CJD: A Case Report

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Abstract

Creuzfeldt-Jakob's Disease (CJD) is a rare neurodegenerative disorder that is included among the transmissible spongiform encephalopathies. The clinical features are those of a rapidly progressive dementia with myoclonic jerks culminating in death in less than one year. We intend to highlight the role of the magnetic resonance imaging (MRI) as a vital tool for the presumptive in vivo diagnosis, thereby obviating the need of histopathologic confirmation of the disease.

INTRODUCTION

Creutzfeldt-Jacob Disease is a rare infectious spongioform encephalopathy. It has four subtypes as sporadic, familial, iatrogenic and variant forms thought to be transmitted with ingestion of infected meat products. Mean age at the onset is 60 years with a yearly incidence of approximately 1/1.000.000. Definitive diagnosis is established with histological examination of brain biopsy or autopsy materials. Observation of cortical signal alterations in diffusion weighted (DW) MRI studies, occurrence of periodical spikes in EEG and detection of protein 14-3-3 in cerebrospinal fluid (CSF) substantiate the diagnosis. Usual age of presentation is 40 – 80 yrs.

In this article 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) is presented.

CASE DISCUSSION

A 55 year old lady was referred presented with chief complaints of memory loss and impaired judgment. She was a school teacher by profession. The relatives reported that patient was developing forgetfulness since past three to six months. She used to enter wrong rooms at home and she lost her way to home on two occasions. Also there was history of making mistake in calculating money. For past three months there was progressive difficulty in walking and the relatives described her gait as that of a drunken person. There was also history of tremulousness of hands on attempt to do some work. There were nonspecific complaints of headache, fatigability and weight loss. Patient was experiencing brief sudden jerky movements occurring synchronously in all four limbs.

On examination, she was partially oriented. Higher mental function as assessed by mini mental examination was grossly impaired. Speech was dysarthric. Action tremors and spontaneous as well as startle myoclonus were noticed. Cogwheeling in both upper limbs and rigidity in lower limbs were present. Deep tendon reflexes were diffusely brisk with extensor plantar response. EEG showed 4–5 cps teta waves in background activity and also slow triphasic waves with higher amplitude on frontal regions. Blood sugar, renal function, serum electrolytes and liver function were all within normal limits.

On MRI brain, neurodegenerative disorders such as fronto-temporal dementia, Alzheimer's disease were ruled out by lack of atrophy on T1W and T2W sequences. T2W FLAIR showed hyperintensity in bilateral basal ganglia and posteromedial aspect of bilateral thalami (pulvinar sign) (Figure 1) and gyriform cortical mild hyperintensity in B/L cerebral hemispheres predominantly involving B/L fronto-temporo-occipital lobes (cortical ribbon sign) (Figure 2). In diffusion weighted sequences, restriction was seen in same areas (Figure 3 and 5) with corresponding low ADC values (Figure 4).

Serology for HIV and syphilis were negative. CSF analysis was normal, CSF VDRL was negative. Thryroid peroxidase (TPO) antibodies were negative and thyroid function test was negative.

Figure 1

Figure 1: T2 FLAIR MR image shows mild hyperintensity seen in bilateral basal ganglia and posteromedial aspect of bilateral thalami ( )

