

Case Report

Sporadic Creutzfeldt - Jakob Disease: Case Report from a Neuroscience Institute in Bangladesh

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Abstract: Sporadic Creutzfeldt-Jakob disease (sCJD) is a rare neurodegenerative disorder characterized by rapidly progressive dementia and myoclonus. Additional clinical features include visual disturbances, cerebellar, and pyramidal/extrapyramidal signs. The rarity of this disease and the wide variety of initial symptoms make the early diagnosis quite challenging. Nevertheless, it can also be diagnosed in a centre with limited resources through good clinical analysis. Here a case of a 53-year-old man is presented who had a 6 weeks history of cognitive deterioration and myoclonus. Brain magnetic resonance imaging (MRI) showed ribbon-like areas of hyperintensity in the bilateral cortex on diffusion-weighted imaging (DWI); bilateral hyperintense caudate nucleus and putamen on T2-weighted and Fluid-attenuated inversion recovery (FLAIR) images. Electroencephalogram (EEG) showed intermittent generalized periodic sharp waves of triphasic morphology. The diagnosis of probable sCJD was reached based on the clinical features and characteristic findings in his MRI and EEG according to WHO criteria. Several other works of the literature were also reviewed for early diagnosis of sCJD and for the exclusion of other differential diagnoses which may mimic sCJD.

Keywords: Creutzfeldt-Jakob Disease, Prion Disease, Myoclonus, Rapidly Progressing Dementia

1. Introduction

Creutzfeldt-Jakob disease (CJD) is a transmissible neurodegenerative disease caused by prion proteins characterized by rapidly developing progressive dementia and myoclonus. This disease is fatal and the mortality is 1-2 people per million annually worldwide. The underlying pathology is an abnormal accumulation of proteins in the brain as well as spongiform changes like neuronal loss and gliosis [1].

CJD has four subtypes; among them, sporadic Creutzfeldt-Jakob disease (sCJD) is the most common subtype (85-95%), while the other subtypes are variant forms (vCJD), iatrogenic (iCJD) and familial (fCJD). Sporadic CJD presents with rapidly advancing dementia, pyramidal/extrapyramidal signs, myoclonic episodes and

cerebellar dysfunction. Moreover, the patient may also present with a subtle change of memory, impaired judgement, subtle behavioural changes like anxiety, irritability, social withdrawal, and some other psychiatric symptoms [2]. The disease usually follows a rapidly progressive course of cognitive impairment followed by functional impairment towards akinetic mutism at the later stage. Most of the patients eventually die within a year of disease onset [1]. Here we have presented a case of a probable sCJD who was admitted to the hospital for evaluation of involuntary movement along with progressive impairment of cognition.

2. Case Report

The index patient was a 53-year-old Bangladeshi, working

as an 'Imam' in a mosque. He was referred to our hospital by a general practitioner for further evaluation suspecting encephalitis. The patient had a two-week history of sudden onset confusion, functional and motor impairment along with myoclonic jerks of both upper limbs. His family reported that his symptoms started around 6 weeks back, which was associated with cognitive impairment in the form of short-term memory loss. Initially, they noticed when he couldn't remember the verses of the Quran while praying even though he knew the whole Quran by heart. Moreover, he was also suffering from loss of functional abilities including dressing up, using the lavatory, and sometimes losing direction to his own house. His wife also added that he had emotional lability followed by mutism. His family denies he had any tremor, unsteadiness of gate or hallucinations. There was no record of significant medical and psychiatric condition, previous surgeries, or drug abuse. He was not taking any regular medication, had no significant travelling history or any exposure to raw livestock or brain matter. None of his family members had dementia or prion disease.

On initial assessment, he was found to be confused. There was the loss of ability to speak and visible myoclonic jerks involving both of his upper limbs. No facial asymmetry was noted and ocular movements were intact, but he was sluggish at following commands. He had rigidity involving all four extremities and there were no Babinski reflexes. There were no signs of meningeal irritation. Due to clouded sensorium, his coordination and gait couldn't be examined. The patient went through a marked cognitive decline by the first week since admission, with episodes of severe agitation, increased stiffness of limbs, and frequency of myoclonic jerks. He also suffered from rapid functional decline to the point of being bedridden with associated bowel and bladder incontinence.

