

Case Report

Rapidly Progressing Sporadic Creutzfeldt-Jakob Disease Presenting as a Stroke

Maxim Oliver^a Lisa Dyke^a Alex Rico^a Mario Madruga^a
Jorge Parellada^a Steve J. Carlan^b

^aDepartment of Medicine, Orlando Regional Healthcare, Orlando, FL, USA; ^bDivision of Academic Affairs and Research, Orlando Regional Healthcare, Orlando, FL, USA

Keywords

Creutzfeldt-Jakob disease · Neurodegenerative disorder · Central nervous system · Stroke · Prion

Abstract

Sporadic Creutzfeldt-Jakob disease (sCJD) is a rare, fatal human prion disease that is characterized by progressive dementia and neurologic degeneration. It can mimic multiple other neurological disorders, and a high index of clinical suspicion is necessary to make a diagnosis. A 74-year-old woman with a 3-month history of a stroke and progressive neurologic deterioration was found to have sCJD. She expired within a week of her diagnosis. Autopsy revealed spongiform encephalopathy consistent with prion disease, and genetic analysis revealed 129 polymorphism and no pathologic mutation, confirming the diagnosis of nonfamilial human prion disease. No pathologic evidence of a stroke was found. Awareness of the disease by clinicians is important not only at the time of initial presentation but also during the following months. Since there is no treatment, invasive medical procedures should be limited to only those that are required for either diagnosis or hospice care.

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Introduction

Sporadic Creutzfeldt-Jakob disease (sCJD) is an exceedingly rare, fatal, and rapidly progressing neurodegenerative human prion brain disease [1]. It is classically characterized by ataxia, myoclonus, progressive dementia, and periodic sharp wave complexes (PSWCs) on electroencephalogram (EEG) [2]. The severity of symptoms on presentation reflects both background unrelated neurodegenerative disease and the length of the prion insult. Delays in diagnosis and misdiagnosis are not uncommon since sCJD mimics other neurologic disorders, including autoimmune encephalitis, infectious encephalitis, and stroke. There is no proven effective therapy, but an early diagnosis allows patients and their families to prepare for the predictable clinical progression and avoid inappropriate interventions [3]. We present a case of sCJD diagnosed clinically as a stroke months before presenting with end-stage disease.

Case Report

A 74-year-old female presented from a skilled nursing facility for evaluation of worsening mental status over 3 months. The patient's family reported a history of a recent stroke 3 months earlier and residual deficit of ataxia and declining memory with now worsening neurological status. She had incomprehensible speech during interview, only responding to painful stimuli.

On examination, her vital signs were stable, and she was afebrile. Her Glasgow coma scale score was 10. Her gaze was fixed to the right lower quadrant. Cardiopulmonary and abdominal exams were normal. Extremities were hyperspastic with marked paratonic rigidity throughout. She followed no commands and was subsequently admitted to the inpatient ward. Noncontrast computed tomography imaging of the head showed only chronic changes compatible with age. Diffusion-weighted magnetic resonance imaging (MRI) of the brain showed restricted diffusion in the bilateral medial cortex of the frontal and parietal lobes, insula, and basal ganglia (Fig. 1). The continuous EEG was only significant for encephalopathy and was unchanged throughout her hospital stay. Initial cerebrospinal fluid (CSF) labs were negative for infectious, malignant, or autoimmune etiologies. CSF analysis for concern for sCJD done with 14-3-3 protein was negative; however, there was markedly high neuron-specific enolase enzyme and S100B protein.

During inpatient workup, despite negative continuous EEG, oral levetiracetam was added to home valproic acid regimen for concern for nonconvulsive status epilepticus. With the final resulting markers in the CSF noted in cases of sCJD, a presumptive diagnosis of sCJD was made, and the family decided to proceed with hospice. The patient expired the day after admission to hospice and within 1 week of presentation. The diagnosis was confirmed via autopsy, showing positive 3F4 immunostaining with characteristic features of spongiform encephalopathy along with PRNP gene sequence analysis with 129 polymorphism valine homozygosity (VV2) (Fig. 2).

Results

This case is unique for several reasons. First, sCJD is extremely rare with an annual incidence of 1 per million worldwide [4]. It mostly affects those over 50 years of age, and the median survival is 6 months from symptom onset [5]. The second unusual element of this case is

