A case report on Creutzfeldt-Jacob disease: early diagnosis through multidisciplinary lens

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ABSTRACT

Background: Creutzfeldt Jacob disease is a rapidly progressive neurodegenerative disorder, which is invariably fatal and results in death within 1 year of onset. The patient presents with a variety of non-specific neuropsychiatric symptoms, such as myoclonus, cerebellar symptoms, visual impairment, and behavioral abnormalities. The symptoms are rapidly progressive and cause early functional impairment in the patient.

Case Presentation: In this report, we discussed a case of 49-year-old male presented with multiple neuropsychiatric symptoms. After a series of extensive diagnostic examinations and follow-up, the patient was diagnosed as having probable sporadic Creutzfeldt-Jakob disease based on 2018 Centres for Disease Control and Prevention criteria, with key findings of myoclonus, behavioral and cerebellar problems, visual abnormalities, abnormal hyperintensity signals on diffusion-weighted magnetic resonance imaging and characteristic electroencephalogram waves. CSF 14-3-3 protein was significantly high.

Conclusion: Sporadic CJD is a rare and fatal rapidly progressive neurodegenerative disorder, that claims prompt and precise diagnosis to help clinicians distinguish it from potentially treatable neuropsychiatric disorders. This aspect elevates the significance of our report, as it aids not only the medical professionals but also the affected families. Early diagnosis enables the family to prepare for the disease course and appropriate management strategies.

Keywords: Case report, sporadic Creutzfeldt-Jakob disease, prion disease, rapidly progressing dementia, fatal neurodegenerative disorder.

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Background

Creutzfeldt-Jakob disease (CJD) is a transmissible spongiform encephalopathy that manifests as rapidly progressive dementia and causes devastating consequences like death usually within a year from symptom onset [1,2]. CJD has a global incidence of approximately 1 to 2 cases per million [3]. This rare and fatal brain disorder, characterized by fast cognitive decline and rapidly progressive neurological deterioration, presents a real challenge in both diagnosis and treatment. There are comprehensive studies on CJD, digging into its etiology, pathogenesis, clinical manifestations, diagnostic modalities, therapeutic approaches, and ongoing research endeavors. The different facets of this complex disorder are being investigated through a multidisciplinary lens including neurology, neuroradiology, neuropathology, genetics, epidemiology, and public health [4]. Four types of CJD have been described: sporadic(sCJD), which accounts for 85%-90% of cases [5]. Other forms of CJDs are variant, familial, and iatrogenic. Every form of CJD has some unique features. It needs to be navigated through the labyrinth of CJD's clinical presentation, from the subtle cognitive changes to the profound neurological deficits and death within a year of onset [6]. Different phenotypic variants of sCJD are the amyotrophic variant (initial presentation: amyotrophic lateral sclerosis-like), [7] Brownell-Oppenheimer variant (cerebellar ataxia as initial presentation), Heidenhain variant (initial visual symptoms such as visual hallucinations, impaired visual acuity and distortions of shapes and colors), and Stern-garcin variant: (initial presentation: extrapyramidal features) [8,9]. Moreover, the intricate landscape of CJD poses challenges to diagnosis due to its rarity, variety of presentation, and the limitations of current diagnostic modalities. From clinical assessment and neuroimaging techniques to cerebrospinal fluid (CSF) analysis and electroencephalography, several tools are available to clinicians in their quest to disentangle the diagnostic puzzle of CJD [10,11]. Furthermore, the therapeutic options of CJD are also required to be explored, although the disease is invariably fatal with a mean

survival of 7 months. Despite the lack of disease-modifying therapies, clinicians are exploring emerging avenues of research, from immunotherapeutic approaches to different novel pharmacological agents, offering a twinkle of hope in the pursuit of effective treatments for CJD [12].

Here, we report a unique case of CJD, where the patient's progressive neurological deterioration has led to an early diagnosis of the disease by a multidisciplinary approach.