Routine blood counts, sugar levels, hepatic and kidney function tests, electrolytes were normal. Thyroid studies, vitamin B12, folate levels, lactic acid, arterial blood gas (ABG), urinary ketones, venereal disease research lab (VDRL), plasma calcium, serum ceruloplasmin and anti-HIV Antibody were also normal. Cerebrospinal fluid (CSF) was negative for infection and other tests of CSF for protein, glucose, cell count, Adenosine Deaminase (ADA), and Gene Xpert MTB/RIF were also unremarkable. CSF 14-3-3 protein level could not be done due to the unavailability of the test in Bangladesh. A contrast MRI of his brain revealed cerebral atrophy. In addition, Diffusion-weighted images (DWI) showed ribboning in cortical areas (shown in Figure 1); T2-weighted image and fluid-attenuated inversion recovery (FLAIR) images revealed hyperintensity in the putamen and caudate nucleus (shown in Figures 2 and 3). There was no intracranial space-occupying lesion (ICSOL) or any infarcts. An EEG showed an abnormal pattern due to the presence of intermittent generalized periodic sharp waves of triphasic morphology at a frequency of 1Hz with occasional diffuse slow waves of 5-6 Hz between the bursts (shown in Figure 4). His clinical presentation, as well as his imaging and EEG findings, satisfied the criteria for probable Creutzfeldt-Jakob disease (sCJD) as per World Health Organizations (WHO) Criteria (Table 1). Several other

differentials were considered and assessed through pertinent investigations. Table 2 shows the tests executed and diagnosis that are ruled out based on their results.

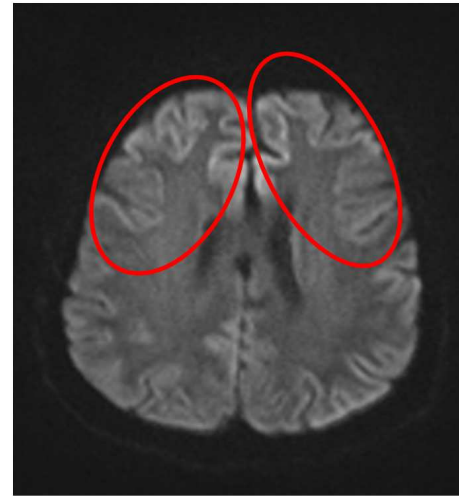


Figure 1. Diffusion-weighted imaging (DWI) showing ribbon-like areas of hyperintensity involving the bilateral frontoparietal cortex (red circle).

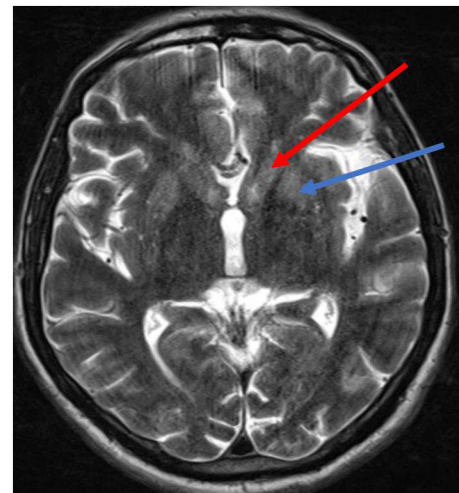


Figure 2. T2-weighted imaging showing Increased abnormal signal intensities in the Caudate nucleus (red arrow) and Putamen (blue arrow).

