Creutzfeldt-Jakob Disease in Nonagenarian: A Rare Presentation from India

Sir,

Creutzfeldt-Jakob disease (CJD) is a transmissible, progressive, and fatal human prion disease. It is divided into four categories: sporadic (sCJD), familial (fCJD), variant forms (vCJD), and iatrogenic (iCJD). sCJD accounts for 85-95% of total CJD cases and the incidence is about 1–1.5 people per million annually; 10% of CJD cases are familial CJD, and iatrogenic and variant forms compose of 2–5% CJD cases[1] A recent study from south India by Divya *et al*.[2] suggest that the mean onset age of sCJD is 59 years, and most of the cases are distributed within the age group between 43 and 75 years. sCJD in patients aged beyond this age limit are rare.[3] The clinical features such as myoclonus, visual disturbances, cerebellar, and pyramidal/extrapyramidal signs. The disease course follows rapid progression of cognitive and functional impairment toward akinetic mutism in the late stage, and eventually death, most often within 12 months of the disease onset[2] Cases of elderly sCJD have been reported in the literature, although the presentation around the age of hundred is probably the first from India. We present here a case of sCJD at the age of 99 with typical clinical and radiological features of sCJD.

A 98-year-old retired farmer, non-smoker, non-alcoholic, and enjoying his daily routine activities with his family was referred to our hospital for evaluation of rapidly progressive dementia for last 10 weeks. History from the son revealed that initially patient had progressive short-term memory loss and it was associated with emotional liability. Then patient developed cognitive dysfunction in the form of repetition of words, inability to recognize familiar objects, inability to perform his daily routine activities, and inability to dress/undress himself. Soon patient developed gait and stance unsteadiness around 3 weeks prior to presenting to us. It was rapidly followed by development of tremulousness in both hands, particularly while reaching for a target. On detailed questioning, his son admitted the presence of intermittent brief rapid involuntary focal and generalized jerks suggestive of myoclonic jerks. Three to four days prior to admission, his higher mental function deteriorated severely enough amounting to akinetic mute state.

The son denied any history of fever, vomiting, trauma, seizure, any drug intake or intake of raw meat or brain matter. Past history and family history were not contributory. His general examination was unremarkable.

On neurological examination, he was drowsy and disoriented. Speech was not accessed as patient was mute. Patient had normal extra-ocular movement and pupils. Although there was no facial asymmetry, difficulty in swallowing was noted. He was moving all his extremities equally and found to have rigidity in all limbs. Postural and action tremors and focal intermittent myoclonus emerging spontaneously and response to auditory or tactile stimuli were observed. Deep tendon reflexes were brisk and planter reflexes were flexor bilaterally. Though detailed higher mental functions, cranial nerve, sensory, or cerebellar examination was not possible, there was no overt cranial nerve, sensory deficit. There were no meningeal signs.

He was investigated thoroughly; his routine blood count, metabolic parameters, thyroid function tests were normal. Anti-nuclear and anti-TPO antibodies levels were negative. CSF cytology and biochemical parameters were within normal limits and culture of CSF was negative. Paraneoplastic and autoimmune encephalitis antibody in CSF were absent. CSF for neurotrophic viruses were also negative. Tests for syphilis, HIV, vitamin B12, erythrocyte sedimentation rate, and homocysteine levels were all normal. Brain MRI showed extensive high intensities with restricted diffusion in the bilateral cortex, more on left side and left caudate nucleus in diffusion-weighted imaging (DWI), resembling ribbon pattern. [Figure 1] An EEG showed diffuse slowing of background activity with periodic sharp wave complexes along with intermittent triphasic waves. [Figure 2]. The closest differential diagnosis of hepatic encephalopathy has been ruled on the basis of normal serum ammonia, liver function test, absent Hepatitis B and C-reactive protein and negative history of alcoholism.

Based on the CDC criteria, this case was diagnosed with probable sCJD with the key findings of rapidly progressive dementia, multimodal myoclonus, cerebellum symptoms, extrapyramidal signs, and a kinetic mutism with typical MRI and EEG findings. Protein 14-3-3 was not send due to patient's unaffordability and unwillingness.