Case Presentation

A 49-year-old male presented with complaints of difficulty in walking associated with impaired balance, and jerky movement in left lower and upper limbs for 5 days followed by jerky movements in right upper and lower limbs for 2 days associated with restlessness and agitated behavior with altered mental status. He had a recent history of double vision and vertigo in the last 15 days. His past medical history was non-contributory to the clinical presentation. However, he has a few comorbidities such as type 2 diabetes mellitus and hypertension. He got his blood sugar tested and his HbA1c came as 9.3. He was admitted to Apollo Multispeciality Hospital, Kolkata, for a re-evaluation. He had no history of any previous surgeries, and his family history was significant for fatal leukemia in his mother, but there was no family history of dementia or prion disease. He had no known allergies. There was no recent travel history or exposure to raw livestock or brain matter. He was an engineer by profession, working in Punjab, India. On doing a physical examination, he had significant anomic aphasia and apraxia. His muscle tone was normal in all four extremities and his power was also 5/5 in all four extremities. His cranial nerves were grossly normal. He had normal sensation and normal coordination. His reflexes were symmetric and no Babinski reflexes were demonstrated. He had a slow but non-ataxic gait. He was able to complete the Mini-Mental State Examination. His blood work included a basic metabolic profile, complete blood count, thyroid profile, liver studies, lactic acid, erythrocyte sedimentation rate, vitamin B1, B12, and folate levels, human immunodeficiency virus, angiotensin-converting enzyme levels, and ceruloplasmin; all came normal. Serum tests for pyruvate kinase, Purkinje cell antibody screen, anti-jo antibody, and anti-Hu antibody were also normal. Serum ammonia was sent which was within normal limits. CSF studies were also performed for oligoclonal bands, autoimmune encephalitis panel, neuromyelitis optica (NMO), and myelin oligodendrocyte glycloprotein (MOG). A serum paraneoplastic panel has also been sent. CSF 14- 3- 3 was also sent. A non-contrast magnetic resonance imaging (MRI) of her brain was significant for global parenchymal loss. Relatively asymmetrical areas of subtle diffusion restriction and FLAIR hyperintensities were noted involving the bilateral caudate nuclei, bilateral putamina, bilateral frontal cortical region (right > left), right fronto-parietal parasagittal location, right posterior cingulate gyrus, and right parieto-occipital cortex (Figure 1a-h).

His PET CT was done which showed moderate to severe large areas of hypometabolism in the bilateral occipital cortex, right frontal and parietal cortex, bilateral posterior cingulate cortex, severe hypometabolism in the right thalamus, bilateral basal ganglia, and right mesial temporal lobe (Figure 2a-d).

He was administered intravenous immunoglobulin (IVIG) with the possibility of autoimmune encephalitis after explaining to the patient's attendant the nature of the disease and costs related to treatment and the need for starting IVIG with its outcome on the overall disease score. His venereal disease research laboratory (VDRL), anti-nuclear antibody, ANCA, ANTI MOG, and ANTI NMO came negative. His serum paraneoplastic and autoimmune encephalitis panel were negative. Cell counts, glucose, and protein were within normal limits. Toxoplasma gondii, Leptospiral antibodies were negative. An electroencephalogram (EEG) was done and it showed background slowing in the delta-Theta range with an intermittent transient triphasic wave, moreover right hemisphere (Figure 3). He had aspiration pneumonia with a WBC count of 11,600 for which appropriate treatment was started. His H1N1 and COVID tests were negative. As his Glasgow comma score deteriorated to E2V1M3 along with pooling of secretion, he was planned for airway

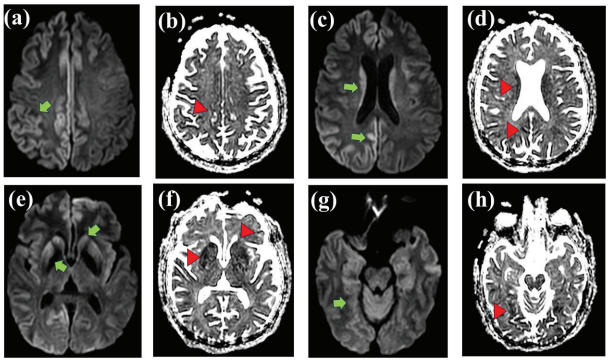

Figure 1. *Non-contrast MRI BRAIN demonstrates hyperintensities on DWI sequence (green arrow) in (a)Right parieto-occipital (c) Body of right caudate nucleus and posterior cingulate gyrus (e)Bilateral putamina and (g) Right mesial temporal lobe. It shows hypointensities on ADC map (red arrow head) in (b) Right parieto-occipital, (d) Body of right caudate nucleus and posterior cingulate gyrus, (f) Bilateral putamina, and (h) Right mesial temporal lobe. This represents diffusion restriction.*

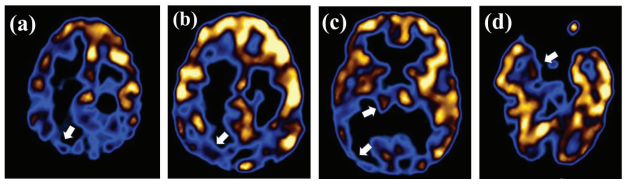

Figure 2. *18 FDG PET-CT shows hypometabolism in (a) Right frontal lobe, (b) Right parieto-occipital, (c) Right thalamus and right parieto-occipital, and (d) Right mesial temporal lobe*

