

Case Report

A rare case of sporadic Creutzfeldt-Jakob disease in an 83 years old female

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ABSTRACT

Sporadic Creutzfeldt-Jakob disease is a rare invariably fatal neurodegenerative prion disease. Prion disease are associated with the conversion of alpha-helix rich cellular prion protein (PrP^C) into a beta-structure rich insoluble conformer scrapie isoform (PrP^{Sc}) thought to be infectious isoform. Here we present a case of an 83 years old woman with findings of rapidly progressive dementia, cognitive disturbance, myoclonic jerks and extrapyramidal signs (cogwheel rigidity). Following a series of clinical and diagnostic (diffusion-weighted magnetic resonance imaging (MRI) brain, electroencephalogram (EEG)) examination she was diagnosed with sporadic Creutzfeldt-Jakob disease based on Centers for disease control and prevention (CDC) criteria.

Keywords: Creutzfeldt-Jakob Disease, Prions, Dementia, Myoclonus, Prognosis

INTRODUCTION

Prions are unparalleled proteinaceous infectious particles that causes invariably fatal neurodegenerative diseases. Prion diseases presents as genetic, infectious or sporadic disorders. Prions are devoid of nucleic acid.¹

Prion diseases are caused by accumulation of scrapie isoform (PrP^{Sc}) which is beta helix predominant instead of the normal alpha helix predominant cellular prion protein (PrP^C). Prion proteins despite their same primary structures can possess a variety of conformations which can be inherited epigenetically.²

Each conformation has specific phenotypic properties leading to a variety of human and animal prion diseases. A rapidly progressing dementia syndrome associated with rigidity and myoclonus should evoke suspicion of prion disease as underlying etiology.²

CASE REPORT

A 83 years old female presented with complaints of involuntary jerky movements of hands, increased forgetfulness and decreased oral intake since 2 weeks. The family members gave a history of the patient's inability in remembering names, performing daily task and also involuntary bowel and bladder habits. Her symptoms progressed to such an extent that she stopped responding to verbal conversations, avoided food intake and remained confined to her bed. However, there was no history of infectious contacts, head injury, seizures or intake of raw livestock or brain matter. Hallucinations, illusion, delusions and weakness in any part of the body or difficulty in swallowing was not found. Family members denied any history of alcohol or illicit substance use but reported that she was a chain smoker for 40 years. Patient was also a known hypertensive individual for the last 5 years and was on oral Ramipril.

On examination the patient recorded blood pressure of 110/78 mmHg, oxygen saturation 96% at room air, pulse rate of 96/minute, respiratory rate 22 per minute and axillary temperature was 96.7° F. On systemic examination patient was conscious, uncooperative and disoriented to time, place and person. The Glasgow Coma Scale was E3V4M5 and her pupils were normal in size, bilaterally reacting to light and fundus examination was normal. Cranial nerve examination was normal, motor system examination showed lead pipe rigidity of bilateral upper limbs with myoclonic movements more in the right upper limb. Muscle stretch reflexes were normal with flexor plantar responses bilaterally. Bilateral lung field was clear on auscultation with no added sounds. Cardiovascular examination revealed normal S1S2, no rub, gallop or murmur. Abdomen was soft, non tender with normal audible bowel sounds. Chest X-ray showed no remarkable findings. Electrocardiogram showed normal sinus rhythm.

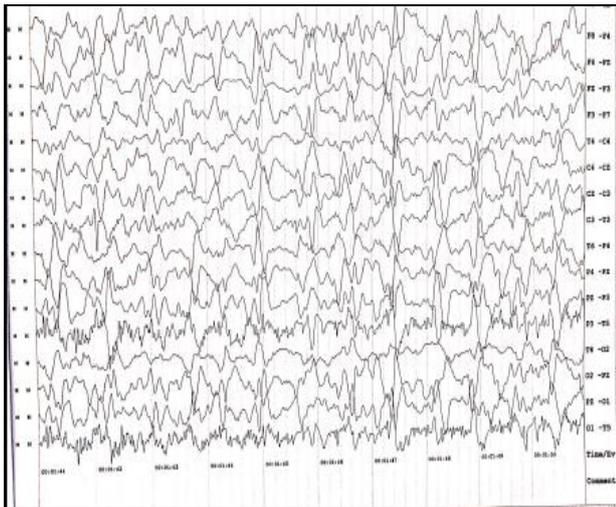


Figure 1: EEG shows diffuse slowing of background activity accompanied by intermittent slow biphasic and triphasic waves.



Figure 2: MRI Brain diffusion-weighted sequence images showing hyperintensities in sporadic Creutzfeldt-Jakob disease.

Routine investigations including complete blood count, liver and renal panels, lipid profile, serum electrolytes, blood sugar level, urinalysis and vitamin B12 level were within normal limits. Serum calcium was low at 7.5 mg/dl. Thyroid function test showed T3 and T4 within normal range with TSH of 0.09 µIU/ml. Mantoux test was normal. Cerebrospinal fluid (CSF) analysis showed slightly elevated protein levels at 67mg/dL and 6 cells/cu.mm with 100% lymphocytes and adenosine deaminase level was within normal limits. CSF culture showed no growth of microorganisms. The opening pressure on lumbar puncture was not raised.

Table 1: 2010 CDC criteria for sporadic CJD.