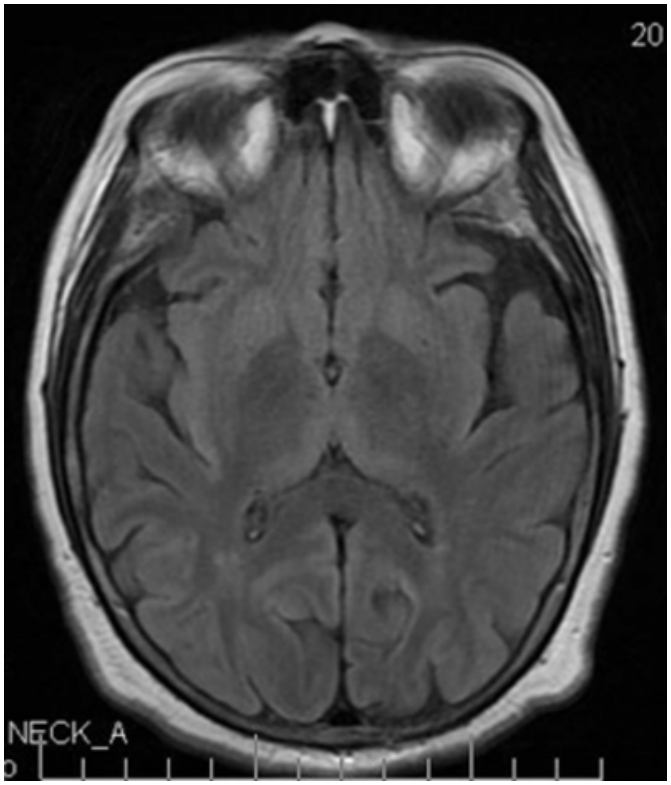


Figure 2

Figure 2: T2 FLAIR MR image shows gyriform cortical mild hyperintensity in bilateral cerebral hemispheres predominantly involving fronto-temporo-occipital lobes ( ). It also shows multiple scattered hyperintensities in bilateral centrum semiovale.

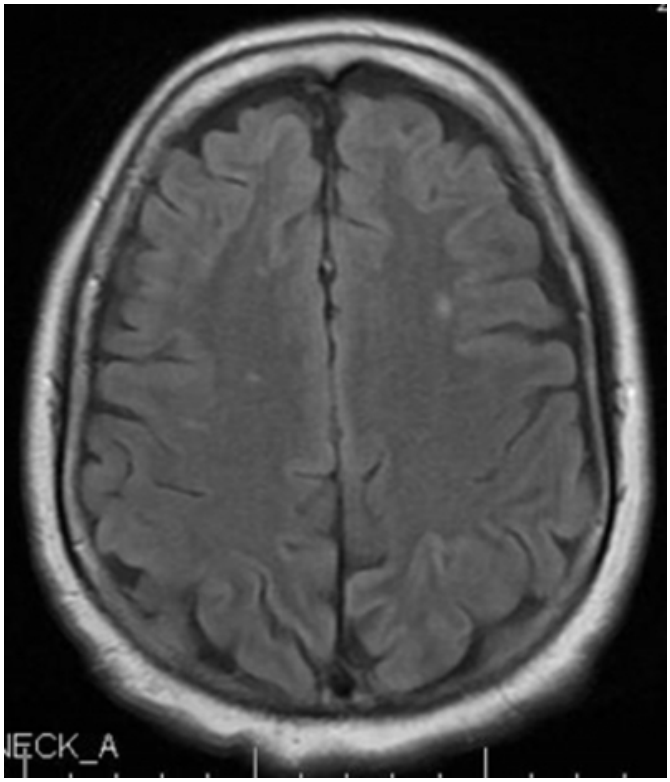


Figure 3

Figure 3: Diffusion weighted MR image shows more conspicuous and as hyperintense areas.

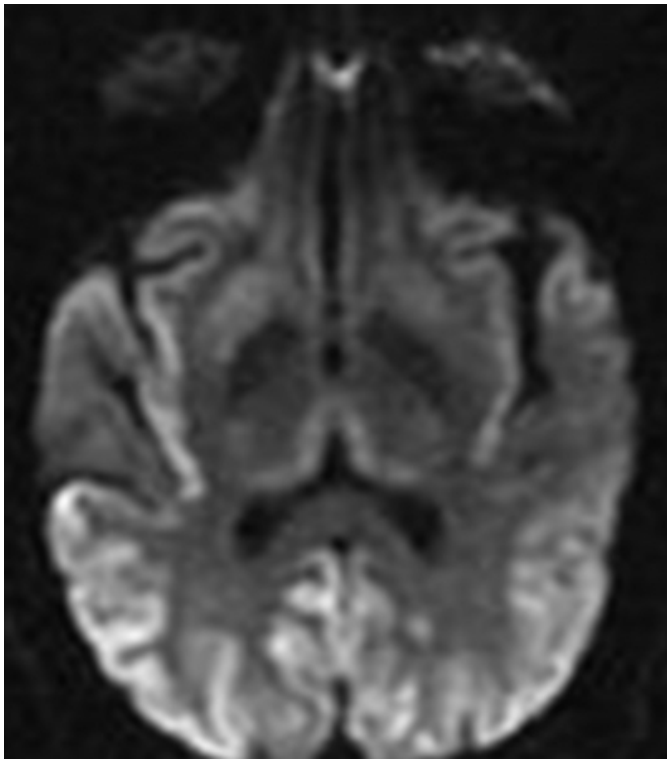


Figure 4

Figure 4: corresponding ADC image showing hypointensity in the corresponding areas (low ADC values) suggesting true restriction.

