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Case Report

Psychiatric Predominant Prion Disease: A Case of Rapidly Progressive Creutzfeldt-Jakob Disease

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Abstract

This case is of particular interest due to its unusually rapid clinical progression from initial symptom onset on March 23rd to death on June 2nd representing one of the fastest documented courses of Creutzfeldt-Jakob disease (CJD). While CJD typically presents with rapidly progressive dementia, ataxia, visual disturbances, and myoclonus, this report underscores the predominance of early psychiatric and behavioral manifestations preceding the classic neurologic findings. The significance of this case lies in emphasizing that initial psychological or psychiatric symptoms may represent the earliest indicators of CJD, warranting prompt neurologic evaluation and advanced diagnostic testing. Recognizing these early psychiatric presentations may facilitate earlier diagnosis, reduce unnecessary investigations, and allow families more time to prepare for the disease's inevitable progression. Ultimately reinforcing the need for heightened clinical suspicion and multidisciplinary assessment in patients presenting with the rapidly evolving psychiatric and cognitive decline.

Keywords: *Creutzfeldt-Jakob Disease (CJD); Prion Disease; Dementia; Transmissible Spongiform Encephalopathies (TSEs)*

Introduction

Creutzfeldt-Jakob Disease (CJD) is characterized by rapidly progressive cognitive decline within several weeks to death within 4 - 6 months [1,2]. Early manifestations can include personality changes, memory loss, impaired thinking, blurry vision or blindness, insomnia, coordination problems, trouble speaking or swallowing, and sudden, jerky movements [3,4]. Most patients die within one year ending with multi end organ failure [5]. As the disease advances weakness of the arms and legs will develop with blindness, inability to move or speak problems swallowing and eventually a coma [6]. Early clinical features of CJD may overlap with Alzheimer's and Huntington's disease [7].

CJD belongs to a group of Prion diseases, also known as transmissible spongiform encephalopathies (TSEs) [8]. Prions are a type of protein found primarily in the brain, their function is not well understood [9]. They are able to induce abnormal folding of normal cellular prions which build up in the brain and cause neurodegeneration [8]. The pathogenesis of CJD is believed due to a conformational change in normal prion proteins (PrP) to a pathologic misfolded form referred to as scrapie prion proteins (PrPsc) [10]. Approximately 350 cases are reported per year in the United States and roughly 70% of people with CJD die within one year of getting the disease [7].

Atypical presentations of Creutzfeldt-Jakob disease may present with overt dementia and motor dysfunction, resulting in misdiagnosis and delayed recognition [11]. Our current case emphasizes the importance of early neurologic evaluation, repeat advanced neuroimaging, and timely cerebrospinal fluid biomarker testing in patients with rapidly progressive psychiatric and cognitive decline.

Case Presentation

A 66-year-old male with a past medical history of hypertension, obstructive sleep apnea on continuous positive airway pressure at night, left eye amblyopia, experienced an abrupt change in his sense of well-being on March 23rd, 2024, reporting that he "didn't feel right". Past surgical history consists of a gallbladder mass followed by elective radical cholecystectomy with partial hepatectomy in 2011 with pathology coming back as benign. His home medications included losartan 50 mg every day for hypertension. Family history was significant for chronic kidney disease in mother and unknown leukemia in father.

Initial symptoms include lightheadedness, gait instability, anxiety, paranoia, and impaired coordination. Symptom onset followed consumption of a single alcoholic beverage, prompting initial suspicion of intoxication. Initially, symptoms were vague and nonspecific, leading clinicians to suspect psychiatric causes. Over the following days, symptoms remained vague and fluctuating. He subsequently developed mild confusion, word-finding difficulty, and behavioral changes including anxiety and paranoia. These findings were initially interpreted as psychiatric in nature. Sleep disturbance, emotional lability, and intermittent agitation were also reported. The patient did not have a history of any substance abuse.

