

# A case of probable sporadic Creutzfeldt-Jacob Disease in a tertiary care hospital in Malaysia

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## SUMMARY

The diagnosis of Creutzfeldt-Jacob disease (CJD) can be challenging as findings are non-specific and there is low awareness of the disease. We present a case of an 83-year-old man with a two months history of rapidly progressive dementia. After a series of extensive diagnostic examinations, he was diagnosed with probable sporadic CJD with key findings of rapidly progressive dementia, myoclonus, pyramidal signs, abnormal hyperintensity signals on diffusion-weighted magnetic resonance imaging (DW-MRI) and typical electroencephalograph (EEG). His symptoms progressively worsened and he died four months after the onset of symptoms.

## INTRODUCTION

Creutzfeldt-Jacob disease (CJD) is a rare, incurable and invariably fatal neurodegenerative disorder. It remains relatively unknown in Malaysia outside of tertiary hospitals with a neurology unit. It carries a grave prognosis, unfortunately has no specific treatment. Creutzfeldt-Jacob disease is increasingly being reported in most countries in Asia as a consequence of the heightened awareness of the disease. However, sporadic CJD may be misdiagnosed as a variety of other illnesses, as it can present with non-specific symptoms and due to various limitations of accessibility to diagnostic investigations. We report a case of probable sporadic CJD in a tertiary centre in Malaysia.

## CASE REPORT

An 83-year-old man presented with two days history of twitching over the left side of his body. He had developed memory impairment, and his concentration had deteriorated for two months; e.g., he could not recall how to get back home after going for his evening walks and forgot how to drive. However, he was able to ambulate. He was easily angered by minor stressful events, and began isolating himself, had minimal conversations with family members and lost interest in reading newspapers which was his hobby previously. He also had difficulty initiating sleep for the last one week before admission. The patient's family reported that he had visual hallucinations as he claimed that he was visualising unearthly creatures. There were abnormal, jerky limb movements on the left side of body for two months, more in the upper limbs, which were intermittent and did not result in significant disability. However, the abnormal, jerky movements progressively worsened, and he began to have

weakness over the same side. There was no history of fever, previous epilepsy, head trauma, recent travel or any significant family history.

At arrival to emergency department, he was not obeying commands, Glasgow Coma Scale was 11/15. He was moving his right upper and lower limbs and had brief myoclonic jerks, predominantly over left upper and lower limbs with slight flexion to pain. There were spontaneous eye movement with no apparent ophthalmoplegia. Pupils were sluggish and startle myoclonus were observed on a few occasions. Cranial nerve examination was unremarkable and there was generalised rigidity, hyperreflexia, clonus and extensor plantar responses, over the left side. The patient was unable to cooperate during Mini Mental State Examination for cognitive assessment. He eventually required nasogastric feeding due to his worsening consciousness level.

Baseline full blood count; renal, liver, and blood chemistry; autoimmune and paraneoplastic screenings, thyroid function test and blood cultures revealed no abnormalities. Chest radiograph and the initial computed tomography scan of his brain were unremarkable. Lumbar puncture was performed. A cerebrospinal fluid 14-3-3 protein immunoassay was done, however, sample sent for analysis was heavily blood stained and could not be interpreted, family members subsequently refused a repeat investigation due to financial burden. Family members were also counselled for a brain biopsy to which they declined.

Brain magnetic resonance imaging (MRI) scan was performed which showed bilateral cortical and deep grey matter changes, with diffusion-weighted/apparent coefficient diffusion (DWI/ADC) changes. An electroencephalography (EEG) was performed, and it showed diffuse, severe cortical dysfunction, with generalised periodic discharges that were mostly over the right cerebral hemisphere.

Considering the clinical history, physical findings and investigations results, the patient was diagnosed as probable sporadic CJD. He was given four different anti-epileptic drugs. He was also empirically treated for meningoencephalitis with intravenous antibiotics. No clinical improvement was observed over the course of one month.

He finally succumbed to his illness four months from the onset of symptoms.

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**Table I: Diagnostic criteria for sporadic CJD based on the Protocol Surveillance of CJD in the UK, National Creutzfeldt-Jakob disease Research & Surveillance Unit (NCJDRSU), University of Edinburgh**

|     |                 |   |
|-----|-----------------|---|
| 1.1 | <b>DEFINITE</b> | Progressive neurological syndrome <b>AND</b><br>Neuropathologically <b>or</b> immunohistochemically <b>or</b> biochemically confirmed   |
| 1.2 | <b>PROBABLE</b> | 1.2.1 I + two of II and typical EEG*<br><b>OR</b> 1.2.2 I + two of II and typical MRI brain scan**<br><b>OR</b> 1.2.3 I + two of II and positive CSF 14-3-3<br><b>OR</b> 1.2.4 Progressive neurological syndrome and positive RT-QuIC in CSF or other tissues |
| 1.3 | <b>POSSIBLE</b> | I + two of II + duration < 2 years<br>I Rapidly progressing cognitive impairment<br>II A Myoclonus<br>B Visual or cerebellar problems<br>C Pyramidal or extrapyramidal features<br>D Akinetic mutism  |

\*Generalised periodic complexes, \*\*High level of signal in the caudate/putamen upon MRI brain scan or at least two cortical regions (temporal, parietal, occipital) either upon DWI or FLAIR

