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# CREUTZFELDT-JAKOB DISEASE: A CASE REPORT PRESENTING TO THE EMERGENCY DEPARTMENT

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## ABSTRACT

Creutzfeldt-Jakob disease is lethal and most common spongiform encephalopathy worldwide and is rarely encountered in the Emergency department. For the benefit of patients and healthcare workers, rapid consideration of this condition needs to be sought in the setting of rapid neurological decline and myoclonic jerky movements. We present a case of a 54-year old male with behavioral changes, jerky body movements, cognitive dysfunction and left sided weakness developing over the course of few months and presented to our Emergency Department for the evaluation for stroke. Due to the non-specific nature of psychiatric and neurologic complaints, the initial diagnosis remained unclear. Magnetic Resonance Imaging of Brain demonstrated global atrophy with periventricular and subcortical T2 hyperintensities. Electroencephalogram showed continuous generalized periodic sharp wave activity with triphasic configuration. Investigations were highly supportive of probable Creutzfeldt-Jakob disease. Brain biopsy was planned but was not an acceptable option for suffering family. Our report showcased the symptoms, investigations, diagnostic challenges and raising concerns regarding this condition. It is advantageous for the emergency physician to be aware of clinical presentation of this rare condition. The prognosis for this disease is very poor and there is currently no cure.

## INTRODUCTION

Creutzfeldt-Jakob Disease (CJD) is the rapidly progressive transmissible spongiform encephalopathy, but with the incidence of 0.4-1.8 cases per million, it is the rare presentation in the emergency room. <sup>1</sup> Diagnosis of CJD is based on the triad of rapidly progressive dementia, myoclonus and periodic sharp wave electroencephalography (EEG). Definitive diagnosis is made through histological examination of brain on autopsy. With increasing concerns about prion diseases, awareness of behavioral symptoms and investigations associated with CJD will be helpful in management of these cases by the emergency physicians.

## Case report

A 54-year-old retired army engineer was brought in by his family as a neurological emergency in the ED with progressive decline in cognition including memory impairment for the past 2 months. He had clumsiness of upper limbs. Family denies the history of illicit drug use, headaches, seizures, any loss of consciousness, trauma or gait or visual abnormalities. Family did

consult general physician once before the ER presentation without any resolution of symptoms. He was admitted in a local hospital before coming to our hospital for 6 days where his clinical deficits remained unchanged and referred to our facility to investigate unexplained clinical worsening.

He also had mild left sensory-motor hemiparesis that had progressively worsened. Symptoms worsened in the form of myoclonic jerks and progressive confusion. In retrospect, the family had noted behavioral and neuropsychiatric symptoms such as fear from loud noise, forgetfulness of routine activities such as offering prayers or changing clothes, irritability, anxiety, anger followed by decreased responsiveness, unfocused gaze, difficulty in numerical calculation and coordination and a decline in the daily living activities. Remote memory was intact. Previous medical history revealed longstanding hypertension and diabetes. Family history was unremarkable for neuropsychiatric disorders. On examination, he appeared disoriented with limited response to verbal or non-verbal cues. He had a flattened affect. His heart rate, blood pressure and oxygen saturations were under normal limits. Complex hyperkinetic-dystonic movement disorder with rigidity and myoclonic jerks, mainly involving the

extremities were noted. There were no signs of meningeal irritation. CJD was included in the differential diagnosis. Due to altered mental status and declining health, limited physical exam was performed. Mini-mental status was not recorded. Detailed lab work up was performed including tests for B12, folate, thyroid profile and ammonia were ordered which was unremarkable and probable diagnosis of CJD was made during his hospital stay.

Magnetic Resonance Imaging (MRI) of brain showed global involucional changes in brain as suggested by dilated ventricular system and prominent cortical sulci with micro-ischemic changes involving the midbrain and basal ganglia territory. Cerebrospinal fluid (CSF) studies showed glucose of 169 mg/dl, protein of 39 mg/dl and TLC 02/cu mm. EEG was concerning as it showed continuous generalized periodic sharp waves with a triphasic configuration at 0.5-1 second interval, sometimes time-locked with visible clinical jerks (Figure 1). We were unable to grasp the detailed EEG reports to comment on epoch. Subsequent EEGs were consistent with these findings and antiepileptics with single antiplatelet agent, statin and antibiotics were administered. Nutritional support and intravenous hydration were started. At this point, the differential diagnosis was almost completely narrowed down to CJD. Other causes such as autoimmune encephalitis, thiamine deficiency, heavy metal toxicity, aminoacid, organic acid or carnitine deficiencies were all ruled out. Family was counselled regarding grim prognosis and definitive method for diagnosis as brain biopsy which was refused due to poor disease outcome. He was discharged from the hospital on oral anti-epileptics and regular neurology clinic follow up. To this date, there has been no correspondence with patient or his family.

#### Discussion

Disorientation, jerky limb movements and decreased responsiveness had been present for few months when patient's history was tracked back. This length of time is also significant in this case. We thought about sporadic CJD due to subtle early symptoms, myoclonic jerks were seen later in the course.