Over the subsequent weeks, additional symptoms emerged that further contributed to the diagnostic uncertainty. The patient reported ear fullness and visual disturbances, prompting evaluation by internal medicine, otolaryngology, and ophthalmology. An internist considered cerumen impaction and performed ear irrigation, which did not reveal obstruction or pathology. These evaluations were otherwise unrevealing. An outpatient brain MRI without contrast was performed showing subtle asymmetry of cortical hyperintensity on diffusion without definitive equivocal of unclear significance.

During early April, progressive behavioral and cognitive changes developed, including insomnia, emotional lability, mild confusion, word-finding difficulty, and increasing anxiety. Psychiatric evaluation raised concern for a primary psychiatric or stress-related disorder. The patient was treated with anxiolytics and antidepressants for presumed acute psychosis or mood disorder. There was no history of seizures, myoclonic movements, transfusions, transplantation, or known prion exposure. His only history was the cholecystectomy and partial hepatectomy.

Approximately three weeks after symptom onset, symptoms progressed with worsening agitation, paranoia, disorganized speech, and behavioral disinhibition. Cognitive decline became more apparent with increasing difficulty communicating and impaired executive function. Family members reported progressive personality change and unsafe impulsive behaviors with no reports of any seizures.

By early to mid May 2024, rapid neurological deterioration occurred with worsening confusion, impaired language, gait instability, and functional dependence. The patient then became unable to ambulate independently and demonstrated severe behavioral dyscontrol such as a manic outburst and psychosis. This prompted hospitalization for further neurologic evaluation and was put on seizure and fall protocol.

During hospitalization, neurological decline progressed over several weeks. Lumbar puncture was performed, and repeat brain MRI demonstrated cortical abnormalities suspicious for early neurodegenerative disease. Continuous electroencephalographic monitoring revealed diffuse encephalopathic changes. On May 16th, 2024, the patient had rhythmic jerking of the chin and associated rhythmic upward eye movements lasting approximately 1 minute, which was concerning for a seizure.

On May 28, 2024, cerebrospinal fluid testing returned positive for 14-3-3 protein, confirming the diagnosis of sporadic Creutzfeldt-Jakob disease. The patient continued to decline and died on June 2, 2024, approximately 10 weeks after symptom onset and five days after diagnostic confirmation.

Investigations

Initial outpatient brain MRI without contrast was interpreted as unremarkable, demonstrating only subtle asymmetric cortical diffusion hyperintensity without definitive restriction. No abnormal enhancement was identified, providing false reassurance early in the disease course.

Serial electroencephalography (EEG) demonstrated progressive abnormalities. An EEG performed May 4, 2024 showed continuous moderate generalized background slowing with focal right frontotemporal slowing and prominent bihemispheric triphasic discharges. Repeat EEG on May 9 revealed generalized 1-2 Hz triphasic waves with intermittent upper extremity myoclonic jerks without clear electrographic correlation. A subsequent study on May 13 demonstrated persistent moderate generalized slowing with superimposed right frontotemporal focal slowing and triphasic discharges. These findings raised concern for a diffuse encephalopathic process with possible prion disease.

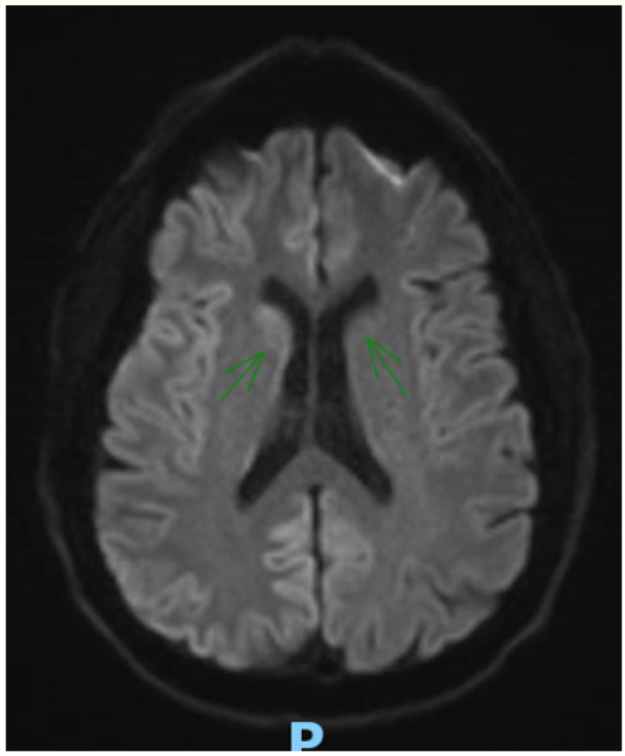

Figure 1: *MR brain without and with IV contrast. Series Desc AX DWI (Resolve SMS TraceW).*

