Cognitive impairment - goodness of fit: Case report on intricacies in diagnosis

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Abstract

Sporadic Creutzfeldt-Jakob disease (sCJD) is a rare neurodegenerative disorder characterized by rapid onset dementia and neurological symptoms, often challenging to differentiate from other neuropsychiatric conditions such as Wernicke-Korsakoff syndrome, especially in patients with alcohol dependence. We present a case of a 61-year-old female with a history of alcohol dependence, who initially presented with hallucinatory behaviour, memory impairment, and ataxic gait. Diagnostic evaluation revealed features reflecting Wernicke-Korsakoff syndrome on initial evaluation. However clinical profile, aided with MRI findings were suggestive of sCJD. The overlapping symptoms of sCJD and Wernicke-Korsakoff syndrome constitute a diagnostic dilemma, which gets further complicated with resource constraints for assessment. This case underscores the importance of enhancing our skills as clinician in neurocognitive assessment to locate specific brain network dysfunction to conclude on a brain disorder, among cases presenting with neuropsychological symptoms.

Keywords:

Cognitive Impairment, Wernicke-Korsakoff syndrome; Creutzfeldt-Jakob disease;

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INTRODUCTION

Sporadic Creutzfeldt-Jakob disease (sCJD) is a fatal neurodegenerative disease caused by misfolded prion proteins Scrapie (PrPSc) in the brain affecting 1-1.5 cases per 1,000,000 per year worldwide. [(1)] The classical clinical features of sCJD are rapidly progressive dementia, ataxia, and myoclonic involuntary movements. [(2)] CJD exhibits symptoms similar to other neuropsychiatric illnesses; however, only a few reports have been published concerning the association between CJD and alcohol-related illnesses. CJD complicated by a neuropsychiatric disorder may be difficult to identify from the disorder itself. [(3)] Early clinical symptoms may resemble those of other neurodegenerative diseases like Alzheimer disease and frontotemporal dementia leading to a misdiagnosis or a delayed diagnosis, and thus affecting the management. [(4)]

CASE PRESENTATION

61-years-old female with a significant history of alcohol use with prior diagnosis of Alcohol Dependence Disorder (ADS), presented with hallucinatory behaviour, impaired memory and difficulty in walking for about 4 months. Hallucinatory behavior was observed in the form of self-smiling/self-muttering. The family noted she was forgetting events (especially recent ones) and misplacing items. She was noted to have difficulty in standing, with a tendency to fall down frequently, which later progressed to getting almost bedridden. She was also mostly noticed to be confused and distracted, unable to engage in productive bilateral communication, talking out of context. She also had disturbed sleep and sudden jerky movement of her limbs times and again.

Her vitals were stable. Neurological examination revealed ataxic gait. Mental State Examination revealed increased psychomotor activity, hallucinatory behaviour and impaired recent memory. She appeared drowsy and was unresponsive during most of the assessment.

On initial evaluation, features suggested rapid-onset

dementia. Laboratory investigation showed low Vitamin B12 levels with rest of the blood parameters within normal limits. She was treated with Memantine 5 mg, Quetiapine 25mg and Vitamin B12 supplementation.

After 2 weeks, the patient presented again to our center with aggravation of prior symptoms. A CT scan of the brain was requested, which revealed bilateral basal ganglia calcification, and subtle asymmetrical hypodensity in right subcortical white matter. Thereafter an MRI brain was done that revealed bilateral symmetric T2/FLAIR (fluid- attenuated inversion recovery) hyperintensities involving caudate head, globus pallidus, putamen, insular cortex and dorsomedial thalamic nuclei The hyperintensities appeared like a hockey stick. (which is pathognomonic of CJD) with corresponding high signal intensities on diffusion-weighted imaging (DWI). Electroencephalography (EEG) revealed paroxysmal activities from the left temporoparietal region in the form of spikes, sharp waves followed by slowing involving the entire hemisphere. Unfortunately, tests for CSF markers of sCJD couldn't be performed.