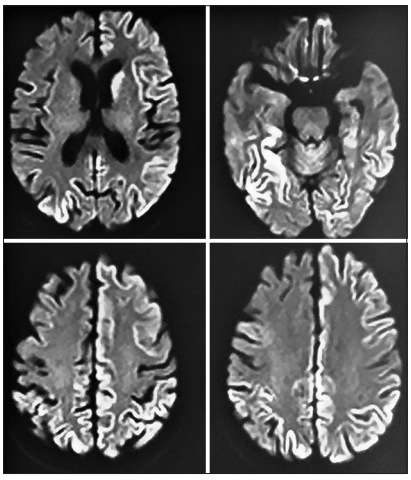

Figure 1: Diffusion-weighted imaging (DWI) showed increased abnormal signal intensities with restricted diffusion in the cerebral cortex bilaterally (Left > Right) and left caudate nucleus

Table 1: Sporadic Cjd

Definitive	Probable	Possible
Diagnosed by standard neuropathological techniques; and/or immunocytochemically; and/or Western blot confirmed protease-resistant PrP; and/or presence of scrapie-associated fibrils.	Neuropsychiatric disorder plus positive RT-QuIC in cerebrospinal fluid (CSF) or other tissues OR Rapidly progressive dementia; and at least two out of the following four clinical features: Myoclonus Visual or cerebellar signs Pyramidal/extrapyramidal signs Akinetic mutism AND a positive result on at least one of the following laboratory tests a typical EEG (periodic sharp wave complexes) during an illness of any duration a positive 14-3-3 CSF assay in patients with a disease duration of less than 2 years High signal in caudate/putamen on magnetic resonance imaging (MRI) brain scan or at least two cortical regions (temporal, parietal, occipital) either on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR) AND without routine investigations indicating an alternative diagnosis.	Progressive dementia; and at least two out of the following four clinical features: Myoclonus Visual or cerebellar signs Pyramidal/extrapyramidal signs Akinetic mutism AND the absence of a positive result for any of the four tests above that would classify a case as "probable" AND duration of illness less than two years AND without routine investigations indicating an alternative diagnosis

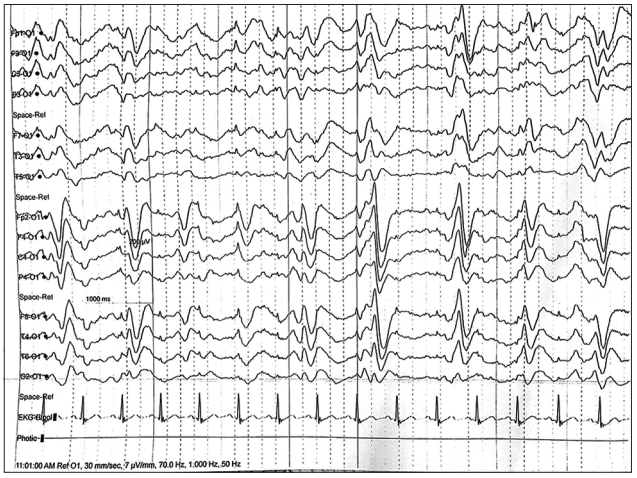

Figure 2: Periodic synchronous triphasic sharp wave complex in electroencephalography

Once the diagnosis and prognosis were conveyed to our patient's relatives, they decided to take him back to a local hospital for terminal care. The details of the follow-up, therefore, could not be obtained in this case.

CJD belongs to a group of prion diseases also known as transmissible spongiform encephalopathies. It constitutes around 85% of all cases of prion diseases.[4] The clinical features such as myoclonus, visual disturbances, cerebellar, and pyramidal/extrapyramidal signs. The disease course follows rapid progression of cognitive and functional impairment toward akinetic mutism in the late stage, and eventually death, most often within 12 months of the disease onset.[5] Based on the CDC criteria for sCJD [Table 1], this case was diagnosed with probable sCJD with the key findings of rapidly progressive dementia, multimodal myoclonus, cerebellum symptoms, extrapyramidal signs, and a kinetic mutism with typical MRI findings EEG findings. Protein 14-3-3 was not send due to patient's unwillingness. In contrast to other neurodegenerative diseases, sporadic Creutzfeldt–Jakob disease (sCJD) is rarely diagnosed in patients older than 75 years. Data describing the characteristics of sCJD in the very old are rare and inconclusive. Older patients showed a faster disease progression represented by an earlier point of diagnosis and a shorter survival time. In the early stages of disease, older patients presented slightly more often with dementia or dysarthria whereas disorders of the extrapyramidal and visual system were more common in the younger group.[6] Overall, sCJD is a rapidly progressive, fatal neurodegenerative disease that can present in a variety of ways and is difficult to diagnose in elderly considering the wide array of differential illness presenting at this age and disease itself present rarely above the age of 90. This case highlighted the need for clinical vigilance to search for this disease even in nonagenarian if the patient present with rapidly progressive dementia. Repeated assessments and diagnostic testing maybe required.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 18-Oct-2020 **Revised:** 22-Nov-2020
Accepted: 01-Jan-2021 **Published:** 14-Dec-2021

DOI: 10.4103/aian.AIAN_1069_20