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Sporadic Creutzfeldt-Jakob Disease Mimicking a Stroke

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Abstract

Creutzfeldt-Jakob disease (CJD) is a rare neurodegenerative disorder (1-1.5 cases per million populations annually) that causes a rapidly progressive dementia, often with accompanying symptoms of ataxia, myoclonus, mutism, visual changes, and cognitive decline. Given these non-specific findings, the diagnosis of CJD is often delayed or missed, particularly in patients with a history of prior central nervous system insults. We report a case of a 70-year old male who initially presented with left arm weakness and was found with bi-occipital infarcts on MRI and was discharged with diagnosis of stroke. He subsequently developed seizures with acute delirium, repeat MRI found further findings of increased intensity in the right frontal cortex. After extensive electroencephalographic, radiologic, and laboratory workup, the patient was ultimately diagnosed with sporadic CJD, by the presence of 14- 3-3 protein in the CSF.

Keywords: Creutzfeldt-Jakob Disease, Prion Disease, Case Report

Introduction

Creutzfeldt-Jakob disease (CJD) is a prion disease, occurring in approximately one in every million people. Prion diseases are characterized by the abnormal folding of proteinaceous particles (prions). Normal prion proteins (PrPC) are primarily alpha-helical, water soluble, and resistant to proteases.

Abnormal prion proteins (PrPSc) result when the alpha-helical structure of the protein is replaced by beta-pleated sheets. These PrPSc then function to self-propagate, converting normal prions (PrPC) to abnormal PrPSc forms. Overtime, these abnormal proteins accumulate in tissues such as the brain, nerves, and skeletal muscle causing neuronal damage, rapidly progressive spongiform encephalopathy and ultimately death [1].

Etiologically, 85% of CJD are termed sporadic as there is no identifiable source. 10-15% of cases are familial and attributed to various mutations affecting the PRNP gene. Very few (<1%) of cases are acquired via iatrogenic causes such as neurosurgery, organ transplantation, or blood transfusions [2]. The age of onset is in the age range of 60-80 years old, with men and women being affected equally.

The clinical manifestations of CJD include prodromal symptoms such as sleep impairment, headaches, and generalized weakness followed by the rapid progression of neurological and neuropsychological symptoms such as dementia, mutism, cerebellar dysfunction, myoclonus, ataxia, and seizures. Most cases lead to death within 12 months of disease onset. Given the rarity of this clinical entity and cross-over of symptoms with more common medical diagnoses, there is often a delay in diagnosis or attribution of the disease symptoms to an alternative cause.

Case Report

Here, we present the case of a 70-year-old male with past medical history of transient atrial fibrillation only seen 7 years ago associated with sepsis and diverticulitis infection, bladder and prostate cancer with spinal metastasis with recent chemotherapy, hypertension, hyperlipidemia, and recent history of COVID-19 respiratory infection 6 months ago. He presented to our emergency department with symptoms of acute left upper extremity weakness described as left arm clumsiness, bilateral tremors, and headache. Family added he was complaining of visual "flashes", "floaters", progressive weakness, and difficulty walking for one month. CT of the brain was unremarkable. MRI images with diffuse- weighted imaging where interpreted as acute cortical infarcts involving the right occipital lobe with right posterior parietal involvement, and to a lesser degree the left occipital lobe. The patient was discharged with the diagnosis of bilateral occipital infarcts which likely secondary to cardioembolic infarcts from atrial fibrillation, despite no capture of atrial fibrillation on monitor or EKG. He began anticoagulation with apixaban.

