Case Report | Journal of Anaesthesia and Critical Care Case Reports | 2024 May-August; 10(2): 01-03

Creutzfeldt–Jakob Disease, a Diagnostic Challenge and Management in ICU: A Case Report

Arshad Zia[1], Srivastava Vinod[1], Singh Digvijay[2], Prakash Ravi[1], Singh Gyan P[1], Prabha Rati[1]

Abstract

Prion disease is a group of neurogenerative disorders caused by misfolding of prion proteins into abnormal proteins. It is presented with multiple central nervous system-related disorders such as decreased cognitive function, movement disorder, seizure, speech problems, dementia, visual blurring, and limb weakness. It is rapidly progressive and highly fatal with an annual incidence of about one per million all over the world. A 65-year-old lady presented in our hospital with all the above mix-up complaints in poor general condition. All workups relevant to the above scenario were done to find the diagnosis. All possible metabolic cause was ruled out; however, magnetic resonance imaging of the brain led to suspicion of Creutzfeldt–Jakob disease. Electroencephalogram was done further to make this diagnosis confirm. The patient responded to the general supportive treatment and discharge with stable and improved status.

Keywords: Creutzfeldt-Jacob disease, Prion, Intensive care unit, Electroencephalogram, Dementia.

Introduction

Creutzfeldt–Jakob disease (CJD) is a progressive neurogenerative disorder of human beings which is rare and fatal. It is either sporadic (90%), genetic (5–10%), or another iatrogenic variant (<1%), and annual incidence is about one per million [1]. The cause of this disorder is basically the alteration of prion protein to abnormally shaped prion protein (PrPC to PrPSc). The sporadic form of the disease is mainly due to misfolding of prion protein because of the aging process of cellular machinery, so the usual age of manifestation is in the elderly group [2]. In addition to abnormal prion protein accumulation in the brain, CJD is characterized by spongiform change, neuronal loss and gliosis. Early symptoms include memory loss, behavior abnormality, impaired coordination, and visual disturbance. Later, it is complicated by dementia, involuntary movements, limb paresis, blindness, and sometimes coma. Duration of disease varies from weeks to years and once it is diagnosed usually fatal in 2–3 months. Diagnosis can be made by magnetic resonance imaging (MRI) brain, cerebrospinal fluid examination, and electroencephalogram [3, 4]. Although there is no specific and characteristic finding in MRI, diffuse-weighted imaging (DWI) sequences are mostly sensitive and informative in the aspect of diagnosis and showing "cortical ribbon sign" [5]. There is no specific treatment regarding CJD, opioids can be used for pain control, and sodium valproate and clonazepam used for involuntary movement [6].

Case Report

We reported a case of 65-year-old lady presented in the emergency department of the institute with abnormal body movement, memory loss with altered sensorium, and fever on and off. She has developed all these symptoms for the past 2 months which were progressive in nature. After initial resuscitation, she was shifted to our intensive care unit. After starting supportive treatment, she was properly evaluated and examined.

According to the history given by the patient's relative, she was a known case of diabetes and hypothyroidism and was on regular medication for the past 7–8 years. The first symptom noticed by a relative was forgetfulness about 2 months back which was limited to daily routine activities. Later, she developed some abnormal body movements with a decline in cognitive function. All symptoms were progressive in nature for which she has taken consultation in the past 2 months. She had also complained of weakness in all four limbs and decreased vision.

She was managed conservatively with a high-flow nasal cannula. The patient was given antihypertensive (telmisartan 40 mg daily and amlodipine 5 mg daily), antiepileptic (levetiracetam 500 mg BD), anticholinergic (trihexyphenidyl 1 mg TDS), and other supportive treatment. She was also diagnosed to have pneumonia on X-ray findings and was taken care of with oxygen therapy, antibiotics (piperacillin + tazobactam), and azithromycin (500 mg) daily.

All the possible causes of altered sensorium with low Glasgow Coma Scale (GCS) (E3V2M5) were searched out. Metabolic causes such as hypo or hyperglycemia were excluded. Thyroid hormones, serum electrolytes (Na+, k+, Ca++, Mg++, and PO4- -), vitamin B12, liver function test, and folate levels were all within normal limits. Laboratory reports of another routine blood and cerebrospinal fluid

[1]Department of Anaesthesiology, King George's Medical University, Lucknow, Uttar Pradesh, India.
[2]Department of Anaesthesiology, Hind Institute of Medical Sciences, Lucknow, Uttar Pradesh, India.

Address of Correspondence
Dr. Srivastava Vinod,
Assistant Professor, Department of Anaesthesiology, King George's Medical University, Lucknow, Uttar Pradesh, India.
E-mail Id: vinod123.doctor@gmail.com

Submitted: 06/06/2023; Reviewed: 02/07/2023; Accepted: 27/04/2024; Published: 10/08/2024

DOI: https://doi.org/10.13107/jaccr.2024.v10.i02.236

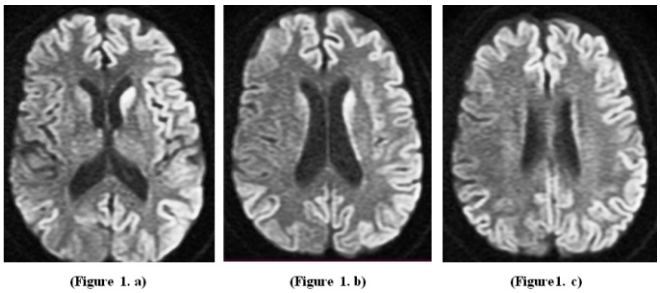

Figure 1: MRI Brain (showing cortical ribboning and hyperintensity of caudate nucleus)

(CSF) were unremarkable. Neurology opinion was taken regarding the above scenario and contrast enhanced computed tomography (CT) head was done.

