Case Report

Creutzfeldt-Jakob Disease (CJD) in Southeast Asia: a diagnostic challenge

Anna Misya'il Abdul Rashid, Mohamad Syafeeq Faeez Md Noh, Fan Kee Hoo, Wan Aliaa Wan Sulaiman, Liyana Najwa Inche Mat, Hamidon Basri

Departments of Medicine and Imaging, Universiti Putra Malaysia

Creutzfeldt-Jakob disease (CJD) is a rare disorder that presents with a myriad of symptoms. MRI has a role in providing a clear diagnosis. We report a patient presenting with dementia, pyramidal symptoms and later had myoclonic jerks. He refused lumbar puncture and EEG changes were not typical of CJD. Only on MRI were we able to prove his diagnosis as workup for alternative diagnoses were negative. Supportive treatment proves of utmost importance during the course of illness. (Rawal Med J 201;42:587-589)

Keywords: Creutzfeldt-Jakob disease (CJD), dementia, pyramidal signs

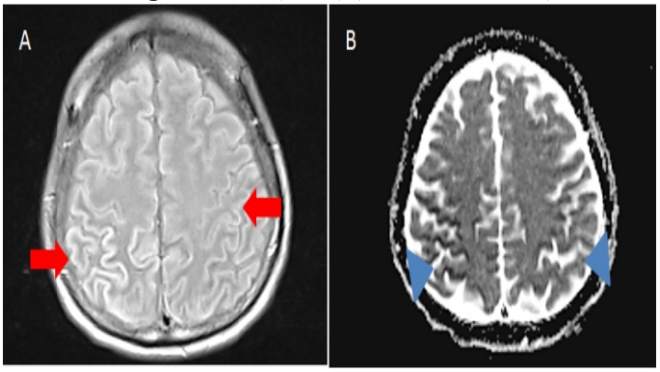
INTRODUCTION

Creutzfeldt-Jakob disease (CJD) is a rare neurodegenerative disorder that leads to rapidly progressing dementia and inevitably, death.[1] It is caused by abnormal folding of scrapie prion protein (PrP^{Sc}) leading to disruption of cellular function; producing characteristic spongio form changes of grey matter and neuronal loss.[2] It can be genetic, sporadic or iatrogenic, although the most commonly seen is sporadic type.[3] Worldwide, incidence is estimated at 1 per million population.[4] However, the incidence of CJD in the region of Southeast Asia is not known as there are no national surveillance programs, thus making epidemiological study of this rare disorder nearly impossible.[4]

CASE PRESENTATION

Patients was previously healthy 61-year-old Malay man who was admitted for aspiration pneumonia secondary to recurrent episodes of choking and difficulty in swallowing. On further history, he had a 2-month history of progressive forgetfulness and altered behaviour. He had fluctuating consciousness level and occasional aggressive behaviour. On clinical examination, he had pseudo-bulbar palsy and myoclonic jerks present predominantly in upper limbs.

Fig. 1A and B. MRI findings, A. Gyral hyper-intensities in the right parieto-occipital and left parietal regions on T2 FLAIR (red arrows) and B. Cortical ribboning seen in diffusion weighted MRI (DWI) (blue arrowheads).



Thyroid function test, vitamin B12, folate, viral screening and VDRL were normal. The cerebrospinal fluid (CSF) protein status was unknown since patient was unwilling to consent for a lumbar puncture. EEG only revealed non-specific slowing pattern. However, MRI brain T2 fluid-attenuated inversion recovery (FLAIR) images showed gyral hyper-intensities in the right parieto-occipital and left parietal regions. Diffusion-weighted (DWI) MRI revealed restriction on diffusion as cortical ribboning (Figures 1A and 1B). He was diagnosed with sporadic CJD based on the clinical history and suggestive MRI findings. Supportive treatment with antibiotics, oral risperidone and nasogastric tube feeding was

commenced. He remains under neurology follow up.

DISCUSSION

The Center for Disease Control and Progression has sought to redefine diagnostic criteria of this disease in 2010 into definite, probable and possible CJD by including MRI findings associated which was not previously included in the WHO criteria (Table 1). However, these presentations are not all present at diagnosis, as the spectrum of symptoms vary from patient to patient, thus rendering definitive diagnosis difficult. Due to the lack of national and regional surveillance programs in Southeast Asia, the actual incidence of this disease is unknown. Literature search in this region only reveals scattered case reports and case series from Singapore, Thailand and Malaysia. This scarcity is made worse by the fact that this disease is not always clinically suspected unless seen by neurologists. Thus, CJD is often misdiagnosed as other more common causes of dementia.