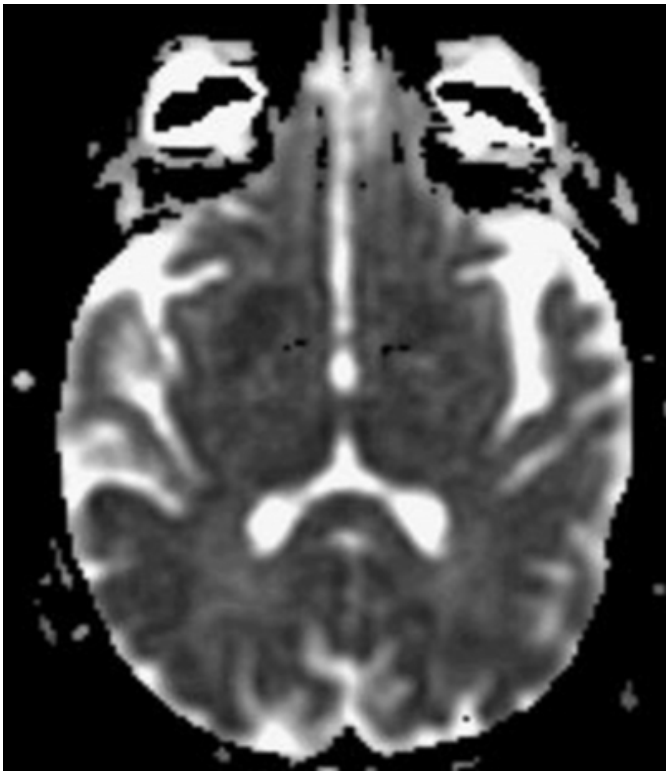


Figure 5

Figure 5: Cortical ribbon sign in bilateral frontal and parietal regions.

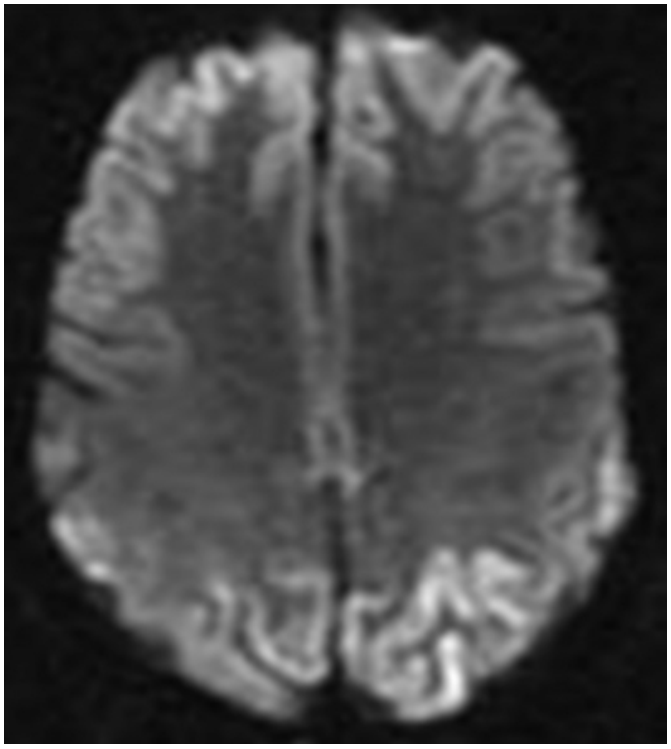
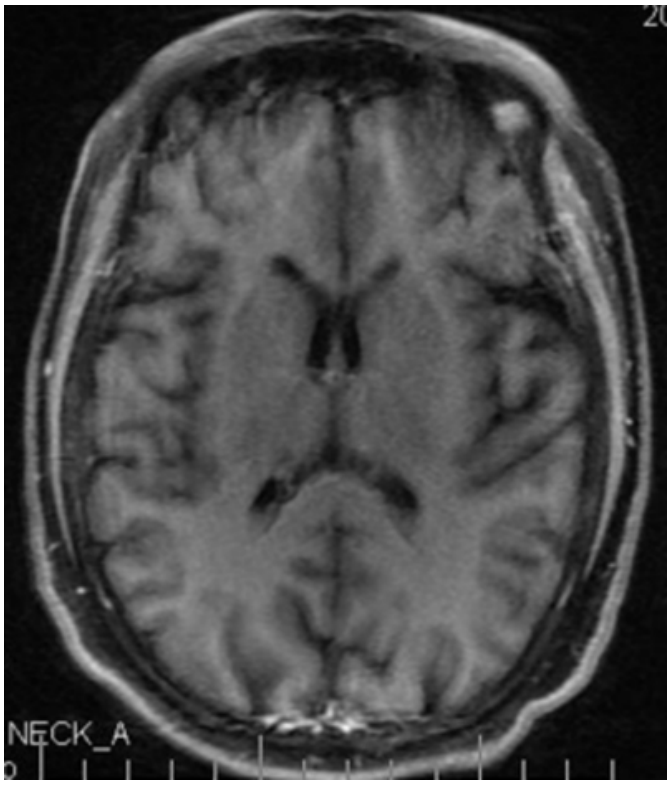


