

Creutzfeldt-Jakob disease presenting with unusual psychiatric symptoms: Report of an Asian patient

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Abstract

Creutzfeldt-Jakob disease (CJD) is increasingly being reported over the last three decades from most countries as a result of heightened awareness of the disease. Various studies have been reported with annual incidence of 0.5-1.5 cases of CJD per million of general population. Here we describe a case who is an ethnic Bangladeshi manifested with unusual psychiatric symptoms together with an autopsy proven CJD.

INTRODUCTION

Creutzfeldt-Jakob disease (CJD) is a member of the group of transmissible neurological diseases known as the transmissible spongiform encephalopathies, or prion diseases. These fatal neurodegenerative brain diseases, are caused by the abnormal folding of the infectious agent, or prion protein. The abnormally folded isoform of the host encoded prion protein (PrP^C), designated PrP^{Sc} protein forms toxic aggregates, which after many years of progressive accumulation, cause clinical neuropathology showing spongiform degeneration in the brain.¹ Prion diseases are generally characterised by progressive dementia and ataxia, and once symptoms appear, then mortality is inevitable.

CJD is increasingly being reported over the last three decades as a result of heightened awareness of the disease. Various studies have been reported annual incidence of 0.5-1.5 cases of CJD per million of general population. The incidence of CJD is around 1 per million in the UK. The report from Singapore General Hospital of 5 cases over 2 years, in an island with a population of 4 millions, is consistent with the incidence elsewhere.²

This paper describes the clinical experience with an autopsy proven case of CJD managed at the Department of Clinical Neurosciences, St Bartholomew's Hospital, London, UK, who is an Asian presenting with psychiatric symptom.

CASE REPORT

A 52-year-old ethnic Bangladeshi woman was referred to our Hospital, in October 2003, with a 2 months history of depressive symptoms accompanied by confusion and disorientation. Three months earlier her family members noted her having insomnia, loss of appetite and periodic agitation. She was anxious in some days and had some delusions, especially of guilt and jealousy. Her interest and pleasure in almost all activities diminished remarkably. She was referred to a psychiatrist because of these symptoms and the diagnosis of depression was made and treatment with antidepressants (amitriptyline 75mg/day and haloperidol 15mg/day) was prescribed. Some improvement in symptoms was noted but after a few weeks she deteriorated. Subsequently, her speech and mentation became less and less, and eventually she became mute. She had no significant family history and past medical history.

On examination, she was in catatonic stupor state. There was lack of spontaneous speech or movement, absence of goal-directed behaviour, and rigidity in all body movements. Brain imaging with computed tomography scan and MR imaging were unremarkable. Electroencephalography (EEG) revealed generalized background slowing with a few irregular sharp waves. Biochemical and microbiological studies of cerebrospinal fluid (CSF) were normal. Routine blood counts and chemistries including thyroid function tests were normal.

Psychiatric opinion was consulted and the diagnosis of “bipolar catatonia” was made and electroconvulsive therapy was begun but after three electroconvulsive sessions she deteriorated and was intubated for airway support. During the last few days of admission, spontaneous and startle myoclonic jerks were seen predominantly in the upper extremities. Extraocular eye movements demonstrated full range of movements with impaired smooth pursuit. In the final stage of the disease, the patient lost all mental and physical capacities. The serial EEGs showed generalized periodic sharp waves, 0.5 to 1 Hz, typical for CJD (Figure 1). The patient lapsed into coma and died in November 2003 from bronchopneumonia precipitated by the bedridden and unconscious state.

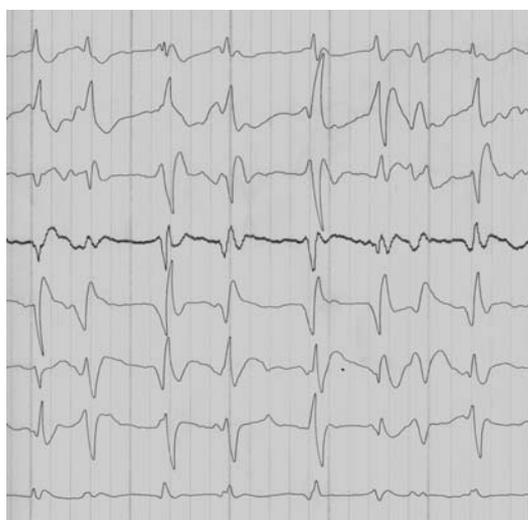


Figure 1: The EEG of patient in late stage of disease shows generalized periodic sharp waves 0.5 to 1 per second and burst suppression, characteristic for CJD.

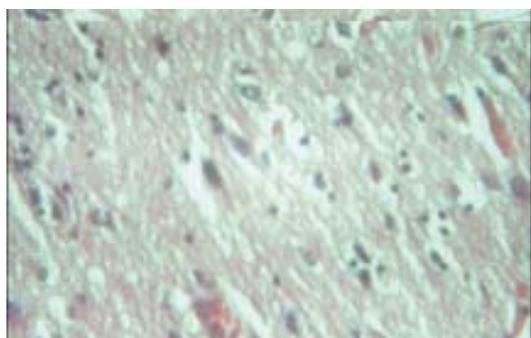


Figure 2: Spongiform encephalopathy: Non inflammatory vacuolization of the cerebral cortex is the dominant alteration evident in the biopsy specimen.