the short time interval from suspecting sCJD to the patient's death. The clinical presentation can be highly variable with sCJD, and significant overlap exists with other neurodegenerative disorders posing a challenge to clinicians [6]. In addition, up to 10% of cases present atypically and may mimic Alzheimer dementia, nonconvulsive status epilepticus, and stroke or other nonlethal or treatable conditions. In fact, our patient was progressively deteriorating for 3 months as a resident in a skilled nursing facility with a stroke diagnosis, which resulted in a significant delay before the sCJD diagnosis was made. Moreover, based on the final autopsy findings, the patient never had pathologic evidence of a stroke. This finding suggests that one of the most important components of diagnosing sCJD is to maintain a high clinical awareness after an initial diagnosis of a central nervous system event in an elderly individual. Indeed, the clinical progress of the patient may be a basic diagnostic element when an elderly patient suffers from a neurological impairment. sCJD is invariably characterized by progression of behavioral change, intellectual impairment, and rapidly progressive dementia, often followed by ataxia, visual disturbance, and myoclonus [1]. If these elements are present, consideration of more targeted sCJD workup may be indicated. The third unusual feature in our case was the laboratory findings. Our patient had both a negative 14-3-3 protein from CSF and no PSWCs on EEG. CSF protein 14-3-3 is a marker of neuronal death [7] and has been reported to have 80–90% sensitivity and 90% specificity for the diagnosis of sCJD [8]. PSWCs on EEG occur in about two-thirds of patients with sCJD, but her only EEG abnormality was a nonspecific encephalopathy. The other diagnostic criteria were, however, consistent with sCJD. Our patient's MRI findings were typical with cortical ribbon hyperintensities, a highly sensitive finding in sCJD [9]. Also, S100B protein is a biomarker that has 65–90% sensitivity and specificity as high as 90% in diagnosing sCJD; however, it has been proposed to have greater diagnostic utility when combined with typical proteins, such as 14-3-3 [3, 4]. S100B is not typically used alone for a diagnosis [10]. The gold standard for definitive diagnosis, however, remains brain biopsy, but oftentimes this invasive technique is avoided given the lack of treatment and risk of further brain injury [11]. Regardless of the discordant lab and EEG values, both autopsy and prion analyses were definitively positive for CJD. Genetic analysis revealed VV2 at the polymorphic codon 129 of PRNP and no pathogenic mutations [12], suggesting her prion disease was not familial and even more unusual. VV2 is the second most frequent genotype accounting for around 16% of cases of sCJD [13]. The central nervous system anatomic findings were positive for cerebral atrophy without Alzheimer disease, Parkinson disease, Pick disease, Lewy body dementia, or dementing neurological disorders other than spongiform encephalopathy, consistent with prion disease.

Conclusion

In conclusion, sCJD is a fatal, progressive, untreatable neurodegenerative disorder that can mimic other serious neurologic conditions at initial presentation. Since it is extremely rare, a very high index of suspicion is necessary, not only at diagnosis, but also in the months that follow. Indeed, as the neurodegeneration progresses beyond the expected trajectory of a stroke, it is imperative that attention is directed toward possible fatal neuropathology. Our patient was in constant contact with providers trained in caring for stroke victims, but her rapidly declining neurologic function was reported by her family rather than the trained staff. Compassionate hospice care, family education, and restriction of invasive medical procedures are recommended.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

There are no potential conflicts of interest for any of the authors with products or techniques discussed in the paper.

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Author Contributions

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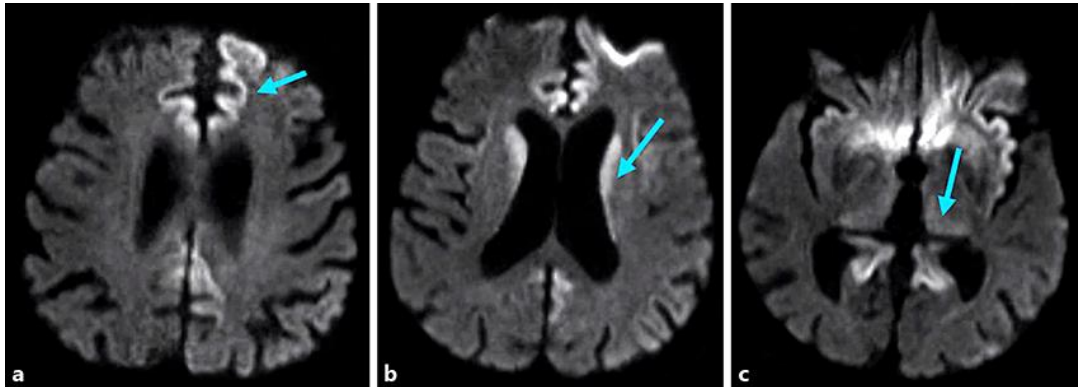


Fig. 1. **a** Restricted diffusion in bilateral frontoparietal cortex also called “cortical ribbon” sign (arrow). **b** Bodies of both caudate nuclei showing restricted diffusion (arrow). **c** Involvement of the posteromedial thalami giving the classic “hockey stick” sign (arrow).

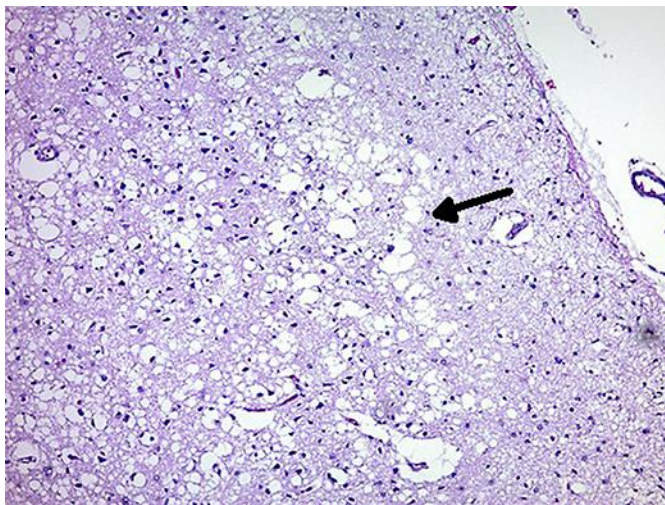


Fig. 2. Cortical spongiosis (arrow) with sparing of the molecular layer (HE; original magnification $\times 10$).