Neurological findings revealed limb and truncal ataxia as well as myoclonus in the upper limb; however, no visual abnormalities, motor weakness, or parkinsonism was observed. There was no any gross abnormality of CT head in context to low GCS except age-related cortical atrophy. Later, MRI brain was done which revealed cortical ribboning (inverted hockey stick sign) suggestive of CJD. Further, this diagnosis is supported by specific electroencephalogram (EEG) changes. The patient was responding to above-mentioned supportive treatment and she was discharged after improvement with GCS (E4V3M6) and controlled abnormal movement with the advice of regular follow-up and taking prescribed treatment. She also visited in follow-up clinic 1 time after 15 days of discharge and was stable and the same status at which she was discharged.

Discussion

Diagnosis of CJD is very challenging as patients present with symptoms and signs that mimic a typical neurological cause. Although the gold-standard method of diagnosis of CJD can be made by pathological detection of abnormal prion protein deposition in brain tissue. However, a suspected diagnosis can be made by a clinical scenario supported by combined MRI brain finding, EEG finding, and CSF examination.

The mean age of presentation of the disease is around 60 years with no gender preferences. The common features are neuropsychiatric symptoms with classical triad including progressive dementia, myoclonus, and ataxia [7]. Additional features may include behavioral abnormalities with higher cortical function abnormalities, such as aphasia, apraxia, and frontal lobe syndrome. Extrapyramidal signs such as hyperreflexia, extensor plantar response, and spasticity can be met in these patients [8].

Diagnosis of sporadic Creutzfeldt-Jakob disease

Definite:

Progressive neuropsychiatric syndrome **AND** neuropathological or immunocytochemical, or biochemical confirmation

Probable:

I + 2 of II and typical EEG*

or

I + 2 of II and typical brain MRI**

or

I + 2 of II and positive CSF 14-3-3

or

progressive neuropsychiatric syndrome and positive RT-QuIC in CSF or other tissues

I		Rapidly progressive cognitive impairment
II	A	Myoclonus
	B	Visual or cerebellar disturbance
	C	Pyramidal or extrapyramidal signs
	D	Akinetic mutism

+ exclusion of other causes in complete diagnostic workup

Possible:

I + 2 of II + duration < 2 years

Figure 3: Diagnostic criteria based on NCJDRSU and WHO

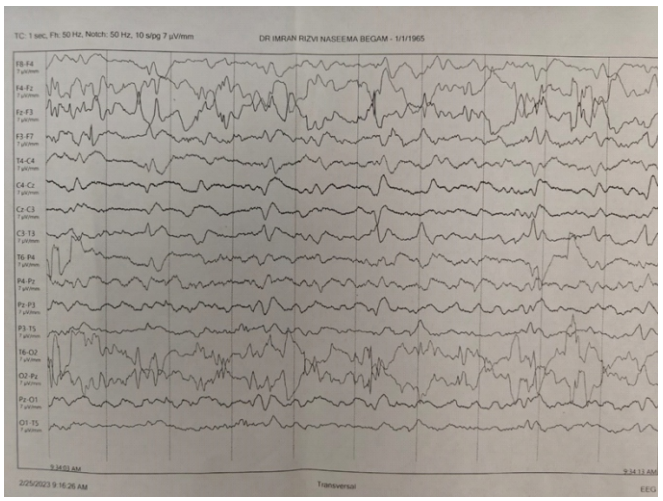

Figure 2: EEG (periodic sharp wave)

MRI brain may show hypertense signal on DWI, fluid-attenuated inversion recovery, and T2-weighted image in the cerebral cortex, corpus striatum, caudate head and putamen nucleus [9, 10]. Similarly, our patient has a high signal intensity in the caudate nucleus and cortical ribboning sign in DWI (Fig. 1).

EEG may also have some characteristic features such as periodic bi- or triphasic sharp wave complexes [11]. Our patients EEG showed periodic sharp occurring at the frequency of 1.5–2 Hz (transverse montage, sensitivity 7 microvolt/mm), a peculiar feature of CJD (Fig. 2).

The presence of CSF TAU protein is more specific for diagnostic purposes than 14–3–3 protein in CSF examination [12]. In our patients, CSF dose does not show any significant finding suggestive of CJD.

The diagnosis of CJD can be made on criteria shown in Fig. 3 which was taken from National CJD Research and Surveillance Unit criteria [13] based on the World Health Organization criteria [14] and later amended by RT-QuIC as an additional biomarker. It is well established that CJD is progressive in nature and worsens with time. Since the patient was improved with supportive treatment, it could be possible that the patient presenting neurological symptoms may be due to the contributory septic component.

Conclusion

CJD diagnosis was made on the basis of clinical scenarios suggestive of CJD. Further, supporting and specific features of MRI and EEG, it was concluded that the patient has sporadic CJD (sCJD) which was conservatively managed and symptomatic improved. Although the condition is fatal and invariably non-curable, early diagnosis makes help in family members to make up for the disease course and possibly give palliative care till survival.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his/her consent for his/her images and other clinical information to be reported in the Journal. The patient understands that his/her name and initials will not be published, and due efforts will be made to conceal his/her identity, but anonymity cannot be guaranteed.
Conflict of interest: Nil **Source of support:** None

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How to Cite this Article

Zia A, Srivastava V, Singh D, Ravi P, Singh GP, Rati P | Creutzfeldt-Jacob Disease, a Diagnostic Challenge and Management in ICU: A Case Report | Journal of Anaesthesia and Critical Care Case Reports | May-August 2024; 10(2): 01-03.