Non-convulsive Seizures Mimicking Creutzfeldt-Jakob Disease with Rapid Resolution and Recurrence of MRI Abnormalities

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Abstract

An 88-year-old man presented with acute altered mental status. Brain magnetic resonance imaging (MRI) demonstrated "cortical ribboning," which is classically associated with Creutzfeldt-Jakob disease. His rapid clinical improvement prompted a follow-up MRI three days after presentation, which showed resolution of the acute abnormal signals. The patient was eventually diagnosed with non-convulsive seizure. Five months later, he returned with a similar clinical presentation and MRI findings after self-discontinuation of anticonvulsant. It is important for clinicians to be aware that neurological changes associated with non-convulsive seizures can acutely mimic Creutzfeldt-Jakob disease, and to consider a short interval follow-up MRI for diagnostic challenges in acute settings.

Keywords

Non-convulsive seizure, Creutzfeldt-Jakob disease, mimic, MRI, transient

Abbreviations and Acronyms

CJD = Creutzfeldt-Jakob disease
CSF = cerebrospinal fluid
DWI = diffusion-weighted imaging
EEG = electroencephalogram
FLAIR = fluid-attenuated inversion recovery
MRI = magnetic resonance imaging
RT-QuIC = real-time quaking-induced conversion assay
sCJD = sporadic Creutzfeldt-Jakob disease
SITMA = seizure-induced transient MRI abnormalities

Introduction

Creutzfeldt-Jakob disease (CJD) is a non-curable, rapidly progressive neurodegenerative disease for which MRI may assist in the diagnosis. Non-convulsive seizure epilepticus refers to prolonged seizures that may manifest primarily as an impaired level of consciousness or behavioral changes rather than movements of extremities. A variety of conditions are reported as CJD mimics, including seizure-induced transient MRI abnormalities (SITMA). SITMA may pose particular clinical challenges in cases where the clinical history is unhelpful or unavailable. This paper discusses a patient who presented with convincing CJD-like symptoms, who clinically and radiographically improved over 3 days, and experienced a recurrent episode with clinical symptoms and MRI abnormalities 5 months later.

Case Report

An 88-year-old man presented to the emergency department with acute confusion, altered vision, and gait instability. He had a past medical history of non-Hodgkin's lymphoma in remission, right posterior parietal meningioma, and progressive memory loss over a few years with rapid deterioration over a few months. The patient's proxy reported that he woke up at 3 am on the day of admission complaining of lightheadedness. He woke up again at 5 am exhibiting confusion, repeatedly dropping and picking up an object on the floor, and inability to leave his bathroom. Additionally, he complained that his vision was altered.

In the emergency department, he was not in acute distress, with a body temperature of 36.6 °C, heart rate 59 beats/min, blood pressure 146/72 mmHg, respiratory rate 13/min, and oxygen saturation 99% on room air. He was alert and oriented to person and place, but not to time. Neurological exam revealed impaired attention span and concentration, left visuospatial neglect, and mildly increased muscle tone throughout. There was no obvious myoclonus. The remainder of the neurological exam was unremarkable.

Laboratory studies revealed a white blood cell count of 7,600 /μL with 76% neutrophils. His hemoglobin was 10.7 g/dL and platelets were 242,000 /μL. Electrolyte, liver, and renal panels were unremarkable. Urinalysis had no major findings. MRI of the brain without contrast demonstrated diffusion-weighted imaging (DWI) lesions in the posterior right thalamus extending in the right hypothalamic region and right parietal-occipital-temporal and occipital lobes with cortical ribboning, in addition to an unchanged 3.2 cm right posterior parietal extra-axial mass, consistent with meningioma (Figure 1). Meanwhile, T2 fluid-attenuated inversion recovery (FLAIR) remained without acute changes as seen on DWI (Figure 2).

Given the scant history and characteristic findings on MRI, CJD and encephalitis were considered in the differential diagnosis. The patient was admitted for further investigation including: extensive laboratory testing (Vitamin B12, methylmalonic acid, folate, thyroid stimulating hormone, ammonia, erythrocyte sedimentation rate, C-reactive protein, lactic dehydrogenase, HIV antibody/antigen, rapid plasma reagin (RPR), paraneoplastic autoantibody panel, cerebrospinal fluid (CSF) analysis (cell count, protein, glucose, bacterial culture and gram stain, herpes simplex virus 1 and 2 PCR, venereal disease research laboratory test (VDRL), 14-3-3 protein, real-time quaking-induced conversion (RT-QuIC) assay), electroencephalogram (EEG), and repeat brain MRI.

On the second day of admission, the patient began to clinically improve. Upon neurological exam, he was alert and oriented to person, place, and time. He still exhibited mild visuospatial neglect on the left, as well as ideomotor apraxia, which was not evaluated on admission. Additional work up was unremarkable, except for CSF total protein 91 mg/dL, ESR 75 mm/hr, and ammonia 88 μmol/L. EEG revealed diffuse slowing, with focal slowing over the right parietal area. CJD, autoimmune encephalitis, and non-convulsive seizures with prolonged postictal state remained as differential diagnoses.