After thorough assessment, diagnosis of Wernicke-Korsakoff syndrome with Alcohol Dependence syndrome with possible dementia of Creutzfeldt Jakob disease and vitamin B12 deficiency was considered. The patient exhibited two out of four, Caine operational criteria (ataxia and confusion), in the background of chronic alcohol use. He also met the probable criteria for sporadic CJD on account of rapidly progressive features of cognitive decline as in dementia, with neurological signs (myoclonic Jerks), high signal bilaterally on DWI and FLAIR imaging supported by abnormal EEG findings.

DISCUSSION

Sporadic CJD is an uncommon disease that presents with rapid onset dementia and, unfortunately, has a poor prognosis. Its overlapping presentation with other common diseases may result in delayed diagnosis. Comorbid Alcohol dependence poses a significant diagnostic challenge in the diagnosis of CJD, as witnessed in this case. [3] .

The presence of rapidly progressive cognitive impairment, cerebellar dysfunction, pyramidal or extrapyramidal signs and akinetic mutism should help us consider sCJD. A thorough history and examination with diagnostic tests including EEG, MRI, and tests for CSF protein markers such as RT-QuIC, neuron-specific enolase, T tau protein, and 14-3-3 protein and neuropathologic examination detecting protease- resistant PrPSc (PrPres) provide a confirmatory clue to the diagnosis of sCJD. [5,6] (Table 1), at state-of-the-art facilities.

SJCD has no effective long term curing treatments available yet [7]. The care and management of affected patients are directed towards symptomatic relief for a better quality of life [8].

Definite:
Progressive neuropsychiatric syndrome and neuropathological or immunocytochemical, or biochemical confirmation
Probable: I + two of II and typical EEG or typical brain MRI or
positive CSF 14-3-3 or progressive neuropsychiatric syndrome and positive
RT-QuIC in CSF or other tissues
+ exclusion of other causes in complete diagnostic workup
Possible:
I + two of II + duration <2 years
I-Rapidly progressive cognitive impairment
II A. Myoclonus B. Visual or cerebellar disturbance
C. Pyramidal or extrapyramidal signs D. Akinetic mutismv

Table 1 : Diagnosis of sCJD Adapted from National Creutzfeldt-Jakob Disease Research & Surveillance Unit criteria13 based on the WHO criteria.[9], [10]

Wernicke-Korsakoff syndrome is a condition caused by a deficiency of thiamine or vitamin B1. Patients classically present with a clinical triad of ophthalmoplegia, altered mental status, and ataxia. [11]. Caine et al, proposed operational criteria for the diagnosis of Wernicke encephalopathy- that requires two out of four features: dietary deficiency (signs such as cheilitis, glossitis, and bleeding gums), oculomotor abnormalities (nystagmus, ,ophthalmoplegia and diplopia), cerebellar dysfunction (gait ataxia, nystagmus), either altered mental state (confusion) or mild memory impairment.[12] Adequate and timely thiamine administration improves the eye movement abnormalities (within days or weeks) and ataxia (may take months to recover), but the effects on memory, in particular, are unclear.[13]

In our case, the patient with the history of chronic alcohol use presented with hallucinatory behaviour, loss of memory and difficulty in walking for 4 months, aggravated

since past 2 weeks. Both conditions, sCJD and Wernicke's Korsakoff syndrome share common symptoms such as ataxia and cognitive impairment, complicating the diagnostic clue. The patient's rapid progression of dementia and specific MRI findings supported a probable sCJD diagnosis. Definitive diagnosis could not be made in this case, owing to overlapping symptoms, limitations with availability and affordability of sophisticated laboratory investigations along with lack of our skills and availability of validated tools for detailed neurocognitive assessment. Such limitations make the process of prognostication more daunting and challenging.

CONCLUSION

Accurate diagnosis makes the task of clinical management easier. There are major overlaps in clinical presentation of various diseases originating from the brain. This overlap poses challenges on timely and accurate diagnosis. Recent advances on tools and techniques for neurocognitive assessment can provide clarity to precisely locate ongoing pathological processes inside the brain, obviating reliance on expensive imaging techniques and laboratory investigations. Training on expanding skills in the domain of neurocognitive assessment and research on various types of cognitive impairment in the cross-cultural aspect is a pressing priority.

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