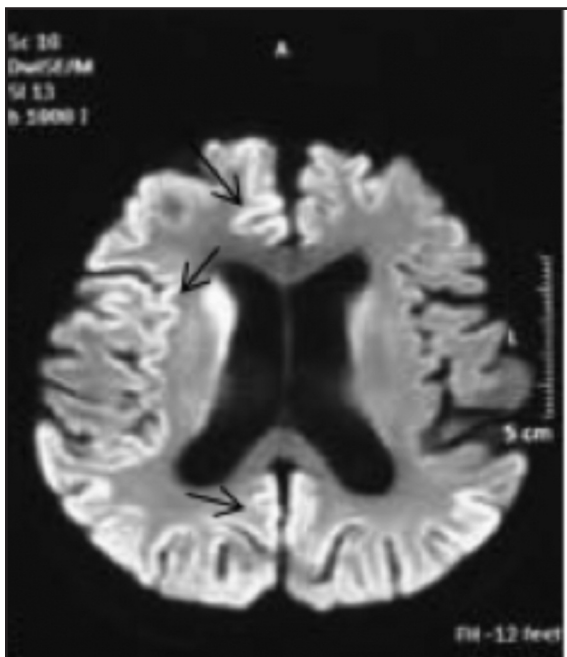


Fig. 1a

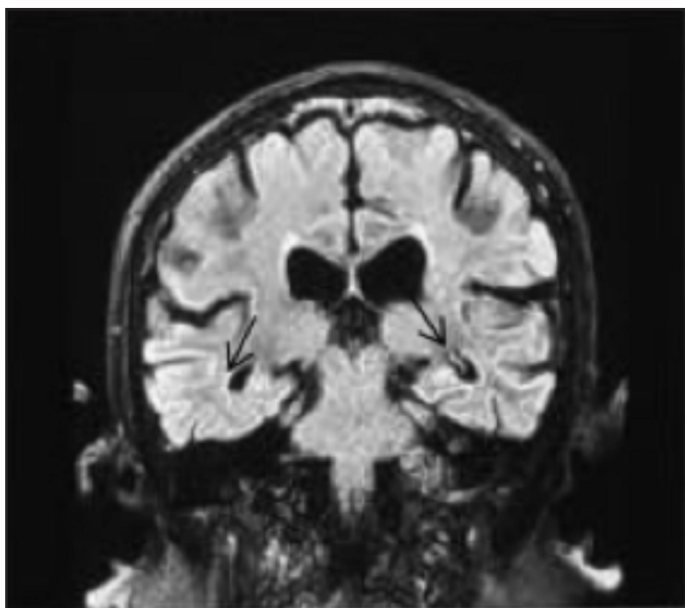


Fig. 1b

**Fig. 1:** a) There is bilateral asymmetric restricted cortical diffusion involving predominantly the right cerebral hemisphere. There is fronto-temporo-parieto-occipital cortical ribboning, including the cingulate gyrus. Further diffusion restriction of the bilateral caudate head and putamen are also noted. There is no white matter involvement. b) There is mild corresponding high Fluid-Attenuated Inversion Recovery (FLAIR) signal intensity in these regions. There is diffusion restriction involving bilateral cortical and deep grey matter area. The pattern of diffusion restriction and abnormality indicate Creutzfeldt-Jakob disease.

**DISCUSSION**

Creutzfeldt-Jakob disease is a fatal progressive prion disease characterized by rapidly deteriorating dementia. Sporadic human prion diseases are seen in 85-90% of cases. Of the remaining cases, 1-2% are the infectious form, acquired from an established source with the prion disease, while 5-15% are the familial autosomal dominant type, which is inherited secondary to the mutation of the prion protein gene localised on chromosome 20.<sup>1</sup>

The hallmarks of CJD are rapidly progressive dementia with myoclonic jerks.<sup>2</sup> In sporadic CJD, there is cerebral atrophy, and increased signal intensity in the putamen, caudate nucleus and cerebral cortex can be detected in imaging studies. Increased signal intensity in the cortex is called ribboning. These characteristic MRI findings are an important clue for an accurate premortem diagnosis. Shiga et al. revealed 92.3% sensitivity and 93% specificity for DW MRI in their patients with definitive (n=9) and probable (n=36) diagnoses of CJD.<sup>3</sup>

In spite of the fact that brain biopsy and cerebrospinal fluid real-time QuIC, which both confer high specificity, were not performed in our patient, the diagnosis of probable sporadic CJD was made as he had rapidly progressing cognitive impairment, myoclonus, pyramidal features, diagnostic DWI MRI and typical EEG. He fulfilled the diagnostic criteria for sporadic CJD, which is believed to be at least 95% accurate.<sup>4</sup> Brain biopsy for the sake of diagnosis would not be recommended, because a diagnosis can be made with a fair degree of confidence without the need for invasive tests and due to the transmissible nature of the disease. Furthermore, family members declined brain biopsy and their decision were respected.

Investigations such as CSF 14-3-3 protein are not readily available in many developing countries in Southeast Asia. The question of whether CJD is actually rarer in Southeast Asia, under-diagnosed or under-reported remains unanswered.<sup>2</sup> Further research and national surveillance is necessary to ascertain the true prevalence of the disease.

#### CONCLUSION

Although sporadic CJD is incurable, it is vital to make an early and accurate diagnosis because other rapidly progressing dementia-causing diseases, such as

paraneoplastic syndrome, Hashimoto encephalopathy, steroid-responsive encephalopathy, autoimmune encephalitis, and viral encephalitis are treatable if detected early.<sup>5</sup> Early diagnosis will allow patients and their family members to prepare for the expected disease course, focusing on the goal of care in helping to improve the patient's quality of life and facilitate end of life care. In our case, the patient's family members had the opportunity to discuss this disease thoroughly and had the freedom to choose how they want to care for the patient.

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