Definite	Detection of protease-resistant Prion Protein or scrapie-associated fibrils by neuropathology, immunochemical technique, and/or Western blot.
Probable	No findings indicating alternative diagnoses AND progressive dementia with at least 2 of (i)-(iv) AND at least one of (a)-(c).
Possible	No findings indicating alternative diagnoses AND progressive dementia with duration of less than 2 years AND with at least 2 of (i)-(iv) AND at least one of (a)-(c).
Myoclonus	
Visual or cerebellar problems	
Pyramidal or extrapyramidal features	
Akinetic mutism	
a. Periodic sharp wave complexes on electroencephalography	
b. Positive 14-3-3 protein in the cerebrospinal fluid with a disease duration of less than 2 years	
c. High signal abnormalities in caudate nucleus and/or putamen on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR) MRI	

Electroencephalography was obtained with 10-20 system of electrode application. Background activity consist of 3-4Hz, 40-50 mv activity over the occipital regions. Periodic generalized sharp waves (Biphasic or triphasic) 70-80 mv was seen occurring every 1 second. Suggestive of biphasic or triphasic periodic discharge typical of Creutzfeldt-Jakob Disease.

Magnetic resonance imaging (MRI) brain showed bilateral gyriform pattern diffusion restriction at left parieto-temporal, left cingulate gyrus and right superior temporal cortical regions and bilateral thalami. Multiple patchy areas of T2WI/FLAIR sequences showed hyper intensities in bilateral centrum semiovale, corona radiata and periventricular white matter suggestive of Creutzfeldt-Jakob disease.

Considering the presenting features a diagnosis of sporadic CJD was made according to CDC criteria.⁶

Management

She was started on levetiracetam for myoclonus with minimal improvement of symptoms. Relatives of the patient were explained about the course of the disease and poor prognosis was explained. The family members opted to take the patient home so regular monthly follow up was advised. However, her symptoms progressively deteriorated and she passed away 6 months later.

DISCUSSION

Sporadic Creutzfeldt-Jakob disease (sCJD) despite being the commonest (about 85%) among human PrP prion diseases, is a rare disorder with a reported incidence of 1 in million per year. The disease is reported worldwide. The average age of occurrence is 68 years, with no specific difference in incidence between genders. However, cases as young as 13 years and as old as 83 as in this case has been reported.³ Symptoms include cognitive, behavioral and personality changes, difficulties in movement and coordination. Sporadic Creutzfeldt-Jakob disease typically presents as a rapidly progressive dementia as well as motor abnormalities.² Early behavioral symptoms and constitutional symptoms are often overlooked as they are nonspecific and is common in geriatric population. These include irritability, anxiety, depression, fatigue, malaise, light headedness etc. Cognitive symptoms occur early in the course of illness and myoclonus occurs later in the course of the disease. An often unaddressed group is visual symptoms.⁴ As sporadic Creutzfeldt-Jakob disease does not have a proper treatment, making proper diagnosis after ruling out possible differential diagnosis becomes a priority. Important differentials include Lewy body dementia, Hashimoto encephalopathy, intracranial vasculitis, paraneoplastic conditions especially limbic encephalitis and cortical encephalitis.² Presence of fever, elevated ESR, leukocytosis of blood and pleocytosis of CSF should alert the physician about an alternate diagnosis.⁴ Lewy body dementia is the most common disorder to be mistaken for CJD. Absence of abnormalities on DWI and FLAIR MRI almost always distinguishes these neurodegenerative disorders from sCJD.⁵ Presence of high titres of antithyroglobulin or anti thyroid peroxidase antibodies, fluctuations in severity of symptoms are features in favour of Hashimoto's encephalopathy. EEG changes found in CJD are also seen here. Diagnosis of this condition is important as it responds to steroids. Prominent headache, absence of myoclonus, stepwise change in deficits, abnormal CSF and focal white matter changes on MRI or angiographic abnormalities favour intracranial vasculitis. Issue with paraneoplastic conditions is that dementia may appear prior to tumor or in some cases no tumor is ever found.²

There are several diagnostic criteria for probable sporadic Creutzfeldt-Jakob disease including WHO 1998 criteria,

UCSF 2007 criteria, European 2009 criteria and 2010 CDC Criteria for Sporadic CJD. These criteria variably incorporate typical presenting features such as EEG pattern, MRI Brain findings or biopsy findings. The specific diagnostic test for sporadic Creutzfeldt-Jakob disease measure PrPsc (scrapie isoform of the prion protein) prions.² The preferred test is limited proteolysis followed by conformation dependent immunoassay. Diagnosis can be established from brain biopsy specimens by detection of PrPsc. However a reasonably secure diagnosis can be made if constellation of pathologic changes are present.²

There is no known effective therapy for preventing or treating CJD. Drugs like quinacrine have failed to slow the cognitive decline. Animal studies for molecules like anti-PrP antibodies, pentosan polysulphate, phenylhydrazine derivatives are under progress. Adequate biosafety level 2 precautions must be followed during the management. Explaining the time course and prognosis is an important aspect in management of this condition as it is relentlessly progressive and generally causes death within 9 months of onset.²

CONCLUSION

Elderly patients presenting with rapidly progressive dementia, behavioral abnormalities and myoclonus should be suspected for sCJD and evaluated thoroughly. Investigations such as DW MRI Brain, EEG, CSF for 14-3-3 protein and Real-time quaking-induced conversion' (RT-QuIC) assays will help clinch early diagnosis of this rare and fatal disease. However definitive diagnosis of CJD is possible only through histological examination of the brain. The diagnosis is challenging in resource-limited settings. Sporadic CJD is incurable and no treatment is available at present. Early diagnosis and symptomatic management can help improve quality end of life care for the patient as treatment remains supportive in nature. This rare disease require further research and studies to mitigate the fatality of the disease.

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