

CASE REPORT

CREUTZFELDT-JAKOB DISEASE: A CASE REPORT

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ABSTRACT: Prion diseases are a group of fatal neurodegenerative diseases caused by the transformation of an endogenous protein, PrP (prion-related protein), into an abnormal conformation, the most common of which in humans is Creutzfeldt-Jakob disease. We report the case of a 40 year old lady who presented with rapidly progressive dementia with pyramidal, extra-pyramidal, cerebellar symptoms, myoclonus and akinetic mutism. Her EEG showed typical periodic sharp wave complexes and MRI Brain revealed DWI>FLAIR intensity in bilateral caudate nuclei, putamen & bilateral subcortical frontal lobes. The clinico-radiological correlation was consistent with the diagnosis of Creutzfeldt-Jakob disease.

KEYWORDS: Prion, Myoclonus, Akinetic mutism, Creutzfeldt-Jakob.

INTRODUCTION: Prions are the only known infectious pathogens that are devoid of nucleic acids. They may manifest as infectious, genetic or sporadic disorders. The sporadic form of CJD is the most common form of prion disorder in humans which accounts for about 85%. The incidence of sporadic CJD is approximately one case per million population. In mammals prions reproduce by binding to the normal cellular isoform of the prion protein (PrP^c) located on the short arm of chromosome 20 and stimulating conversion of PrP^c into the disease causing isoform (PrP^{Sc}).⁽¹⁾ The constellation of dementia, myoclonus, and periodic electrical bursts in an afebrile patient generally indicates CJD.^(2,3) The clinical abnormalities in CJD are confined to central nervous system. Studies have suggested an incubation period of 1.5 to 2 years before the development of clinical disease. Most patients with CJD live only for 6 to 12 months after the development of clinical disease. The diagnosis can be established by PrP^{Sc} in brain biopsy. The high sensitivity and specificity of cortical ribboning and basal ganglia hyperintensity on FLAIR and diffusion-weighted MRI for the diagnosis of CJD have greatly diminished the need for brain biopsy in patients with suspected CJD. CSF study is mostly normal but may show protein 14-3-3. The EEG is useful in the diagnosis of CJD, although only about 60% of individuals show the typical pattern. A typical EEG in sCJD has sharp or triphasic waves (periodic sharp wave complexes, or PSWCs) occurring about once every second.⁽¹⁾

CASE REPORT: 40 year old lady from Thirupathur, Tamilnadu presented with altered behaviour for 10 months, slowness of speech for 5 months, jerky movements both upper limbs for 3 months, seizures for 3 days. Her complaints started as pain and burning sensation involving right side of the body 10 months ago. She then developed insomnia, irritability, intolerance to loud sounds, and behavioural alteration in the form of apathy. In about 1 month she had slowness of gait, low volume speech, urge incontinence. For these complaints she took psychiatric treatment for 3 months. With treatment sleep and bladder disturbances improved. But gait and speech

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disturbances persisted. While on treatment she developed memory disturbances, inappropriate laughter frequent falls grasp like movements of both hands, dragging of right leg, urinary and fecal incontinence. She was deteriorating and in a month she was unable to recognize her daughter and husband, had screaming episodes, assaultive behavior, difficulty in swallowing, truncal ataxia, myoclonic jerks involving both upper limbs and fine tremor of hands. In about 2 weeks she was not communicating, had difficulty in comprehending, was not able to walk even with support and soon she was completely bedridden, there was no spontaneous eye opening and developed recurrent episodes of generalised tonic clonic seizures. On examination she was unconscious, not responding to call, was localizing pain. Vitals were stable. Grasp reflex was present. Pupils were equally reacting to light. Fundus examination was normal. Downbeat nystagmus was present. Corneal, conjunctival reflex absent, Dolls Eye Movement present. On motor system examination bulk of the muscles were equal bilaterally. Rigidity was present bilaterally. All deep tendon reflexes were brisk, plantar extensor bilaterally. Myoclonic jerks were present. Sensory and cerebellar system could not be examined. Other system examinations were normal. Her blood picture was normal. ECG, Ultrasonogram of abdomen, Chest X-ray were normal. There was no Kayser –Fleischer ring. Serum Copper and ceruloplasmin levels were normal. Cerebrospinal fluid analysis was normal. Anti-thyroid peroxidase antibodies were negative. Electroencephalography showed background poorly formed theta intermixed with alpha, bilateral biphasic, triphasic wave complex at 1Hz/sec and bilateral periodic sharp wave complexes. MRI Brain showed T1 iso- hypointense T2 hyperintensity in bilateral caudate nuclei, putamen and bilateral subcortical frontal lobes. Lesion showing diffusion restriction on DWI. In addition there was shrinkage of cerebellar hemisphere.