Figure 6

Figure 6: Post-Gadolinium T1 weighted MR image shows no abnormal contrast enhancement.



DISCUSSION

Creutzfeldt-Jakob's Disease (DCJ) is a rare, neurodegenerative disorder that is part of a larger group of transmissible spongiform encephalopathies[1]. It was first described by Gerhard Creutzfeldt e AlfonsJakob in Germany during the twenties[2]. It was initially believed to be an infectious disease transmitted by an unconventional virus, which was later termed "prion" (proteinaceous infectious particle) by Prusiner in 1982. In fact, 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. Methionine/valine polymorphism on codon 129 of this gene is found to be associated with CJD. 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. [3].

CJD is a fatally progressive prion disease and an important etiology of rapidly progressive dementia. 85-90% of human prion diseases are sporadic. Prion diasease acquired from a source accounts for 1-2% of all cases. 5–15% of cases are familial autosomal dominant type inherited secondary to the mutation of prion protein gene localized on chromosome 20 [4]. New variant CJD (nvCJD) has been reported since middle of 90's. The mean age at the onset of the disease is 29 years, and its mean survival is 16 months. This variant leads to cerebral prion plaques, contrary to spongioform alterations in the brain tissue [5,6].

Sporadic CJD has onset in age group of 50-70 and is characterized by rapidly progressive dementia and myclonus. Personality changes accompany cerebellar and visual symptoms. Ataxia occurs in advanced cases and most patients have myoclonus manifesting as a response to auditory and tactile stimuli. In late stages patient can be akinetic and mute and the myoclonus may disaapear. The important cause of death in these patients includes infection, cardiac and respiratory failure within the first year [4]. CSF analysis is usually normal. Presence of a proteinase inhibitor, 14-3-3 protein released from damaged neurons into CSF fortifies the diagnosis [5,6]. This protein can be detected in viral encephalitis, Hashimoto's encephalitis, amyotrophic lateral sclerosis, and other types of dementia. Besides 14-3-3 protein, markers such as neuron specific enolase, amyloid beta, tau protein, astrocytic protein S 100 and neopterin are being investigated [6]. In early stages EEG may show

diffuse slowing, and frontal rhythmic delta activity. Periodic biphasic or triphasic, synchronized sharp wave complexes occuring during middle or late stages of disease are typical and found 90% of the patients[7]. EEG changes are absent in the terminal changes when the myoclonus are absent.

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. Hyperintensities in posteromedial aspects of thalami is known as pulvinar sign. Conventional MRI sequences may not show characteristic changes in 21% cases of CJD, though changes are seen in DWI sequences. Shiga et al. revealed 92.3% sensitivity and 93% specificity for DW MRI in their patients with definitive (n = 9) and probable (n = 36) diagnoses of CJD [8]. Recent studies demonstrated that even in very early stages of the disease pathological findings can be detected with DW MR [8-11]. Definitive diagnosis of CJD requires neuropathological examinations.

Spongiform alterations, astrogliosis and neuronal losses are detected in brain tissues obtained with biopsy or post-mortem sampling.

CONCLUSION

According to diagnostic criteria of World Health Organization (WHO) for the probable diagnosis of CDJ, the presence of at least one criterion among typical EEG findings and 14-3-3 positivity for CSF samples or at least 2 criteria among myoclonus, visual disturbances, cerebellar, pyramidal or extrapyramidal findings and akinetic mutism together with progressive dementia are required. [12]. Among these criteria pathological EEG findings and the presence of 14-3-3 protein in CSF samples were mentioned without considering MR findings. We thought that DW MRI should be appropriately considered among diagnostic armamentarium, because it is a non-invasive screening tool with higher sensitivity and specificity than biopsies.

Patients who have progressive dementia and associated atypical features should be investigated especially with DW MRI. Cortical ribboning is a very useful diagnostic sign for CJD.

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