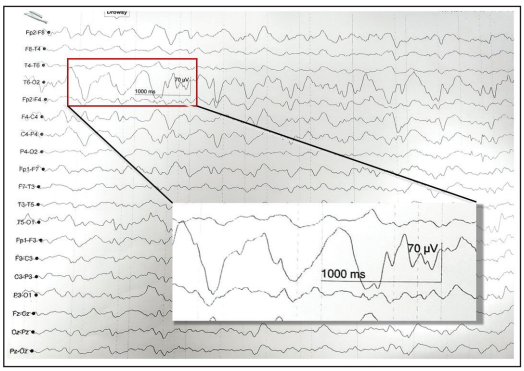

Figure 3. *EEG showing background slowing in the delta-Theta range with intermittent transient triphasic waves.*

protection (intubation or ventilation followed by tracheostomy) but as his neurological status did not improve, so a repeat MRI brain was done which showed no significant change. His CSF 14-3-3 came positive (>2 ng/ml, normal value <1 ng/ml).

Discussion

CJD is a fatal neurodegenerative disorder caused by an abnormal host-encoded protein called prions [13]. Varying presentation and lack of knowledge make it tough and challenging to diagnose a case of CJD [14]. Confirming prion protein at autopsy or on a brain biopsy is considered the gold standard and conclusive method but is an invasive technique. Therefore, a resource-limited CJD can be diagnosed through meticulous clinical analysis and non-invasive diagnostic workup.

Considering the Centre for Disease Control and Prevention (CDC) criteria for CJD (given below), our case fulfilled the criteria of that of a "*Probable case"* of sporadic CJD (Table 1).

Our patient exhibited multiple neuropsychiatric symptoms such as cognitive decline and myoclonus along with behavioral abnormalities and higher cortical dysfunctions such as aphasia and apraxia. Signs of cerebellar involvement such as impaired balance, vertigo, and double vision were also seen in the patient. According to Schröter et al. [16] FLAIR, and T2-weighted hyperintensities involving the cerebral cortex, corpus striatum, caudate head, and putamen are some of the most common presentations of sporadic CJD on MRI [16]. A combination of isolated cortical hyperintensity and cortical and deep gray matter (basal ganglia) hyperintensity are two patterns of DWI and/or FLAIR abnormality that have been well described [17]. Another study also demonstrated that 95% of CJD cases show signal abnormality in at least three out of four discrete areas, including the insula, cingulate gyrus, superior frontal gyrus, and occipital gyrus [18]. Similarly, our patient on DWI showed restricted cortical diffusion on parieto-occipital, cingulate gyrus, bilateral parietal, and mesial temporal lobe (Fig 1a-h). Another major advantage of using DWI sequences is that they rule out typical

Table 1. *CDC's diagnostic criteria for CJD, 2018 [15].*

DEFINITE
• Diagnosed by standard neuropathological techniques; and/or immunocytochemically; and/or Western blot confirmed protease-resistant PrP; and /or presence of scrapie-associated fibrils.
PROBABLE
• Neuropsychiatric disorder plus positive real-time quaking-induced conversion in CSF or other tissues OR • Rapidly progressive dementia; and at least two out of the following four clinical features: 1) Myoclonus 2) Visual or cerebellar signs 3) Pyramidal/extrapyramidal signs 4) Akinetic mutism AND a positive result on at least one of the following laboratory tests 1) a typical EEG (periodic sharp wave complexes) during an illness of any duration 2) a positive 14-3-3 CSF assay in patients with a disease duration of less than 2 years 3) High signal in caudate/putamen on 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.
POSSIBLE
• Progressive dementia; and at least two out of the following four clinical features: 1) Myoclonus 2) Visual or cerebellar signs 3) Pyramidal/extrapyramidal signs 4) Akinetic mutism AND the absence of a positive result for any of the four tests mentioned above that would classify a case as "probable" AND duration of illness less than 2 years AND without routine investigations indicating an alternative diagnosis.