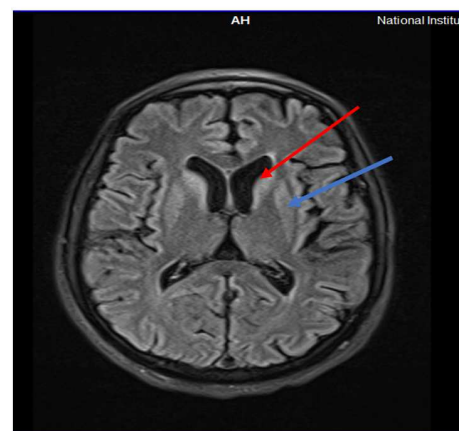


Figure 3. Fluid-attenuated inversion recovery (FLAIR) imaging showed Increased abnormal signal intensities in the Caudate nucleus (red arrow), and Putamen (blue arrow).



Figure 4. Intermittent generalized periodic sharp waves of triphasic morphology in electroencephalogram (EEG).

Table 1. The World Health Organization (WHO) criteria for probable sporadic CJD (Adopted from World Health Organization Emerging and other Communicable Diseases, Surveillance and Control [Internet]. Available from: <http://www.who.int/emc>).

No.	Description
i	a) Progressive Dementia a) Myoclonus
ii	b) Pyramidal or extrapyramidal disturbance c) Cerebellar or visual disturbance d) Akinetic mutism
iii	a) Typical EEG (Generalized triphasic periodic complexes at approximately one per second) b) Positive 14-3-3 assay in Cerebrospinal fluid (CSF)
Possible case: 1 plus at least 2 of ii and duration <2 years	
Probable case: Possible case criteria with at least 1 of iii	
Definite case: Neuropathological confirmation and/or confirmation of protease-resistant prion protein (PrP) (immunocytochemistry or Western Blot) and/or presence of scrapie-associated fibrils	

Table 2. Investigations for ruling out differential diagnoses.

Differential Diagnoses	Investigations
Stroke, normal pressure hydrocephalus, Alzheimer's disease metastases to brain, brain abscesses,	MRI of brain
Electrolyte imbalance	Electrolyte assay
Hypoglycaemic encephalopathy	Blood sugar
Hepatic encephalopathy	Liver panel
Uremic encephalopathy	Renal panel
Hashimoto encephalopathy	Thyroid function test
B ₁₂ , folate deficiency dementia	B ₁₂ , Folate assay
Meningitis or encephalitis of bacterial, viral, tubercular aetiologies	CSF study for microbiological, cytological, biochemical examination, ADA and gene Xpert.
Cerebral vasculitis	Serum VDRL
Hypoxic Encephalopathy	cANCA, pANCA ABG, serum lactate

MRI: Magnetic resonance imaging

CSF: Cerebrospinal fluid

ADA: Adenosine deaminase

VDRL: Venereal Disease Research Laboratory

ANCA: Antineutrophil cytoplasmic antibodies

ABG: Arterial blood gas analysis

As the patient became comatose, a nasogastric tube was inserted for feeding and to prevent aspiration pneumonia. Without waiting for the test results, he was empirically treated with intravenous acyclovir for viral encephalitis, but there was no significant improvement. A trial of 5 days of intravenous Dexamethasone, commenced on day 7 for autoimmune encephalitis, showed no clinical improvement either. He was commenced on valproic acid for myoclonic jerks with minimal improvement. By day 16 postadmission, nasogastric feeding was continued as the patient remained comatose. Eventually, the patient was referred to palliative care and discharged to hospice in the local nursing home.

3. Discussion

The common age of onset of Sporadic CJD ranges from 41 to 81 years and the survival duration is half a year with a 3–18 month range [3]. It is typically presented with rapidly progressive dementia, myoclonus, ataxia, or behavioural changes. Eye symptoms can be present in the form of cortical blindness, distorted vision, and ophthalmoplegia or gaze palsy. However, psychiatric manifestations, including psychosis, mood disorder, and altered sleep pattern, maybe the only feature of early sporadic CJD [4]. The diagnosis is confirmed by demonstrating prion protein deposition in the brain by biopsy/autopsy and supported by investigation including CSF study, EEG and blood examination for certain proteins such as 14-3-3 protein, S-100 and atypical signal changes in putamen and/or caudate nucleus on DWI or FLAIR image on MRI [1]. The present case displayed the importance of early attention to rapidly deteriorating dementia as it might be an early presentation of sCJD. The diagnosis of probable sCJD was made, based on the clinical features and EEG results and as per World Health Organization (WHO) diagnostic criteria [5].