The challenge in diagnosing CJD lies in the fact that its clinical manifestations vary. Patients may not always present with dementia, which is the main clinical prerequisite. There have been reports of patients presenting with stroke like symptoms such as hemiparesis.[5] Others, such as ours, present with pyramidal signs.[5,6] When present, dementia is often mistreated as the commoner etiologies: vascular, metabolic, infectious and vitamin deficiencies which are more common in our region.[1] It is not until later when typical symptoms of myoclonus and akinetic mutism appear that clinicians begin to suspect an alternative diagnosis.

The criteria for definitive diagnosis require histological evidence from brain biopsy, which is not always feasible. Detection of 14.3.3 protein in the CSF supports the diagnosis of sporadic CJD, however its sensitivity is low (44%).[7] Its presence should not be considered pathognomonic as it can also be detected during stroke, encephalitis, hypoxic brain injury, intracranial bleed and Alzheimer's disease.[4,8] Additionally, in the region of Southeast Asia, laboratory diagnosis is limited as CSF examinations for 14.3.3 protein is not always readily available to many healthcare facilities. Even if it is available, not all patients may consent for a lumbar puncture. This is due to social circumstances and financial restrictions as these investigations are often expensive.

Table 1. Center for Disease Control and Prevention's (CDC) Diagnostic Criteria for Creutzfeldt-Jakob Disease (CJD), 2010.

Definite CJD	Probable CJD	Possible
Diagnosed by standard neuropathological techniques; and/or immunocytochemicall y; and/or Western blot confirmed protease-resistant PrP; and /or presence of scrapie-associated fibrils	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	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: • a typical EEG • a positive 14-3-3 cerebrospinal fluid (CSF) assay in patients with a disease duration of less than 2 years • Magnetic resonance imaging (MRI) high signal abnormalities in caudate nucleus and/or putamen on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR)	**AND** the absence of a positive result for any of the three laboratory tests that would classify a case as "probable
		AND duration of illness less than two years
	AND without routine investigations indicating an alternative diagnosis	**AND** without routine investigations indicating an alternative diagnosis

Therefore, a more noninvasive approach is preferable. EEG, where available, allows a diagnosis to be made if characteristic findings of periodic short wave complexes (PSWCs) are found. However, the sensitivity and specificity of EEG is only 32% and 94%, respectively.[7] The typical EEG findings may also be absent during the initial stages and only becomes more apparent with the progression of the disease.[2] This makes diagnosis even more difficult and challenging.

Thus, in recent years, neuroimaging has proved useful as a tool for diagnosis. In 2010, characteristic MRI findings were added to the diagnostic criteria of CJD. Findings of high signal intensity lesions in the striatum (caudate or putamen or both), lesions in the thalamus including the pulvinar, and lesions along the cortical ribbon (cerebral or cerebellar) are accepted as CJD associated MRI changes on DWI and/or FLAIR and/or T2-weighted sequences.[9] Although these findings may be missed due to low suspicion of radiologists and clinicians alike, their presence is highly suggestive of CJD and provides room for prognostication and planning of therapy. The utilization of CT imaging is irrelevant, as it only shows nonspecific atrophy or no abnormality at all.[7] Unfortunately, not all patients in our region have access to neuroimaging such as MRI unless clinically indicated; which is not always the case. Typical symptoms such as akinetic mutism and myoclonus often present later in the course of the disease, and death ensues within months.[6,8]

In summary, due to the rarity of the disease, CJD is not always clinically suspected. The variety of clinical symptoms makes it difficult to recognize and diagnose. Invasive investigations such as lumbar puncture or brain biopsy, along with the associated social taboo and costs may not be feasible in daily practice. MRI, with characteristic imaging findings proves invaluable in aiding the diagnosis of CJD, in addition to a high index of clinical suspicion, as seen in our case.

Author Contributions:
Conception and design: Abdul Rashid AM
Collection and assembly of data: Abdul Rashid AM
Analysis and interpretation of the data: Md Noh MSF, Hoo FK
Drafting of the article: Wan Sulaiman WA
Critical revision of the article for important intellectual content: Inche Mat LN, Basri H
Final approval and guarantor of the article: Abdul Rashid AM
Corresponding author email: Anna Misya'il Abdul Rashid: annamisyail@yahoo.com
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