

A Case Report of Creutzfeldt-Jacob Disease

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Abstract- Creutzfeldt-Jacob Disease is the most frequently seen type of prion diseases. Its clinical findings consist of predominantly progressive dementia with a rapid onset, myoclonus, and also cerebellar, pyramidal, extrapyramidal and visual signs. Occurrence of periodical spikes in EEG, observation of cortical signal alterations during diffusion weighted (DW) MRI studies, and detection of protein 14-3-3 in cerebrospinal fluid (CSF) substantiate the diagnosis. Definitive diagnosis is established with histological examination of brain biopsy or autopsy materials.

Index Terms- Creutzfeldt -Jakob Disease (CJD), prion (PrPC), Infective prion (PrPSc), periodic sharp-wave complexes (PSWCs).

I. INTRODUCTION

Creutzfeldt -Jakob Disease (CJD) is a rarely seen neurodegenerative disease. It has four subtypes as sporadic, familial, iatrogenic and variant forms thought to be transmitted with ingestion of infected meat products¹. Mean age at the onset is 60 years with a yearly incidence of approximately 1/1.000.000. Firstly in 1982, Prusiner hypothetically proposed prions as causative infectious agents of CJD¹. In fact, normally a prion (PrPC) is a glycoprotein found in normal cells of humans and animals. In humans prion protein gene is localized on the short arm of the chromosome 20. Infective prion (PrPSc) is a posttranslational product resulting from defective folding of the normal prion. These abnormal prions accumulate in cells leading to the formation of vacuolar degeneration and some fibrillar structures; subsequently brain takes the form of a sponge resulting in death.²

Here we presenting a case with a probable sporadic CJD, in which diagnosis was established based on medical history, clinical presentation, findings of diffusion weighted (DW) MRI, EEG and CSF in accordance with clinical diagnostic criteria of World Health Organization (WHO).

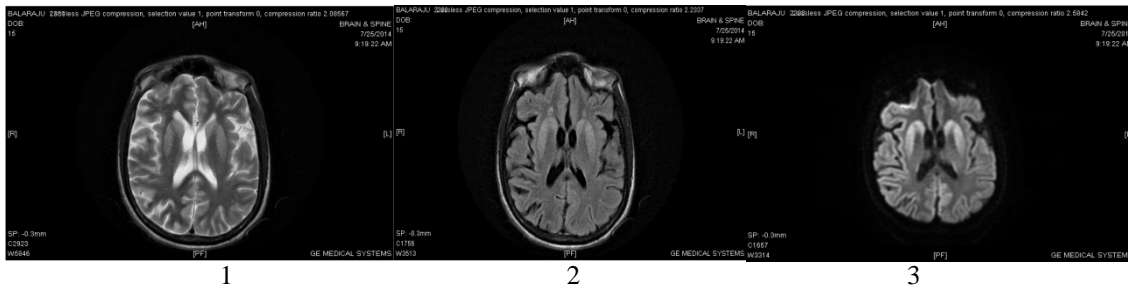
II. CASE HISTORY

50yr old male presented with rapidly progressive dementia, rigidity, akinetic mutism, myoclonus of 3 months duration with loss of memory and behavioural abnormalities, in the form of formed visual and auditory hallucinations of 3 months duration. This was followed by slowness of all activities and stiffness of whole body, predominantly axial. There was exaggerated startle myoclonus.

Neurological examination revealed expressionless face with loss of speech and difficulty in swallowing, loss of all movements with stiffness of whole body. Not following commands but maintaining eye-to-eye contact with preserved reflexive eye movements. Normal pupillary responses to light. He was having diffuse myoclonus emerging spontaneously and response to auditory or tactile stimuli were observed. Deep tendon reflexes were normal, and planter reflexes were bilateral flexors. Sensory system examination is normal. Past medical history and family history was unremarkable. No abnormality in laboratory test was detected. **Complete blood picture** Hb 11.0gms, WBC count 6500 cells/cm³, Differential count: N-65, L-30, M-03, E-02, Platelets – adequate, ESR-10MM, SERUM UREA-26mg/dl, SERUM CREATININE-0.8mg/dl, sodium-150 meq/l.

Potassium-4.0meq/l, RBS-74mg/dl, Thyroid profile, LIPID PROFILE-NORMAL, Serum B12 and folic acid: normal, LFT – normal, CUE-normal, Chest x ray –normal, HIV AND HBSAG: negative, 2DECHO: NORMAL, Carotid Doppler: normal, CSF ANALYSIS: Normal, ADA 4U/ L, Cell count <5 cells with lymphocytes Sugar (54mg/dl) and protein(35mg/dl) levels normal, Gram staining and cultures negative, CT SCAN Brain: normal study.