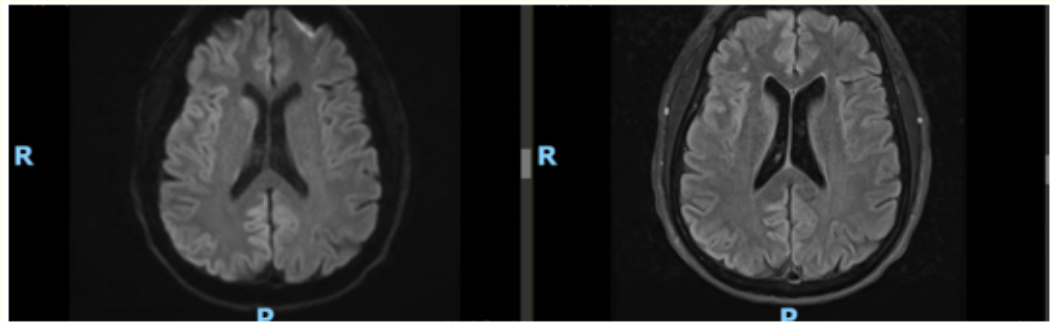

Figure 2: *Left - MR Brain with and without IV contrast. Series Desc: AX T2 FLAIR.*

Repeat neuroimaging demonstrated evolving abnormalities. MRI brain on May 17, 2024 showed abnormal diffusion signal and FLAIR hyperintensity involving the right greater than left cerebral cortex and right caudate without enhancement. These findings were considered indeterminate but concerning for encephalitis, postictal state, metabolic or toxic etiologies, and early neurodegenerative disease. In retrospect, the cortical diffusion abnormalities were consistent with early cortical ribboning seen in Creutzfeldt-Jakob disease.

Extensive laboratory evaluation for infectious, metabolic, inflammatory, and autoimmune etiologies was unrevealing. Testing included HIV, syphilis, Lyme disease, tick-borne panel, fungal studies, hepatitis panel, respiratory viral panel, blood cultures, urinalysis with culture, vitamin B12, folate, homocysteine, methylmalonic acid, ACE level, autoimmune encephalitis panel, MOG antibody, and heavy metal screening, all of which were negative or within normal limits.

Lumbar puncture performed May 4, 2024 demonstrated cerebrospinal fluid with glucose 89 mg/dL, protein 100 mg/dL, 0 nucleated cells, and 2 red blood cells. CSF IgG index and oligoclonal bands were normal. Autoimmune encephalitis panel and infectious PCR testing were negative. Myelin basic protein was mildly elevated. The absence of pleocytosis argued against inflammatory or infectious encephalitis. Subsequent cerebrospinal fluid testing returned positive for 14-3-3 protein, supporting the diagnosis of sporadic Creutzfeldt-Jakob disease. RT-QuIC testing was also sent for confirmatory evaluation.

Additional investigations for paraneoplastic etiologies included MRI cervical spine, CT imaging, thyroid ultrasound, and abdominal imaging, which demonstrated incidental thyroid and hepatic nodules without evidence of malignancy. These findings were not felt to explain the patient's neurological deterioration.

Given rapidly progressive cognitive decline, abnormal EEG findings, cortical diffusion abnormalities on MRI, and unrevealing infectious and autoimmune evaluation, prion disease became the leading diagnostic consideration. The diagnosis of sporadic Creutzfeldt-Jakob disease was confirmed following positive CSF biomarker testing on May 28, 2024.