On the third day, the patient reported improvements of his subjective symptoms. He remained alert and fully oriented. His ideomotor apraxia and left-sided visuospatial neglect had completely resolved. Ammonia level was normalized to 29 μmol/L. This clinical improvement argued against a diagnosis of CJD. On the fourth day, repeat brain MRI with and without contrast demonstrated near-complete resolution of the right thalamic and right parietal-occipital-temporal cortical lesions, suggesting SITMA (Figure 3). All of the other tests returned normal, including the RT-QuIC. Based on the resolution of the MRI abnormalities, the diagnosis of SITMA was established. The patient was discharged with newly started lacosamide, an anti-epileptic medication, to prevent subclinical seizures thought to be provoked by his meningioma, which he subsequently self-discontinued due to insomnia.

Five months later, the patient returned with left-sided neglect, left-sided weakness, and acute confusion. MRI (Figure 4) and EEG were similar to the previous findings. The patient was discharged home on second day of admission with levetiracetam, a different anti-epileptic medication. Since the discharge, the patient has not had any recurrence of seizures.

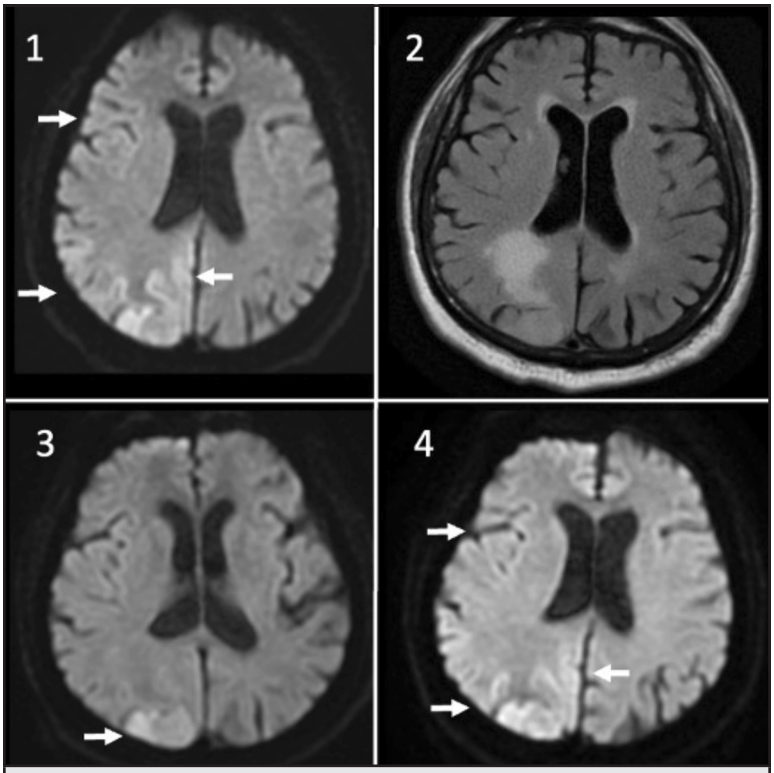

Figure 1. MRI DWI at presentation with altered mental status, showing cortical restricted diffusion in the right parietal-temporal-occipital lobes (arrows).
Figure 2. T2 FLAIR at presentation, showing unremarkable changes in the right parietal-temporal-occipital lobes.
Figure 3. MRI DWI on day 3 of admission, showing near-complete resolution of right cortical restricted diffusion. Please note the unchanged 3.2 cm right posterior parietal extra-axial meningioma (arrow).
Figure 4. MRI DWI after 5 months during another episode of altered mental status, showing recurrent restricted diffusion in the right parietal-temporal-occipital lobes (arrows).

Discussion

CJD most commonly presents as a rapidly progressive dementia. Sporadic CJD (sCJD) accounts for 90% of human Prion diseases. Diagnostic criteria for probable sCJD proposed by the US Centers for Disease Control and Prevention (CDC) includes the following:[1]

(A) neuropsychiatric disorder plus positive RT-QuIC in CSF or other tissues, or (B) rapidly progressive dementia and at least 2 of the following 4 clinical features: myoclonus, visual or cerebellar signs, pyramidal/extrapyramidal signs, or akinetic mutism, with supportive findings on at least one of the following tests: typical EEG finding (eg, periodic sharp wave complexes), positive 14-3-3 CSF assay with a disease duration of less than two years, or an MRI showing hyperintensity in caudate/putamen or at least two cortical regions (temporal, parietal, and occipital) on DWI or FLAIR. There are reports of many conditions that can mimic CJD, such as encephalitis, hepatic failure, thyroid dysfunction, and the CNS manifestation of autoimmune disorders (eg, lupus, Sjögren syndrome, Hashimoto encephalitis).[2-4]

In the present case, declining memory with rapid deterioration, visual disturbance, increased muscle tone, and MRI abnormalities with ribboning on DWI were consistent with the diagnostic criteria of probable sCJD. Although seizure is rare in CJD, prior case studies have reported seizures and several cases of non-convulsive status epilepticus, as an initial manifestation.[5] Abnormal labs were retrospectively thought to be non-specific seizure-related changes, as elevated CSF protein, ammonia, and inflammatory changes have been reported with seizure activity.[6-8] Ammonia level improved to 29 μmol/L in two days spontaneously, while other liver function tests remained normal. CJD was ruled out by hospital day 4 given clinical improvement without treatment, unremarkable labs, non-specific EEG, and resolution of MRI findings.