CJD is an iconic prion disease where proteolysis of cell membrane and misfolding of protein further led to neuro-degeneration and inevitable death. 1 Diagnosis of CJD is mainly clinical including myoclonus, cerebellar, pyramidal, extra-pyramidal or visual signs on physical examination however MRI, EEG and CSF studies may aid in the diagnosis. Brain biopsy is the definitive test for diagnosis. The differential diagnosis would be CNS infections, seizure disorder, toxins, delirium, electrolyte abnormalities and psychiatric illnesses. Emergency physicians can initiate their

investigations by ruling out the common causes of altered sensorium. CJD may initially manifest as psychiatric symptoms. Our patient developed neurological symptoms later and a probable diagnosis of CJD was made. MRI demonstrates T2 hyper-intensities in basal ganglia 1 as it did in our case however; these findings are evident later in the disease course. Repeated EEG played a pivotal role in the evaluation of our patient. The presence of periodic sharp wave complexes on the EEG is characteristic of CJD and is observed in two-thirds of patients 2, 3.

The diagnostic criteria for CJD outlined by the World Health Organization and Centers for Disease Control and Prevention (CDC) classify CJD into definite, probable, or possible based on symptomatology, EEG findings, CSF analysis, and MRI (Table 1). 4

There are 4 subtypes of CJD which are sporadic, familial, iatrogenic and variant forms thought to be acquired from infected meat ingestions however can be transmitted from medical procedures or blood transfusions. All humans have prion proteins in brain. As a result of CJD, damaged prion proteins accumulation caused neurodegeneration. Sporadic CJD is the most common type and diagnostic evaluation of patients with suspected sCJD involves assessment of the 14-3-3 protein assay, MRI, and EEG. Elevated tau and/or 14-3-3 protein is seen on CSF analysis which was unavailable in our case. Studies have demonstrated that CSF 14-3-3 may be the most accurate test, with a sensitivity of 92% and a specificity of 80%. 5 Typical EEG findings of sCJD show periodic sharp and slow wave complexes (PSWC) with a reported sensitivity and specificity of 66% and 74%, respectively. 6

MRI is the most suitable neuroimaging technique in the diagnosis of CJD, with T2W, FLAIR and DWI sequences being the most essential sequences of the MRI protocol. 6 MRI has shown to be the superior test by demonstrating areas of hyperintensity in the cortical and/or subcortical areas with sensitivity and specificity of 92.3% and 95%, respectively. 7 The key MRI features in CJD are T2W/FLAIR hyperintensity in the caudate, putamen, anterior cingulate gyrus and thalamus. Widespread involvement of the cerebral cortex is also a characteristic feature. 7 DWI is very sensitive and shows diffusion restriction, especially in early stage of the disease, with no visible changes on T2W/FLAIR sequences. 7 Generalized atrophy is usually noted in late or terminal CJD. Variant CJD (vCJD) commonly presents with psychiatric symptoms and selective T2W/FLAIR hyperintensity with diffusion restriction in the medial and dorsal thalami (pulvinar), giving the appearance of "hockey-stick" or "pulvinar sign". 8 A combination of clinical, neuroimaging and

neuropathological findings frequently leads to the definitive diagnosis of CJD.

Due to the low incidence and varying clinical presentations, CJD remained a devastating condition and needs to be quickly considered based on clinical features and exclusion of other causes of rapidly progressive dementia. Myoclonus with rapid dementia should raise the suspicion for CJD. Early neurological and palliative teams involvement would help navigating the course of the disease, decreased number of ER visits and medical cost for families.

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**Figure 1**



**Figure 1: EEG showing continuous generalized periodic sharp waves with a tri phasic configuration at 0.5-1 second interval.**

**Table 1. Diagnostic Criteria for Sporadic Creutzfeldt-Jakob Disease (sCJD)**

Possible Case	<p>Progressive dementia; and</p> <ul style="list-style-type: none"> <li>• Atypical EEG; and</li> <li>• &lt;2 year duration; and</li> <li>• At least two of the following: <ul style="list-style-type: none"> <li>o Myoclonus</li> <li>o Visual or cerebellar disturbance</li> <li>o Pyramidal or extra pyramidal dysfunction</li> <li>o Akinetic mutism</li> </ul> </li> </ul>
Probable Case (in the absence of alternative diagnosis)	<p>Progressive dementia;</p> <ul style="list-style-type: none"> <li>• Two of the four clinical features mentioned above for possible case, with <ul style="list-style-type: none"> <li>o A typical EEG of generalized triphasic periodic complexes at the rate of one per second; and/or</li> <li>o Positive 14-3-3 assay in CSF; and</li> <li>o MRI showing high signal abnormalities in the caudate nucleus and/or putamen on diffusion-weighted imaging (DWI) or fluid-attenuated inversion recovery (FLAIR).</li> <li>o Akinetic mutism</li> </ul> </li> </ul>
Definite Case	<p>Neuropathological confirmation post-mortem; and/or</p> <ul style="list-style-type: none"> <li>• Presence of protease-resistant prion protein by either Western Blot or immunochemistry; and/or</li> <li>• Presence of scrapie associated fibrils</li> </ul>

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Muhammad Akbar Baig; concept, data collection, data analysis, manuscript writing, manuscript review

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