Discussion

This case highlights an atypical presentation of sporadic Creutzfeldt-Jakob disease characterized by early predominant psychiatric and behavioral symptoms preceding classic neurologic findings. The patient initially presented with anxiety, insomnia, paranoia, and behavioral disinhibition without clear focal neurologic deficits, leading to an initial working diagnosis of a primary psychiatric disorder. This presentation contributed to delayed neurologic evaluation and fragmented care across multiple specialties. Rapid progression of cognitive decline over weeks, however, was inconsistent with a primary psychiatric condition and should raise concern for an underlying neurodegenerative process.

Several diagnostic distractors further complicated recognition. The patient underwent ENT and ophthalmologic evaluations for ear fullness and visual complaints, both unrevealing. Behavioral symptoms including paranoia and agitation led to treatment with anxiolytics and antipsychotics, reinforcing a psychiatric diagnosis. The absence of prior psychiatric history paradoxically contributed to the interpretation of an acute stress-related disorder. These factors, combined with initially normal imaging, delayed consideration of prion disease.

Early MRI findings can be falsely reassuring. Nearly half of initial MRIs may miss sCJD if the DW/FLAIR findings are subtle or overlooked [12]. The diagnosis can also be missed due to the MRI changes not being identified on the initial scan [13].

Common misdiagnoses of CJD include viral encephalitis, paraneoplastic disorder, depression, vertigo, Alzheimer disease, stroke, unspecified dementia, central nervous system vasculitis, peripheral neuropathy, Hashimoto encephalopathy [14]. The symptoms being vague and sporadic cause CJD to not be a top differential for physicians. CJD imaging abnormalities are missed in approximately two-thirds of initial radiology interpretations [14].

Prior reports describe similar presentations of sporadic Creutzfeldt-Jakob disease initially attributed to psychiatric disorders or cerebrovascular events before rapid neurologic decline clarified the diagnosis. Typical cases of CJD consist of a 4 - 6 months survival time from diagnosis to death [2]. A documented case of a 64-year-old female who was misdiagnosed for a stroke [15]. Another documented case of a 58-year-old female who was misdiagnosed for hysteria being in a psychiatric hospital for 32 days [2]. This patient was ill for 2.5 months from onset of symptoms to death. This patient's timeline seemed to be quicker than most. It is common for the cases of CJD to present with progressive dementia, psychiatric symptoms that slowly progress and eventually progress rapidly including neurological symptoms [16]. In this case, the patient started to lose his balance being unable to stand up on his own, talking in word jumble with things that did not make any sense and, neurological decline. Similarly to the case of Samra., *et al*. 2024, they both underwent stressful lives causing the psychiatric diagnosis more relevant at the time. The psychiatric changes in the patients masked the diagnosis of CJD.

Although early diagnosis does not alter the fatal course of sporadic CJD, timely recognition has important clinical implications. Earlier diagnosis may reduce unnecessary invasive testing, limit empiric immunotherapies, and allow for appropriate goals-of-care discussions and hospice planning. In addition, early recognition minimizes exposure risk and allows implementation of appropriate infection control precautions [17].

This case emphasizes that sporadic CJD should be considered in patients presenting with rapidly progressive psychiatric symptoms, particularly when accompanied by subtle neurologic findings, abnormal EEG, or evolving diffusion-weighted MRI abnormalities. Early repeat imaging and CSF biomarker testing are critical to avoiding diagnostic delay.

Conclusion

This case illustrates how sporadic Creutzfeldt-Jakob disease can initially present with prominent psychiatric and behavioral symptoms, leading to misdiagnosis and delayed neurologic evaluation. Early frontal-lobe behavioral changes, absence of prior psychiatric history, and rapid clinical progression over weeks should consider an underlying neurodegenerative process, even when initial MRI findings are unrevealing. Fragmented subspecialty care and false reassurance from early imaging contributed significantly to diagnostic delay in this patient. Earlier neurologic consultation, repeat MRI with diffusion-weighted and FLAIR sequences, EEG, and cerebrospinal fluid biomarker testing may facilitate earlier recognition of CJD. Heightened awareness and clinical vigilance is essential when psychiatric symptoms obscure rapidly progressive cognitive and neurologic decline.

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