Eighteen days later he returned to our hospital with intermittent confusion, myoclonus, and progressive weakness in all extremities. Initially attributed to stroke related epilepsy, he was admitted and had an extensive workup. He had witnessed right arm convulsions while inpatient. EEG found periodic sharp waves noted in the right temporal region consistent with epileptiform activity. He was placed on anticonvulsant therapy with levetiracetam 500 mg intravenously twice a day. He developed mental status changes including hallucinations, lethargy, combativeness requiring restraints. Initially he required assistance eating, but later refused diet. He also developed signs of pseudobulbar affect including long periods of crying and intermittent laughter. Due to development of protracted delirium, lumbar puncture was obtained and an encephalitis panel was ordered. CSF was acellular, with mildly elevated protein. Subsequent analysis of CSF 14-3-3 protein level was elevated to 19,131 resulting in the diagnosis of sporadic Creutzfeldt-Jakob disease. His clinical course continued to worsen as he ultimately developed mutism and lost his ability to eat. Subsequent family discussions were held, and family elected hospice and the patient expired in several weeks on comfort care.

Discussion

In summary, this case report outlines a patient who presented with a one-month history of visual abnormalities, cerebellar ataxia, and progressive weakness originally diagnosed with was thought to be subacute cortical infarctions based on radiographic imaging and a medical history of atrial fibrillation. Upon his re-presentation, the patient developed worsening confusion, tremors, and myoclonus. At this time with his atypical clinical progression, special consideration was given to expand the differential diagnosis to include epilepsy, herpes simplex temporal lobe encephalitis, autoimmune encephalitis, paraneoplastic encephalitis and prion disease [3].

Extensive workup was performed including repeat neuroimaging, EEG monitoring, laboratory evaluation of metabolic abnormalities, lumbar puncture with CSF analysis for infectious etiologies and CSF sample send-outs for a paraneoplastic panel and 14-3-3 protein. Early results were non-revealing, with the exception of continuous EEG monitoring revealing periodic sharp wave activity and repeat MRI-results showing progression of diffusion weighted imaging (DWI) of the caudate nucleus and frontal cortex, sparing white matter. The initial MRI showed right parietal involvement and the subsequent MRI showed right frontal involvement demonstrating a progressive restricted diffusion on the MRI correlating to his worsening clinical findings. Although no post-mortem examination was performed, levels of 14-3-3 protein were elevated at 19,131, strongly supporting the diagnosis [4].

Our case aims to outline the importance of considering CJD given the proper clinical scenario due to the overlap of symptoms seen in the condition with other conditions causing rapidly progressive dementia. The question becomes that once CJD is on the differential, how can we confirm our suspicion of this clinical entity. According to the CDC, definitive diagnosis of CJD can be made only by neuropathological study done at autopsy. However, a probable diagnosis can be made in patients who present with a rapidly-progressive dementia who present with 2/4 of: myoclonus, visual or cerebellar signs, pyramidal/extrapyramidal symptoms, or akinetic mutism in addition to a positive EEG result, 14-3-3 CSF analysis, or typical MRI findings in the absence of findings consistent with an alternative diagnosis (table 1).

In the case of our patient, we identified the symptoms of rapidly progressive dementia, myoclonus, visual abnormalities, cerebellar ataxia, and akinetic mutism, demonstrated periodic sharp waves on EEG, and obtained a positive 14-3-3 CSF analysis. Additionally, we ruled out potential alternative diagnosis, making the diagnosis of CJD highly likely

MRI of the brain with DWI sequence upon presentation (left image) show some changes which were suspected to be bioccipital infarcts with cortical involvement. Upon progression 33 days later (right image) there was noted increased hyper intensity of the right frontal cortex and progressive restricted diffusion on

Table: Diagnostic Criteria for CJD[4]

Sporadic CJD

Definite:

- Diagnosed by standard neuropathological techniques; and/or immunocytochemically; and/or Western blot confirmed protease-resistant PrP; and /or presence of scrapie-associated fibrils.

Probable:

- Neuropsychiatric disorder plus positive RT-QuIC in cerebrospinal fluid (CSF) or other tissues

OR

- Rapidly progressive dementia; **and** at least two out of the following four clinical features:
  1. Myoclonus
  2. Visual or cerebellar signs
  3. Pyramidal/extrapyramidal signs
  4. Akinetic mutism

AND a positive result on at least one of the following laboratory tests

- a typical EEG (periodic sharp wave complexes) during an illness of any duration
- a positive 14-3-3 CSF assay in patients with a disease duration of less than 2 years
- High signal in caudate/putamen on magnetic resonance imaging (MRI) brain scan or at least two cortical regions (temporal, parietal, occipital) either on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR)

AND without routine investigations indicating an alternative diagnosis.