Seizure-induced transient MRI abnormality (SITMA) of the brain was first reported in 1987 by Kramer et al,[9] though the specific pathophysiology has remained elusive. Incidence of seizure-induced MRI abnormalities provoked by status epilepticus, a severe form of seizure, widely varies from 11.6% to 100% in the literature.[10-11] The recovery from SITMA also ranges from complete recovery, partial recovery, to persistent changes.[12] It is important to be aware that seizures can cause acute MRI changes, which often complicate clinical decision making.

In the present case, the SITMA closely approximated the typical MRI findings seen in CJD. However, the recovery in 3 days is more rapid than previously reported in the literature. Cianfoni et al reported reversibility of seizure-induced brain-MRI abnormalities between 15 and 150 days (average, 62 days) in an observation of 26 patients.[13] Yaffe et al reported a case of normalized MRI in 5 days.[14] In addition, the SITMA mimicking CJD reappeared in 5 months, when the patient developed another episode of altered mental status. Although there are some reports of recurrence of seizure-induced MRI abnormilities,[14-15] it is not commonly documented in the literature. The patient's condition was thought to be postictal confusion after an unwitnessed non-convulsive seizure, given the focal slowing noted without epileptiform activity on EEG. Thus, it is important to consider a short interval follow-up MRI to avoid diagnostic ambiguity.

In conclusion, we report a case of a non-convulsive seizure mimicking CJD with a rapid SITMA recovery in 3 days and recurrence in 5 months. It is important for clinicians to be aware that confusion associated with non-convulsive seizures can acutely mimic CJD, and to consider a short interval follow-up MRI for diagnostic challenges in acute settings.

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References

1. Centers for Disease Control and Prevention. Diagnostic Criteria | Creutzfeldt-Jakob Disease, Classic (CJD) | Prion Disease | CDC. Published January 25, 2019. Accessed December 24, 2020. https://www.cdc.gov/prions/cjd/diagnostic-criteria.html
2. Mead S, Rudge P. CJD mimics and chameleons. *Pract Neurol*. 2017;17(2):113-121.
3. Rudge P, Hyare H, Green A, Collinge J, Mead S. Imaging and CSF analyses effectively distinguish CJD from its mimics. *J Neurol Neurosurg Psychiatry*. 2018;89(5):461-466.
4. Matsuo K, Saburi M, Ishikawa H, et al. Sjögren syndrome presenting with encephalopathy mimicking Creutzfeldt–Jakob disease. *J Neurol Sci*. 2013;326(1-2):100-103.
5. Espinosa PS, Bensalem-Owen MK, Fee DB. Sporadic Creutzfeldt–Jakob disease presenting as nonconvulsive status epilepticus case report and review of the literature. *Clin Neurol Neurosurg*. 2010;112(6):537-540.
6. Süße M, Saathoff N, Hannich M, von Podewils F. Cerebrospinal fluid changes following epileptic seizures unrelated to inflammation. *Eur J Neurol*. Published online February 5, 2019:ene.13924.
7. Hung T-Y, Chen C-C, Wang T-L, Su C-F, Wang R-F. Transient hyperammonemia in seizures: A prospective study: Confounders, Duration, and Outcome. *Epilepsia*. 2011;52(11):2043-2049.
8. Sohn HS, Kim SK, Lee S-Y. Inflammatory markers associated with seizures. *Epileptic Disorders*. 2016;18(1):51-57.
9. Kramer RE, Lüders H, Lesser RP, et al. Transient focal abnormalities of neuroimaging studies during focal status epilepticus. *Epilepsia*. 1987;28(5):528-532.
10. Milligan TA, Zamani A, Bromfield E. Frequency and patterns of MRI abnormalities due to status epilepticus. *Seizure*. 2009;18(2):104-108.
11. Szabo K, Poepel A, Pohlmann-Eden B, et al. Diffusion-weighted and perfusion MRI demonstrates parenchymal changes in complex partial status epilepticus. *Brain*. 2005;128(Pt 6):1369-1376.
12. Xiang T, Li G, Liang Y, Zhou J. A wide spectrum of variably periictal MRI abnormalities induced by a single or a cluster of seizures. *J Neurol Sci*.. 2014;343(1-2):167-172.
13. Cianfoni A, Caulo M, Cerase A, et al. Seizure-induced brain lesions: A wide spectrum of variably reversible MRI abnormalities. *Eur J Radiol*. 2013;82(11):1964-1972.
14. Yaffe K, Ferriero D, Barkovich AJ, Rowley H. Reversible MRI abnormalities following seizures. *Neurology*. 1995;45(1):104-108.
15. Doherty CP, Cole AJ, Grant PE, et al. Multimodal Longitudinal Imaging of Focal Status Epilepticus. *CanJ Neurol Sci*. 2004;31(2):276-281.