Brain autopsy showed no abnormal macroscopic appearance. Histological examination revealed spongiform transformation of the cerebral cortex consisted of presence of many variable sized vacuoles within the neurophiles and sometimes in the perikaryon of neurons, and occasionally expansion of the vacuolated areas (microcyst like spaces). There was no inflammatory infiltrate (Figure 2).

DISCUSSION

CJD can occur in sporadic, familial and acquired forms; the most common of which is sporadic CJD (80-90%).³ A diagnosis of CJD should be considered when an adult patient develops dementia rapidly and myoclonus. Unfortunately, confirming the diagnosis of CJD has historically been difficult as traditional laboratory tests are ineffective. According to WHO criteria, probable diagnosis of CJD require that the patient has progressive dementia and at least 2 of following 4 clinical features: myoclonus, visual or cerebellar dysfunction, pyramidal/extrapyramidal signs or akinetic mutism; a typical EEG and/or a positive 14-3-3 CSF assay and a clinical duration of less than 2 years before death; and exclusion of alternative diagnoses with routine investigations. For definite diagnosis, in addition to above criteria, one of the two followings should be established: characteristic pathological changes in brain or positive Western blot to confirm the presence of PrP^{Sc}.⁴

The frequency of the prodromal psychiatric manifestations in sporadic CJD ranges between 18-39% with mainly depressive disorders, personality changes, and emotional lability.⁵ In the study of Brown *et al.* the prevalence of myoclonus at the onset of disease was 1%, and in later stages it was 78%.³ Infrequently, the myoclonus may not appear for weeks or even months after the initial mental changes (as observed in our patient). Also the pathognomonic EEG was seen only in the middle and late stages of the disease.

Patients with sporadic CJD may have abnormal patterns of hyperintensity in the basal ganglia on diffusion-weighted MRI sequences, but the specificity and sensitivity of these patterns remain uncertain. Many patients with sporadic CJD have abnormal proteins in their CSF, most notably the 14-3-3 protein. The specificity of this finding may be as high as 95%, but the sensitivity ranges vary from 45 up to 85%.⁶

A definitive diagnosis of CJD has traditionally

required a brain biopsy or autopsy which can detect the characteristic changes in the brain tissue caused by the disease. Because these procedures pose risks to those handling the brain tissue, they are not always performed. Biopsy of the nasal epithelium has recently been reported to be a less invasive and reliable way to obtain tissue for the identification of PrP protein.⁷

CJD may be mistaken for a variety of psychological illnesses because the behavioural changes were seen in 30% of patients at onset of disease and in 57% of patients in later stages.³ There is a limited literature on CJD in Asia, especially from Southeast and South Asia as the disease was under reported or perhaps under diagnosed and misdiagnosed. Many of the patients might not present to hospitals because of the rapidly progressive course, and death usually occurs within a few weeks to a few months. However, CJD is being increasingly reported from various regions in South Asia and at least two cases presented with psychiatric symptoms were reported from Sri Lanka (personal communication, Dr Padma Gunaratne). Five of the 8 cases of Yen *et al.* from Taiwan with CJD had psychiatric symptoms including changes of mood, thought, behaviour and perception during their course of illness. Four cases had been sent to the psychiatric unit and received treatment under different psychiatric diagnoses.⁸ In these cases, it is likely that it was the psychiatrists who will first met CJD patients in the early stages of disease. There might be a history of neuroleptic use and the patients are often wrongly diagnosed as neuroleptic malignant syndrome. On the other hand, the presence of the behavioural and mood abnormalities as in this case, could lead to a diagnosis of catatonia, affective disorders or schizophrenia; but an abnormal EEG is an important pointer against these disorders.⁹ We agree with Yen *et al.* that, if the cognitive functions of the patients with unusual neurological symptoms deteriorate quickly and their psychiatric symptoms fail to respond to any treatment, CJD should be kept in mind and serial EEGs with detailed neurological workups should be considered.⁸

The disease is fatal within 1 year in 90% of cases. In 10 reported cases from North India, the mean duration of disease from the onset of symptom to death was 6.6 (\pm 6.11) months.¹⁰ Our patient had a rapid course of approximately 3 months, which is similar to a case of CJD from Korea in which the patient fell into vegetative state within 3 months.¹¹

In conclusion, our experience with this patient showed that in any adult patient with catatonic state or who presents with clinical features similar to a bipolar mood disorder, CJD should be considered. In such cases EEG has a very important role and should be done. The characteristic EEG findings of CJD are rarely seen in other diseases. Serial EEG recordings is a valuable tool in early diagnosis, as frontal intermittent rhythmical delta activity (FIRDA) might occur at an early stage of CJD and is later replaced by the classical periodic sharp wave complexes.^{12,13}

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