The diagnosis of sCJD can be difficult as some of the clinical features are nonspecific and may also exist in other neurodegenerative conditions. Uncharacteristic symptoms not satisfying the diagnostic criteria, absence of any remarkable features in EEG or MRI may make the diagnosis more challenging. The clinical pictures of sCJD can be incorrectly attributed to other common disease conditions. Thus, it is fairly common to miss the diagnosis of CJD or make a delayed diagnosis, [6]. In addition, often physicians may ask for an antemortem brain biopsy due to a lack of non-invasive tests to confirm the disease which may delay the diagnosis [6].

The gold standard for the diagnosis of sCJD is the neuropathological examination of brain tissue obtained either by carrying out a brain biopsy or post-mortem examination of the brain [7]. Other tools of diagnosis are MRI and EEG. MRI is a very valuable test for diagnosis, as it has characteristic features in sCJD, relatively noninvasive and easily available. Classic MRI features of sCJD include hyperintense signal changes in the putamen, caudate nuclei, and/or cortex on diffusion-weighted image and FLAIR sequences [7]. These MRI abnormalities are included within the diagnostic criteria for CJD, increasing the sensitivity and specificity by around

90% [8]. It is worth mentioning that periodic triphasic sharp-wave complexes are observed in EEGs and its specificity can also be as high as 90% [7].

The detection of the 14-3-3 protein in the cerebrospinal fluid (CSF) can be helpful in the diagnosis of sCJD. It is normally present in various neural tissues, but when there is the destruction of neural tissue, it is released into the cerebrospinal fluid. Therefore, the elevation of the 14-3-3 protein may also be found in ischemic stroke and encephalitis [9]. Nonetheless, if it is used in the background of fitting the clinical context of rapidly progressive dementia, this test may become an excellent tool and a guiding marker in the diagnosis of sCJD [10]. This assay of CSF 14-3-3 protein possesses a sensitivity of 92% and specificity of 86% [9]. In our patient, the symptoms like progressive impairment of cognition with myoclonus were consistent with sporadic CJD (sCJD). Moreover, suggestive MRI with a typical EEG finding, 14-3-3 protein supports the diagnosis of sporadic CJD (sCJD).

Soon, CSF analysis for CJD will likely include real-time quaking-induced conversion (RT-QuIC) which is an assay for prion protein conversion. This test can confirm the diagnosis of CJD from the CSF sample by detecting PrP^{Sc} (prion protein). This test is approximately 80%–90% sensitive and up to 100% specific. Though this test is still not a part of the diagnostic criteria, this new test has a great potential to increase the precision of antemortem diagnosis of CJD [6]. The confirmation of the diagnosis of sCJD needs histological evidence. In a postmortem study of brain tissue or premortem brain, a biopsy may show multiple areas of neuronal loss, spongiform changes in the grey matter of the brain, amyloid plaques, without any signs of inflammation and widespread proliferation of astroglial cells [11].

4. Conclusion

Even though there is no evidence-based curative medical therapy available for sCJD, it is vital to make a precise and timely diagnosis because some of the differential diagnoses such as meningoencephalitis and metabolic encephalopathy are remediable. A timely diagnosis will make give the patient party time to prepare for the natural outcome of the disease and they can also choose options of treatment like palliative care.

Footnotes

Abbreviations: CJD=Creutzfeldt–Jakob disease, sCJD=sporadic CJD, DWI=diffusion-weighted imaging, EEG=electroencephalography, CSF=cerebrospinal fluid, PrP^{Sc}=Prion protein.

Statement of Ethics

An informed written consent was taken from the patient's guardian for their anonymous information to be published in

this case study. This case report has been approved by the Ethics Board of the National Institute of Neurosciences and Hospitals, Bangladesh.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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