Possible:

- Progressive dementia; **and** at least two out of the following four clinical features:
  1. Myoclonus
  2. Visual or cerebellar signs
  3. Pyramidal/extrapyramidal signs
  4. Akinetic mutism

AND the absence of a positive result for any of the four tests above that would classify a case as "probable"
AND duration of illness less than two years
AND without routine investigations indicating an alternative diagnosis.

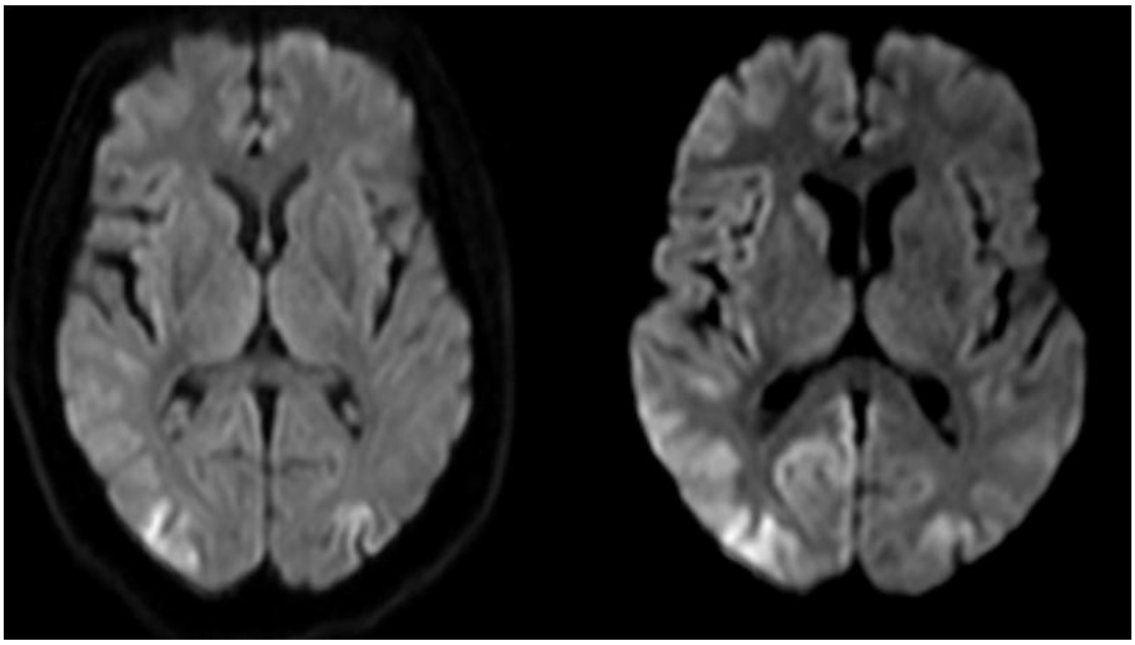

Figure 1: MRI (left image) show bioccipital infarcts with cortical involvement and 33 days later (right image)there was noted increased hyper intensity of the right frontal cortex and progressive restricted diffusion on DWI of the right caudate which was highly suggestive of CJD.

DWI of the right caudate which was highly suggestive of CJD.

In summary, this case presented with a clinical scenario suggestive of a cardioembolic stroke with unilateral weakness and visual changes. The clinical progression was atypical and with the added symptoms of seizures and encephalopathy. Thes features made it necessary to entertain a broader differential diagnosis. Our case identifies a rare presentation of CJD and highlights the opportunity for medical community to continue to work to increase clinical awareness, improve the accuracy of diagnostic options, and develop potential goals of care guidelines

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