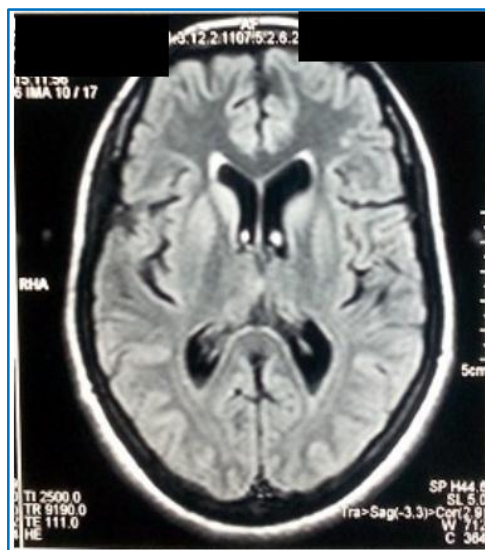


Fig. 1: T1 FLAIR image showing cortical ribboning and Bilateral basal ganglia hyperintensity

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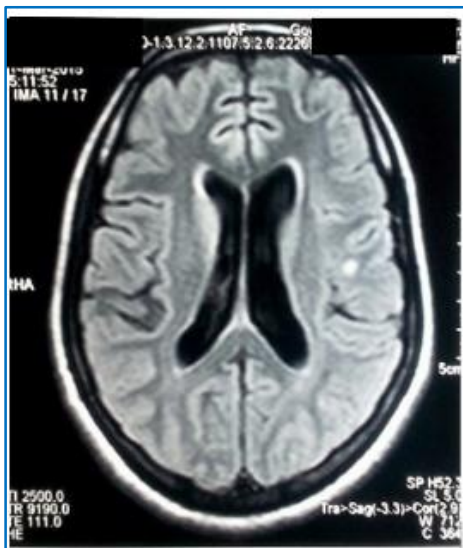


Fig. 2: T1 FLAIR image showing cortical ribboning

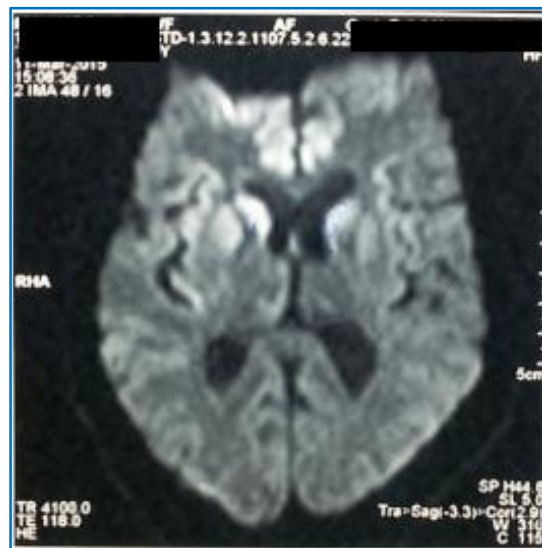


Fig. 3: DWI showing bilateral cortical and basal ganglia hyperintensity



Fig. 4: EEG showing bilateral periodic sharp wave complex

DISCUSSION: Prion diseases are neurodegenerative diseases^(3,4) that have long incubation periods and progress inexorably once clinical symptoms appear. Several criteria exist for the diagnosis of sCJD. Unfortunately, most patients will only fulfill existing criteria at later stages of the disease, because most criteria are designed for epidemiological purposes.⁽⁵⁾ The most commonly used probable criteria are the World Health Organization Revised Criteria (1998).⁽²⁾

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Several Diagnostic Criteria for Probable Sporadic Creutzfeldt-Jakob Disease		
WHO 1998 Revised Criteria (WHO, 1998)	UCSF 2007 Criteria (Geschwind et al., 2007)	European Criteria 2009 [*] (Zerr et al., 2009)
1. Progressive dementia and/or 2. At least two of the following four features: a. Myoclonus b. Visual or cerebellar disturbance c. Pyramidal/extrapyramidal signs d. Akinetic mutism and 3. PSWCs on the EEG and/or a positive 14-3-3 CSF assay and a clinical duration to death <2 years 4. No alternative diagnosis on routine investigations	1. Rapidly progressive dementia and 2. At least two of the following: a. Myoclonus b. Pyramidal/extrapyramidal signs c. Dysfunction d. Visual disturbance e. Cerebellar signs f. Akinetic mutism g. Other higher focal cortical sign* and 3. A typical EEG or MRI and 4. Routine investigations should not suggest an alternative diagnosis	1. Progressive dementia 2. At least two of the following four features: a. Myoclonus b. Visual or cerebellar disturbance c. Pyramidal/extrapyramidal signs d. Akinetic mutism and 3. One of more of the following: a. Periodic discharges on the EEG b. A positive 14-3-3 CSF assay and a clinical duration to death <2 years c. High signal abnormalities in caudate nuclear and putamen or at least two cortical regions (temporal-parietal-occipital but not frontal, cingulate, insular, or hippocampal) either in DWI or FLAIR MRI 4. No alternative diagnosis on routine investigations
<small>CSF, Cerebrospinal fluid; DWI, diffusion-weighted imaging; EEG, electroencephalogram; FLAIR, fluid-attenuated inversion recovery; MRI, magnetic resonance imaging; PSWCs, periodic sharp wave complexes; WHO, World Health Organization. *Higher focal cortical signs include such findings or symptoms as apraxia, neglect, acakulia, aphasia, etc. [*]N.B. There were errors in the table summarizing the criteria in the paper; criteria shown here are derived from the text of the paper. </small>		

Our patient had rapidly progressive dementia with myoclonus, cerebellar symptoms, pyramidal and extra pyramidal signs and akinetic mutism with typical EEG and MRI findings. Definitive diagnosis is by demonstrating the abnormal protein in brain biopsy specimen.

CONCLUSION: Creutzfeldt-Jakob disease is one of the rare cause of dementia. The rapid progression of dementia with myoclonus and typical EEG or MRI features suggest the diagnosis. To date no curative treatment has been found.

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