EEG in Creutzfeldt-Jakob disease. Clinical Neurophysiology, 117(5), (2006), 935–951.
8. Atarashi, R., Satoh, K., Sano, K., et al. Ultrasensitive human prion detection in cerebrospinal fluid by real-time quaking-induced conversion. Nature Medicine, 17(2), (2011), 175–178.
9. Rudge, P., Jaunmuktane, Z., Adlard, P., et al. Diagnostic criteria for sporadic Creutzfeldt–Jakob disease: Analysis of the updated National CJD Research & Surveillance Unit criteria. Journal of Neurology, Neurosurgery & Psychiatry, 89(5), (2018), 535–541.