EEG showed diffuse slowing; with periodic sharp-wave complexes (PSWCs), most often triphasic or biphasic, occurring approximately every second. The discharges are diffuse and symmetrical. MRI brain showed altered signal intensities in bilateral basal ganglion which were hyperintense on T2 and Flair images with restriction on DW images. Gyri appear bulky with subtle T2 hyper intensities and showed restriction of DW images.



MRI brain axial images T2 (1), Flair (2), DWI (3) showing T2 and flair hyperintensities of bilateral basal ganglion with bulky gyri showing diffusion restriction of bilateral basal ganglion and gyri.



EEG showing periodic sharp-wave complexes (PSWCs), most often triphasic or biphasic, occurring approximately every second.

III. DISCUSSION

CJD is a fatally progressive prion disease characterized with rapidly deteriorating dementia. Four different forms of the disease are recognized:

1. Sporadic – which accounts for 87% of all cases;
2. Genetically transmitted (familial) – accounts for another 10% of reported cases; inherited secondary to the mutation of prion protein gene localized on chromosome 20.
3. Iatrogenic – which can either be transmitted by contaminated surgical instruments or human tissues (dura-mater grafts; growth hormone preparations, cornea grafts and intracranial cortical electrodes)³

4. Variant form – which is the clinical form related to the bovine spongiform encephalopathy epidemic (the so-called "Mad Cow Disease")⁴.

Symptoms of sporadic CJD can appear at 50–70 years of age. Personality changes accompany cerebellar and visual symptoms. Ataxia is more marked in advanced cases and most patients have myoclonus manifesting as a response to auditory and tactile stimuli. In late stages patient develops akinetic mutism and myoclonus can disappear. 80% of the patients die from infection, cardiac and respiratory failure within the first year. CSF protein levels rarely rise in CJD. Detection of a proteinase inhibitor, 14-3-3 protein released from damaged neurons into CSF fortifies the diagnosis. Zerr et. al. found that 14-3-3 protein is 94% sensitive and 84% specific for the disease⁵

This protein can be detected in many other neurological disorders. Besides 14-3-3 protein, markers such as neuron specific enolase, amyloid beta, tau protein, astrocytic protein S 100 and neopterin are being investigated. EEG with Periodic biphasic or triphasic, synchronized sharp wave complexes occurring during middle or late stages of disease are typical and found 90% of the patients.

In sporadic CJD cerebral atrophy, increase in signal intensity in putamen, caudate nucleus and cerebral cortex can be detected in imaging studies. Increased signal intensity in the cortex is called ribboning. Shiga et al. revealed 92.3% sensitivity and 93% specificity for DW MRI in their patients with definitive and probable diagnoses of CJD⁶.

Recent studies demonstrated that even in very early stages of the disease pathological findings can be detected with DW MR. Definitive diagnosis of CJD requires neuropathological examinations. Detection of PrPSc reactivity with immunohistochemical staining and demonstration of protease resistant PrPSc have diagnostic value⁶.

Infective prion (PrPSc) is resistant to boiling, treatment with formalin, alcohol and UV rays but it can be inactivated by autoclaving at 132⁰ C and 15 lb per Sq inch for 1 hr or by immersion for 1 hr in 5% sodium hypochlorite (House hold bleach)⁷.

Table 53D.3 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 ⁷ (Zerr et al., 2009)
1. Progressive dementia <i>and/or</i> 2. At least two of the following four features: a. Myoclonus b. Visual or cerebellar disturbance c. Pyramidal/extrapyramidal signs d. Akinetic mutism <i>and</i> 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 <i>and</i> 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* <i>and</i> 3. A typical EEG or MRI <i>and</i> 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 <i>and</i> 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

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, acalculia, aphasia, etc.
¹N.B. There were errors in the table summarizing the criteria in the paper; criteria shown here are derived from the text of the paper.

In our case, patient is having progressive dementia akinetic mutism, myoclonus, visual Hallucination, both pyramidal and extrapyramidal symptoms and on EEG – PSWC most often triphasic occurring every second and MRI brain showing hyper intensities on bilateral basal ganglia. All these findings are fulfilling the criteria for the diagnosis of sporadic Creutzfeldt-Jacob Disease as per WHO guidelines.

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