imaging findings of stroke and confirm the presence or absence of an alternative differential diagnosis. According to many studies, the presence of 14–3-3 protein in CSF is considered a complementary test rather than a diagnostic test for prion disease. CSF tau protein levels (>1,150 picogram/ml) have superior accuracy and specificity as compared to 14-3-3 protein as a diagnostic test [19]. Due to financial constraints of the patient party only underwent a 14-3-3 CSF protein test which gave a positive result. EEG was also performed which showed background slowing of delta-theta waves with intermittent and transient triphasic morphology (Fig 3) [20]. Taking into consideration the above features our case fulfilled the diagnostic criteria of sporadic CJD which consists of progressive dementia, with at least two out of the four clinical signs (myoclonus, visual or cerebellar impairment, pyramidal or extrapyramidal dysfunction, and atypical mutism) along with

atypical EEG pattern and identification of CSF protein 14-3-3. In addition, on doing PET CT, our patient showed moderate to large areas of hypometabolism (Figure 2a-d). According to many studies [18F], fluorodeoxyglucose positron emission tomography (FDG-PET) is said to be a sensitive investigation in CJD and could be used to differentiate CJD from other neurodegenerative disorders [10]. Before proceeding to the diagnosis, we ruled out other vascular, ischemic, infectious, toxic, metabolic, auto-immune, metastatic, neoplasm-related, iatrogenic, systemic, seizures, and demyelinating causes of rapidly progressive dementia, on the basis of clinical presentation and relevant investigations which were available in our hospital [21]. To conclude cortical diffusion-restriction with positive CSF protein and atypical EEG workup along with PET hypometabolism is a multidisciplinary approach which if used efficiently is an important tool in suspecting prion disease.

Conclusion

Sporadic CJD is a rare and fatal rapidly progressive neurodegenerative disorder, that claims prompt and precise diagnosis to help clinicians distinguish it from potentially treatable neuropsychiatric disorders. This aspect elevates the significance of our report, as it aids not only the medical professionals but also the affected families. Early diagnosis enables the family to prepare for the disease course and appropriate management strategies.

What is new?

Sporadic Creutzfeldt Jacob disease is a rare and fatal rapidly progressive neurodegenerative disorder, which claims prompt and precise diagnosis to help clinicians distinguish it from potentially treatable neuropsychiatric disorders. This aspect elevates the significance of our report, as it aids not only the medical professionals but also the affected families. As it is a relatively rare disease, reporting this case helps clinicians to understand further what to expect as clinical presentation and how to diagnose early by a small seed of suspicion.

List of Abbreviation

CJD	Creutzfeldt-Jakob disease
DWI	Diffusion weighted imaging
EEG	Electroencephalogram
FDG PET CT	Fluorodeoxyglucose positron emission tomography
GCS	Glasgow comma score
IVIG	Intravenous immunoglobulin
MMSE	Mini mental State Examination
MOG	Myelin oligodendrocyte gycloprotein
MRI	Magnetic resonance imaging
NMO	Neuromyelitis optica
RT-QuIC	Real-time quaking-induced conversion

Conflict of interest

The authors declare that they have no conflict of interest regarding the publication of this report.

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Consent for publication

Informed consent was obtained from the patient.

Ethical approval

Ethical clearance was taken from the Institutional committee.

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References

1. Kobayashi T, Miyata Y. Early symptoms of Creutzfeldt-Jacob disease mimicking alcohol-related disorder. Psychogeriatrics. 2009;9(3):143–6. https://doi.org/10.1111/j.1479-8301.2009.00275.x
2. Asher DM, Gregori L. Human transmissible spongiform encephalopathies: historic view. Handb Clin Neurol. 2018;153:1–17. doi: 10.1016/B978-0-444-63945-5.00001-5
3. Rong LL, Lannen NJ, Tank EC, Feistel JL, Therasse CJ, Potluri A, et al. Case report: two clusters of Creutzfeldt-Jakob disease cases within 1 year in West Michigan. Front Neurol. 2023 Mar;14:1134225. https://doi.org/10.3389/fneur.2023.1134225
4. Koeller KK, Shih RY. Viral and prion infections of the central nervous system: radiologic-pathologic correlation: from the radiologic pathology archives. Radiographics. 2017;37(1):199–233. https://doi.org/10.1148/rg.2017160149
5. Shi Q, Chen C, Xiao K, Zhou W, Gao C, Gao L, et al. Characteristics of different types of prion diseases - china's surveillance. China CDC Wkly. 2022;4(33):723–8.
6. Gençer AG, Pelin Z, Küçükali CI, Topçuoğlu ÖB, Yilmaz N. Creutzfeldt-Jakob disease. Psychogeriatrics. 2011 Jun;11(2):119–24. https://doi.org/10.1111/j.1479-8301.2011.00361.x
7. Panegyres PK, Armari E, Shelly R. A patient with Creutzfeldt-Jakob disease presenting with amyotrophy: a case report. J Med Case Rep. 2013 Aug;7(1):218. https://doi.org/10.1186/1752-1947-7-218
8. Appleby BS, Appleby KK, Crain BJ, Onyike CU, Wallin MT, Rabins PV. Characteristics of established and proposed sporadic Creutzfeldt-Jakob disease variants. Arch Neurol. 2009;66(2):208–15. doi:10.1001/archneurol.2008.533
9. Manix M, Kalakoti P, Henry M, Thakur J, Menger R, Guthikonda B, et al. Creutzfeldt-jakob disease: updated diagnostic criteria, treatment algorithm, and the utility of brain biopsy. Neurosurg Focus. 2015 Nov;39(5):E2. https://doi.org/10.3171/2015.8.FOCUS15328
10. Kiliç AK, Kaymakamzade B, Saka E, Tan E. The sole initial imaging finding in creutzfeldt-jacob disease: focal FDG-PET hypometabolism. Noro psikiyatr Ars. 2018 Jul 4;56(3):226–8.
11. Fragoso DC, Gonçalves Filho AL, Pacheco FT, Barros BR, Aguiar Littig I, Nunes RH, et al. Imaging of Creutzfeldt-Jakob disease: imaging patterns and their differential diagnosis. Radiographics. 2017;37(1):234–57. https://doi.org/10.1148/rg.2017160075

12. Papageorgiou SG, Koros C. Rapidly progressive dementia - clinical aspects and management. Eur Neurol Rev. 2011;6(4):238. https://doi.org/10.17925/ENR.2011.06.04.238
13. Ae R, Hamaguchi T, Nakamura Y, Yamada M, Tsukamoto T, Mizusawa H, et al. Update: dura mater graft-associated Creutzfeldt-Jakob disease - Japan, 1975-2017. MMWR Morb Mortal Wkly Rep. 2018 Mar;67(9):274–8. https://doi.org/10.15585/mmwr.mm6709a3
14. Caobelli F, Cobelli M, Pizzocaro C, Pavia M, Magnaldi S, Guerra UP. The role of neuroimaging in evaluating patients affected by Creutzfeldt-Jakob disease: a systematic review of the literature. J Neuroimaging. 2015;25(1):2–13. https://doi.org/10.1111/jon.12098
15. U.S. Department of Health & Human Services. CDC's diagnostic criteria for Creutzfeldt-Jakob disease (CJD). Atlanta, Georgia: Centers for Disease Control and Prevention; 2021 [cited 2022 Sep 07].
16. Schröter A, Zerr I, Henkel K, Tschampa HJ, Finkenstaedt M, Poser S. Magnetic resonance imaging in the clinical diagnosis of Creutzfeldt-Jakob disease. Arch Neurol. 2000 Dec;57(12):1751–7. https://doi.org/10.1001/archneur.57.12.1751
17. Ukisu R, Kushihashi T, Kitanosono T, Fujisawa H, Takenaka H, Ohgiya Y, et al. Serial diffusion-weighted MRI of Creutzfeldt-Jakob disease. AJR Am J Roentgenol. 2005 Feb;184(2):560–6. https://doi.org/10.2214/ajr.184.2.01840560
18. Tschampa HJ, Kallenberg K, Kretzschmar HA, Meissner B, Knauth M, Urbach H, et al. Pattern of cortical changes in sporadic Creutzfeldt-Jakob disease. AJNR Am J Neuroradiol. 2007;28(6):1114–8. https://doi.org/10.3174/ajnr.A0496
19. Collins SJ, Sanchez-Juan P, Masters CL, Klug GM, van Duijn C, Poleggi A, et al. Determinants of diagnostic investigation sensitivities across the clinical spectrum of sporadic creutzfeldt-jakob disease. Brain. 2006 Sep;129:2278–87. https://doi.org/10.1093/brain/awl159
20. Steinhoff BJ, Räcker S, Herrendorf G, Poser S, Grosche S, Zerr I, et al. Accuracy and reliability of periodic sharp wave complexes in Creutzfeldt-Jakob disease. Arch Neurol. 1996 Feb;53(2):162–6. https://doi.org/10.1001/archneur.1996.00550020074017
21. Geschwind MD, Murray K. Differential diagnosis with other rapid progressive dementias in human prion diseases. Handb Clin Neurol. 2018;153:371–97. https://doi.org/10.1016/B978-0-444-63945-5.00020-9

Summary of the case

1	**Patient (Gender/Age)**	49 years/Male
2	**Final diagnosis**	Probable case of sporadic CJD
3	**Symptoms**	Cognitive decline, myoclonus with behavioral abnormalities and higher cortical dysfunctions like aphasia and apraxia. Impaired balance, vertigo, and double vision.
4	**Medications**	Symptomatic management and palliative care
5	**Clinical procedure**	No evidence of surgery. MRI and PET/CT imaging. CSF study and EEG.
6	**Specialty**	Neuroradiology